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COMPLICATIONS ASSOCIATED WITH EPIDURAL ANALGESIA FOR POSTOPERATIVE PAIN RELIEF AND THEIR MANAGEMENT AT A TERTIARY CARE UNIVERSITY HOSPITAL

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Abstract

Epidurals are well recognized for providing high quality postoperative pain relief and facilitating postoperative recovery. However, epidurals have an inherent risk of minor, or rarely, major complications. We assessed the frequency of complications associated with epidurals for postoperative pain relief at our university hospital and the steps taken to manage them. Data was collected from January 01, 2012 to December 31, 2013 during which 1030 patients received continuous epidural infusion. Overall incidence of complications was 28.8% (297/1030). Lower limb motor block was the commonest complication, observed in 22.71% (234/1030) cases, followed by hypotension 5.92% (61/1030), nausea and vomiting 5.34% (55/1030), while dural tap, catheter pullout, pruritus were observed in less than 1% cases. There were no serious or long-standing complications. All patients were managed successfully by the acute pain service with conservative symptomatic management.

Keywords: *epidural analgesia; complications; postoperative pain; pain relief*

1. Introduction

Epidurals are well recognized for providing high quality postoperative pain relief and facilitating postoperative recovery. Like all interventional procedures, epidurals have an inherent risk of minor, or very rarely, major complications. The most common complications / side effects of epidural analgesia include lower limb motor block, hypotension, pruritis, nausea, vomiting, dural tap leading to post-dural puncture headache, urinary retention, respiratory depression, neurological damage, premature catheter pull out, and inadequate analgesia. The incidence of complications related to epidural analgesia has not been fully established for each complication and estimates quoted are often based on extrapolation from

controlled trials. An earlier study in our center in 2007 reported an overall incidence of complications of 26.6%. Common complications were motor block (13.4%), dural tap (1.2%), ineffective pain control (2.4%), accidental catheter pull outs (3.8%) and problems associated with the delivery system of drugs (1.7%).

Safe and effective epidural analgesia requires, not only expertise on the part of the anaesthesiologists performing the procedure, but also regular follow-up and monitoring of the patient by experienced and trained staff. Acute pain service (APS) plays a vital role in this aspect of patient care. APS was established at our tertiary care university hospital in 2001 and is dedicated to safe and effective delivery of pain relief with an evidence-based practice. APS conducts regular studies and audits to ensure patient safety, enhancement of practices and continuous quality assurance. As a part of this important responsibility, we conducted an observational study to assess the frequency of various complications associated with epidurals for postoperative pain relief at our hospital and the steps taken by APS to manage these complications. The objectives of the study were to assess the frequency of various complications / side effects associated with epidurals for postoperative pain relief at our university hospital and to assess the steps taken by APS to manage these complications.

2. Methods

Approval was granted by the Anaesthesiology Research Committee and exemption was obtained from the institution Ethics review Committee. All adult patients who received continuous epidural infusion for postoperative pain relief from January 01, 2012 to December 31, 2013 were included. Anesthesiology based acute pain service was established at our university hospital in 2001. The APS team comprises of three consultants, one fellow, one resident (on rotation) and three pain nurses. Regular morning, afternoon and evening rounds are conducted by the rotating resident and pain nurse covered by a consultant. Patients receiving continuous epidural infusions, intravenous patient controlled analgesia (IV-PCA) and continuous IV opioid infusions are followed up by APS. An acute pain register is kept in the post-anaesthesia care unit of the main operating room suite and relevant details of all patients who receive pain management under the supervision of acute pain service (APS) are

entered in this register on an ongoing daily basis until the patient is discharged from the service.

A structured form was designed for the purpose of this study and a designated pain nurse collected relevant data from the register and filled out the forms on a daily basis. Parameters that were recorded included level of epidural insertion, length of catheter in space, local anaesthetic concentration used with or without fentanyl, number of days infusion was continued and complications like hypotension, motor block, sedation, dural tap, catheter pull-out, nausea, vomiting, urinary retention, and pruritis. Furthermore, the intervention done to manage these complications was also recorded. No names or patient identification numbers were noted during data collection to ensure confidentiality. Filled forms were kept in the custody of the primary investigator.

Statistical analysis was performed using statistical packages for social sciences version 19 (SPSS Inc., Chicago, IL). Frequency and percentages were computed for categorical variables including adjustments made and side effects treated by APS. Mean ±SD, and median (IQR) were reported for quantitative variables.

3. Results and Discussion

1030 patients received continuous epidural infusion for postoperative pain relief from January 01, 2012 to December 31, 2013. The overall incidence of complications was 28.8% (297/1030). Out of 297 patients who developed complications, 75.4% cases were observed with single complication while 24.5% patients had two and more than two complications. The average age of the patients having any complication was 49.04 ±17.32 years [range: 15-84]. There were 96 (32.3%) male and 201 (67.7%) female patients. Information regarding epidural analgesia and co-analgesia provided to the patients is presented in table 1. An infusion of bupivacaine 0.1% with fentanyl 2 mcg/ml was used in majority of patients for continuous epidural analgesia and L3/L4 space was the most commonly used level for insertion of epidural catheter.

Motor block was the commonest complication, observed in 22.71% (234/1030) cases, followed by hypotension 5.92% (61/1030), nausea and vomiting 5.34% (55/1030), while dural tap, catheter pullout, pruritus were observed in less than 1% cases. Interventions for the above complications are listed in table 2. Epidural analgesia was discontinued in 1.46% (15/1030) cases due to complications and patients were shifted to intravenous patient controlled

analgesia (IV-PCA) with morphine, while there were 2 cases in whom epidural analgesia did not work adequately and therefore these patients were switched over to intravenous morphine infusion.

The overall incidence of complications following epidural analgesia for postoperative pain relief was found to be similar to that observed in an earlier study done in 2007 at our hospital. However, a very remarkable finding of this study is that we found a difference in the types of complications observed. Incidence of motor block was markedly higher compared to the earlier study (22.7% vs 13.4%), whereas incidence of dural tap (0.51% vs 1.2%), catheter pullouts (< 1% vs 3.8%) and ineffective analgesia (0.19% vs 2.4%) was much lower in the present study compared to the earlier study conducted at our hospital in 2007.

A considerable number of patients who received epidural analgesia at our university hospital during the study period experienced motor weakness. Lower limb motor weakness delays patient's rehabilitation process and must be addressed and resolved promptly. Most of our patients had their epidurals inserted at the lumbar intervertebral spaces (213/297). Konigsrainer et al found in their audit that postoperative motor weakness of the legs occurred in 52.4% of patients with epidurals placed in lumbar intervertebral space, compared to only 4.8% of patients with epidural catheters in thoracic intervertebral space. After a change of practice to lower thoracic epidurals for abdominal surgeries (T8-T11), they found that there was a significant decrease in postoperative lower limb motor weakness, with the overall incidence decreasing from 14.7% to 5.7%. We plan to make similar recommendations in our department in an effort to decrease the incidence of motor weakness and thus facilitate rehabilitation. An audit will then be required to assess change in incidence of motor weakness after epidural analgesia. Chisakuta et al in their comparison between lumbar and thoracic epidural for major upper abdominal surgeries, concluded that the thoracic epidural route proved significantly more reliable than the lumbar and provided effective analgesia in all patients. They found that the incidence of side effects was significantly higher with lumbar epidural route. They supported the use of thoracic epidural for postoperative pain management after upper abdominal surgery.

Hypotension was seen in 61 patients receiving epidural analgesia. Lowering the concentration of local anaesthetic might be helpful in this respect. Bupivacaine 0.1% was used in most of our patients. Randomized controlled trials comparing lower concentrations of local anaesthetic agents must be conducted to discover the concentration that would be effective in

providing adequate pain relief while keeping side effects to the minimum. Other variables, such as patients' fluid status, co-morbids, etc. must also be kept in mind when working on preventing hypotension in these patients.

Postoperative nausea and vomiting is a major cause of patient dissatisfaction after surgery. The incidence of 5.3% in our patients may be due to systemic absorption of fentanyl in the epidural solution. Timely administration of antiemetic is important to treat and prevent this undesirable symptom. Pruritis is another side effect of opioids administered through an epidural. In our study nine patients complained of pruritis and anti-histamines were found to be effective in all of these patients. After several accidental epidural catheter pull-outs in recent years, APS had introduced a 'locking' device and made strict protocols for fixation of epidural catheters to the skin. Adherence to these protocols has markedly decreased the incidence of catheter pullouts (< 1% versus 3.8%).

Effective training and continuing experience due to increasing patient volumes is evident from the observation of an increase in the overall effectiveness of epidural analgesia and a decreased incidence of dural tap in our study compared to the earlier study at our hospital. Lack of facilities and dearth of trained staff has made it difficult to provide epidural services even in many major healthcare centers of our country. Therefore less than 1% incidence of ineffective analgesia is very encouraging for us and we plan to share this knowledge at national anaesthesiology forums and conduct training sessions so as to promote the initiation of epidural services in other tertiary care centers.

We recommend the use of lower concentrations of local anaesthetics whenever feasible, increased use of thoracic epidurals, more frequent follow-up in the early postoperative period and taking steps at the earliest to avoid progress of motor block or other complications. These recommendations need to be further strengthened through randomized controlled trials. Furthermore, audits should be conducted after any change of practice that may follow the conduct of these studies.

Table 1: Epidural analgesia and co analgesia provided to patients (n=297)

Level of Insertion of epidural	
T7T8	1(0.3%)
T8T9	5(1.7%)
T9T10	8(2.7%)
T10T11	21(7.1%)
T11T12	21(7.1%)
T12L1	28(9.4%)
L1L2	26(8.8%)
L2L3	34(11.4%)
L3L4	124(41.8%)
L4L5	29(9.8%)
Length of catheter in space (cm), *Mean ± SD*	4.94±0.48 [Range: 4-7]
Epidural Drugs	
Bupivacaine 0.1% with fentanyl 2 microgram/ml	277(83.3%)
Bupivacaine 0.0625% with fentanyl 2 microgram/ml	17(5.7%)
Other (0.1% or 0.125% Bupivacaine without fentanyl)	3(1%)
Rate of infusion, *Mean ± SD*	10.12±1.47 [Range: 6-16]
Co-Analgesia	
Paracetamol	236(79.4%)
Diclofenac Suppositiory	13(4.3%)
Ketorolac	01(0.34%)
Paracetamol + diclofenac	33(11.1%)
Paracetamol + Ketorolac	7(2.4%)

Table 2: Rate of complications /side effect associated with epidural analgesia for postoperative pain relief and their management

Complications*	***Epidural Bupivacaine***	***n (%)***	***Intervention for Management***
Hypotension	0.1% = 57 0.625% = 04	61(5.92%)	- 58, Fluid bolus given, shifted to lower concentration of local anaesthetic - 03, discontinued epidural, Shifted to PCA
Motor block	0.1% = 220 0.625% = 11 Other = 03	234(22.7%)	- 20, Change in position, shifted to lower concentration of local anaesthetic - 12, discontinued epidural - 202, change in patient's position
Dural Tap	0.1% = 6 0.625% =1	7 (0.67%)	07, conservative treatment
Catheter pullout	0.1% =6	6 (0.53%)	- 04, Shifted to PCA morphine - 02, shifted to morphine infusion
Nausea/Vomiting	0.1% = 50 0.625% = 4 Other =1	55 (5.3%)	- 51, Inj. Metoclopramide 10mg I/V 8h - 02, Inj. Metoclopramide 10mg, Ondansetron 8mg - 02, Inj. Ondansteron 8mg I/V 8h
Pruritis	0.1% = 8 0.625% = 1	9 (0.87%)	09, I/V anti-histamine
Other	0.1% = 2 0.625% = 1	3 (0.29%)	02, epidural not working in recovery room, shifted to infusion

4. Conclusion

This study helped us in identification of side effects and complications associated with continuous epidural analgesia and has highlighted the importance of early interventions by APS to prevent serious complications. The most common side effect observed was lower limb motor weakness and we recommend the insertion of lower thoracic epidurals instead of lumbar epidurals to prevent this side effect.

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PREDICTION OF DIFFICULT LARYNGOSCOPY IN PREGNANT WOMEN UNDERGOING CESAREAN SECTION USING THE RATIO OF HYOMENTAL DISTANCE RATIO IN COMPARISON WITH NECK CIRCUMFERENCE TO THYROMENTAL DISTANCE RATIO, HEIGHT TO THYROMENTAL DISTANCE RATIO, MODIFIED MALLAMPATY TEST AND UPPER LIP BITE TEST: A PROSPECTIVE BLINDED STUDY

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Abstract

Background: Unexpected difficult intubation, which may be considered a failed intubation, is a major factor relating to mortality and morbidity, following general anesthesia. We aimed to elucidate the role of five usual tests and their possible correlation in predicting difficult laryngoscopy in parturient patients undergoing cesarean section.
Materials and Methods: 716 consecutive parturient scheduled for elective cesarean section under general anesthesia, requiring endotracheal intubation, were enrolled into this study. Each patient was evaluated regarding HMD ratio, NC/TMD, RHTMD, MMT and ULBT before surgery. Laryngoscopy was assessed by a skilled anesthesiologist, blinded to the preoperative airway assessment. The laryngoscope result was graded according to Cormack-Lehane classification. Sensitivity, specificity, positive predictive value and area under curve (AUC) or receiver operating characteristic (ROC), for each airway predictor in isolation and in comparison with each other, were established.
Results: The sensitivity of HMD ratio was 45.4%, with AUC=0.551(P=0.071). MMT, as an old predictive test (AUC=0.582, 95%CI, 0.545–0.619), NC/TMD (AUC= 0.600, 95%CI, 0.563–0.637), HMDe (AUC=0.672, 95%CI, 0.636 –0.706) and HMDn (AUC=0.651,95%CI, 0.614–0.686) are good predictors for difficult intubation. The differences of the last four ROCs were statistically significant(P<0.05).
Conclusion: We consider that, in addition to MMT (as an ancient predictor), NC/TMD, HMDn and HMDe in parturient patients with higher incidence of difficult visualization of larynx (DVL) rather than general population, are good and reliable predictors of difficult laryngoscopy and intubation.

Keywords : Cesarean Section; Laryngoscopy; Intubation; Airway management; Anesthesia .

1. Introduction

Failure to achieve endotracheal intubation is a tangible endpoint that causes morbidity and mortality[1]. The incidence of failed intubation has been reported to a range of 0.7–31.3%[2]. However, in obstetrics, this has been considered to approximately ten times greater incidence than in the general population (1 in 250 patients). Most of the airway difficulties occur when they are not predictable before anesthesia. Therefore, a skilled anesthesiologist should have the ability to determine the difficulties with airway management[3,4]. Although performing of general anesthesia in obstetrics has significantly declined in recent years, it is still inevitable in special situations, such as massive maternal hemorrhage, overt coagulopathy, fetal bradycardia, which is life threatening, and finally, patient refusal towards neuraxial techniques. The last reason mentioned above is one of the most frequent indications of general anesthesia in obstetrics, in developing countries.

Recently, studies have shown that neck circumference to thyromental distance (NC/TMD) is a sensitive test to predict difficult airway in general population[5] and obstetric patients[6]. Also, the ratio of height to thyromental distance (RHTMD), that has high sensitivity, is sufficiently sensitive to detect possible difficulties with laryngoscopy and intubation in obstetrics [area under the curve (AUC) = 0.627, 95% confidence interval(95%CI), 0.589–0.664][7].

The modified Mallampati classification has poorprognostic value[2,6,7,8]in many studies. In addition, Savva[8]showed that modified Mallampatitest (MMT) was neither sensitive, nor specific enough, as a single test, in predicting difficult intubation in parturient patients.

In one study, Honarmand et al.[9]showed that HMDR(hyomental distance ratio) is comparable with RHTMD and upper lip bite test (ULBT) in predicting difficult airway. Also,Takenaka et al.[10]showed that HMDR is a clinically reliable predictor of difficult visualization of larynx (DVL) in the general population.

Recently, the description of ULBT, by Khan et al.,[11,12] has come under scrutiny.

No published study has compared HMDR with ULBT,RHTMD, MMT, and NC/TMD by their sensitivity, specificity, and positive and negative predictive values for prediction of difficult laryngoscopy in pregnant patients, yet.

Therefore, the hypothesis underlying this study was to develop predictors for difficult intubation in paturients candidate for cesarean section under general anesthesia, and to test if HMDR has a positive correlation with other mentioned indices, and which of them has a direct correlation with the difficult laryngoscopic view and difficult intubation.

2. Patients and methods:

With approval of the institutional Ethics Committee from our university, informed consent was obtained before each parturient anesthesia.
Patients with a history of trauma to the airway or cranial and cervical spine fracture, cervical and facial regions pathology, or who were edentulous or requiring awake intubation, patients with restricted motility of the neck and mandible (e.g., cervical disc disorders or rheumatoid arthritis), or inability to sit were not included in the study.
During the 18-month period, 716 consecutive American Society of Anesthesiologists (ASA) physical status I and II adult patients, who were undergoing cesarean delivery under general anesthesia, with tracheal intubation, were enrolled into this prospective observational study. Each parturient data collected included age, weight, height and body mass index (BMI). A skilled anesthesiologist, with at least 5-year experience in anesthesia, not imparted to the noted preoperative airway assessment, carried out laryngoscopy and rating of the difficulty of intubation (as per Cormack-Lehane's classification[13,14]).
The Cormack-Lehane grading system for laryngoscopic view is defined as:grade 1 - visualization of the entire laryngeal aperture;grade 2 - visualization of only the posterior portion of the laryngeal aperture;grade 3 - visualization of only the epiglottis;and grade 4 - no visualization of the epiglottis or larynx.
Difficult visualization of larynx (DVL) was defined as grade 3 and 4 of laryngoscopy.

The subsequent five measurements of predictive test were performed in all patients:

- HMDR: The ratio of hyomental distance in full extension of neck to this distance in neutral position(as shown inFigure 1)[10].

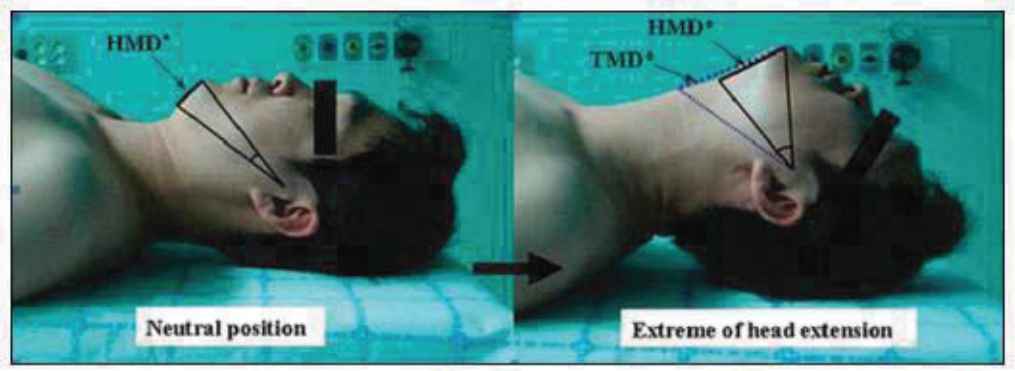

Figure 1: Method for measuring the hyomental distance ratio. The HMDR was defined as the ratio of the hyomental distance at the extreme of head extension (expressed as HMDe) to that in the neutral position (expressed as HMDn). Thyromental distance at the extreme of head extension was expressed as TMD

- NC/TMD: The neck was measured at the level of cricoid cartilage and thyromental distance was measured from the bony point of the mentum, while the head was fully extended, with mouth closed. TheNC/TMD ratio was calculated[5].
- RHTMD: Thyromental distance was measured from the bony point of the mentum, while the head was fully extended with mouth closed.Then, the RHTMD was calculated[7].
- MMT: Modified Mallampati testas described bySamsoon and Young. Classes are differentiated on the basis of thestructures visualized: class I:soft palate, fauces,

uvula, tonsillar pillars;class II: soft palate, fauces, uvula; class III: soft palate, base of theuvula; class IV: soft palate not visible[15].

- ULBT: ULBT was introduced as follows: Class I: the lower incisors can bite the upper lip above the vermilion line; Class II: lower incisors could bite the upper lip below the vermilion line; Class III: lower incisors could not bite the upper lip[11].

After arrival of the patient to the operating theatre and complete monitoring of the vital signs , each parturient who received the aspiration prophylaxis[15], was preoxygenated for 5 minutes and anesthesia was induced intravenously,with sodium thiopental (5mg/kg) and suxamethonium chloride (2mg/kg) for facilitating endotracheal intubation. Sellick maneuver[16] was applied until the patient was intubated and the cuff was inflated and confirmation of successful intubation was made by bilateral auscultation of lungs and capnography.
Laryngoscopy was performed with a 5-year experienced anesthesiologist, not imparted of the noted preoperative airway assessment. For the first laryngoscopy in each case, a size 3 Macintosh laryngoscope blade was used.
Difficult visualization of larynx has been defined as grades 3 and 4 in the Cormack-Lehaneclassification, and grades 1 and 2 of this classification are defined as easy visualization of larynx(EVL).
Patient data were presented as mean ± SD. The BMI and value of the airway predictors were compared using *t*-tests for continuous variables and U-test for MMT or ULBT. Sensitivity, specificity, and positive predictive value (PPV) were obtained and compared amongst predictors. Differences between the AUC values for the five predictor tests were analyzed using MedCalc statistical software,version 9.3.6.0 (MedCalc Software bvba, Ostend, Belgium). The data were analyzed using SPSS version 20 (SPSS Inc., Chicago, IL, USA).

3. Results:

A total of 716 patients were enrolled into this study. Three cases had grade IV Cormack-Lehane, which tracheal intubations were performed with the aid of a videolaryngoscope. There are no significant differences in demographic data between EVL and DVL. (Table 1)
The distribution of ASA, MMT, ULBT and the Cormack- Lehane grading are presented in Table 2.
Table 3 shows that the differences on NC/TMD, HMDe and HMDn are statistically significant, in comparison with the other tests.
The predictive value of MMT, ULBT, NC/TMD, RHTMD, HMDe, HMDn, HMDR are presented in Table 4. The main end point in this study, the AUC of the ROC, were lower for ULBT(AUC=0.532; 95%CI, 0.494–0.569) and HMDR (AUC=0.551; 95%CI, 0.514–0.588) and RHTMD (AUC= 0.555; 95%CI, 0.517–0.591) in comparison with MMT(AUC=0.582,95%CI, 0.545–0.619), NC/TMD (AUC= 0.6; 95%CI, 0.563–0.637), HMDe (AUC=0.672, 95%CI, 0.636–0.706) and HMDn (AUC=0.651,95%CI, 0.614–0.686). The differences of the last four ROCs were statistically significant($P<0.05$).
In discrimination analysis, MMT grade >I, ULBT grade ≥II, RHTMD ≥19.2, NC/TMD ≥4.1, HMDe≤6, HMDn≤4 and HMDR ≥1.4 were considered as the cutoff points in predicting DVL. The RHTMD is the least sensitive of the tests, with the sensitivity of 41.6%.The MMT and NC/TMD had the highest sensitivities, among the predictors (73.4% and 58.3%, respectively).

4. Discussion:

Difficult laryngoscopy and intubation can cause irreparable sequels for the patient, if not handled properly. Studies to find predictive tests with high accuracy continue even at this moment. Little works have been published, based on the use HMDR, MMT, ULBT, RHTMD and NC/TMD, in obstetrics airway management. This study was designed to evaluate the efficacy of the five tests above in forecasting difficult laryngoscopy and to reveal a possible correlation between the tests and Cormack-Lehane grade of laryngoscopy. The previous studies have shown the incidence of difficult intubation to range between1.3%–17%[2,20] and it is ten times more in parturient[6]. In this study, the incidence of DVL was 18.4%,which was comparable with the previous studies. In Merah et al.[21] study, the incidence of DVL in Nigerian parturients was 10%. We can support our findingson the presence several differences in head position, degree of muscle relaxation and different anthropometric features.
Several studies have related weight increase and BMI with the risk for DVL[22], although others,[23,24] similar to the present study in parturients, have found that the incidence of DVL was not correlated with BMI. This may be due to not using general anesthesia in these parturient candidates for elective cesarean section.
In this study, ULBT failed to be a reliable bedside test in predicting DVL. The descriptive reason was the limited amount of cases with ULBT grade III(0.8%), of which only 0.1% had DVL. On the other hand, in patients who had ULBT I and II, the probability of DVL was exceedingly low, that is comparable with previous studies[11,12].
The accuracy of NC and NC/TMD for prediction of DVL in non-obstetric patients was documented by Gonzalez[25] and Kim et al.[5] In this study and the previous one[6], we found that NC and NC/TMD were the most useful predictors in parturients with AUC of ROC 0.564(P=0.022) and 0.6(P=0.000), respectively.
The 73.4% sensitivity of the MMT combined with 22.9% PPV, suggests that, for a reliable prediction of difficult laryngoscopy, Mallampati scoring should be combined with other predictors. However, in this study, the AUC of ROC of MMT is 0.582(P=0.003).
The HMD (measured in supine position, with the head fully extended and with the mouth closed, as the straight distance from the lower border of the mandibular mentum to the superior border of the hyoid bone, in centimeters) that was described as HMDe in this study, had a significant difference in DVL(P<0.001). Also, HMDn(measured in supine position, with head in neutral position) is a good predictor of difficult intubation(P<0.001).The study of Khan et al.[12]described the HMD as a valuable predictor of DVL. However, HMDR has the sensitivity of 45.4% and is not a good predictor in the parturients.
In conclusion, there are stepwise increases in the incidence of Cormack-Lehane grades III and IV, as the MMT class shows a rise form II to III and more, the NC/TMD increases from the value of 4.1, the HMDe and HMDn decrease from their predetermined values of 6 and 4 cm, respectively. Therefore, we consider that NC/TMD, HMDe, HMDn are good predictors of difficult laryngoscopy and intubation, in obstetric patients.

5. Tables:

Table 1: Patients characteristics

Variables	Patients(n=716)	EVL(n=584)	DVL(n=132)	Pvalue
Age(years)	28.8±4.9	28.7±4.9	29.1±4.9	0.428

Weight(kg)	76.7±12	76.5±12	77.4±12.1	0.440
Height(cm)	161±6.1	161±6.3	160±5.6	0.082
BMI(kg/m²)	29.6±4.3	29.5±4.3	29.8±4.2	0.398

EVL: Easy visualization of larynx, DVL: Difficult visualization of larynx, BMI: Body mass index, Data are presented as mean ± SD. P<0.05 statistically significant.

Table 2: Distribution of ASA, MMT,ULBT and laryngoscopic view of all patients

Variable	Number(%)
ASA	
I	573(80)
II	143(20)
Mallampati Class	
I	293(40.9)
II	263(36.7)
III	*124(17.3)*
IV	36(5)
ULBT	
I	390(54.5)
II	320(44.7)
III	6(0.8)
Laryngoscopic view	
I	362(50.6)
II	222(31)
III	129(18)
IV	3(4)

ASA: American Society of Anesthesiology, ULBT: Upper Lip Bite Test

Table 3: Distribution of Statistically differences in all tests in DVL and EVL

Variables	DVL(n=132)	EVL(n=584)	P value

TMD	8.9± 1.5	9.2±1.4	0.025
RHTMD	18.5±3.6	17.8±2.9	0.010
NC	36.5±2.5	35.9±2.8	0.018
NC/TMD	4.2±0.8	3.9±0.6	0.000
HMDe	6.6±1	7.2±1	0.000
HMDn	4.9±1.1	5.4±1.1	0.000
HMDR	1.38±0.2	1.37±0.2	0.497

DVL: Difficult view of laryngoscopy, EVL: Easy view of laryngoscopy, TMD: Thyromental distance ratio, RHTMD: Ratio of height to thyromental, NC: Neck circumference, NC/TMD: Neck circumference to thyromental distance, HMDe: hyomental distance in extention of neck, HMDn: Hyomental distance in neutral position of neck, HMDR: ratio of HMDe/HMDn. Data is presented as mean ± SD. P value < 0.05 is significant.

Table 4: Predictive value for MMT,ULBT, RHTMD,NC/TMD, HMDe, HMDn and HMDR to predict the occurrence of DVL according to the modified Cormack- Lehane Classification

Test	Sensitivity	95%CI	Specifisity	95% CI	+LR	-LR	PPV (%)	NPV (%)	AUC of ROC curve	P value
MMT	73.4	65.1-80.8	44.1	40.1-48.3	1.32	0.6	22.9	88.1	0.582	0.003
UBLT	50.7	41.9-59.6	55.6	51.5-59	1.14	0.88	20.6	88.3	0.532	0.262
RHTMD	41.6	33.2-50.6	75	71.3-78.1	1.67	0.78	27.4	85	0.555	0.053
NC/TMD	58.3	49.4-66.8	64.3	60.3-68.3	1.64	0.65	27	87.2	0.600	0.000
HMDe	49.2	40.4-58.1	79.2	75.8-82.5	2.38	0.64	34.9	87.4	0.672	0.000
HMDn	47.7	39-56.5	82.8	79.5-85.8	2.78	0.63	38	87.5	0.651	0.000
HMDR	45.4	36.8-54.3	73.4	69.6-77	1.71	0.74	27.9	85.6	0.551	0.071

MMT: Modified Mallampati Test, ULBT: Upper lip bite test, RHTMD: Ratio of height to thyromental distance, NC/TMD: Ratio of neck circumferences to thyromental distance,HMDe: hyometal distance in head fully extended with closed mouth, HMDn: hyomental distance in neutral position, HMDR: hyomental distance ratio, CI: Confidence Interval, AUC: Area under curve, ROC: Receiver- operating characteristic curve. $P< 0.05$ statistically significant.

6. Conclusion

Our study demonstrated that, in addition to MMT (as an ancient predictor), NC/TMD,HMDn and HMDe, in parturients with higher incidence of DVL, rather than general population, are good and reliable predictors of difficult laryngoscopy and intubation, using a standard laryngoscope.

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PROSPECTIVE EVALUATION OF CORRELATION OF DEPTH OF DEXMEDETOMIDINE SEDATION AND CLINICAL EFFECTS FOR RECONSTRUCTIVE SURGERIES UNDER REGIONAL ANAESTHESIA

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Abstract

This study evaluated the correlation of efficiency and depth of dexmedetomidine sedation, parameters of haemodynamics and breathing, and the time and quality of recovery under regional anaesthesia. 32 ASA I-II patients who received dexmedetomidine sedation under regional anaesthesia during reconstructive surgeries were assessed in this prospective study. The loading dose of dexmedetomidine was 1 μg/kg over 10 min intravenously (IV) followed by a continuous infusion of 0.1-0.6 μg/kg/h until the end of the surgery. Standard monitoring was used. The depth of the sedation was measured with Narcotrend electroencephalogram (EEG) index and Richmond Agitation Sedation Scale (RASS). The time and quality of the recovery were evaluated. Dexmedetomidine did not cause any significant haemodynamic instability and did not induce bradycardia while EEG index was 20-80. According to RASS the level of sedation was 0 to -3 during all surgeries. Dexmedetomidine provided fast and good quality of recovery without impaired cognitive and psychomotor functions. The loading dose of dexmedetomidine 1 μg/kg over 10 min IV followed by 0.1-0.6 μg/kg/h provided sufficient sedation according to EEG index 50-70 during reconstructive surgeries under regional anaesthesia maintaining spontaneous breathing.

Keywords: dexmedetomidine, regional anaesthesia, sedation

Introduction

The result of the surgery under regional anaesthesia can be affected by fear and anxiety of the patient and discomfort from lying on the operating table [1]. In order to reduce

the patient's stress of being awake during the surgery under regional anaesthesia and to increase surgeon's and anaesthetist's satisfaction of the surgery sedation is widely used [1, 2, 3, 4]. For surgeries under regional anaesthesia midazolam and propafol are the most common sedatives [4].

Dexmedetomidine is a selective α-2 receptor agonist with an anxiolytic, sedative and analgesic effect, and is not associated with respiratory depression [4, 5, 6, 10]. Compared to sedatives we have used so far, dexmedetomidine causes the 'natural sleep' through inhibition of neuronal firing in the locus coeruleus in the brain stem which means the patient is easily arousable on verbal stimulation without impaired cognitive abilities and psychomotor functions [4, 7, 8, 9, 10, 13]. Dose dependent bradycardia and hypotension are the most frequently reported adverse reactions of dexmedetomidine [4, 6, 14, 16].

The purpose of this study was to investigate correlation of the efficiency and depth of dexmedetomidine sedation, parameters of haemodynamics and breathing, and the time and quality of recovery under regional anaesthesia.

Methods

32 ASA I-II patients scheduled for reconstructive surgeries under regional anaesthesia (RA) with dexmedetomidine sedation were enrolled in a prospective study, after an ethical committee's approval and receiving written consent from all patients. The following inclusion criteria were used: men or women over the age of 18, normal liver and renal function and no acute diseases. And the following exclusion criteria were used: second or third degree heart block, bradycardia and arrhythmia, uncontrolled hypotension, mechanical ventilation, history of sleep apnea, liver failure, acute cerebrovascular accident, psychiatric disorder or currently being on psychotropic medication, pregnancy and coagulation disorders.

All patients received premedication with tablet of 7.5 mg midazolam before regional anaesthesia. Intravenous catheter (IV) was inserted in the non-operated arm and a 5 ml/kg/h infusion of 0.9% NaCl solution was given. Standard monitoring was used – noninvasive systolic (SBP) and diastolic (DBP) blood pressure, heart rate (HR), respiratory rate (RR), peripheral oxygen saturation (SpO_2) was recorded before and after regional anaesthesia was administered and recording continued until the end of the surgery. The respiratory depression was defined as oxygen saturation <90% or RR under 12 breaths/min. HR <50 beats/min for more than 5 minutes was considered to be bradycardia and patients received a solution of 0.5 mg atropine IV. HR >100 beats/min for more than 5 minutes was considered to be

tachycardia. SBP >180 mmHg was considered to be hypertension and SBP <90mmHg was considered to be hypotension.

EEG monitoring with EEG monitor Narcotrend - Compact M was used during sedation. After regional anaesthesia was performed, three self-adhesive disposable electrodes were placed on the forehead using electrode gel, the patient's leads were connected with Narcotrend - Compact M monitor and the EEG recording was started monitoring the depth of sedation or hypnotic status of the patient during sedation. The monitor automatically classified EEG stages on a scale from stage A (conscious) to stage F (very deep sedation), this division refers explicitly to a range of EEG indexes: EEG stage A – awake (EEG index 95-100); EEG stage B, C – light sedation (EEG index 65-94); EEG stage D – moderate sedation (EEG index 37-64); EEG stage E, F – deep sedation (EEG index < 36) [11].

Patients were divided into 3 groups depending on their type of RA to be used which again depends on the type of reconstructive surgery they would have had planned. Axillary brachial plexus blockade was done for reconstructive surgeries in hands, this was performed while patients were in the supine position with the upper arm abducted and flexed 90 degrees at the elbow. A solution of 20 ml 0.5% bupivacaine and a solution of 20 ml 1% lidocaine was used for axillary brachial plexus blockade. Spinal anaesthesia (SA) was done for reconstructive surgeries in legs, this was performed with a 25 gauge needle in L3-L4 interspace while patients were sitting on the operating table placing feet on a stool, head flexed and arms hugging a pillow providing maximum flexion of the lumbar spine. A solution of 4 ml 0.5% levobupivacaine was used for spinal anaesthesia. Axillary brachial plexus blockade and spinal anaesthesia was done for free flap microvascular surgeries not exceeding the maximum recommended doses of local anaesthetics. After confirmation of successful regional anaesthesia, loading dose of dexmedetomidine 1 μg/kg over 10 min was administered IV followed by a continuous infusion of 0.1-0.6 μg/kg/h until the end of the surgery. To provide an efficient sedation during surgery the continuous infusion of dexmedetomidine was adapted by EEG index maintaining a definite target EEG index of 50-70 (complies with EEG stage $C_2 – D_1$).

An independent observer rated the level of sedation of the patients using RASS. Measurements were obtained before and after the loading dose and then every 20 minutes until the end of the surgery. The sedation was considered too deep when RASS was -4 or -5 [12]. The time and quality of the recovery were evaluated at the end of each surgery. In the

recovery room at 30 minutes patients' satisfaction with the quality of sleep was assessed by the use of handed out questionnaires.

Statistical analysis was performed with Microsoft Excel 2010 and SPSS (Statistical package for social sciences) 20. Data was evaluated with ANOVA (Analysis of variance) and Student's t-test. Results with p values of <0.05 were considered statistically significant.

Results

The demographic data and surgical characteristics were similar in all patients (Table 1). Types of RA used: 24/32 had an axillary brachial plexus blockade (75.0 %) for reconstructive surgeries in hand, 5/32 had a spinal anaesthesia (15.6 %) for reconstructive surgeries in leg, 3/32 – SA with plexus blockade (9.4 %) for free flap microvascular surgery.

Table 1. Demographic data and surgical characteristics

Gender (F/M)	14 (43.8 %) female	18 (56.2 %) male
Age (years)	46.44 ± 16.88 (20 to 74)	
Weight (kg)	75.00 ± 14.11 (50 and 120)	
Height (cm)	172.85 ± 8.31 (163 and 185)	
Type of surgery	28 (87.5 %) elective	4 (12.5 %) acute
Duration of surgery (minutes)	89.38 ± 67.46 (min 20, max 300)	
Duration of sedation (minutes)	102.81 ± 67.52 (min 35, max 310)	

Cardiovascular and Respiratory Measurements

The mean HR during sedation was 62.86 ± 7.90 beats/min. After dexmedetomidine loading dose the mean HR decreased by 8.44 ± 7.16 beats/min (p = 0.000) (before loading dose 73.75 ± 10.34 beats/min). We observed bradycardia below 50 beats/min requiring a single minimum dose of atropine in 2/32 patients (6.3 %), 5/32 patients (15.6 %) had a temporary bradycardia that does not require treatment and in 25/32 cases (78.1%) sedation with dexmedetomidine did not cause bradycardia. After the loading dose bradycardia did not appear in any of the patients while EEG index was 20-80 (Table 2). 2 patients with

bradycardia requiring atropine had a Narcotrend EEG stage A – awake (EEG index of 95-100). Out of those two patients – one patient was a 28-year-old professional athlete, he had bradycardia during loading dose when EEG index was 98, other patient was a 71-year-old man who had an acute surgery and bradycardia occurred 20 minutes after the start of continuous infusion at EEG index 96.

When comparing all types of RA used, HR was similar in all three RA groups after the loading dose (Table 3).

Table 2. Changes of HR after loading dose according to EEG index (20-80).
The number printed on bars indicates the number of patients in current group of EEG index.

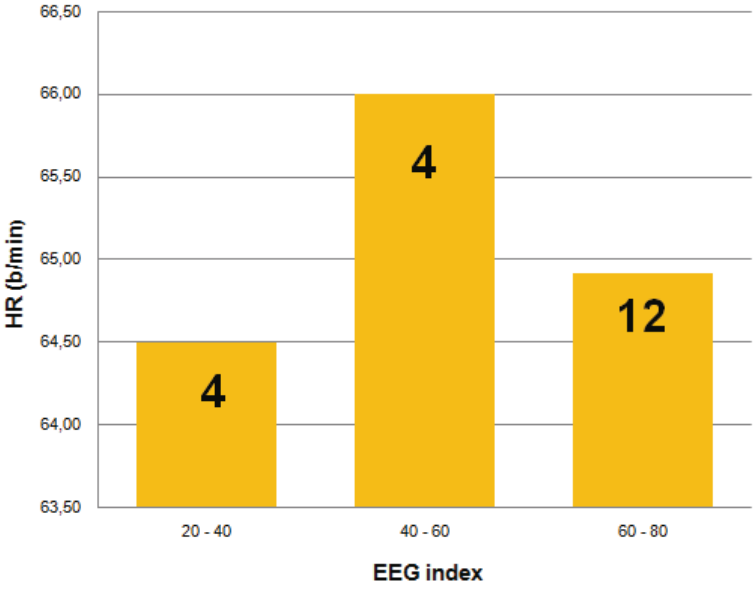
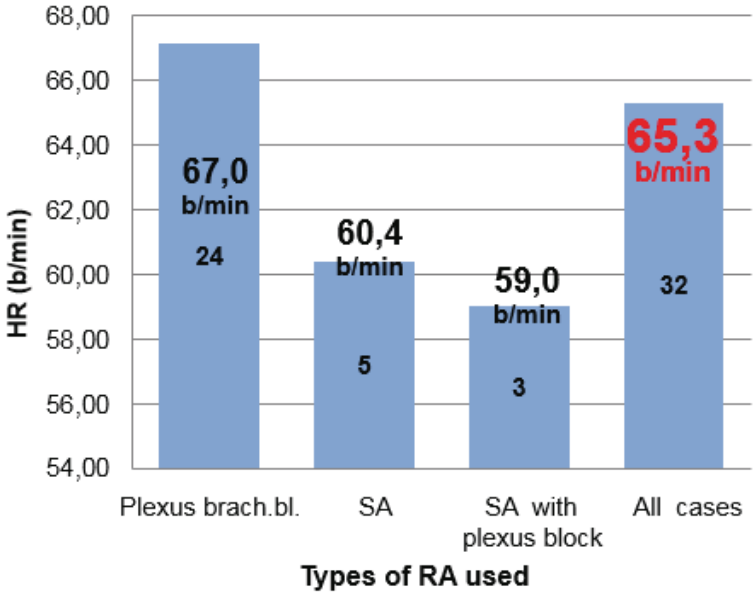


Table 3. Changes of HR after loading dose according to types of RA used.



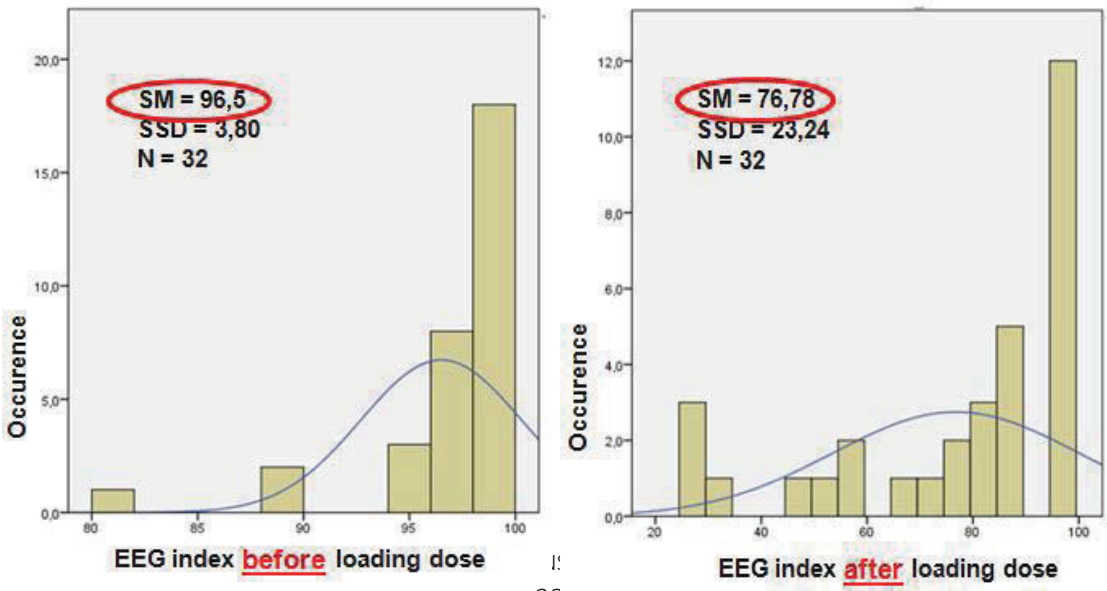
We did not observe any significant changes in SBP and DBP after dexmedetomidine loading dose was administered – the mean SBP decreased by 7.31 ± 12.03 mmHg (p = 0.002) and the mean DBP decreased by 4.75 ± 7.15 mmHg (p = 0.001). The mean SBP during the sedation was 119.39 ± 15.16 mmHg, the mean DBP was 71.99 ± 9.83 mmHg. Results showed that sedation with dexmedetomidine caused neither of the following in any of the patients: hypotensia, the need to stop the continuous infusion or add other sedatives.

We observed minimal decrease in SpO_2 levels after the loading dose (1.28 ± 2.37 %, p = 0.005) without the need to use assisted ventilation or any airway device. All patients had adequate spontaneous breathing during their sedation.

Sedation Measures

The mean EEG index after loading dose decreased by 19.72 ± 23.85 (p = 0.000) indicating light to moderate sedation (Table 6). During dexmedetomidine sedation the mean EEG index was 68.53 ± 21.70 which was within the target EEG index rage. The target level of sedation was reached 10 minutes after the start of continuous infusion. The mean lowest recorded EEG index was 53.10 ± 25.00 after a continuous infusion of 30 minutes. The environment had a significant negative impact to the quality of dexmedetomidine sedation. Increased noise levels rose the EEG index during surgery therefore the patients woke up. However, those patients were able to quickly fall back asleep. According to RASS the level of sedation during surgery was from 0 to -3. We observed that at the end of the surgery all patients were promptly arousable with verbal stimulation without impaired cognitive abilities and psychomotor functions. According to answers from their questionnaires all patients were satisfied with the sedation they received.

Table 6. Changes of EEG index before and after loading dose of dexmedetomidine.



Discussion

The aim of the study was to investigate correlation of the efficiency and depth of dexmedetomidine sedation, parameters of haemodynamics and breathing, and the time and quality of recovery under regional anaesthesia. We found that low doses of dexmedetomidine (loading dose 1 μg/kg/10 min, a continuous infusion 0.1-0.6 μg/kg/h) during reconstructive surgeries under RA sedation did not cause any significant haemodynamic instability and bradycardia was not seen while EEG index 20-80. Similar results were reported by Arain S. R. at al. and Kilic N. et al. using dexmedetomidine loading dose of 1 μg/kg over 10 minutes followed by a continuous infusion of 0.4-0.7 μg/kg/h and 0.2-0.7 μg/kg/h providing efficient sedation [***34***, 15]. Ok H. G. et al. study results showed that dexmedetomidine loading dose of 1 μg/kg over 10 minutes is sufficient for surgeries up to 60 minutes long. A continuous infusion of dexmedetomidine of 0.2 μg/kg/h is sufficient for surgeries up to 80 minutes long and a continuous infusion of 0.4 μg/kg/h provides efficient sedation for surgeries up to 120 minutes long under spinal anaesthesia [4].

The incidence of bradycardia and hypotension is the most frequently reported dexmedetomidine adverse hemodynamic response associated with increased dosage and concentration [4, 6, 14, 16]. A study by Ok H. G. et al. reported that the frequency of bradycardia and hypotension does not increase when a low dose of dexmedetomidine is administered IV for sedation under spinal anaesthesia. In our study the incidence of bradycardia requiring atropine was low (2 out of 32 patients) in addition – hypotension was never recorded.

Authors report dexmedetomidine as a useful sedative for procedures because of its minimal effects on the respiratory system [15, 17]. Belleville J.P. et al. reported a study of examined ventilatory effects of a 2 minute intravenous four different dose level of dexmedetomidine infusion. Results showed that right after the maximum infusion of 2.0μg/kg irregular breathing with periods of apnea were noticed. However, the authors also report that there was no significant arterial oxygen desaturation below 90% [19].

In this study the level of sedation was assessed by RASS (the level was from 0 to -3 during sedation) and the depth of sedation or hypnotic status was measured by Narcotrend EEG monitor maintaining the pre-set target level EEG index between 50 and 70. Authors emphasize that there are some limitations using assessment scales like Richmond Agitation Sedation Scale, Ramsay Sedation Scale or Observer's Assessment of Alertness/Sedation scale. Assessment scales are subjective interpretations by the observers of patients' alertness.

The quality of sedation is compromised because the assessments require the patient to be awaken every time an assessment is done [4]. Therefore authors recommend using Bispectral Index System (BIS) or Narcotrend EEG monitoring for measuring the depth of the sedation instead of the assessment scales [4, 20]. BIS and Narcotrend EEG monitoring provide real time assessment and the quality of sedation is not compromised by external stimulation [20]. Ekin A. et al. in a study measuring the depth of sedation with BIS reported that environmental stimuli and the application of tourniquet increase values of BIS, although it does not affect the patient's satisfaction with his sedation [3].

There are reports about dexmedetomidine's advantages of providing fast recovery after procedures, patients are easily arousable on verbal stimulation and able to perform the psychomotor testing without impaired cognitive abilities and psychomotor functions [10, 15, 18]. In our study at the end of each surgery all patients were promptly arousable with verbal stimulation.

Conclusion

The loading dose of dexmedetomidine of 1 μg/kg administered intravenously over 10 minutes and a continuous infusion of 0.1-0.6 μg/kg/h until the end of the surgery provides safe management of sedation according to pre-set target for Narcotrend electroencephalogram index of 50-70 during reconstructive surgery under regional anaesthesia.

After the loading dose of dexmedetomidine bradycardia did not appear while Narcotrend electroencephalogram index was 20-80, all patients maintained spontaneous breathing and sedation did not cause any significant haemodynamic instability. Dexmedetomidine sedation under regional anaesthesia provides fast and good quality recovery and ensures a high patient satisfaction rate of sleep quality during reconstructive surgery.

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Assessment of Patient Satisfaction with Acute Pain Management Service: Monitoring Quality of Care in Clinical Setting

INTRODUCTION

Timely and effective management of acute pain has been one of the biggest challenges of modern medicine. About two thirds of patients admitted to hospitals still suffer from uncontrolled pain despite extensive research and education vis-à-vis pain management.[1] It is also an established fact that uncontrolled pain leads to many deleterious effects.[2] Quality assurance efforts in pain management consist of methods to establish pain management protocols, to monitor their application, and to assess the benefits they provide to the patients. Quality of pain management that results from these efforts can be evaluated by assessment of various pain management outcomes;[3] patients' satisfaction being one of them.[4] Health care facilities routinely use patient satisfaction evaluations to identify methods of practice improvement and better care provision.

Patient satisfaction with postoperative pain management depends upon a number of variables including patients' expectations, intensity of pain experienced, promptness of acute pain service response, effectiveness of treatment and health-care professionals' attitude.[5] The American Pain Society in Quality Assurance Standards (Table 1) for Relief of Acute and Cancer related pain specifies that patient satisfaction with pain management must be surveyed in clinical practice [6] .The current study was conducted to monitor the quality of care provided by Acute Pain Service (APMS), to develop a reliable tool for assessing patient satisfaction with APMS, and to identify different variables affecting patient satisfaction with an aim to improve the overall quality of service.

Materials and Methods

Approval for the study was granted by institutional Ethics Review Committee (ERC). Data were collected over a 3-month period on 102 consecutive, adult patients, who were provided care by APMS and consented to participate. A questionnaire was designed and administered to each patient on the day of discharge, before going home. The questionnaire was delivered, explained to the patient and filled out by an independent, unbiased person who had no link with APMS. This was achieved by assigning this task to a medical student visiting from another medical school, and not known to the APMS team or patients, except for one of the authors who briefed her about the questionnaire.

Acute Pain Management Service

Authors' institute is a tertiary care hospital situated in a city riddled with violence and insecurity. It caters to multiple emergency situations including bomb blasts, mass causalities and road traffic accidents and is hence faced with a huge burden of trauma and injury. It also provides care to a range of complicated tertiary care surgical patients brought in from all parts of the country besides elective surgical patients. Formal Acute Pain Service has been

established in the institute since 2001. It is an anaesthesia consultant led service where everyday care is provided by dedicated pain nurses and anaesthesia residents with the help of ward nurses. The service provides care to post-operative patients and others suffering from medical or non-surgical acute pain.

Primary anesthesiologist devises the post- operative pain management plan and initiates its implementation in the operating room. APMS team takes over the pain relief responsibility of patients in the PACU, carry out regular pain assessments, responds and trouble shoots all problems related to acute pain management. On duty pain nurse and the rotating anesthesia resident conduct regular bed side rounds 3 times in a day, more often if indicated, and report to the covering anesthesia consultant. In between the rounds, regular pain assessment is the duty of ward nurses, who pages the on duty pain nurse whenever required. Everyone uses a combination of Verbal rating scale and Numeric-rating scale for uniform assessment of pain scores. The reliability of these tools is in general high. Ward nurses as well as AMPS staff carry out documentation of pain scores, pain-management interventions used, and patient condition at regular intervals in patient's records. APMS also maintains electronic data of all the patients under its care. To ensure effectiveness and safety of the pain management regimes employed, APMS members regularly make adjustments to the originally prescribed analgesic strategies and treat side effects as required. APMS also provides round the clock consultative service to all patients suffering from acute non-surgical pain. Besides provision of clinical care, conducting regular audits, satisfaction surveys, implementing quality assurance measures, giving regular feedbacks to all concerned, is the duty of APMS. APMS with its efforts has made pain visible.

Instrument

The questionnaire consisted of 2 parts:

Part I comprised of patient's demographics including age, gender, surgical specialty, surgical procedure, post-operative analgesic modality and co-analgesics used. This part was completed from patients' medical records.

Part II of the questionnaire included 10 questions (table 2). Six of these questions had options to respond on a 5 point Likert scale arranged from highest to lowest. Four questions had 'yes' or 'no' options while at the end, patients were encouraged to give their comments/opinions in an open ended manner.

All statistical analysis was performed using statistical packages for social science version 19 (SPSS Inc., Chicago, IL). Mean and standard deviation were computed for age, and frequency and percentages were reported for qualitative observations.

RESULTS

A total of 132 patients were managed by APMS during the three months of the survey, of which 102 agreed to participate. The average age of patients was 45.27 ± 16.47 years. There were 55.9% female and 44.1% males. Different analgesic modalities were employed but

majority (66.7%) received epidural analgesia. The analgesic modalities used and the surgical specialties are provided in table 3. For co-analgesia, patients received paracetamol, a combination of paracetamol with tramadol or ketorolac. Diclofenac suppository and paracetamol were administered as co-analgesics to patients undergoing gynaecological operations. The expectation of experiencing severe pain was higher than the pain actually experienced, as shown in figure 1.

Of the patients followed up by APMS during the study period, 56.9% received interventions within half an hour of the call given for inadequate pain relief or management of side effects, 13.7% were managed within 1 hour, 2% within 1 to 2 hours and 1% after 2 hours of the call, while 26.4 % did not require any intervention by APMS and were free of pain and side effects. After interventions by APMS, excellent to very good pain relief was reported by 72% of the patients, moderate pain relief by 25.3%, while 2.7% reported poor pain relief. Attentiveness and sensitivity of APMS staff was considered very good to excellent by 91% of patients, fair by 8%, while 1% considered the service as poor.

Only 46% patients were aware that APMS is a part of anaesthesia department. The intention to be treated with the same analgesia modality in future and to recommend it to their family and friends was reported by a large majority of the patients (Table 4). All participants except one found APMS staff courteous and professional (Table 4). The overall experience with APMS was considered good to excellent by 97% of the patients (Fig2). The comments of the patients are presented in Table 5.

Discussion

The results of this study show that multimodal analgesia was used in all patients included in the survey which is part of current recommendations for best analgesic practice.[7] There is a scarcity of strong opioid analgesics in our country and, even in centers where morphine and fentanyl are available, their supply is limited and erratic. In resource limited set-ups, careful selection of the available drugs and techniques is the best hope for provision of optimal pain relief to the patient. It has rightly been said that the solution to the problem of inadequacy of postoperative pain management does not actually lie in the acquisition of expensive medication or development and use of new techniques, but rather in the optimal utilization of already available drugs, techniques and facilities.[8,9] Thus, a combination of regional technique and multimodal analgesia, which most of our patients received, was the best available option for providing effective pain relief in the postoperative period.

Campbell and colleagues define assessment of quality care as determining "whether individuals can access the healthcare structures and processes of care which they need, and whether the care received is effective".[10] One method of evaluating users' perception of a service is to assess their satisfaction with the care they receive. The American Pain Society in Quality Assurance Standards for Relief of Acute and Cancer related pain specifies that patient satisfaction with pain management must be surveyed in clinical practice.[11] Assessment of

patient satisfaction is of particular importance if the aim is to improve service to achieve better outcomes and improved quality of life.[12] Furthermore, a satisfied patient is said to be more likely to comply with the prescribed treatment [13,14] and hence has a better chance of earlier recovery.

Satisfaction is a subjective feeling dependent upon patients' past experiences and future expectations.[15] It is easy to assume that effective pain relief would correlate highly with patients' satisfaction with their pain management. However, earlier research has shown that patients may be highly satisfied with their pain management even when they have reported considerable levels of pain during their hospital stay.[3,16-18] This imposes difficulty in interpreting the results of patient satisfaction surveys on pain management,[16-18] and explanation needs to be sought for the high satisfaction scores even with inadequate pain relief. In our survey, even though pain management interventions by APMS were required in a significant number of patients and 28% of the patients had moderate to poor pain relief despite the interventions, 97% of the patients reported their overall experience regarding pain management as good to excellent. The response time of APMS staff and their attitude and attentiveness might have played a role in defining the level of patient satisfaction, since more than 70% of our patients received pain management interventions within one hour of the call given to APMS. Furthermore, 91% of our patients reported attentiveness and sensitivity of the APMS staff as very good to excellent. Thus, one of the reasons for the high rate of patient satisfaction in our study could be a professional and courteous attitude of APMS. Lin has provided a similar explanation for high satisfaction scores even with high pain levels in his patients and states that caring attitude of the staff may be one of the reasons for high overall satisfaction levels in patients suffering with pain.[3]

Our results show that patients' expectation of experiencing severe pain was higher than the pain actually experienced by them. It has been claimed that patient's expectations have a strong effect on degree of patient's satisfaction about an experience. Squires states that the ratio between expectations and perception of an experience results in the level of satisfaction for the person making the judgment.[19] The fact that majority of our patients (70.6%) expected severe pain postoperatively, but not as many (44%) suffered from it, could have been one of the reasons for majority being satisfied with the service.

More than half of the patients included in the survey (54%) were not aware that APMS was a part of anaesthesia department. This identifies the need for conduct of public awareness sessions regarding pain management by dedicated acute and chronic pain physicians and nurses. Such sessions would make the patients aware that pain relief is their basic right, pain relieving medicines are accessible and who to turn to in case of unrelieved pain. In addition, APMS staff needs to introduce the team members and the service provided by them to the patients and their families in adequate detail during APMS rounds so that they can be traced back whenever patients need help.

Despite the high satisfaction scores in our study, some shortcomings were identified by us, which need to be addressed with the aim of formulating and implementing strategies for improvement. More than 4% patients waiting for over an hour to receive analgesia is one of the identified parameters requiring improvement. Similarly, at least four patients complained

of severe pain on waking up from anaesthesia in the recovery room (Table 4), which was not addressed in a timely manner. This highlights the need for APMS team to make a process for timely provision of pain management in the recovery room and wards. Evaluation of any service by its providers has the potential of bringing in an element of bias. In our survey a medical student of another medical school was employed for data collection. Utilizing an evaluator, unrelated to APMS, eliminated the factor of bias and is thus a major strength of our study.

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Table 1: American Pain Society's Quality Assurance Pain-relief Standards

1. Recognize and treat pain promptly.
   - Chart and display pain and relief (process).
   - Define pain and relief levels to initiate review (process).
   - Survey patient satisfaction (outcome).
2. Make information about analgesics readily available (process).
3. Promise patients attentive analgesic care (process).
4. Define explicit policies for use of advanced analgesic technologies (process).
5. Monitor adherence to standards (process).

Table 2: Questionnaire.

Questions	No pain	Mild	Moderate	Less than severe	Severe
What type of pain did you expect in the post-operative period?	1	2	3	4	5
What type of pain did you experience in the post-operative period?	1	2	3	4	5
	Within ½ hr	Within 1hr	Within 2hr	After 2hr	Never
When you were in pain, APMS responded:	1	2	3	4	5
	Excellent	Very Good	Good	Fair	Poor
What was the quality of pain relief after APMS management?	1	2	3	4	5
How would you rate the attentiveness and sensitivity of APMS staff?	1	2	3	4	5
How was your overall experience with your pain management service?	1	2	3	4	5
	Yes		No		
Would you use the same	1		2		

analgesia modality again if required?		
Would you recommend the same modality to your family/friends?	1	2
Was the APMS team courteous and professional during your entire interaction?	1	2
Are you aware that a team of specialist pain doctors looked after your pain relief that is a part of anesthesia department?	1	2

Table 3: Analgesic modality and surgical specialty of the patients (n=102)

Variable	**Percentage**
Intraoperative Analgesic Modality (%)	
Epidural	67.6%
Continuous opioid infusion	2.0%
Patient controlled analgesia	27.5%
Others	2.9%
Surgical Specialty	
General Surgery	44.1%
Gynaecology	30.4%
Urology	3.9%
Neurosurgery	1.0%
Orthopaedic Surgery	20.6%

Table 4**:** Responses regarding future preferences of patients and awareness about pain specialist

Questions	**Yes**	**No**
Would you use the same analgesia modality again if required?	79.4%	20.6%
Would you recommend the same modality to your family/friends?	81.4%	18.6%
Was the APMS courteous and professional during your entire visit?	99%	1%
Are you aware that a team of specialist pain doctors looked after your pain relief that is a part of anesthesia department?	46.1%	53. 9%

Table 5: Patients' comments regarding their pain management. (n=12)

Pain medication/Analgesia - Drugs like paracetamol should be available in post-op period readily so we do not suffer. (1 patient) - Another pain-killer instead of paracetamol was given which was not effective. (2 patients) - Pain relief was really bad with epidural alone. Will use spinal block + epidural for any of my next surgery. (1 patient) - PCA* dose was not effective enough. I would prefer epidural over PCA next time. (1 patient) Nursing Care - PCA got disconnected on way to the ward and APMS staff reached late. (1 patient) - In recovery I was in severe pain, but staff responded late. I had to call them more than twice. (2 patients) Pain related factors - I had severe bursts of pain as soon as I gained consciousness (2 patients) - I had severe pain during sleep and I woke up in pain in the ward (2 patient)

*PCA: Patient controlled analgesia

Figure 1: Comparing pain expected by patients and pain actually experienced in post-operative period (n=102)

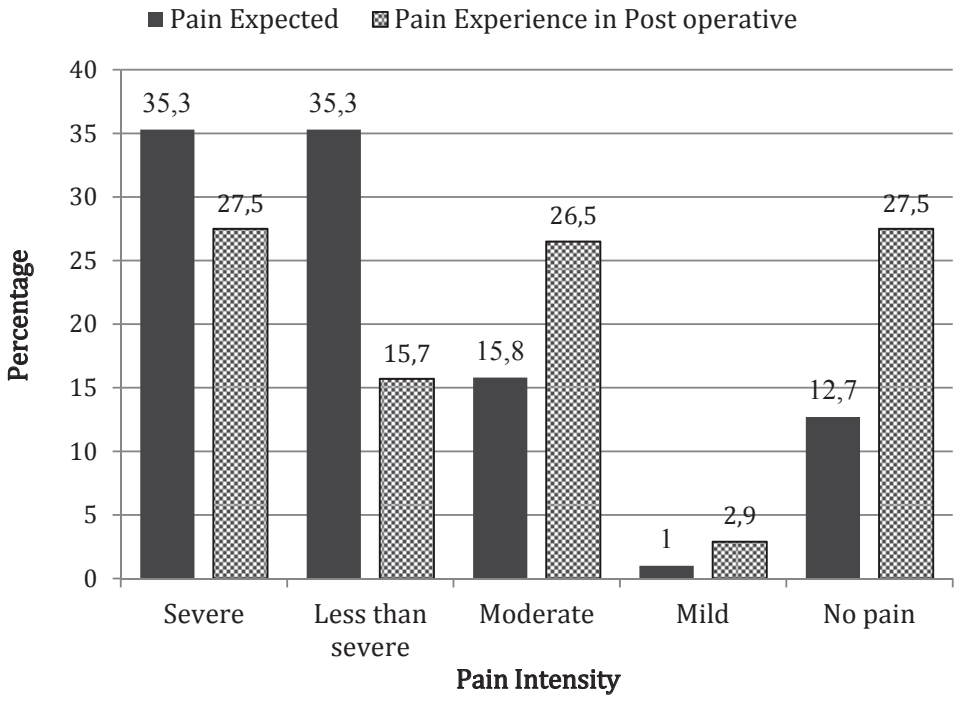
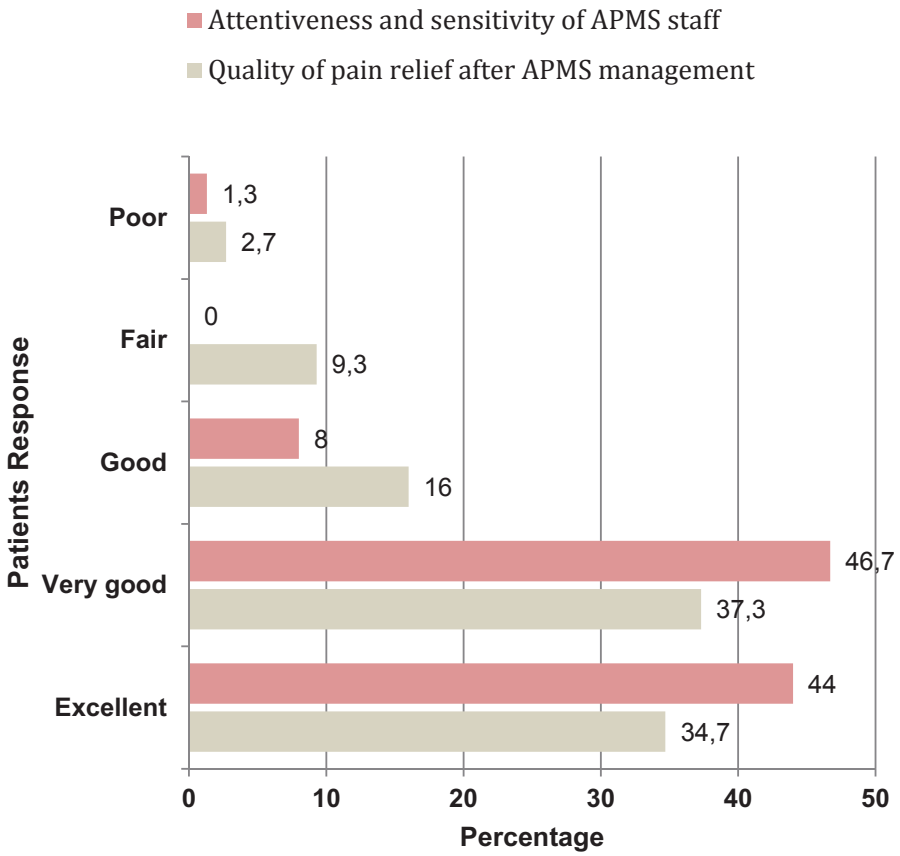


Figure 2:- Response of patients regarding APMS Staff and management progress



THORACIC AORTIC DISEASE - AORTIC DISSECTION

Experiences of the University Clinic for Cardiology

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Abstract:

The term Thoracic Aortic Disease (TAD), covers a wide range of degenerative, structural, acquired, genetically based and traumatic diseases, conditions and presentations of the thoracic aorta. In 2010 several professional associations published joint Recommendations for diagnosis and treatment of TAD, and last year ESC published new Guidelines for diagnosis and treatment of Aortic Disease. Interesting enough is the fact that, 2010 Guidelines were the first recommendations accompanied by a campaign designed for the general population, with a purpose to increase awareness of the existence and importance of these conditions. It was explained by the fact that dissection of the thoracic aorta, the most distinguished acute clinical manifestation of TAD, is recognized as one of the twenty most common causes of death.

This is a condition that is diagnosed mainly based on data obtained by a detailed history and clinical examination, for the existence of high-risk situations, high-risk features of the chest pain and high risk clinical findings. Unfortunately, yet, there isn't sensitive and specific biomarker that could help in the diagnosis of this acute condition. The definitive confirmation of the disease is made by imaging of the aorta with one of the imaging modalities such as transoesophageal echocardiography (TOE), computed tomography (CT) or magnetic resonance (MRI). And in terms of rapid diagnosis, this condition is still characterized with high mortality.

This paper is an attempt to give an overview of the situation with TAD in our country, through a retrospective analysis of the medical database at the University Clinic

of Cardiology of all patients hospitalized during the year 2009 with a working diagnosis of AoD.

Key words: ***thoracic aortic disease (TAD), thoracic aortic dissection (AoD), morbidity, mortality***

INTRODUCTION

The term THORACIC AORTIC DISEASE (TAD) covers a wide range of degenerative, structural, acquired, genetically based and traumatic diseases, conditions and presentations covering the thoracic aorta. In the year 2014 ESC published Guidelines - recommendations for diagnosis and treatment of these conditions. This description covers wide range of clinical situations that according to their clinical presentation are divided into:

Chronic aortic syndromes: atherosclerosis and calcification, dilatation and aneurysm, vasculitis and inflammatory diseases, genetic syndromes associated with TAD: *Marfan, Loeys-Dietz, Ehlers-Danlos, Turner Syndrome*, bicuspid aortic valve, inflammatory diseases associated with TAD: *Takayasu Arteritis and Giant Cell Arteritis*, Ankylosing Spondylitis Infective Thoracic Aortic Aneurysm, and

Acute aortic syndromes: aortic dissection (AoD), intramural hematoma, (IMH), penetrating atherosclerotic ulcer (PAU), pseudo aneurism, traumatic rupture of thoracic aorta (TRA).

Acute aortic dissection is the most important clinical presentation of TAD, because of the distinguish clinical presentation and high mortality even when diagnosis is made, which imposes the urgency of diagnosis and treatment of this condition.

The population-based studies point to an incidence of 2 to 3.5 / 100 000 inhabitants, while Sweden's author Olsson even refers to an incidence of 16/ 100000, but for men. There is a trend of increasing not only of the incidence, but of the prevalence of this condition also. Unfortunately, we have no data on the approximate frequency of TAD in the Macedonian population, but we tried to make a comparative analysis of the prevalence of it in the subpopulation of hospitalized patients due CVD at the University Clinic for Cardiology during the year 2009, compared with data from a group of academic medical centers (UHC-University Health system Consortium), which together with the connected hospitals, covers about 100 hospitals in the United States.

MATERIAL AND METHODS

Single center retrospective analyze was performed, on all comers in ICCU (Intensive Cardiac Care Unit) at University Clinic of Cardiology during the 2009. Medical files were analyzed, from which data for patients' history, physical findings, results from clinical examinations, and therapeutic treatment were analyzed. Only patients with confirmed diagnosis were included in our study.

RESULTS AND DISCUSSION

At our clinic, from a total of 3000 patients hospitalized in the ICCU in the year 2009, 2% were diagnosed with TAD, or from a total of 6500 hospitalizations annually, for the all hospitalizations at our University Clinic (utility with the highest volume of treatment of

patients with cardiac conditions), 0.9% hospitalized patients were diagnosed with TAD. Compared with the data from the UHC database (Table 1), it correlates with the frequency of hospitalizations due to some of the clinical forms of TAD in US, which in the period from 2002 to 2007 shows an increasing trend from 0.8% in 2002, over 0.9% in 2004, to 0.99 in 2006 and 0.9% in 2007. This growing trend is explained by the increase in the average span of life, but also with the rising influence of known risk factors for TAD.

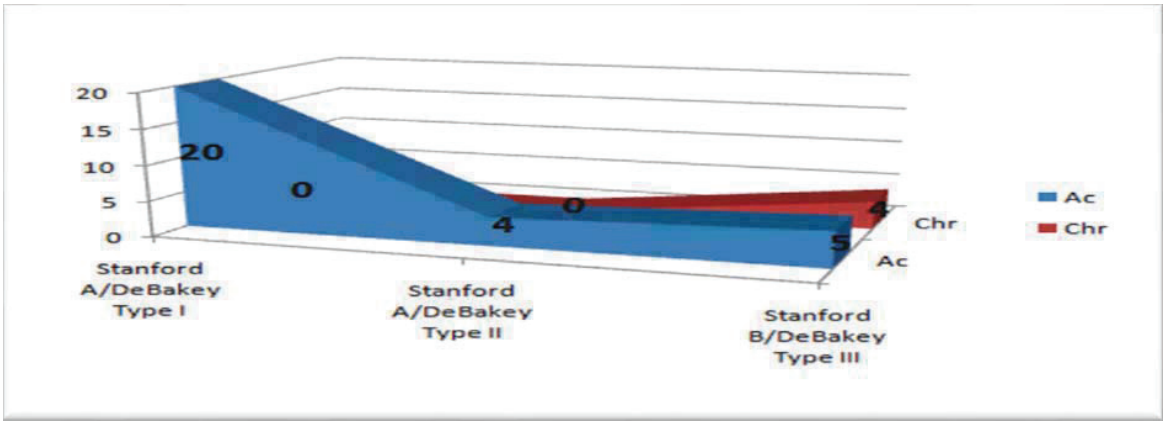
Table 1. Prevalence of hospitalizations due to TAD, according to the UHC database

Total No. of cases	**20 525**	**23 098**	**27 651**	**31 201**	**32 797**
Total No. of inpatient discharges	2679334	2777880	3018141	3222542	3297834
%	0,8	0,9	0,9	0,99	0,9

Type of dissection

Of the 33 patients analyzed, 29 (87.9%) were with an acute dissection, defined when the symptoms were present two weeks of the initial presentation, versus 4 (12.1%) patients with chronic dissection. According to the standard classification, predominating were patients with Stanford type a dissection 72.7%, all with acute dissection, 60.6% of type I and 12,1% of type II after DeBakey. Only 15.5% of the patients had Stanford type B dissection, or type III DeBakey. (Chart 1) Statistically significant difference in distribution was observed for the acute clinical presentation vs. DeBakey classification (p = 0,002), as well as vs. Stanford classification (p = 0,003) with OR 3,2 (CI 0,9 -10,8; p = 0,009) for type A in patients with acute dissection.

Chart 1. Distribution of the patients according to the type of dissection



Although it is known that dissection can occur in the absence of pre-dilatation of the dissected segment, in our population only one patient's dissection was registered in the absence of dilatation of the corresponding segment of the aorta. (Table 2)

Table 2.Correlation of dissection and the concomitant dilatation of the aorta

TAD	*Acute*	*Chronic*	*total*	*Sig (p)*
Without dilatation	1 (3,0%)	0 (0%)	1 (3,0%)	
With dilatation	28 (84,8%)	4 (12,1%)	32 (97,0%)	ns
total	29 (87,8%)	4 (12,1%)	33 (100%)	

Risk factors for TAD

Three groups of risk factors are important for TAD development. They are:

- **Conditions associated with increased wall stress**: hypertension (especially uncontrolled), pheochromocytoma, use of cocaine or other stimulants, lifting weight or other Valsalva maneuvers, trauma, deceleration or torsical injuries, coarctation of the aorta.

- **Conditions associated with abnormalities of the aortic media**: **Genetic**: Marfan syndrome, Ehlers-Danlos syndrome (vascular form), Turner syndrome, Loeys-Dietz syndrome, Bicuspid aortic valve (including prior aortic valve replacement), anuloaortic ecstasy, familial thoracic aneurysm and dissection; **Inflammatory**-vacuities: Takayasu arteritis, Giant cell arteritis, Becket arteritis

- **Other**: Pregnancy, autosomal dominant polycystic kidney, chronic corticosteroid or immunosuppressive therapy, infections of the aortic wall due to bacteriemia or spread of local infection, iatrogenic causes (cardiac catheterization), syphilis, metabolic disorders (dislipidemias).

The presence of risk factors in our patients was as follows: uncontrolled arterial hypertension was by far the most common risk factor, present in 76% of the patients with TAD, which correlates with the data from the literature. It was followed with cigarette smoking 33,3% and dyslipidemia 18,2%.

Only 18,2% of analyzed patients had previously known condition associated with an increased risk of aortic dissection. (Table 3) In addition, one patient with a Marfan syndrome, and one with bicuspid aortic valve. Three of the patients were previously operated from aortic aneurism (one with replacement of aortic valve and aortic root, while two with previous operation of the abdominal Aorta, one with known chronic dissection. In three of the patients during the interrogation data for a family burden were obtained.

This is especially emphasized because of the fact that in none of these patients were implemented the recommendations for monitoring patients with genetic syndromes associated with TAD, a family outbreak of TAD and patients operated or with known TAD.

Table 3. Distribution of patient according to known previous condition

Previous condition	*frequency*	*Percentage (%)*
Without previous condition	27	81,8
Bicuspid aortic valve	1	3,0
Ao valve implantation + aortic root repair	1	3,0
Marfan syndrome	1	3,0
Chronic dissection	1	3,0
Abdominal Ao operation	1	3,0
Chronic dissection +Abdominal Ao operation	1	3,0
Total	6	18,0

Initial diagnostic evaluation of patients with suspected acute TAD

The initial assessment of a patient who presents with symptoms that make the possible diagnosis of TAD is based on the so-called pretest probability for TAD. (Table 4)

Table 4. Clinical data useful to assess the a priori probability of acute aortic syndrome

High-risk conditions	High-risk pain features	High-risk examination features
• Marfan syndrome (or other connective tissue diseases) • Family history of aortic disease • Known aortic valve disease • Known thoracic aortic aneurysm • Previous aortic manipulation (including cardiac surgery)	• Chest, back, or abdominal pain described as any of the following: - abrupt onset - severe intensity - ripping or tearing	• Evidence of perfusion deficit: - pulse deficit - systolic blood pressure difference - focal neurological deficit (in conjunction with pain) • Aortic diastolic murmur (new and with pain) • Hypotension or shock

Adopted from 2014 ESC Guidelines on Diagnosis and Treatment of aortic disease

This evaluation was made based on the data we got from the detailed history, especially the features of chest pain (as a dominant symptom), other symptoms of the disease, medical and family history, as well as detailed and focused clinical examination (Class I, le B). The list of high-risk features that define risk of TAD is presented in Table 4.

Based on the presence of any of these symptoms or signs, patients belong to one of the three risk categories that determine further diagnostic algorithm:

1. Patients with a low risk of TAD: patients who do not have any of the above high risk features.

2. Patients with an intermediate risk of TAD: patients who have one of high risk features; and

3. Patients with a high risk of TAD: patients who have at least two of the high risk features.

Clinical findings in patients with TAD

The blood pressure level is one of the specifics of TAD. According to Hiratzka and co-workers, about half of the patients with acute TAD are hypertensive at the time of presentation, 71% of patients with type B, and 36% of patients with Stanford type a dissection. About 20% of patients with acute TAD are hypotensive or in shock at the time of presentation. The hypotension in these patients may be due to cardiac tamponade, severe aortic valve insufficiency, compression of the false lumen on the right, intraabdominal complications or aortic hemorrhage. Patients that are hypotensive at the moment of presentation, often have neurological complications, myocardial, mesenterial or limb ischemia.

In our study population, only 27% of patients were normotensive at the moment of clinical examination. Hypertensive patients predominated (39%), while 18% were hypotensive, and an additional 15% were in cardiogenic shock at the time of first examination. As it can be seen from Table 5, there are no significant differences in this respect with patients from the IRAD registry.

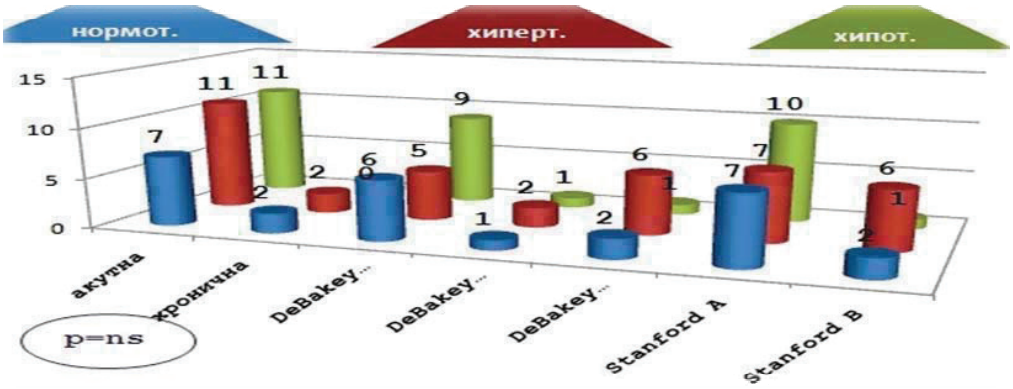
Table 5. Physical findings in patients with acute TAD

Physical findings	Referred (%)	Our study (%)
Normal blood pressure	45	27,3
Hypertension	32	39,4
Hypotension	14	18,2
Shock	13	15,1
Cardiac tamponade	5	3
Aortic regurgitation	45	54,5
Pulse deficit	26	27,3
Pericardial friction edge	2	0
CVI	8	3
Ischemic peripheral neuropathy	3	3
Ischemic spinal damage	2	3
Lower limbs ischemia	10	9,1
Comma	12	6,2
Congestive heart failure	5	0

**Referred according to International Registry of Acute Aortic Dissection (IRAD)*

When we tried to assess what is the linkage between blood pressure and the type of dissection, we found domination of the hypotension in patients with acute, Stanford tip A, DeBakey type I dissection *(Chart 4)*, while hypertension was present in patients with chronic, Stanford type B, DeBakey type III dissection, however recorded differences were without statistical significance.

Chart 4. Distribution of patients by type of dissection and value of BP



When it comes to target organ damage, cardiovascular complications were predominant. In 54% of the patients murmur indicating aortic insufficiency was registered, although we are not entirely sure whether it was always newly created. Although pericardial effusion was common finding (27% of patients), only in one patient we confirmed cardiac tamponade. The literature refers the incidence of syncope as clinical presentation in 13%, while in our series it was registered in only one patient. We are not shore that there weren't cases of "misdiagnosis", so that some of these patients were 'wrong' estimated as CVI and diverted to other facilities that may have waste valuable time for such patients. 15% of patients at the time of presentation in our institution were already in a shock condition, a figure which is significantly higher than referred in the literature. If we want to speculate, that may be due to the fact that patients reach too late our institution, loosing time. Renal complications were predominant clinical manifestations other that cardiovascular. Renal failure was present in 15% of patients. Pulse deficit, limb ischemia, neurological deficit, are conditions that should always focus our attention to this condition. *(Table 6)* Only 24.2% of our patients were without signs of target organ involvement at the time of presentation.

Table 6. Target organ damage as a consequence of acute TAD

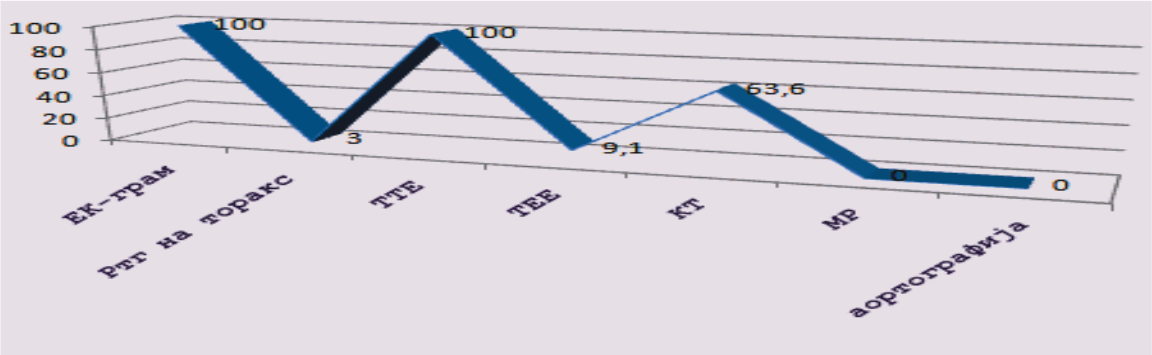
Type	***manifestation***	***referred****	***found***
CV complications	*Aortic valve insufficiently*	*41-76%*	*18(54,5%)*
	Syncope	*13%*	*1(3%)*
	Pericardial effusion/tamponade	*30 (8-10)*	*9(27,3%)*
	Myocardial ischemia/infarction	*7-19%*	*3(9,1%)*
	Heart failure/Shock	*6%*	*5(15,1%)*
Neurological	*CVI/TIA*	*17-21%*	*1(3%)*
	Peripheral neuropathy	*околу 12%*	*1(3%)*
	Paraparesys	*1-3%*	*1(3%)*
Pulmonal	*Aorto-pulmonary fistula*	*3%*	*1(3%)*
	Pleural effusion	*16%*	*0*
GIT complications	*Mesenterial ischemia/ infarction*		*0*
	Aorto-enteric fistula		*1(3%)*
Renal	*Renal failure*	*7%*	*5(15,1%)*
	Ischemia/infarction		*0*
Extremities	*Ischemia*	*10%*	*1(3%)*

** referred frequency according to the International Registry of Acute Aortic Dissection (IRAD)*

Diagnostic modalities that we utilized

ECG - done on all patients with symptoms of suspected acute TAD. Biomarkers (D-dimer test as a rule out procedure, if negative). Rtg of the chest that according to the Guidelines is recommended for the patients with low clinical probability was performed in only 3% of our patients. TTE is the first imaging modality in all patients with suspicion for TAD, and it was performed in all of our patients. Emergent and definitive diagnosis is made with TOE (Class IIa, Loe C), CT or MRI in patients with high risk for acute TAD *(Class I,le C)*. The choice of the imaging modality depends on the patient's characteristics, the institutional capacities, including the immediate availability. Due to the existence of high clinical suspicion of dissection in terms of negative results from the first imaging, second imaging modality should be performed. *(Class I, le C)* In our patients only 9.1% were subjected to TOE while in most of the cases, 63.6%, definitive diagnosis was made with a computerized tomography. *(Chart 5)*

Chart 5. Screening tests applied in our patients



Legend: ЕК-грам-ECG; Ртг на торакс- chest radiogram; TTE- TT echocardiography; TEE- TOE; KT- CT; MP- MRI; аортографија-aortography

Features of TAD by sex and age

What are the data in the literature in terms of gender distribution? According to the IRAD database, the gender significantly affects the presentation of acute TAD. Only 32% of patients included in this database were female, at higher age than males, asking for medical help in the later hours of clinical presentation (not in the first six hours), rarely had an abrupt beginning of the symptoms, and more often first signs were heart failure and alterations of the mental status. This all leads to delay in the diagnosis of acute TAD, that is rarely confirmed in the first 24 hours, and consequently leads to higher hospital mortality compared with men (30% vs. 21%, p = 0,001).

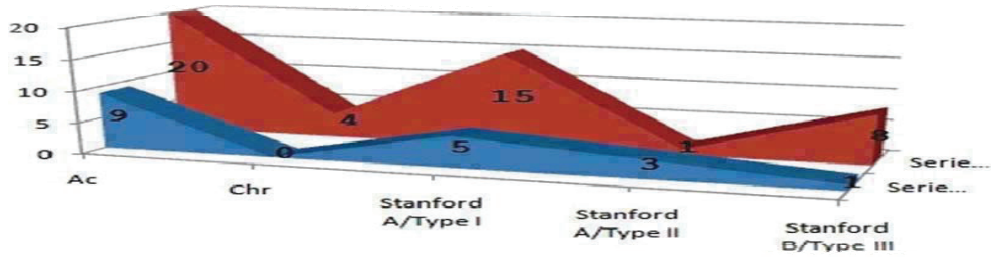
Same distribution by sex (3:1) at the expense of males was found in our population also. Female patients were at higher mean age, although statistically insignificant. In the male population, males at age 40-60 predominated, while among women the same was with the age 50-70 years. Females had significantly lower number of risk factors. *(Table 7)*

Table 7. Distribution of patients according to sex and age

variable	*gender*	*N*	*Mean*	*SD*	*Sig (p)*
age	*female*	*9*	*60,22*	*13,81*	*ns*
	male	*24*	*54,92*	*10,18*	
Nr of risk factors	*female*	*9*	*1,11*	*0,60*	*<0,05*
	male	*24*	*1,92*	*1,17*	

Regarding the type of dissection, no statistical significance was found between genders, although female patients had statistically insignificant increased risk for development of acute dissection (OR = 1,7; p = ns), as well as triple higher risk of developing Stenford type A dissection (p = 0,054; OR = 3,0; p = ns), while in terms of classification according to DeBakey, no statistically significant difference was found (p = ns). *(Chart 6)*

Chart 6. Distribution of patients by sex and type of dissection



The comparison of patients of the opposite sexes in our study in terms of clinical presentation of the disease showed, contrary to findings from the literature, that women were the ones that asked for medical help earlier, and had significantly shorter time to the definitive diagnosis. (Table 7)

Table 7. Comparative characteristics of clinical presentation by gender

	females	*males*				
	Mean±SD	*Mean±SD*	*Min-max*	*Mediane*	*Mode*	*Sig (p)*
Time to first medical contact (h)	*43±110*	*139±305*	*2-336-f* *1-1440-m*	*3* *5,5*	*2*	*0,002*
Time from first medical contact to definitive diagnosis(h)	*15±23*	*16±24*	*2-72-f* *1-72-m*	*4* *2*	*2*	*<0,000*

Table 8. Comparative characteristics of clinical course by gender

variable		*females*	*males*	*Sig (p)*	*OR females*	*Sig (p)*
Target organ damage	***no***	*3*	*5*	*ns*	*1,6*	*ns*
	y	*6*	*19*			
In-hospital mortality	***no***	*8*	*19*	*ns*	*1,8*	*ns*
	y	*1*	*5*			

Although women had slightly greater risk of target organ damage (OR 1.6), and hospital mortality (OR 1,8), these differences were without statistical significance.

RECOMMENDATIONS FOR A DEFINITE TREATMENT OF ACUTE TAD

1. **Urgent surgical consultation** was done for all of the patients with acute TAD, regardless of the anatomical localization (ascending / descending), right after setting a definitive diagnosis. *(Class I, le C)*
2. **Acute dissection which involved the ascending aorta was immediately reported for immediate surgical correction** because of the high risk of associated life threatening complications such as rupture. *(Class I, leB)*
3. **Acute dissection which involved the descendant thoracic aorta was treated with medications**, unless there was a development of life threatening complications: organ malperfusion syndrome, progression of dissection, aneurysm growing, and pure control of blood pressure and / or symptoms despite optimal drug treatment. *(Class I, le B)*

Why urgency in the treatment of patients with acute TAD?

Urgency of treatment results from the fact that it is a life threatening condition which is characterized by a 40% immediate mortality, while mortality of 1% follows with each passing hour from the time of onset of symptoms. If the patient reaches the operation room he carries a risk of 5-20% for the peri- and immediate post-operative mortality, while the five-year survival is 50%.

The hospital mortality of our patients was 18.2%. Of those who survived, 63.6% were reported and treated surgically, while in 24.2% of the patients after cardio surgical consultation an intensive drug treatment was undertaken. Worth noting is the fact that the total time from the point of the beginning of the symptoms to the point of setting a definite diagnosis was significantly shorter in patients in whom the outcome was hospital death. The time passed since the onset of symptoms until the moment of hospitalization in patients with fatal hospital outcome was about 3,7 ± 1,6 h, compared to 137,8 ± 291,6 h in surviving patients ($p = 0,024$). The time from the first contact with a physician in our institution to the moment of setting a definitive diagnosis was also significantly shorter in patients with hospital death 2 ± 1 h versus 19,1 ± 25,1 h ($p = 0,002$). This leads us to the conclusion that patients, who early after the initial presentation seek for medical help, are exactly those with worse clinical outcome and a higher risk of fatal outcome.

Trying to define which high-risk features overlook the fatal outcome in our patients, we made a multivariable logistic regression analysis in which we included the following risk characteristics: *Stanford type of dissection, DeBakey type of dissection, presence of newly showed aortic insufficiency, presence of pericardial effusion, a reaction of blood pressure (hypotensive), the presence of target-organ involvement*, we created a model with a regression coefficient: Chi square = 24,702; $p = 0,001$, accuracy of prediction of 93.9%, in which none of these features was identified as independent risk factor for in-hospital mortality. Our opinion is that it is due to the small study group.

CONCLUSION:

Acute thoracic aortic disease continuous to be one of the major conditions presenting predominantly with chest pain, together with acute coronary syndrome, but as opposite of the first one is characterized with lower capacity for rapid diagnosis and treatment, and by far worse clinical outcome.

That is the reason, why we are urged to think of this condition and actively source for it in patients presenting with chest pain and other typical and less typical signs and symptoms associative for acute TAD.

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Assessment of Tooth Decay Risk in Children Suffering from Nephrotic Syndrome

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Abstract:

Introduction:The assessment of tooth decay risk is based on a combination of clinical and para-clinical indicators. The last being related with environmental characteristics. One of the most essential criteria of dental caries risk is the individual general health status. The nephrotic syndrome concerns a complex of pathological conditions including reduction of the serum calcium concentration, compensated with an increase of protein-linked one.

Theaim of this study is to be evaluated the risk of tooth decay in children suffering from nephrotic syndrome.

Material and methods:Ten children aged from 3 to 13 years participated in the investigation. All of them were diagnosed with kidney disorder, namely nephrotic syndrome. There have been evaluated indices of epidemiology of tooth decay in primary and permanent teeth and plaque index of Silness-Lὸe. Specifics of fluorides prophylactic cares, frequency of visits by the dentist and carbohydrates' nutrition were also taken into account.

Results:All the participants have been estimated of high decay risk.

Conclusion:These children need prophylactic cares for improvement of the oral-dental status.

Key words: *tooth decay, indicators of risk, nephrotic syndrome;*

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1. Introduction

The most common etiological factor of the nephrotic syndrome in children's age (in approximately 85 % of all the cases) are the minimal glomerular changes. Distribution by gender shows prevalence of boys to girls in a ratio of 2:1. Predominantly affected are children from 1 to 6 years of age. The nephrotic syndrome is characterized with proteinuria of high degree, hypo-proteinemia, hypo-albuminemia, hyper-lipoproteinemia, related with an increase of cholesterol and triglycerides. The clinical manifestation of the disease is most often provoked by infections, procedures of immunization, intoxications, allergic reactions, injuries of burning. An essential para-clinical indicator of this kidney disorder is reduction of the concentration of serum calcium at the expense of increased amount of protein-linked fractions. In order to ensure proper treatment of the disease there has to be applied a specific dietary regime avoiding proteins' compounds and salt. Diuretic medicines, especially the groups of potassium-saving, together with thiazide and loop diuretics are of great importance for overcoming the effects of edema. In condition of bacterial infections are prescribed antibiotics combined with γ-globulin therapy. More than 90 % of children suffering from nephrotic syndrome are very well influenced by application of corticosteroids (De-hydrocortisone, Prednisolone). It is necessary for children and their parents to become acquainted with the fact that the nephrotic syndrome is a long-lasting disorder, related with potential complications as a consequence of the disease and its treatment protocol. [8]

The initiation and progression of the systemic disorder require frequent procedures of hospitalizationof these patients. All the efforts of doctors, parents and children are concentrated upon overcoming the somatic problem. The attempts to cope with the restrictions accompanying dietary regime and medicine programs can result in negligence of preventive cares addressed to oral health status, therefore to its severe deterioration.

Tooth decay is the most widely spread chronic disease among children and adolescents, which often reflects not only upon oral, but also on the general health status of the individual. [7, 5] The intensity of caries impacts correlates with plenty of factors: age of the child, depth of the lesion, topographic characteristics of cavity clinical findings. It has been established that more vulnerable to decay attacks are younger children, these suffering from chronic systemic failures, as well as those who are with limited access to complex, properly performed dental cares. [1]

Models of caries risk assessment accentuate on a great variety of indices:

- Specifics of nutrition, especially frequency and consistency of consumed carbohydrates;
- Exposure to the effects of endogenous and exogenous fluoride products of preventive cares;
- Susceptibility of the host to acid attacks;
- Micro-flora- representatives, quantity characteristics;
- Traits of the social-economic environment;
- Cultural markers;
- Behavioral patterns. [3, 2]

With explicitly strong protective potential against tooth decay are characterized fluorides of systemic and topical application, influencing the development of hard teeth tissues during the periods of pre-eruptive mineralization and post-eruptive maturation, respectively. The following effect of caries reduction concerns primary, as well as permanent teeth. [6, 9]

The accessibility of children and their parents to dental services is related with determination of tooth decay risk level, too.

Some authors, including participants in the National Initiative for improving oral health under the patronage of the American Academy of Pediatrics, put an accent on some significant indicators of tooth decay risk:

- Active at the time of clinical investigation decay lesions;
- Treated decay lesions, registration of present fillings on definite teeth and teeth surfaces;
- Caries lesions on teeth roots' surfaces;
- Performance of oral hygiene procedures;
- Records of oral hygiene status. [4]

The aim of this paper is to be assessed the risk of tooth decay in children of different age suffering from nephrotic syndrome.

The performance of this purpose is related with accomplishment of some tasks.

Task 1 Assessment of tooth decay risk based on clinical signs illustrating the state of hard teeth tissues. Evaluation of the indices of epidemiology of tooth decay in primary and permanent teeth for each participant.

Task 2 Assessment of tooth decay risk according to the level of dental plaque accumulation upon teeth surfaces.

Task 3 Application of environmental criteria of caries risk assessment.

2. Material and methods

A number of 10 children aged from 3 to 13 years took participation in the investigation. All of them were hospitalized at the Department of Pediatrics at the University Hospital "St Marina", Medical University-Varna, city of Varna, Bulgaria. These patients have been diagnosed with nephrotic syndrome.

The actual detailed intraoral status of each of the participants was recorded applying the documentary method of individually addressed medical card. The oral cavity examination was performed in daily light, to the bed of the patient, using sterile kits of dental instruments. Registration of presence or absence of: teeth affected by tooth decay (D-decayed permanent, d-decayed primary); extracted teeth as a consequence of complicated dental caries (M-missing permanent teeth; no registration of missing primary teeth because of processes of physiological exchange); teeth with fillings (F-fillings in permanent teeth, f-fillings of primary teeth).

Calculation of the index of epidemiology of tooth decay in teeth separately for permanent and primary teeth. This index gives information about the percent of teeth affected by caries compared with all the examined teeth. The sum of all the decayed, filled and extracted permanent teeth is divided into the total number of examined permanent teeth and the value obtained is multiplied with 100. Concerning primary teeth this index is calculated as the sum

of decayed and filled primary teeth is divided into all the examined primary teeth and the result is multiplied with 100.

By the means of the plaque index by Silness-Lòe we can evaluate the amount of accumulated dental plaque on teeth surfaces in the role of an essential factor for initiation and progression of the tooth decay process. With scraping movements of the periodontal probe (UNC-15) with the figures from 0 to 3 we record dental plaque upon vestibular, palatal (respectively lingual), medial and distal surfaces of these representative teeth: 16, 22, 36, 42 and 44. In tooth 24 we estimate the amount of dental plaque only on the medial and distal surfaces. 0 means no plaque on tooth surface. The figure 1 equals to a small amount of plaque. 2 corresponds to a moderate level of plaque and equivalent of a great amount of plaque is the figure 3. The sum of all the figures of all the examined teeth surfaces of an individual is divided to the total number of these surfaces (22), thus calculating the average value of the plaque index in each of the examined participants.

Implementing the documentary method of individually addressed inquiry we obtain data about environmental criteria of tooth decay risk assessment. The target-oriented enquiry is associating with information about general health status of the child; application of various modalities of fluorides' exposure- exogenous and endogenous; specifics of carbohydrates' nutrition- frequency of consumption, consistency, content of disaccharides). An indicator of great significance is the frequency of visits by dentist for the child and its parents, respectively.

3. Results:

- The values of epidemiology of tooth decay in primary teeth in the examined patients vary from 25 % to 66 %.
- The values of epidemiology of tooth decay in permanent teeth are in the range from 14% to 44 %.
- One fifth (20 %) of all the examined are with PI equal or less than 1.
- One half of the participants (50 %) are with PI values registered in the interval from 1,1 to 2.
- In 30 % of all these children PI values are equal or more than 2,1.
- No patients apply regular endogenous fluorides' prophylactic cares.
- Sporadic endogenous fluorides' exposure is relevant to 40 % of the children.
- Regular exogenous fluorides' modalities are applied by 70 % of the examined.
- Sporadic exogenous fluorides are used by 10 % of investigated children with nephrotic syndrome.
- Predominant portion of the patients (90 %) consume irregularly and incessantly carbohydrates of the group of disaccharides.
- Prevailing part of these children have never visited dentist (80 %).
- Only 1 of 10 participants visits dentist on each 6 months. And 1 of the 10 examined turns to the dentist on a period longer than 1 year.**[Table 1]**

№ of patient	age	epidemiology of tooth decay in teeth	Plaque Index of Silness-Lòe	Fluoride prophylaxis cares				Frequency of carbohydrates' nutrition	Frequency of visits by the dentist	
				exogenous		endogenous			patient	parents
				regular	sporadic	regular	sporadic			
1	3 years of age	Et = 33%	PI = 2,04	no	no	no	no	all the day incessantly	never	only in emergency
2	5 years of age	Et = 60%	PI = 1,95	no	yes	no	no	all the day incessantly	never	only in emergency
3	6 years of age	Et = 50% ET= 33%	PI=2	yes	no	no	no	all the day incessantly	never	only in emergency
4	6 years of age	Et = 60 %	PI = 2,18	no	no	no	no	all the day incessantly	never	never
5	6 years of age	Et = 38% ET=14%	PI = 1	yes	no	no	yes	all the day incessantly	never	only in emergency
6	6 years of age	Et = 28 %	PI= 0,95	yes	no	no	yes	all the day incessantly	never	never
7	7 years of age	Et = 66% ET = 44 %	PI = 1,14	yes	no	no	yes	only as a dessert once or twice per day	never	on a period longer than 1 year
8	8 years of age	Et = 58% ET= 33%	PI = 1,55	yes	no	no	no	all the day incessantly	never	only in emergency
9	9 years of age	Et = 25% ET = 25%	PI = 1,32	yes	no	no	yes	all the day incessantly	on each 6 months	only in emergency
10	13 years of age	ET = 25%	PI = 2,27	yes	no	no	no	all the day incessantly	on a period longer than 1 year	only in emergency

Table 1 Illustration of tooth decay risk factors in children of different age suffering from nephrotic syndrome

4. Conclusions:

Based on considerable criteria of caries risk assessment, we can conclude that all of the examined children suffering from nephrotic syndrome are in high risk of tooth decay. In order to restrict this tendency of caries progression and stop the deterioration of oral-dental health these measures have to be taken into account:

- Motivation for performance of regular proper oral hygiene procedures.
- Precise age-dosed regular application of fluorides' products with exogenous and endogenous mechanisms of effects.
- Total restriction of carbohydrates' consumption, especially disaccharides- only as a dessert once per day.

- Increased frequency of regular visits by dentist for performance of primary, secondary and tertiary prophylactic cares.

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THE POTENTIAL OF COCOA (*Theobroma cacao L.*) PODS EXTRACT IN PERIODONTAL DRESSING TO RABBIT GINGIVAL WOUND HEALING

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Abstract

Introduction: Anti inflamatory and antibiotic in periodontal dressing are often added but they cause any allergic reaction. Cacao (*Theobroma cacao L.*) has potential as natural anti inflamtory, antioxidant, and antimicrobial because it contains polyphenolics as flavonoid or condensed or polymerized tannin. The aim of this study was to determine increase wound healing rate indicated by fibroblast cells number and to determine the most effective percentage level of cocoa pods extract. **Materials and methods:** This study was experimental laboratories that used post test only control group design. The samples were 36 male rabbits had been given gingiva labial injury. The samples were divided into 4 groups based on percentage of cocoa pod extract addition, there were 0%, 5%, 10%, 15%. Each groups were divided into 3 day decapitation subgroups, they were on day 3, 5, and 7. **Result:** The results showed difference high fibroblast cells number in day 3 but insignificant. Beside it, there were significant difference decrease of fibroblast cells in day 5 and 7 between second treatment group and third treatment group with control group. **Discussion:** In this case the catechins, tannins, and anthocyanin content of cacao pod extract were able to suppress inflammatory cells number and free radicals produced during inflammatory phase. **Conclusion:** The conclusion was addition of cocoa pod extract could potentially increase rabbit wound healing rate and most effective percentage extract to affect fibroblast cells was 15%. **Suggestion:** Need research percentage addition of extract of the cocoa pod which is different to know lethal dose.

Keywords : Cocoa pods, fibroblast, wound healing, polyphenolics

A. INTRODUCTION

Background

Periodontal dressings is material used for dress the wound after surgical periodontal. The addition of anti inflamatory and antibiotic on periodontal dressings often done but also pose an allergic reaction so we need a alternatif material to substitute which it can speed wound healing proscess up without generate side effects. Plants that could potentially anti inflamatory , antioxidants, and a natural antimicrobial is cocoa (Theobroma cacao l.) because contain polyphenols in form flavonoids or condensed tannins.

Baharudin (1996), granting extract of cocoa pod at concentrations 5 %, 10 %, and 15 % have anti inflamation activity against number of macrophages cells[1]. A active macrophage produce factors chemotaxis, growth factor, and cytokines that affect the proliferation, and migration of fibroblas, endothelial cells, and epithelial [2]. This indicates that extracts of cocoa pod capable of accelerating the process of wound healing.

Formulation of the Problems

1. Whether extract of cocoa pod addition in periodontal dressing potential for increase wound healing of rabbit gingiva that is viewed from fibroblast cells number?
2. How percentage of pod cocoa extract in periodontal dressings that is effective for increase fibroblas cells number to wound healing of rabbit gingiva?

Research Purposes

1. To examine the potential addition of cocoa pod extract in periodontal dressing to increase wound healing of rabbit gingiva that is viewed from fibroblast cells number.
2. To know percentage of cocoa pod extract in periodontal dressing that is effective for increase fibroblas cells number to wound healing of rabbit gingiva.

Benefits Of Research

This research is expected to provide benefits such as:

1. As an additional information about the impact of cocoa pod extract addition (*Theobroma cacao L.*) in periodontal dressing to increase speed of wound healing.
2. As a research reference on a dose of cocoa pod extract used *(Theobroma caca L.)* to be additional ingredient in periodontal dressing.

Hypothesis

The addition of cocoa pod extract (*Theobroma cacao L.*) in periodontal dressing able to increase the speed of rabbit gingiva wound healing that is viewed from fibroblast cells number.

B. LITERATURE REVIEW

Cocoa (*Theobroma cacao L.*)

According to Wollgast and Anklam (2000) in Porbowaseso (2005), classifies of cocoa polyphenols in three groups, catechins (flavan-3-ols) 37%, 4% and proantosianidin relationships 58% [3].

Catechin called catechoat acid with the chemical formula $C_{15}H_{14}O_6$, is in a State of pure highly soluble in hot water, alcohol, and ethyl acetate[4]. The relationships with chemically derived pigment, formed from sianidin sianidin with the addition or reduction of

hydroxyl groups or by methylation or a glycosylation. Proantosianidin is another name of condensed tannins. The tannins are bound with sugars soluble in the solvent condensed tannins, while hidroalkohol or tannins are more easily extracted with the solvent acetone 70%.

Wound healing

Wound healing is a dynamic process that includes blood vessels, fibroblasts, epithelial and [5]. The process then happens in the healing of wounds is divided into three phases: the inflammatory phase, a phase of the proliferation, and completion phase [6].

Inflammatory phase lasts for 0-3 days [5]. At the beginning of this phase of the injured area is dominated by platelets. Platelets release a number of factors chemotaxis, growth factors, and cytokines that attract other platelets, and leukocytes to the site of the wound fibroblasts [7]. Next in 24-48 hours phase inflammatory taken over by leukocytes especially pmn, a macrophage, and a lymphocyte played the role to deprive of debris and memfagosit bacteria. Factor chemotaxis, growth factor, and also by a macrophage cytokine that is produced. Growth factor such as PDGF, FGF, EGF, TGF α dan TGF β impact on migration and the proliferation of fibroblas, endothelial cells, and epithelial [2]. Next phase proliferation between 3-24 day depends on the size wound.This phase dominated by tissue formation granulation, synthesis collagen by fibroblas, and process epitelisasi [8]. Last phase remodeling tissue, consists of three part, namely epitelisasi contraction, and reorganization of connective tissue. Duration phase it began at the 3rd sunday and lasting minimum 1 year [9].

Fibroblast cells

Fibroblasts are the cells that produce fibers and ground substance of the connective tissue amorphous. Fibroblasts was instrumental in the formation of extracellsular matrix components of connective tissue such as the synthesis of collagen, elastin, glikosaminoglikan, proteoglycans, and glycoproteins multiadhesif[10].

Periodontal Dressing

Periodontal dressings is material for dress the wounds after surgical periodontal. Periodontal dressing does not contain material that could in healing, but only help healing for the hurt protected [11] .

Periodontal dressing does not contain of eugenol often used because does not have an irritant effect. A formula was introduced by Baer based on the reaction between a metallic oxide with fatty acids [12].

C. RESEARCH METHODS

The research was experimental laboratories with the post test only control group design. Population samples and object were 36 of local guinea (oryctolagus cuniculus). The samples divided into four groups based on the percentage of an cocoa extract in periodontal dressing that were control group (0 %), treatment group one(5 %), group two (10 %) and group three(15 %) with each group consists of 9 rabbits. The treatment of each group divided into subgroups of dekapitasi, day namely subgroup one (3rd), subgroups two (5th day), and subgroups three (7th day) with each group consists of 3 rabbits.

The stage of making cocoa cocoa pod extract was blend the cocoa skin to get a fine powder. A fine powder of cocoa pod was remaseration with solvent acetone 70 % as much

as three times. Filtrat obtained then the solvent was evaporated with rotavapor until not left and obtained extract liquid. Extract liquid concentrated by an oven at a temperature of 60 ^{0}C [13].

Stage making periodontal dressings extract skins of cocoa :

a. The control group (K): periodontal dressings formula Baer already homogeny 100 grams without extra extract rind of cocoa.
b. Treatment group one (KP1): formula periodontal dressing formula Baer already homogeny 95 grams and added extract rinds of cocoa stored 5 grams.
c. Treatment group two (KP2): periodontal dressing formula Baer already homogeny 90 grams and rind cocoa added extract as much as 10 grams.
d. Treatment group three (KP3): periodontal dressing formula Baer already homogeny 85 grams and added extract rinds of cocoa 15 grams

Treatment of animals exercised after adapted for 7 days, then performed anesthesia in combination with ketamin and xylazine, punch biopsy and conducted on the gingiva of dental insisivus right lower jaw section with diameter 2.0 mm labial until it reaches alveolar bone. The wound was closed with periodontal dressings with cocoa skin extract content. Each group is divided into three sub groups according to the day of dekapitasi, on day 3, day 5, and the 7th day. Then do the making of preparations with Mallory and repainting Trichrome fibroblasts cells observed with the light microscope with 1000x magnification.

D. RESULT AND DISCUSSION

Result

Based on the research that has been done, the average fibroblasts number cells of rabbits in the control group (K), treatment group one (KP1), two (KP2), and three (KP3) can be seen in attachment 1. Comparison of the average fibroblasts number cells of each group can be seen in attachment 2.

The Data obtained was tested with Kolmogorof-smirnov test, shows a normal data distribution with the value significance of 0.308 ($P>0.05$). Further Data was tested with test Levene, shows data is not homogeneous with the significance value of 0,018 ($P<0.05$). Then The Data was tested with a non-parametric test of Kruskal-Wallis, the result was a difference with a significance value of 0.001 ($P<0.05$). The next test was a statistical test of the Mann Whitney to find out which groups have significant differences. Mann Whitney test results can be seen in attachment 3.

Discussion

On the day 3 of the treatment group showed a proliferation of fibroblasts cells amounts was higher even though less significant compared to the control group. This happens because the migration and proliferation of fibroblasts cells have started to take place at the inflammatory phase that is on a initial 24 hours post treatment. Migration and proliferation of fibroblasts cells induced by growth factors PDGF and TGF- TGF-β and cytokine factors released by platelets and leukocytes[5] [7] [9]. In this case the catechins, tannins, and anthocyanin content of the cacao pod extract were able to suppress inflammatory cells number

and free radicals produced during inflammatory phase. On the dose addition of as much as 5%, 10%, 15%, and catechins, tannins, and antosisnin gives a bitter taste but the effects did not inhibit the inflammatory process continuity that occurs naturally. It can be concluded that indirectly, catechins, tannins, and the relationships were able to increase the activity of fibroblasts proliferation and migration.

On the day 5 and 7, the average number of fibroblasts cells decreased. There was a significant difference in treatment group two (KP2) and treatment group three (KP3) compared to the control group (K), this happens because the activities of fibroblasts cells are more progressive in synthesis of collagen fibers and the occurrence of cells differentiation of fibroblasts into miofibroblas so that in one point of view of microscope would appear fewer of fibroblasts number cells that can be observed in atachment 5. That was caused by catechins, tannins and anthocyanin contained in the extract of the cocoa pod in periodontal dressing. The presence of condensed tannins, catechins, and influencer relationships with a bitter taste, antibacterial, antioxidant and [14].

As an anti-inflammatory agent, tannin works by inhibiting arakhidonat acid [15]. Anthocyanin and catechin also acted as anti inflamatory agents which in high concentrations block line siklooksigenase and phospholipase A2, while in low concentrations of this compound, just block sikloogsigenase path. Inhibition of primarily from arachidonic acid release from inflammatory cells will lead to less availability of substrate arachidonat for siklooksigenase and lipooksigenase lines, which will ultimately suppress the amount of prostaglandins, prostacyclins, thromboxanes and endoperoksida on one side and acid hydroperoxide, hidroksieikostrenoat acid, and leukotrienes on the other [16]. Less availability of substrate arakhidonat for the siklooksigenase and lipooksigenase process resulting in decreased inflammation characterized by a decrease of inflammatory cells number microscopically on lesions area [17]. Reduction of inflammatory cells cause cytokine produced also reduced so that free radicals released by cytokines also decreases. The decline in number of these free radicals and collagen fibroblasts synthesis activities may soon take place.

As antibacterial agents, tannin works by coagulation or agglomerate bacteria protoplast, thus formed a stable bond with the bacterial proteins [18]. In addition, catechin have a tendency to bind bacterial proteins, thus interfering metabolism of bacteria. Potential of cocoa pods extracts as antibacterials cause inflammatory cells to phagocytes bacteria become easier, so that free radicals released by cytokines are not excessive. Therefore inflammatory phase is short, so it can proceed with proliferation or fibroplasia phase.

As an antioxidants agent, catechin is able to act as antioxidants for inflammatory phase. Free radicals are produced during the inflamatory, a free-radical types of reactive oxygen species (ROS). The working mechanism of catechins in neutralize ROS is through –OH group, so the radicals become pepsinogen. That process is *Catechin (–OH) + R (Free radical)* → *Catechin* (O^{2+}) + *RH* [19]. The neutralizing cause lowering expression of MMP-1, MMP-8, MMP-9, and so barriers on degradation of type-3 collagen and matrix extracellsular is synthesize by fibroblasts caused by ROS directly or by activated MMP.

The effect of antioxidant, antibacterial, and anti inflamatory work together during inflammatory process. They worked together in lowering effect of excessive inflammation so inflammatory phase can last a short time. The next healing phase continues with the

proliferation phase is marked by the increasing activity of fibroblasts in the synthesis of collagen fibers.

E. CONCLUSION AND ADVICE

Conslusion

The addition of extract pod of cocoa (*Theobroma cacao L.*) in periodontal dressing can potentially increase the speed of wound healing with a percentage that most effective way to increase fibroblasts cells number in rabbit gingiva injuries is 15%.

Suggestion

Advice that can be given of this research.

1. Need to reserch the cocoa pod active substances that play a role in wound healing.
2. Need to research the percentage addition of extract of the cocoa pod which is different to know the lethal dose of this material.

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ATTACHMNET 1. THE AVERAGE NUMBER OF RABBITS FIBROBLAST CELLS

Table of average number of rabbits fibroblasts cells in the control group (K), treatment group one (KP1), two (KP2), and three (KP3) after administering treatment

Group	Amount fibroblast day- (X±SD)		
	3	5	7
K	8,2222±1,71053	6,1111±0,19245	4,8889±0,96225
KP1	8,8889±0,38490	5,7778±0,50918	4,1111±0,38490
KP2	9,0000±0,33333	4,4444±0,69839	3,6667±0,33333
KP3	9,1111±0,83887	4,3333±0,66667	3,3333±0,33333

X±SD : averange fibroblast cells number±deviation standart

ATTACHMENT 2. IMAGE GRAPHS OF AVERANGE FIBROBLAST CELLS NUMBER

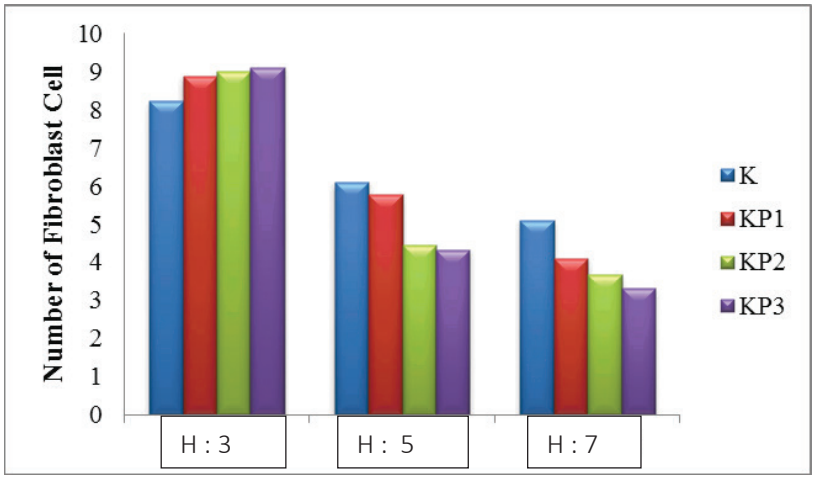


Image graphs of average fibroblasts cells number in the control group (K), treatment group one (KP1), two (KP2), and three (KP3) after administering treatment

ATTACHMENT 3. RESULT OF MANN WHITNEY TEST

The table result of Mann Whitney test that rabbit macrophage cells number on treatment group one (KP1), two (KP2), three (KP3), and four (the garden) after administering treatment (atachmnet 4)

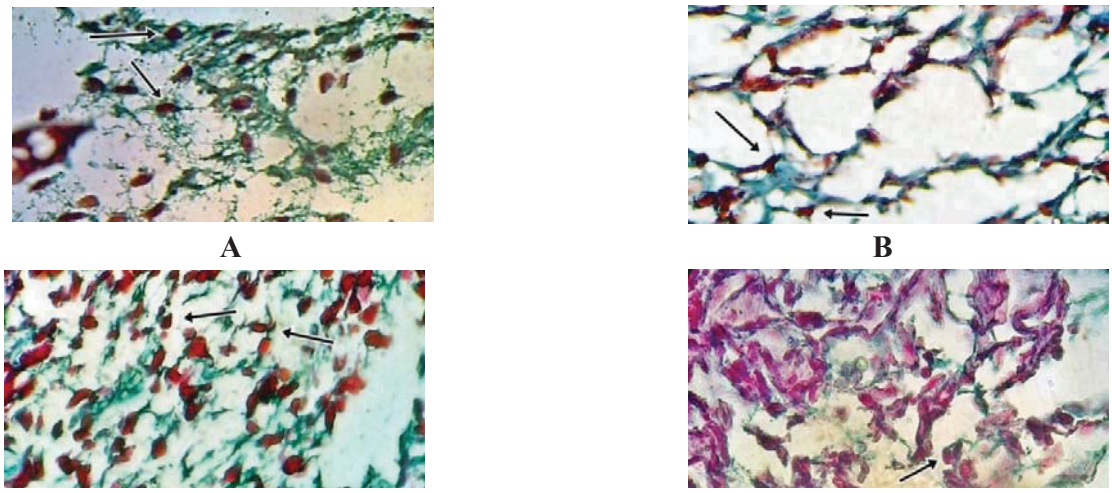
	KH3	KP1H3	KP2H3	KP3H3	KH5	KP1H5	KP2H5	KP3H5	KH7	KP1H7	KP2H7	KP3H7
KH3	-	**0,817**	**0,658**	**0,513**	**0,072**	**0,077**	**0,050**	**0,050**	**0,046***	**0,046***	**0,050**	**0,050**
KP1H3		-	**0,637**	**0,825**	**0,043***	**0,046***	**0,046***	**0,046***	**0,043***	**0,043***	**0,046***	**0,046***
KP2H3			-	**1**	**0,046***	**0,050**	**0,050**	**0,050**	**0,046***	**0,046***	**0,050**	**0,050**
KP3H3				-	**0,046***	**0,050**	**0,050**	**0,050**	**0,046***	**0,046***	**0,050**	**0,050**
KH5					-	**0,369**	**0,046***	**0,046***	**0,099**	**0,043***	**0,046***	**0,046***
KP1H5						-	**0,050**	**0,050**	**0,268**	**0,046***	**0,050**	**0,050**
KP2H5							-	**0,822**	**0,825**	**0,369**	**0,184**	**0,077**
KP3H5								-	**0,487**	**0,637**	**0,184**	**0,077**
KH7									-	**0,197**	**0,046***	**0,046***
KP1H7										-	**0,178**	**0,072**
KP2H7											-	**0,261**
KP3H7												-

H3 declared to day 3 observation, H5 declared to day 5 observation, H7 declared to day 7 observation. Sign (*) indicates the data in the statistical continuation has values of significance (P<0.05;).

ATTACHMENT 4. MAKING OF PERIODONTAL DRESSING

Manufacture of rosin: pour powder as much as 28.5 grams and zinc oxide as much as 21.5 grams. Mix the rosin and zinc oxide until homogeneous. The manufacture of pasta: pour fat and hydrogenated 47,5 g 2.5 g zinc oxide then mix until homogenous. The making of periodontal dressing: mix powder 50 grams and 50 grams of pasta little by little until homogeneous (100 grams).

ATTACHMNET 5. IMAGE OF RESULT

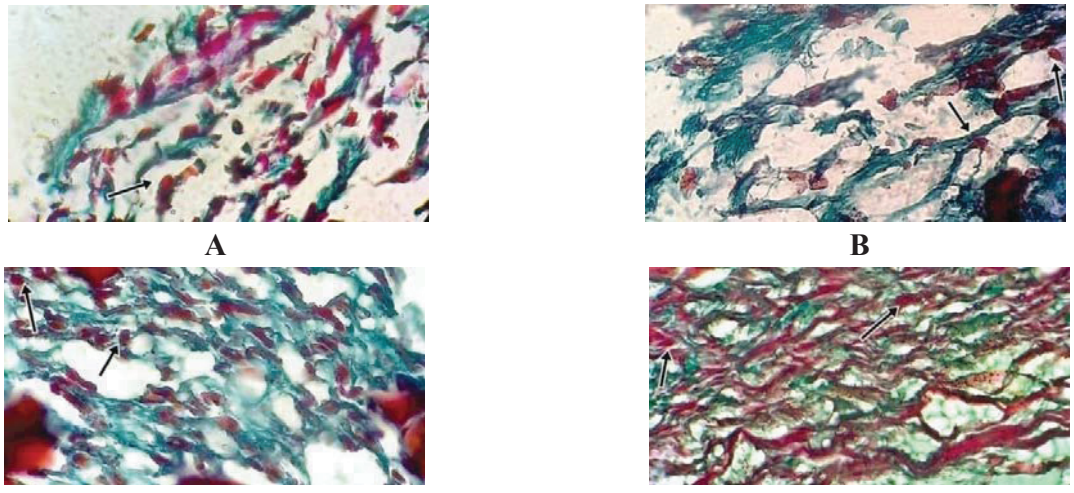


A **B**

C **D**

An arrow indicates fibroblas cells magnification trichrome mallory 1000x

Preparat Day 3 (A: control group; B: Treatment control group 1; C: Group Treatment 2; D: 3 Treatment Groups)

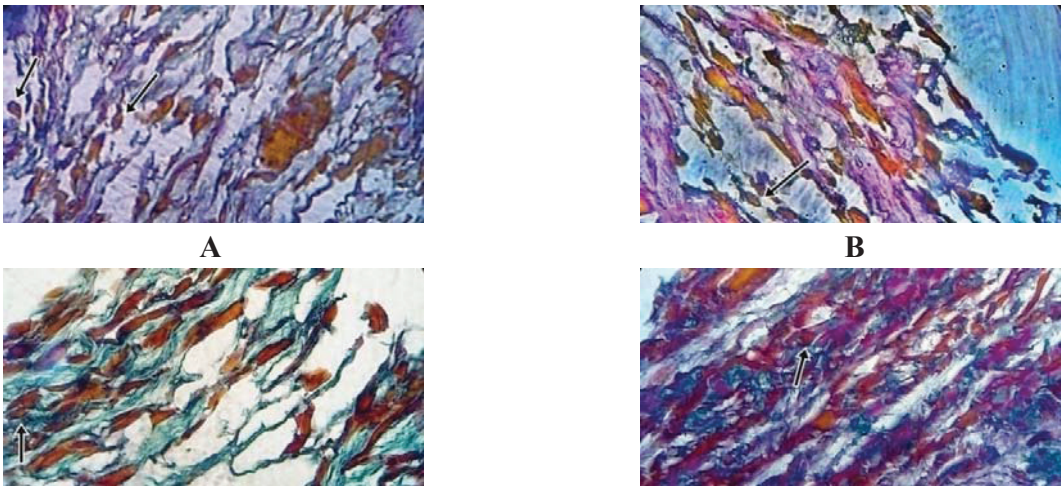


A **B**

C **D**

An arrow indicates fibroblas cells magnification trichrome mallory 1000x

Preparat Day 5 (A: control group; B: Treatment control group 1; C: Group Treatment 2; D: 3 Treatment Groups)



A **B**

C **D**

An arrow indicates fibroblas cells magnification trichrome mallory 1000x
Preparat Day 7 (A: control group; B: Treatment control group 1; C: Group Treatment 2; D: 3 Treatment Groups)

COMPARISON BETWEEN MOLAR BANDS, BONDABLE TUBES AND BONDABLE TUBES WITH FLOWABLE COMPOSITE

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Abstract

Orthodontic treatment is an expensive treatment in dentistry and the treatment period is between two to three years. The cost and treatment time could be significantly increase if metal attachment (brackets, molar tubes and bands) is lost/ broken. The failure of bondable tube and molar band could increase the cost for orthodontic treatment. With additional flowable composite to bondable tube, the failure rate could become lower. The objective of this study is to compare the failure rate between molar bands, bondable tubes and bondable tubes with flowable composite. In this study, 30 patients attending orthodontic specialist clinic in USIM were randomly selected and grouped into Group A, B and C. Group A were cemented with molar bands, Group B with bondable tubes and Group C with bondable tubes with flowable composite. Upper and lower fixed appliances were also bonded. The failure rate (molar bands or tubes become loosed/ need recemented/ rebonded) of each group will be assessed after 1 month, 3 months and 6 months.

Keywords: *flowable composite, bondable tubes, molar bands*

1. Introduction

One of the greatest impacts on orthodontic treatment (braces) is the development of adhesives for bracket bonding. Orthodontic bonding has become as part of routine clinical procedure in orthodontic treatment for fixed appliances since 1980s.This procedure has reduced the need for bands(Trimpeneers *et al.*, 1996). Although many practitioners still band the molar teeth, there are some who choose to bond metal tube to molars. This procedure has eradicated the need to open and close the space for band insertion. The comfort, speed and

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facility of placing the appliances as well as better aesthetics in comparison to banding are reasons for the success with this technique(Reynolds, 1975). A current technique for bracket attachment and bonding is by using light-cure resin composite(Wendl *et al.*, 2008). The advantages of light cure composites are accurate bracket position, longer working time, easy removal of excess adhesive and higher bond strength in comparison to chemical cure composites(Greenlaw R 1989 ; Galindo *et al.*, 1998; Wendl *et al.*, 2008).

Edward H Angle introduced the use of bands with brackets in 1928. The solid metal brackets were welded to the band and had to be customized for each patient. The time needed to fit and cement the band to teeth was considerably long. The introduction of adhesive resins in orthodontics has permitted the practitioner to bond directly bracket onto tooth surface. Meaning that adhesive are most widely used for bonding between brackets and enamel(Shinya *et al.*, 2008; Zachrisson, 1977; Mirza, 1983; Kinch *et al*., 1988). One of the advantages of adhesive bonding is that the procedure has reduced treatment time in clinical procedure (Jenkins, 2005).

In addition, it is more convenient to the practitioner and comfortable for patient. Bryant et al in their study noted that bonding had abolished the need for pre-treatment separation, reduced interdental spaces created from bands, decreased decalcification risk and increased the ability for the detection of caries(Bryant *et al.*, 1987). Jenkins also suggested that bonding had eliminated band seating problems, improved aesthetic appearance, reduced the need for separation, improved oral hygiene, allowed easy access to interproximal area and eradicated the need for space closure at the end of treatment(Jenkins, 2005). In contrast to bonding, banding needed space separations to release the tight contact point between teeth. It is impossible to place a band on a tight contact point. Moreover, the interdental space created from the use of banding on each tooth was also reduced. Decalcification risk decreased because less tooth surface was covered and becomes easier to notice any caries that have occurred.

Another concern of the bonding procedure is related to the adhesive strength, adhesive application and residual adhesive resin on tooth surface at the end of treatment (Sinha *et al.*, 1995).One of the reasons for the use of metal band in posterior teeth is because bonding has inferior physical properties (Jenkins, 2005). The lack of strength in adhesive will lead to bond failure. Powers et al also agree that bond failure could result in additional cost in material, longer treatment time and increase the number of visit for treatment(Powers *et al.*, 1997). Sharma-Sayal et al noted that various designs of bracket bases have been made to improve the mechanical retention between bracket and adhesive (Sharma-Sayal *et al*., 2003).

The aims of this study therefore were to assess the failure rate between molar bands, molar tubes and molar tubes with flowable composite. Thus, the best way to apply attachment to molar teeth can be made. In the end this will reduce failure rate of molar attachment.

2. Materials and methods

A total number of 30 patients were randomly selected for this study. They were divided into 3 groups. Group A patients were cemented with molar bands, Group B with bondable tubes and Group C with bondable tubes and flowable composite.

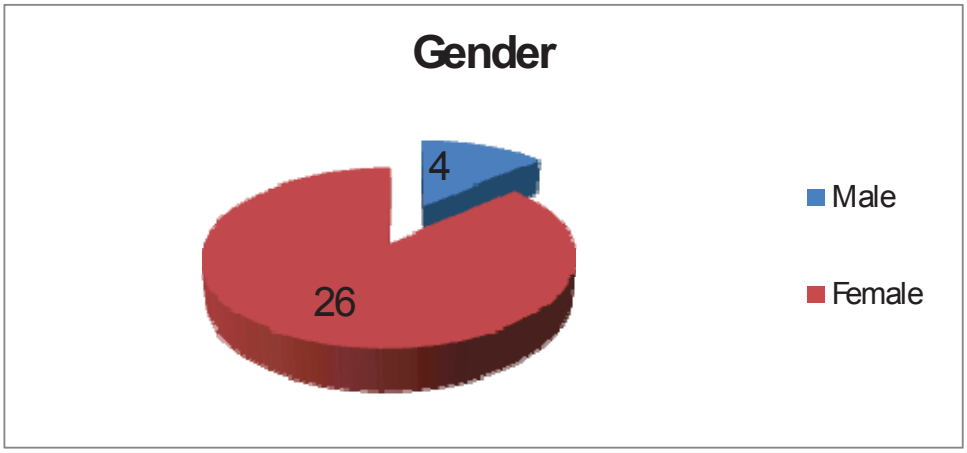
The failure rate is defined as any molar bands or tubes which are loosen, detached or broken. The data collections were done in 1, 3 and 6 months after bond up. The failure rates were compared between each groups and each period. The data collected were then being analyst using SPSS.

3. Results

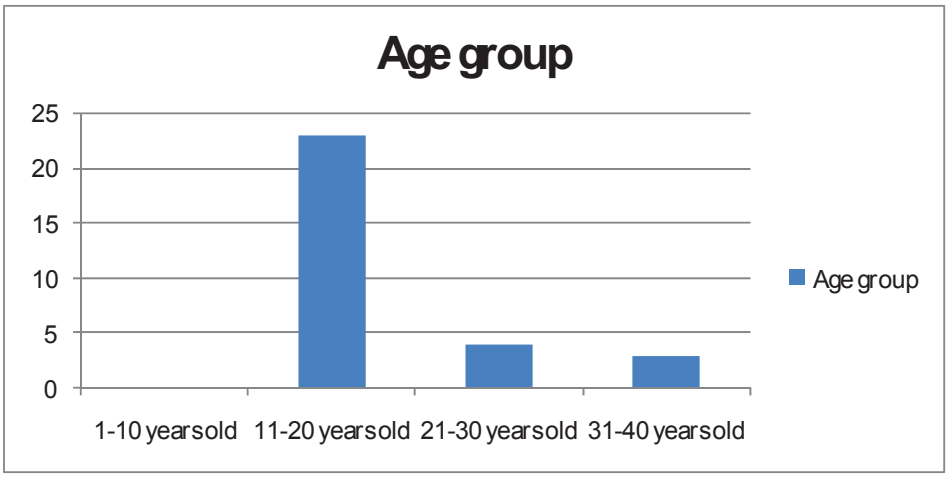
From the sample size, from 30 patients involved in this study, 26 patients are female and only 4 are male. This could be because female are more concern of their appearance and willing to seek for treatment.

The age groups are mainly between 11 to 20 years old patient which consist of 23 patients. Apart from that, there are 4 patients from 21-30 years old and 3 patients from 31-40 years old group. This is because most patients are still studying and could not afford treatment in private clinic.

Chart 1: Gender distribution



Graph 1: Age group distribution



A month after bond up, one patient experienced molar bond failure in Group B which is bondable tube group. The other two groups which are the Group A patients cemented with

band and Group C patients bonded with bondable tube plus flowable composite did not experienced any band or bond failure.

After three months post bond up, the result is still the same as a month after bond up. One patient still experienced bond failure in Group B. The band and bondable tube with flowable composite still did not experience any band or bond failure. Six month post bond up shows the number of bondable tube failure increased to two patients in Group B, one patient experience bond failure in Group C and no band failure in Group A.

However, a One Way ANOVA analysis shows that the differences between groups are not statistically significant of $p > 0.05$ for all periods. This could be because of the small sample size.

Table 1: One month post debond

Group A (band)	*Group B (bondable tube)*	*Group C (bondable tube with flowable)*
30/30	*29/30*	*30/30*

The number of patient after 1 month bond up without molar attachment failure.

Group A (band)	*Group B (bondable tube)*	*Group C (bondable tube with flowable)*
0%	*3.3%*	*0%*

Failure rate of each group comprise of 30 patients.

Table 2: Three months post debond

Group A (band)	*Group B (bondable tube)*	*Group C (bondable tube with flowable)*
30/30	*29/30*	*30/30*

The number of patient after 3 month bond up without molar attachment failure.

Group A (band)	*Group B (bondable tube)*	*Group C (bondable tube with flowable)*
0%	*3.3%*	*0%*

Failure rate of each group comprise of 30 patients.

Table 3: Six months post debond

Group A (band)	*Group B (bondable tube)*	*Group C (bondable tube with flowable)*
30/30	*28/30*	*29/30*

The number of patient after 1 month bond up without molar attachment failure.

Group A (band)	*Group B (bondable tube)*	*Group C (bondable tube with flowable)*
0%	*6.6%*	*3.3%*

Failure rate of each group comprise of 30 patients.

4.0 Statistical Analysis

Statistical analysis was done using One Way ANOVA to compare the relationship between the three groups with p> 0.05. The data summaries are as followed:

Table 4: One month after bond up

	Sample			
	Group A	*Group B*	*Group C*	*Total*
N	*10*	*10*	*10*	*30*
∑X	*40*	*39*	*40*	*119*
Mean	*4*	*3.9*	*4*	*3.9667*
$\sum X^2$	*160*	*153*	*160*	*473*
Variance	*0*	*0.1*	*0*	*0.0333*
Std. Dev	*0*	*0.3162*	*0*	*0.1826*
Std. Err.	*0*	*0.1*	*0*	*0.0333*

Standard weighted-means analysis					
ANOVA Summary Independent Samples k=3					
Source	*SS*	*df*	*MS*	*F*	*p*
Treatment between group	*0.0667*	*2*	*0.0333*	*1*	*0.381099*
Error	*0.9*	*27*	*0.0333*		
Total	*0.9667*	*29*			

p > 0.05

Table 5: Three months after bond up

	Sample			
	Group A	*Group B*	*Group C*	*Total*
N	*10*	*10*	*10*	*30*
∑X	*40*	*39*	*40*	*119*
Mean	*4*	*3.9*	*4*	*3.9667*
$\sum X^2$	*160*	*153*	*160*	*473*
Variance	*0*	*0.1*	*0*	*0.0333*
Std. Dev	*0*	*0.3162*	*0*	*0.1826*
Std. Err.	*0*	*0.1*	*0*	*0.0333*

Standard weighted-means analysis					
ANOVA Summary Independent Samples k=3					
Source	*SS*	*df*	*MS*	*F*	*p*
Treatment between group	*0.0667*	*2*	*0.0333*	*1*	*0.381099*
Error	*0.9*	*27*	*0.0333*		
Total	*0.9667*	*29*			

p > 0.05

Table 6: Six months after bond up

	Sample			
	Group A	*Group B*	*Group C*	*Total*
N	*10*	*10*	*10*	*30*
$\sum X$	*40*	*38*	*39*	*117*
Mean	*4*	*3.8*	*3.9*	*3.9*
$\sum X^2$	*160*	*148*	*153*	*461*
Variance	*0*	*0.4*	*0.1*	*0.1621*
Std. Dev	*0*	*0.6325*	*0.3162*	*0.4026*
Std. Err.	*0*	*0.2*	*0.1*	*0.0735*

Standard weighted-means analysis					
ANOVA Summary Independent Samples k=3					
Source	*SS*	*df*	*MS*	*F*	*p*
Treatment between group	*0.2*	*2*	*0.1*	*0.6*	*0.555966*
Error	*4.5*	*27*	*0.1667*		
Total	*4.7*	*29*			

$p>0.05$

4. Discussion

One of major problem in orthodontic fixed appliances is debond of molar tubes. It could not only cost money but precious time as well. Five to ten minutes of clinical time is requires for rebond and could prolong the waiting time of other patients. Apart from that, to replace and bond molar tube requires good moisture control and lot of concentration. The conventional method of placing band requires two day visits, skills and a wide inventory of band sizes.

Placing additional flowable composite around molar tubes in this study has proven that it could reduce molar tube failure and could be as good as band. Although statistically it is not statistically significant, but clinically it shows that bondable tube with flowable composite have lower failure rate compared to bondable tube alone. However, the case selection is very important because patient must have very good oral hygiene and should be monitor closely to prevent any white sport lesion due to the additional composite around molar tubes.

5. Conclusion

From this study, we could conclude that the failure rate is higher between bondable tubes compare to molar bands and bondable tubes with flowable composite. Application of flowable composite to bondable tubes could increase the bondable tubes strength and thus reduce the failure rate of bondable tubes. However, a study of 18 months post bond up will be done to assess the long term failure rate of each group.

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RAPID METHOD FOR DETECTION OF ETHANOL CONTENT IN MOUTHWASH USING LOCALLY FABRICATED PORTABLE ELECTRONIC NOSE[1]

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Abstract

The purpose of this study is to check for ethanol (EtOH) content in mouthwash products sold in Malaysia market using portable electronic nose (e-nose). For this study, twenty mouthwashes were tested with nine of the samples contain EtOH as part of its ingredients. The problem with those products is that it does not disclose the concentration of the EtOH as part of its labelling. This is important since long-term use of ethanol-containing mouthwash may result in adverse health effect to the consumer. The process parameters used in this study was optimized using Response Surface Methodology (RSM), with strong relations between actual and predicted sensor response yield correlation of determination, R^2 of 0.9756. Optimum process parameters generated by Design Expert 7.1.5 shown that the optimum volume for EtOH sample was 5.84mL for 1.45 min time of detection. While for screening process, it was found that from the detection of alcohol-free mouthwash using portable e-nose, no alcohol content detected with "alcohol free" was displayed on the LCD screen of the device. However, 9 out of 10 mouthwash samples that have no "alcohol free" label on the products contain more than 10% (v/v) EtOH. Hence, this study had successfully optimized the process parameters and screened the mouthwashes sold in Malaysia market for the presence of EtOH.

Keywords: *ethanol; mouthwash; portable e-nose; optimization*

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1. Introduction

Mouthwashes are considered beneficial in the prevention and treatment of variety of oral or orophryngeal diseases such as gingivitis, periodontitis and other inflammatory conditions. Apart from the various therapeutically active ingredients in the mouthwashes such as essential oils, Chlorhexidine, Fluoride, Potassium Nitrate and Benzydamine, one ingredient that is present generally in every mouthwash is ethanol (EtOH). The concentration of ethanol in mouthwash product is between 0-27% that is high compared to the EtOH in beer (4%) and wine (12%). High concentrations of ethanol in mouthwash may have detrimental oral effects such as epithelial detachment, keratosis, mucosal ulceration, gingivitis, petechiae and oral pain [1]. Moreover, there is a possible connection between the long-term uses of ethanol containing mouthwash with oral cancer [2],[3],[5]. To check for the presence of EtOH in mouthwash, a portable e-nose was designed and fabricated for this purpose.

An E-Nose is basically a device that mimics human olfactory system [4] and it is a useful tool for EtOH detection since its allowed identification and fingerprinting of aroma. The use of E-Nose to detect a large number of chemical compounds is appropriate since the detection is based on the principal of gas chromatography, which allows chemical compounds to elute at different times and then the compounds will be detected by the sensitive sensor.

The portable e-nose used for this study, as shown in Figure 1, was designed to be very compact and small, so it can be carried around for an “on-line” detection of the mouthwash or beverage for EtOH detection. The way the device worked was simple which any layman can operate this portable E-Nose. The gas sensor will detect the presence of EtOH which later the output response will be received by the conditioning electronics. The received data were then analyzed by microcontroller and displayed the concentration of EtOH on the LCD display.

Figure 1 The Prototype of the Fabricated Portable E-Nose Used in this Study

The objectives of this study are to check for EtOH concentration in mouthwash product using the fabricated portable e-nose and to test the accuracy and reliability of the sensor used. Various mouthwash products used as samples and been tested by the E-Nose to

detect the presence of EtOH substance in it. This study is important to check whether the concentration of EtOH in mouthwash product contain the specific concentration that is allowed.

2. Materials and Methods

2.1 Materials

Ethanol, 95% (v/v) was purchased from HmBg Chemicals Inc. (Germany). 20 mouthwash samples of different flavours from different brands were bought from a local market in Selangor; with 10 of them have "alcohol free" indication on the products' labelling.

2.2 Methods

2.1.1 Calibration

EtOH dilution of 0.1% (v/v), 1.0% (v/v) and 10.0% (v/v) were prepared for calibration purpose. Later, the result was saved in the e-nose database for further used during screening process. The EtOH sample of certain volume (2mL, 4mL and 6mL) was put inside a bottle and the portable e-nose will take the reading based on the time set for the parameter, which is 0.5 to 1.5 minute with 30 seconds increment.

2.1.2 Screening Process

For screening process, experiments were conducted after optimum time and sample's volume generated from the optimization part in RSM. Then, twenty mouthwashes were tested with nine of the samples contain EtOH as part of its ingredients. Then, reading was taken after the portable e-nose is ready and the concentration of EtOH is displayed on the LCD screen of the device.

3. Results and Discussion

For calibration part, the result of the response will be in terms of an analogue value of the sensor response. While for optimization, process parameters were optimized using Design Expert 7.1.5 to get the optimum values of time and EtOH solution's volume. Lastly, screening of twenty mouthwashes of different flavours from different brands sold in Malaysia market was done, which the results were successfully displayed on the LCD display of the portable E-Nose.

The portable e-nose used for this study can give rapid detection up to 10s at 20% (v/v) and above, of the EtOH concentration. The analogue value starts to spiked rapidly once the EtOH sample was put near the sensor of the e-nose (less than 1s) but will keep on increasing until it goes constant, which reaches its maximum value. Hence, the time chosen as one of the process parameters was up to 1.5 min.

3.1 Calibration Process

Based on the data in Table 1, it was found that the higher the concentration of the EtOH detected, the higher the analogue value of the sensor response recorded by the portable e-nose. Time of the detection as well as the sample's volume is also plays an important role in increasing the response of the sensor. However, from the observation, the highest concentration had consumed more power for the e-nose, which will result in a shorter amount of time to use the device. This happens because the VOC adsorbed by the sensor was too saturated, which will increase the resistance of the sensor, hence increase the voltage needed for the e-nose to operate. This device has to be used when it is in an optimum condition which

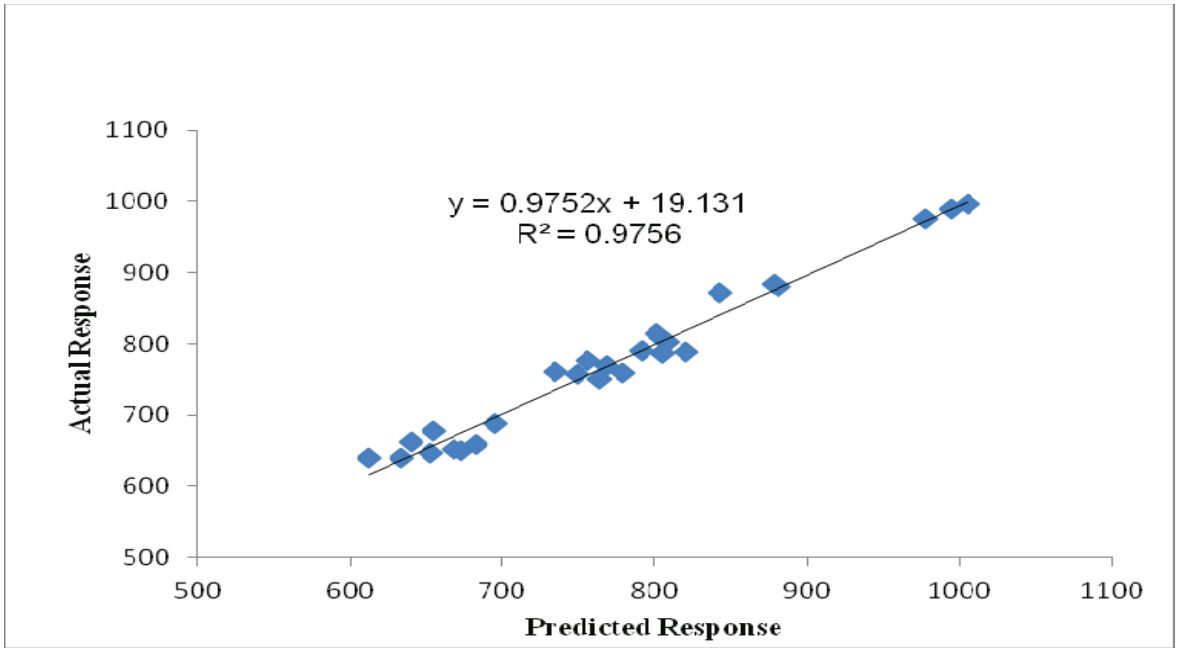
the battery is fully charged, or should be around 7v - 9v left, so the results can be taken accurately.

The data shown in Table 1 is also showing two kinds of result which are the actual and predicted sensor response. Actual reading is actually taken from the experimental result, to observe the sensor response while the predicted sensor response was generated from the RSM of the design expert software. From the data, it was found that the results of both responses are not too deviating from each other and this is shown in Figure 2, as most of the responses showed a close relationship between actual and predicted values. From the plotted graph, the R^2 value is 0.9756, which proves that there is a strong relation between both values.

Table 1 Historical Data Design with Experimental and Predicted Values of the Sensor Response.

Run	*Time (min)*	*Sample Volume (mL)*	*EtOH Conc., % (v/v)*	*Actual Sensor Response*	*Predicted Sensor Response*
1	0.5	2	0.1	613	639
2	0.5	4	0.1	633	640
3	0.5	6	0.1	640	662
4	1	2	0.1	653	647
5	1	4	0.1	668	652
6	1	6	0.1	655	678
7	1.5	2	0.1	673	650
8	1.5	4	0.1	683	658
9	1.5	6	0.1	696	688
10	0.5	2	1	763	750
11	0.5	4	1	779	759
12	0.5	6	1	820	788
13	1	2	1	749	758
14	1	4	1	769	770
15	1	6	1	808	803
16	1.5	2	1	735	760
17	1.5	4	1	756	777
18	1.5	6	1	801	814
19	0.5	2	10	805	786
20	0.5	4	10	843	871
21	0.5	6	10	977	976
22	1	2	10	791	791
23	1	4	10	881	880
24	1	6	10	994	989
25	1.5	2	10	791	791
26	1.5	4	10	878	883
27	1.5	6	10	1005	997

Figure 2 The graph of Actual versus Predicted of the Sensor Response.



3.2 Optimization Process

Another objective of this study is to optimize the process parameters using historical data of RSM. For optimization part, time and sample's volume were set "in a range" while sensor response was set as "maximum". These parameters were set with the specific requirement because optimization process for this particular studies is concerning with the highest sensor response can be detected by the portable e-nose. From the results of those parameters, which have been conducted in 27 runs, the highest sensor response of EtOH generated by the software was 1056.81 which was shown in Figure 3 of the contour plot of the optimization graph. While the optimum volume for EtOH sample was 5.84mL for 1.45 min time of detection. In similar case, Figure 4 shows the same result of the optimization graph, only in 3D surface graph. This is important to show the optimum parameters which represented by the 3D graph.

Figure 3 2D Contour Plots of the Optimization Graph.

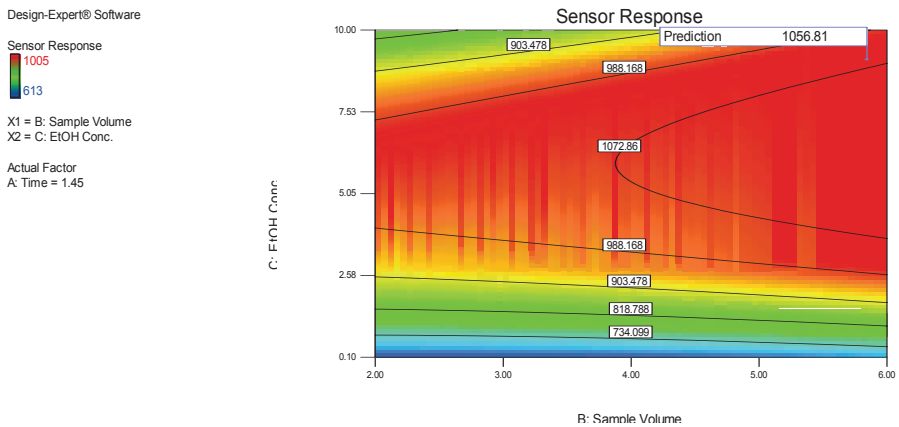
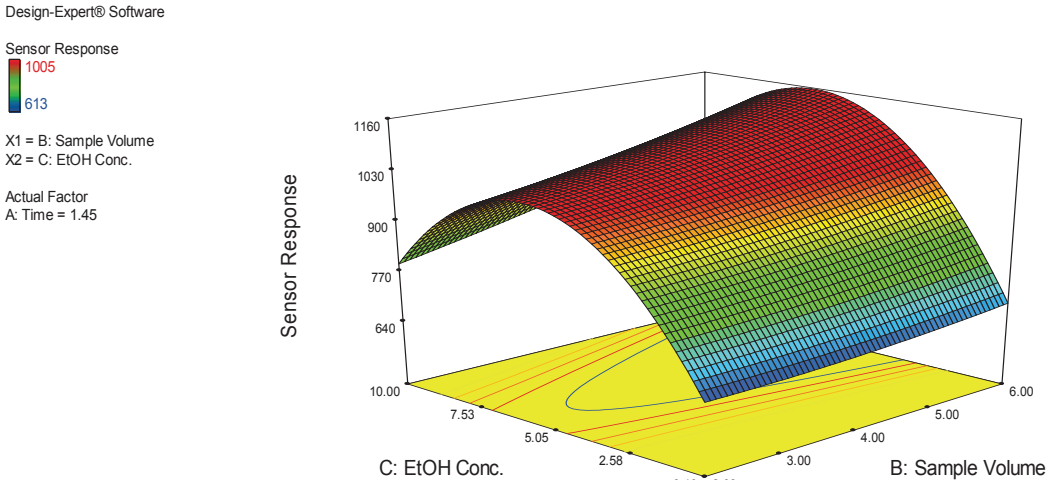


Figure 4 3D Surface Graph of the Optimization Graph



3.3 Screening Process

Detection of ethanol in 20 types of different mouthwash flavours and brands was tested using the portable e-nose prototype for a screening process. Based on the optimum time and EtOH volume from the Design Expert optimization, 5.84mL of mouthwash sample was tested and the result was taken after 1.45 min of the detection. Samples of mouthwash products were tested, as shown in Table 2 which was from alcohol contained mouthwash and non-alcohol contained mouthwash.

For alcohol free mouthwash, all ten samples have halal logo from JAKIM on the product's label. When testing with the portable e-nose, the device has successfully validated the authenticity of the products, since it has shown "Alcohol Free" on the LCD screen of the device. While for the mouthwashes that has no halal logo, only sample L1 has no EtOH content presence in the sample, while others shown ">10% EtOH" displayed on the LCD screen. The concentration displayed is high that long term usage might give side effect to the consumer's oral health.

Apparently, it was also found that only sample L1 resulted in "Alcohol Free" when testing it using the portable e-nose. This result supported by its labelling since it that has no halal logo on the product and EtOH was nowhere to be found as part of its ingredients, All 20 samples except for sample B1 disclose its ingredients as part of its labelling. Hence, the usage of the portable e-nose is important to check the availability of EtOH in the sample. Based on these findings, in can be concluded that the portable e-nose can be used to check for the presence of EtOH in mouthwash.

Table 2 Screening Process of Different Mouthwashes Sold in Malaysia Market.

Description on the product's label	***Sample***	***Result of EtOH conc.***	***Description on the product's label***	***Sample***	***Result of EtOH conc.***
Alcohol Free	C1	Alcohol Free	*Contain Alcohol*	L1	Alcohol Free
	C2	Alcohol Free		L2	>10%
	C3	Alcohol Free		L3	>10%
	C4	Alcohol Free		L4	>10%
	S1	Alcohol Free		L5	>10%
	S2	Alcohol Free		L6	>10%
	O1	Alcohol Free		G2	>10%
	O2	Alcohol Free		G3	>10%
	G1	Alcohol Free		G4	>10%
	G5	Alcohol Free		B1	>10%

4. Conclusion

This study has successfully calibrated, optimized and screened EtOH content in mouthwash samples bought from Malaysia market using portable e-nose prototype. It was found that all three process parameters; time (min), sample volume (mL) and EtOH concentration % (v/v) can affect the sensor response value, as the higher the parameters was set, the higher the analogue value displayed by the device. From the calibration process, the lowest concentration of EtOH detected by the portable e-nose was 0.1% (v/v). Apart from that, the strong relations between actual and predicted sensor response yield correlation of determination, R^2 of 0.9756. While for optimization process, optimum time and EtOH sample generated by RSM was 5.84mL for 1.45 min time of detection. In screening process, it was found that from the detection of alcohol-free mouthwash using portable e-nose, the LCD has displayed "Alcohol Free" upon the detection, while 9 out of 10 mouthwash samples of ethanol-containing-mouthwash showed ">10% EtOH" on the LCD screen. Hence, this study had successfully optimized the process parameters and screened the mouthwashes sold in Malaysia market for the presence of EtOH.

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The combined therapy «PUVA + interferon-α» in cutaneous T-cell lymphoma treatment

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Key words: cutaneous T-cell lymphoma, interferon-α, mycosis fungoides, PUVA

Introduction

Cutaneous T-cell lymphoma (CTCL) is a heterogeneous group of neoplastic diseases caused by the proliferation of the lymphocytes' clone in the skin that shows considerable variation in clinical presentation, histologic appearence, immunophenotype and prognosis. CTCL represents more than 65% of all primary cutaneous lymphomas. Cutaneous lymphomas make 2% of all dermatological diseases. For quite a long time only two types of CTCL had been known: Mycosis fungoides and Sezary syndrome. Many years had passed before the researchers identified new species of CTCL via clinical and immunophenotypic criteria analysis. Usually CTCL begins at an old age, although it can affect younger people and even children. CTCL is more common in men than in women (2:1). Besides, in the U.S. CTCL is more common among African americans than among white citizens. A great increase of the CTCL incidence has been fixed worldwide lately: 3% per year only in the U.S. and E.U.-countries.

The concrete cause of CTCL is unknown. According to the researches lymphocytes become malignant due to changes of the DNA genetic code as a result of the factors increasing risk of the disease development, initiating oncogenic mutations and promoting appearance of malignant T-lymphocytes clone. These factors may be Epstein-Barr virus, human T-lymphotropic virus – HTLV-1, HTLV-2, human herpesvirus 6 (HHV-6) and Borrelia burgdorferi, chemicals (including medicines), the ionizing radiation, even in small doses. The most common type of CTCL is mycosis fungoides (MF).

Mycosis fungoides makes 75% of all CTCL cases. Mostly it arises among men at the age of 40-60 and develops slowly within decades. It is generally accepted to allocate 3 stages of classical form of MF:

1 stage (spotty) is presented with single or multiple shelled spots up to 10-20 cm in diameter, which may be located on any site of cutaneous integument looking like eczematous centers or parapsoriasis plaque. Rashes can exist for years. At the same time their spontaneous regress is also possible. Patients are disturbed by an intense itching. It is quite hard to establish the correct diagnosis at this stage. 5 years or more usually pass since the beginning of the disease till the statement of the correct diagnosis. Patients can be considered to have atopic dermatitis, psoriasis, seborrheic dermatitis. However persistant itching and resistance to the applied therapy help to state the clinical diagnosis of MF.

2 stage (plaque) is characterized by transformation of spots into sharply delimited, intensely itching flat infiltrative reddish-bluish plaques of various degree of density and rising over the skin level or their appearance on visibly healthy skin. The elements can spontaneously regress or merging together they can form large intensely itching centers with clear boundaries due to the center regress. On a surface of some plaques peeling is noted. Rather often it resembles psoriasis. Hyperkeratosis of palms and feet, onychomycosis are an often case. Alopecia develops at affection of the scalp.

3 stage (tumoral) is characterized by domed brownish-red nodes with a smooth surface. There are some frequent places of their appearance: face, neck, skin of axillary, inguinal and femoral folds. Active growth and collapse of the nodes resulting in deep ulcers with the bloody and purulent discharge form are natural for this stage as well. The intense itching, fatigue, appetite loss and body temperature increase are subjectively noted. Lymph nodes and internal organs (lungs, a liver, a spleen) are affected at final stages. The marrow is affected quite rarely.

Erythrodermic variant of mycosis fungoides

In most cases erythroderma develops sharply and spreads throught the skin without any previous rashes. However a long-term period of skin rash may precede the erythroderma. These elements can spread and merge together which leads to the development of partial or full erythroderma. The affected skin becomes infiltrated red with a purple shade; a peeling may appear. Sometimes the skin becomes ashy and brown (melanodermic variant). Patients complain of intolerable itch, burning and swollen skin, shivering. And also sweat secretion disorder, total alopecia, onychodystrophy, hyperkeratosis of palms and feet, the peripheral lymph nodes growth and cachexia are observed.

Mycosis fungoides lasts for ages or even decades. At tumoral stage with throughout spreaded disease and internal organs affected the prognosis is poor. MF may transform into the large-cell cutaneous lymphoma with an aggressive clinical behavior. The life expectancy of such patients doesn’t exceed 3 years.

Nowadays the treatment of CTCL which depends on the stage of the disease makes great difficulties for the clinicians. They use corticosteroids (prednisolone, triamcinolone,

dexamethasone, metypred), chemotherapy using cytotoxic drugs of different groups: alkylating (prospidinum, spirobrominum, cyclophosphan), antimetabolites (methotrexate, 6-mercaptopurine), organic alkaloids (vinblastine, vincristine), antitumor antibiotics (adriamycin, bleomycin), interferon-therapy, which is able to restore the antitumor protecting mechanisms, radiation therapy and retinoids.

Perfect results were obtained by application of PUVA-therapy. Recently the combination of PUVA and antiviral drugs is commonly used. However there are no publicated data on this matter.

Aim

The exploration of the effectiveness of combined therapy: PUVA via antiviral drugs in CTCL-patients treatment.

Materials and methods

This clinical research was conducted at V.A. Rakhmanov Department of Skin and Sexually-Transmitted Diseases (the First Moscow State Medical University, Russia) and the Hematology Science Center (Moscow, Russia). We observed 8 patients with CTCL: 3 (37.5%) men and 5 (62.5%) women at the age of 50-56. The diagnoses were verified with histological, immunochistochemical and clonal hematological research methods. The duration of the disease ranged from 2 to 36 years. The patients had different stages of the CTCL: IA – 3 patients, IB – two patients, IIA – one patient, IIB – one patient. Before the treatment all the patients were fully examined; the contraindications for photochemotherapy were not revealed. The Hematology Science Center prescribed Reaferon (3 million units – 3 times per week). At the same time the photochemotherapy based on skin exposure with UV (wavelength 320-400 nm) in 2 hours after ammifurin intake (photosensitizer) was applied in our clinic. The initial dose of the irradiation depended on the phototype of the patient's skin and was 0.5-1.0 J/cm^2. Photochemotherapy was carried out 4 times a week with gradually increasing dose of 0.5-1.0 J/cm^2 in every 2 sessions to a single dose of 8-10 J/cm^2. The course of therapy consisted of 20-30 procedures.

Results

After the combined therapy we reached the clinical remission in 75% of cases. The clinical behaviour was improved in 25% of cases (reduction and cessation of itching, blanching and flattering of lesions). At IA-IIA stage of CTCL the treatment was noted to be more effective.

Conclusion

Thus, basing on the results of our research, we can maintain that nowadays the photochemotherapy in combination with interferon-α is one of the most effective methods of CTCL-treatment, which can be recommended to practical doctors.

Open preperioneal inguinal hernioplasty is more beneficial compares to Lichtenstein hernioplasty

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Abstract

The objective of this study is to compare that the open preperitoneal hernioplasty technique is shorter in incision length (mm), shorter operating time (minute) and less post operative pain (VAS score) with that of in open Lichtenstein technique.

This study was a prospective experimental study, done by a single operator in private hospitals in August 2010 - August 2012. All the subjects in this study were randomly divided into two groups, the number of samples among the open preperitoneal hernioplasty group was 30 and Lichtenstein group 29. In analysis with student-t test, the length of incision line in open preperitoneal hernioplasty group (39.13 ± 3.01 cm) was shorter (P=0,000) than Lichtenstein group (57.24 ± 7.64 cm). The operating time (32,90 ± 6,73 minute) was shorter (57.24 ± 7.64 minute) (P=0,000). The post operative pain (VAS score 1,90 ± 0,71) was less (VAS score 3.28 ± 0.70) (P=0,000).

It can be concluded that open preperitoneal hernioplasty technique was more beneficial in the event of shorter incision line, shorter operating time and less post operative pain, compares with that of in Lichtenstein technique.

Keywords: Open preperitoneal hernioplasty, Lichtenstein, VAS score

Introduction

Various herniotomy techniques had been introduced in the past, from the open hernioplasty to those using state-of-the-art advanced equipments. Each of these techniques has their own benefits and disadvantages in regards to their outcomes, costs, simplicity of operational procedures and post operative pain (Maurice B, Luke J, Sam S, 2012). The commonly used open hernioplasty method today in Surabaya-Indonesia is the Lichtenstein technique, which is used as a standard technique in many hospitals in

Surabaya. However, the Lichtenstein technique still leaves a relatively long incision mark, which is a cosmetical disadvantage (Amid P, 2007). Also, the Lichtenstein technique has been known to have an 11% rate of chronic post operative pain (Shyam, 2009). Despite the fact that the Lichtenstein Technique is a tension-free technique, it still causes pain due to the mesh fixation to the conjoint tendon and inguinal ligament (Erhan, 2008). The open preperitoneal hernioplasty technique is also an open hernioplasty technique, this method is a combination of open hernioplasty and laparoscopic technique. The technique is found to be simpler, without the use of laparoscopic equipments and tackers, entering through the preperitoneal space. This technique leaves a smaller incision wound and requires a relatively shorter operation time. Post operative pain is expected to be minimum due to the small incision and the positioning of the mesh is without tension, no fixation needed for the mesh to the surrounding tissues. Then comes the question, is the open preperitoneal hernioplasty technique better than the Lichtenstein open hernioplasty technique, to both the operator and to the patient?

Preperitoneal hernioplasty is a combination of open hernioplasty and laparoscopy techniques. It resembles the open hernioplasty (Lichtenstein) because the open preperitoneal also requires an incision in the inguinal region, despite the difference of location, which is 2 cm cranial from the anulus internus and the incision is made horizontally, 3 cm long. This technique is similar to laparoscopy because the open preperitoneal technique also goes inside, creates a cavity and places a mesh in the preperitoneal space. The positioning of the mesh inside the preperitoneal space requires no fixation using the tacker device as the mesh is simply placed and spread over the preperitoneal space, and the mesh shall fixate by itself due to the pressure from the peritoneum (Sinha, 2007). Post operative pain is expected to be at a minimum because the mesh is not fixated to the ligamentum inguinale and the conjoint tendons as it is done in the Lichtenstein technique (Erhan, 2008). The mesh is also not fixated using the tacker to the surrounding tissues, as it is done in the TAPP (Trans Abdominal PrePeritoneal) technique or the TEP (Totally Extra Peritoneal) technique (Pawanindra, Kajla, Chander, et al, 2004).

Not all hospitals in Indonesia is equipped with laparoscopy equipments. Even if such laparoscopic equipments are available, a certain competence and a special set of

skills are required to perform the TAPP or TEP laparoscopic techniques, moreover, the costs to be paid by the patient is higher. The patient's demand to receive minimal access surgery is also difficut to fulfill. On the contrary, the Lichtenstein open hernioplasty is simpler, although leaving a relatively longer incision scar. The surgery department of Dr. Soetomo General Hospital Surabaya had been performing laparoscopic hernia repair selectively since 2009. The data in the surgery department of Dr. Soetomo General Hospital Surabaya indicates that in 2009, from 229 herniotomy procedures performed, only 11 cases (4,80%) was laparoscopic herniotomy.

Ugahary has also performed an open preperitoneal technique, but the incisions is farther cranially from the anulus internus (Simmermacher, 2000), therefore, it is more difficult to perform and require a set of special equipments, thus also demands a special set of skills to perform the technique (Veenendaal , Borst, Davids, et al, 2004). Kugel has also performed an open preperitoneal technique using a specially designed mesh, the mesh uses a ring which can be rolled and will automatically expand itself (Dogru, Girgin, Bulbuller, et al, 2006). Through the open preperitoneal hernioplasty, it is expected to have minimum incision wound, short operation time, and minimum post operative pain complaints.

Research Method

This research was an experimental prospective study, performed on private patients in several private hospitals in Surabaya between August 2010 to August 2012. This research compares the open preperitoneal hernioplasty technique and the Lichtenstein technique, perfomed by the same operator, to men over 18 years old of age with elective cases of reponible and unilateral lateral inguinal hernia. Patients with relapsing lateral inguinal hernia, post incarserated lateral inguinal hernia, and those with systemic illnesses were not included in this research. If any post operative complication occurs, the sample was excluded from this research. Anesthetics was administered with both spinal or general anesthesia. The number of samples in the open preperitoneum hernioplasty group was 30 and the open Lichtenstein group 29. Samples were randomly divided into 2 groups, the open preperitoneum hernioplasty group and the open Lichtenstein group. Comparisons were made on operative incision lengths, operating time

length, and post operative pain between the two groups. Operative incision length was measured in milimeter (mm) before the final dressing of the wound at the end of the operation. The operative time length was counted in minutes, starting from the moment of the skin incision to the moment the final wound stitching was completed. Post operative pain was measured on the 4th (fourth) day after the operation using a VAS score. The antibiotic Cefotaxim 1 gram IV was administered only once, one hour before the operation, and analgetics was administered after the operation using Dynastat® 40 mg IV for only 2 administrations. Patients would go home in the following day without the use of antibiotics or analgetics and then requested to come again for a control visit on the fourth day for a VAS score assessment. The data analysis using a student t-test.

Operating technique

Open preperitoneal hernioplasty is essentially similar to TEP (Totally Extra Peritoneal) laparoscopy, but without the use of laparoscopic equipments. The incision is made 3 cm long horizontally, positioned 2 cm cranial from the anulus inguinalis internus (Pic. 2, Pic. 3). The incision is then deepened to open the aponeurosis of the musculus oblicus externus (MOE) in the direction of the fibers, then splitting the musculus oblicus internus and the musculus transversus until the preperitoneal fat is visible. By using the "peanut" and the tip of the index finger, preperitoneal fat is opened and widened until a sufficiently wide preperitoneal space is formed, allowing clear vision of the funiculus spermaticus and anulus internus structures. The space is made as large as the mesh which will be placed within (Yamac, 2008). The identification of the funiculus spermaticus together with hernial sac entering the anulus internus is performed, then hanging this structure up using a ribbon or a catheter (Pic. 4). The hernial sac is then separated carefully from the funiculus spermaticus using sharp and blunt dissection until the hernial sac is fully separated from the anulus internus (Pic. 4). A mesh the size of 15cm x 10cm in a rolled position, held by long anatomical forceps, is inserted through the incision wound into the preperitoneal space until it slightly exceeds the tuberculum pubicum, and the mesh is unrolled. This mesh shall cover the anulus internus, Hesselbach's trigonum, and fossa ovalis all at once. The mesh will only be placed in the preperitoneal space withought fixation, it is only fixated to the musculus transversus abdominis using only

one stitch to facilitate the mesh remains in place. Unlike those in the TEP or TAPP techniques which uses a tacker to fixate the mesh (Pawanindra, Kajla, Chander, et al, 2004). All the procedure performed in the preperitoneal space including the dissections, need to be done meticulously and carefully as to avoid unnecessary injuries to the peritoneum, vas deferens, and vasa testicularis (Bobby D, 2009).

RESULT AND DISCUSSION

The sample characteristics used in this research fulfills the inclusion and exclusion criteria, and both sample groups have a homogenic age distribution (p = 0.600). The age homogeneity test between the groups can be seen in Table 1.

Table 1: Age difference testing (years) between the groups of open preperitoneal hernioplasty dan Lichtenstein, using a t-test

Var	***Open Preperitoneum***			***Lichtenstein***			**P**
	n	**Mean**	**SD**	**n**	**Mean**	**SD**	
Age (years)	30	46.20	13.12	29	44.45	12.36	.600

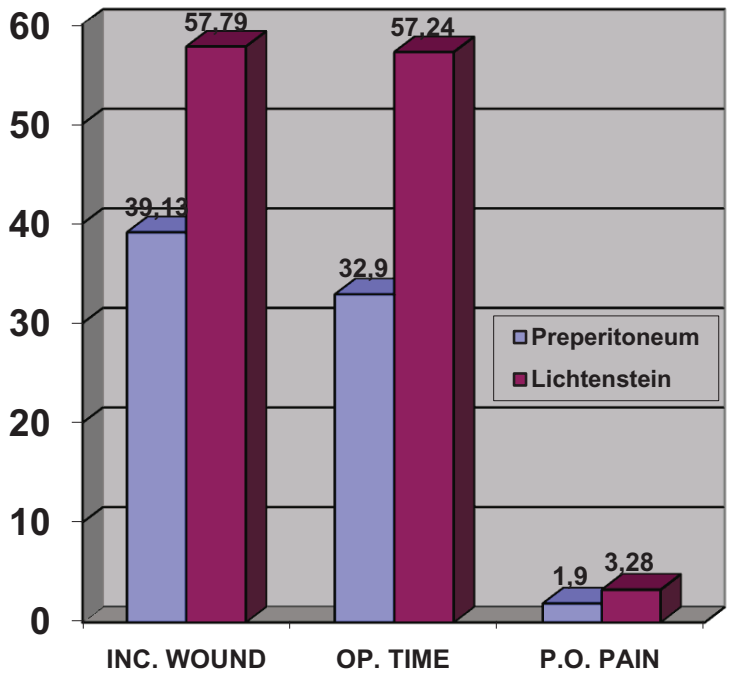
Based on the statistical testing (t-test) on the figures in Table 1, it was found that the age difference of the samples in the open preperitoneal group was at a mean of 46,20±13,12 years old and in the Lichtenstein group was at a mean of 44,45±12,36 years old. The numbers show no significant difference (p=0,600), therefore indicating that both groups have a homogenous age distribution.

The incision length in the open preperitoneal group (39.13 ± 3.01) was shorter (P=0,000) than those of the Lichtenstein group (57.24 ± 7.64). The length of the operation time in the open preperitoneal group (32,90 ± 6,73) was shorter (P=0,000) than those of the Lichtenstein group (57.24 ± 7.64). By using the VAS score, post operative

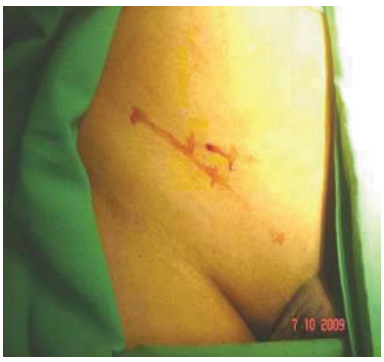
pain in the open preperitoneal group (1,90 ± 0,71) was smaller (P=0,000) than that of the Lichtenstein group (3.28 ± 0.70). (Table 2).

Table 2: Difference in incision length (mm), operation time (minute) and post operative pain (VAS Score) between the open preperitoneum and Lichtenstein technique.

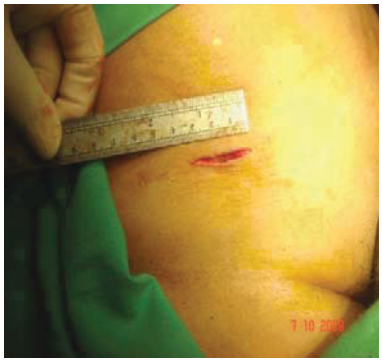
	Open Preperitoneal (n=30)	Lichtenstein (n=29)	P
Incision wound length (mm)	39.13 ± 3.01	57.79 ± 1.70	.000
Operation time Length (minute)	32.90 ± 6.73	57.24 ± 7.64	.000
Post Operative Pain (VAS Score)	1.90 ± 0.71	3.28 ± 0.70	.000



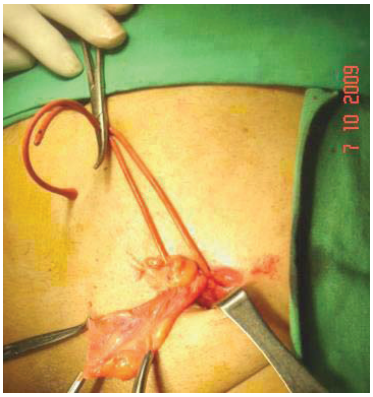
Pic.1. The incision wound (mm), operation time (minutes) and post operative pain (VAS Score) between the open preperitoneal and Lichtenstein techniques.



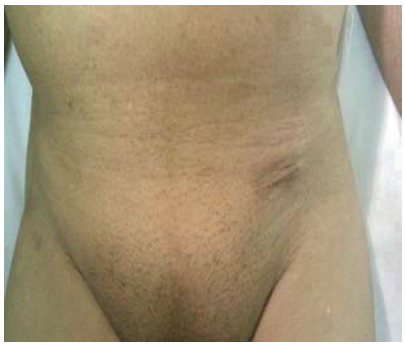
Pic.2. Sketch of incision plan



Pic.3. Incision wound by the end of operation, before stitching



Pic.4. Hernial sac, after separation from the canalis inguinalis



Pic.5. Incision wound after stitching

Stoppa in 1995 had also introduced the open preperitoneal approach using a wide incision to attain bigger exposure through an incision on the median line, but this was cosmetically disadvantageous due to the long incision on the abdominal median line (Bobby D, 2009). However, in cases of bilateral inguinal hernia, the operation time of the Stoppa techique was shorter than that of the Lichtenstein technique, which was 51 minutes and 65 minutes, respectively ($p < 0.01$) (Malazgirt, 2000).

The Lichtenstein technique is known to cause chronic pain (pain for more than 3 months) in an 11% rate (Shyam, 2009), causing significant morbidity after inguinal hernioplasty (Lau, 2006). Several surgery experts had tried to reduce this chronic pain by performing, among many, ileolinguinal prophylactic neurectomy, using a lightweight mesh, mesh fixation using fibrin glue sealant, or by replacing the Lichtenstein technique with laparoscopic TEP repair (Koushia, 2009)

Kugel had also performed the preperitoneal technique with a 3 cm long incision cranially from the anulus internus, with the mesh similarly placed in the preperitoneal space, but the shape of the mesh in the Kugel technique was specially designed using a stiff memory ring which was able to auto-expand after insertion into the preperitoneal space, thus eliminating the need to fixate the mesh (Dogru, Girgin, Bulbuller, et al, 2006)

CONCLUSION

Hernioplasty using the open preperitoneal hernioplasty is more beneficial than the Lichtenstein technique as it has shorter incision wound (39.13 ± 3.01 **vs** 57.79 ± 1.70 mm), shorter operation time (32.90 ± 6.73 **vs** 57.24 ± 7.64 minute) and smaller post operative pain (VAS score 1.90 ± 0.71 **vs** 3.28 ± 0.70).

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CARDIOVASCULAR COMORBIDITY IN ACUTE ISCHEMIC STROKE

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Abstract

Nowadays acute ischemic stroke is the most common cerebrovascular disease. The objective of the present investigation was to outline the co-occurrences of nine cardiovascular diseases and pathological conditions in the patients with acute ischemic stroke. We examined 258 patients, 129 males and 129 females, aged 71 years (range, 49-92 years) and hospitalized in 2007-2013 in the Department of Neurology and Neurosciences, Medical University "Prof. Paraskev Stoyanov" of Varna, Bulgaria. Cardiovascular comorbidity covered the arterial hypertension (AH), hypertensive heart (HH), atrial fibrillation (AF), ventricular tachyarrhythmia (VTA), myocardial infarction (MI), ischemic heart disease (IHD), effort angina pectoris (AP), coronary atherosclerosis (CA) and heart failure (HF). AH occurred most commonly (in 246) followed by IHD (in 154) and HH (in 118 patients). There was a weak correlation between patients' age and the number of accompanying or preceding diseases (Pearson's coefficient r=0,210). There were 63 patients with four diseases but 51 with two ones. Cardiovascular comorbidity should be taken in consideration as a risk factor for worse acute ischemic stroke stoke patient's outcome.

Key words: *acute ischemic stroke; cardiovascular diseases; comorbidity; correlation analysis*

1. Introduction

Acute ischemic stroke is the most common cerebrovascular disease worldwide. This disorder represents a severe burden for the patients themselves, their relatives, medical community and society as a whole. Nowadays there is rising evidence of a variety of cardiovascular, metabolic and neurological diseases in the adult and elderly patients with acute ischemic stroke. Numerous publications deal with isolated co-occurrences of such diseases in individual patients with acute ischemic stroke.

The purpose of the present study was to identify the simultaneous co-occurrences of nine cardiovascular diseases and pathological conditions in adult patients with acute ischemic stroke.

2. Material and methods

Our study covered 258 patients, 129 males and 129 females, aged 71 years (range, 49-92 years). They were hospitalized in 2007-2013 in the Department of Neurology and Neurosciences, Medical University "Prof. Paraskev Stoyanov" of Varna, Bulgaria. The co-occurrences of the following cardiovascular diseases and pathological conditions were analyzed: arterial hypertension (AH), hypertensive heart (HH), atrial fibrillation (AF), ventricular tachyarrhythmia (VTA), myocardial infarction (MI), ischemic heart disease (IHD), effort angina pectoris (AP), coronary atherosclerosis (CA) and heart failure (HF). Statistical data processing was done by means of variation and correlation analysis (Pearson'c coefficient).

3. Results

Our results are summarized in three tables. The counts and percentages of 258 acute ischemic stroke patients with nine co-occurring cardiovascular diseases and pathological conditions are demonstrated in Table 1. It is evident that AH, IHD and HH occupy the leading positions.

Table 1 Co-occurrences of cardiovascular diseases and pathological conditions in acute ischemic stroke patients

	AH	IHD	HH	AP	HF	CA	AF	MI	VTA
n	246	154	118	101	63	58	41	40	28
%	95,35	59.69	45.74	39.15	24.42	22.48	15.89	15.50	10,85

The counts and percentages of 246 patients with AH as the first disease missing or co-occurring with eight other cardiovascular diseases and pathological conditions as second disease in one and the same patient are demonstrated in Table 2.

It can be seen that AH occurs together with IHD in 147 patients, IHD is missing in the presence of AH in 99 other patients, AH is missing in the presence of IHD in 7 other patients, and both AH and IHD are missing in the rest 5 patients.

The counts of the acute ischemic stroke patients presenting with a various number of accompanying or preceding cardiovascular diseases and pathological conditions according to

patient's age are presented in Table 3. There is a weak correlation between patients' age and the number of these diseases and pathological conditions (Pearson's coefficient r=0,210).

Table 2. Co-occurrences of AH with eight cardiovascular diseases and pathological conditions in acute ischemic stroke patients

Second disease	**two diseases**		**no second disease**		**second disease only**		**no cardiovascular disease**	
	n	%	n	%	n	%	n	%
IHD	147	59.76	99	40.24	7	2.84	5	2.03
HH	117	47.56	129	52.44	1	0.41	11	4.47
AP	97	39.43	149	60.57	4	1.63	8	3.25
HF	61	24.80	185	75.20	2	0.82	10	4.06
CA	55	12.91	191	77.64	3	1.22	9	3.66
AF	41	16.67	205	83.33	0	0	12	4.88
MI	38	15.45	208	84.55	2	0.82	10	4.06
VTA	27	10.98	219	89.02	1	0.41	11	4.47

Table 3 Patients' distribution according to their age and the number of accompanying or preceding cardiovascular diseases and pathological conditions

Age groups/ diseases	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**
≤ 60 years	1	3	3	1	3	2	0	1	0	0
61-70 years	3	12	25	18	31	14	9	5	0	0
71-80 years	1	11	19	11	23	16	10	10	2	1
≥ 81 years	0	1	4	2	6	5	4	1	0	0
total	5	27	51	32	63	37	23	17	2	1

4. Discussion

Recent publications worldwide convincingly indicate the presence of cardiovascular comorbidity in adult patients with acute ischemic stroke. However, most often, only single diseases and pathological conditions accompanying or preceding the ischemic stroke have been analyzed in one and the same paper.

We identify a different degree of comorbidity of single cardiovascular diseases and pathological conditions in our patients' contingent. In our opinion, further research covering a greater sample is needed to better illustrate the mutual relationships between these common disorders in acute ischemic stroke and to stratify the cardiovascular risk associated with them.

In a nationwide population-based cohort study using the Danish National Registry of Patients during 1994-2011, the 30-day, one-year, and five-year mortality of acute ischemic stroke was analyzed [14]. Comorbidity categories were defined by Charlson Comorbidity Index. The 30-day mortality rate ratio adjusted for age, sex, and comorbidity decreases by

approximately 45% while the five-year one decreases from 56.4% in 1994-1998 to 46.1% in 2004-2008. Comparing very severe comorbidity with no comorbidity, these rate ratios increase approximately 2.5-fold.

The retrospective assessment of the validity of the modified Charlson Comorbidity Index as a predictor of the short-term outcomes in a cohort of 297 patients with first-ever ischemic stroke, older than 60 years shows a significant association with poor outcome and mortality with higher point estimates of odds ratio (2.74; 95% CI 1.64-4.59) and hazard ratio (2.73; 95% CI 1.51-4.94) [3]. However, this association is dependent on stroke severity and premorbid disability, too.

Among 300 Japanese patients with ischemic stroke and 21 ones with transient ischemic attack, 225 males and 96 females at an mean age of 67.3 years, the comorbidity includes the following: hypertension - in 260 (81.00%), dyslipidemia - in 249 (77.57%), atrial fibrillation - in 47 (14.64%), diabetes mellitus - in 102 subjects (31.78%), and chronic kidney disease - in 98 patients (30.53%) [5].

During a follow-up period of 89,468 person-years, ischemic stroke rate is higher in patients with than in those without atrial fibrillation (5.79 per 100 person-years versus 2.25 per 100 person-years) [2]. The higher prevalence of CHA2DS2-VASc comorbidities (heart failure, hypertension, diabetes mellitus, coronary artery disease, and peripheral artery disease) in atrial fibrillation patients further increases the stroke risk. Combination of data from the nationwide stroke register Riks-Stroke and from the Patient Register in Sweden shows that 31428 (33.4%) ischemic stroke patients present with previously known, or newly diagnosed atrial fibrillation [4].

Among 204 patients with acute ischemic stroke, there is trial fibrillation in 31 patients (15,20%) and paroxysmal atrial fibrillation PAF - in 15 patients (7,35%) [15]. Multivariate analysis reveals that age of ≥70 years (odds ratio 3.52, 95%; CI 1.68-7.35; p=0,001) and heart diseases (odds ratio 4.26; 95% CI 1.14-15.95; p=0,031) are associated with these arrhythmias.

Of 4806830 eligible patients, 14121 (0.29%) are diagnosed with paroxysmal supraventricular tachycardia (PSVT) and 14402 (0.30%) experience an ischemic stroke [7]. The cumulative rate of ischemic stroke after PSVT diagnosis (0.94%; 95% CI 0.76%-1.16%) significantly exceeds the rate among patients without a diagnosis of PSVT (0.21%; 95% CI 0.21%-0.22%). A 56-year-old female with a rapidly changing supraventricular tachyarrhythmia including sinus tachycardia, atrial fibrillation, and atrial flutter that quickly

interchanging to another, without any hemodynamic instability, due acute ischemic stroke without structural heart disease has recently been reported [11].

Between January 2001 and July 2010, acute ischemic stroke has been diagnosed in 106 out of 8485 patients (in 1.25% of the cases) with acute myocardial infarction in a cardiology intensive care unit in France [6]. Between 1998 and 2008, 7185 of 173233 acute myocardial infarction patients in Sweden (4.15% of the cases) have presented with ischemic stroke within one year [16]. ST-segment-elevation myocardial infarction, previous ischemic stroke, atrial fibrillation, heart failure at admission, ACE-inhibitor treatment, age, female sex, and previous diabetes mellitus are independent predictors of ischemic stroke. In the national sample of Medicare in the United States from 1999 to 2010, there are 57848 subsequent hospitalizations for ischemic stroke aged ≥65 years after acute myocardial infarction [17]. The one-year rate of ischemic stroke decreases from 3.4% (95% CI 3.3%-3.4%) to 2.6% (2.5%-2.7%; $p<0.001$). Among the 1924413 patients from the Nationwide Inpatient Sample in the USA, admitted for acute myocardial infarction in 2006-2008, the incidence rate of ischemic stroke is 1.47% [10].

A total of 207 out of 580 chronic heart failure patients at a mean age of 63±13 years have died due to cardiovascular reasons [9]. Multivariable Cox regression analysis shows that history of ischemic stroke (hazard ratio 2.48, 95% CI 1.14-5.37, $p=0.022$) is one of the independent predictors of cardiac death.

The prevalence of hippocampal infarction in 1245 subjects (at a mean age of 79±1 years) is 12% [12]. There are large hemispheric brain infarctions in 31% of the cases. They are strongly associated with cardiovascular risk factors such as hypertension (43%), coronary disease (32%), myocardial infarction (22%), atrial fibrillation (20%), and heart failure (20%).

Between 2006 and 2007, hypertension is the main cardiovascular risk factor for ischemic stroke, either alone or in combination with other risk factors, among 175 patients aged over than 65 years in Greece [8].

There is a decompensated heart failure in 17% of 566 acute ischemic stroke patients at a mean age of 73 years [1]. Such patients are older and more frequently suffer from hypertension, atrial fibrillation, myocardial infarction and diabetes mellitus. The decompensated heart failure is a strong, independent predictor of worse functional outcome after ischemic stroke (OR 2.34, 95% CI 1.12 - 4.89, $p=0.02$).

Long-term excess mortality after ischemic stroke in young adults aged 18 to 50 years is mainly attributable to a cardiovascular disease and most pronounced in men in Nijmegen, the Netherlands, between 1980 and 2010 [13].

5. Conclusion

Our results reveal the different extent of cardiovascular comorbidity in single patients with acute ischemic stroke and emphasize the role of timely diagnosis and regular control of this common pathology for the adequate prevention of the cerebrovascular diseases in adult individuals.

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(18F)-FDG PET/CT AND MRI IN DIAGNOSIS OF IDIOPATHIC LATE-ONSET CEREBELLAR ATAXIA

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Abstract

Adult-onset progressive cerebellar disorders can result from many pathological processes. The diagnosis is usually based on the medical history, neurological examination, laboratory investigations, and presence of cerebellar atrophy on CT and MRI. In addition, SPECT and PET have been used in detection of genetic and non-genetic ataxias. We studied the cerebral glucose metabolism and neurological dysfunction in 7 patients with late-onset cerebellar ataxia. All patients underwent (18F)-fluoro-2-deoxy-D-glucose (FDG) PET scanning with Phillips Gemini TF (16slice) PET/CT. The age at progressive cerebellar symptoms onset was over 45 years. Detailed medical history, physical findings and laboratory tests excluded other acquired causes of cerebellar ataxia. CT scans and MRI revealed presence of cerebellar and brainstem atrophy. (18F)-FDG PET showed moderate to severe cerebellar and brainstem hypometabolism. Based on our own clinical and neuroimaging findings, we support the notion that brain FDG PET scanning may be useful as a complimentary diagnostic tool in evaluation of patients with late-onset progressive cerebellar syndromes.

Keywords: *cerebellar ataxia, (18F)-FDG PET/CT, cerebral glucose metabolism, brain atrophy*

1. Introduction

Adult-onset progressive cerebellar disorders can result from many pathological processes, including malformations, degenerations, vascular diseases, infections, neoplasms, paraneoplastic syndromes, toxic/metabolic disorders, and demyelinating disease (1, 14). The diagnosis of degenerative cerebellar diseases is usually based on the medical history, neurological examinations, laboratory investigations, and presence of cerebellar and brainstem atrophy on Computed tomography scans (CT) and Magnetic resonance imaging (MRI) (2, 6).

In the last decades, nuclear medicine techniques have played a crucial role in the differential diagnosis of various movement disorders. Respectively, single photon emission

computed tomography (SPECT) and positron emission tomography (PET) have been used in the diagnosis of patients with acute or chronic genetic and non-genetic ataxias (7). PET scanning is known as a noninvasive imaging method for assessment of cerebral metabolic and neurotransmitter activity, blood flow, as well as neurotransmitter receptor density (9, 11). Evidently, (18F)-FDG PET has improved the detection of etiology and understanding of underlying pathophysiologic mechanisms in progressive non-genetic cerebellar disorders (4, 8, 10, 12). In accordance with the aforementioned data, we studied the cerebral glucose metabolism and neurological dysfunction in seven patients with late-onset cerebellar ataxia.

2. Material and Methods

Seven patients (2 Males and 5 Females, aged between 31 and 59 years) with idiopathic cerebellar ataxia were included in this study. Neurological status examination and additional laboratory investigations were carried out. All patients underwent MRI and (18F)-fluoro-2-deoxy-D-glucose (FDG) PET/CT. FDG activity was calculated based on body weight (0,14mCi/kg) and administered through an intravenous line. Patients were scanned with Phillips Gemini TF (16slice) PET/CT, using the following parameters - Low Dose CT 120keV, 50mAs from vertex to mid-thigh and corresponding PET scan field with 576mm FOV, 4mm pixel size, 10 minutes per frame (Brain PET/CT protocol). Iterative reconstructions of PET raw data were done, following the standard manufacturer's algorithm for Brain CTAC in two image sets: PREVIEW (3D-RAMLA) and Brain CTAC (LOR-RAMLA) with opportunity for fusion with CT scans. The pattern of cerebral glucose metabolism in cerebellar ataxia was compared to the results of healthy controls. Brain magnetic resonance imaging (MRI) was performed using a GE 1.5 T, Signa Excite HDxt system.

3. Results

All the patients experienced onset of their symptoms beyond the age of 30 years. Detailed medical history, physical findings and laboratory investigations excluded other acquired causes of cerebellar ataxia. The main symptoms involved dysarthria, dysmetria and intention tremor in arms, dysdiadochokinesis, and truncal ataxia. CT/MRI data revealed different severity of cerebellar atrophy. (18F)-FDG PET showed decreased metabolic activity in cerebellum and exceptionally in the pontine region or cerebral cortex. Hereby, we illustrate the clinical and neuroimaging findings in two patients, included in the study.

Case 1

A 59 year old woman without previous medical illness was referred for investigation of vertigo, dizziness, dysarthria, and severe gait imbalance with secondary falls towards the left side. The symptoms have developed progressively for the last 4 years. On admission, her blood pressure, pulse rate, and body temperature were normal. She was alert and had a full range of extraocular movements. There was an evoked bilateral horizontal nystagmus on lateral gaze. She had moderate dysarthria, mild bilateral dysmetria and intention tremor in arms, dysdiadochokinesis as well as truncal ataxia. All laboratory analyses, transcranial Doppler ultrasound, and neurocognitive tests were within normal ranges. Findings of central otoneurological syndrome were recorded. Brain CT revealed mild symmetrical cerebellar

atrophy (Fig.1). (18F)-FDG PET showed dramatically decreased metabolic activity in cerebellum and mild - in both parietal regions (Fig. 2).

Figure 1 Brain CT reveals mild symmetrical cerebellar atrophy.

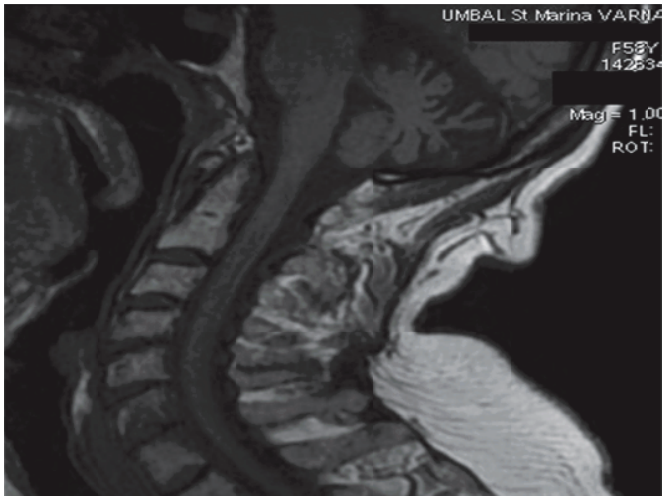
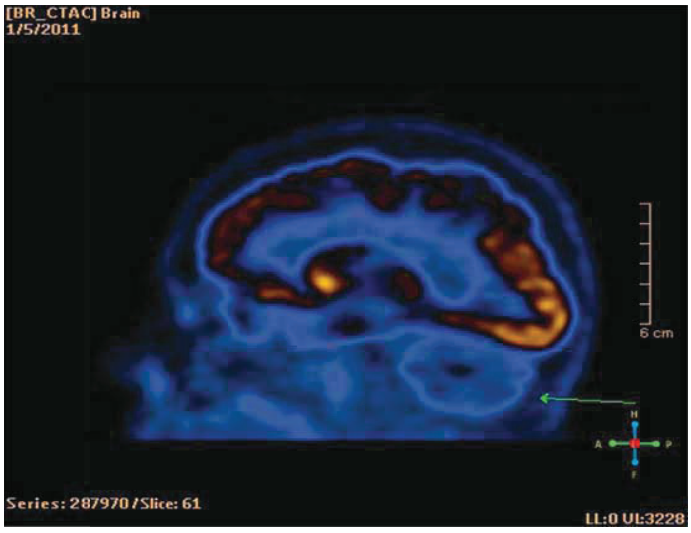


Figure 2 (18F)-FDG PET shows severe hypometabolism in cerebellum and mild - in parietal regions.



Case 2

A 54 year old woman without previous medical illness was referred for investigation of vertigo, voice, speech and handwriting disturbance, head, lower jaw and arms tremor, as well as severe gait imbalance with several incidents of falling. The symptoms have been permanent and progressive for the last 3-4 years. Medical history revealed previous thyrotoxicosis and multinodular goitre. On admission, her blood pressure, pulse rate, and body temperature were normal. She was alert and had a full range of extraocular movements.

There was bilateral horizontal nystagmus on lateral gaze, worse towards the right side. She had moderate dysarthria, lower extremities weakness, bilateral dysmetria and intention tremor in arms and legs, dysdiadochokinesis (all worse on the left side) as well as broad-based ataxic gait. All laboratory analyses, including toxic elements exposure, autoantibodies evaluation, neuroinfections, and evaluation of endocrine function were within normal ranges. Transcranial Doppler ultrasound demonstrated no clinically significant cerebrovascular abnormalities. Neurogenetic and neurocognitive tests (MMSE) were normal. Brain MRI revealed severe cerebellar (both hemispheres and vermis) and distal pontine atrophy (Fig. 3). (18F)-FDG PET showed dramatically reduced metabolic activity in cerebellar hemispheres, vermis, and pons (Fig. 4).

Figure 3 MRI shows cerebellar and pontine atrophy.

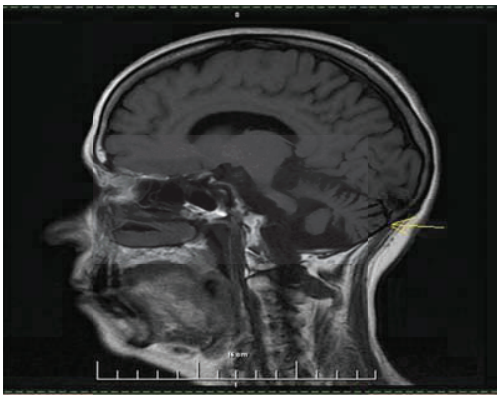
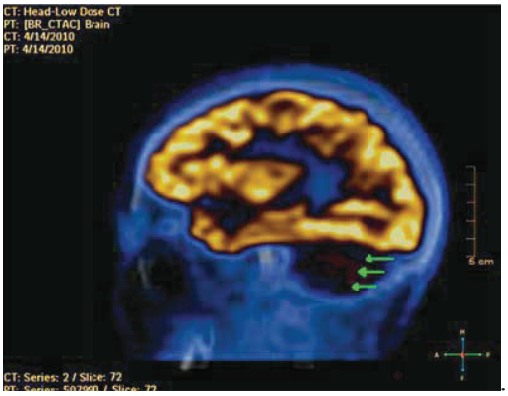


Figure 4 (18F)-FDG PET reveals dramatically reduced radiotracer uptake in the cerebellum.



4. Discussion

In this study, we present clinical and neuroimaging data of seven patients with manifestations of progressive cerebellar disorder. The age at symptoms onset of all patients was over 30 years. Neurological examinations revealed similar to previously described by Abele M, et al (1) clinical features of ataxia that corresponded to cerebellar impairment. Therefore, the final diagnosis of late-onset cerebellar ataxia was considered in all our cases.

Cerebellar dysfunction may result from various genetic and non-genetic causes, e.g. neurodegenerative idiopathic late onset cerebellar ataxia (3, 5, 13). In this study, detailed medical history, physical findings and laboratory investigations excluded other acquired causes of cerebellar ataxia, such as vascular, neoplastic, paraneoplastic, inflammatory, toxic, etc.

According to the literature, CT scans and MRI show evidence of cerebellar and sometimes brainstem atrophy in approximately 50% of patients (2, 6). In this context, our structural brain scans demonstrated cerebellar atrophy in all patients and found no evidence for other structural lesions. Respectively, we supposed a diagnosis of idiopatic neurodegenerative cerebellar ataxia.

In the last decades, a large number of PET studies in patients with ataxia have revealed a dramatic reduction of glucose metabolism in cerebellar hemispheres, vermis, brainstem, and dentate nuclei (3, 8, 10, 12). In addition to aforementioned anatomical imaging results, we performed further functional brain scanning with (18F)-FDG PET. Our findings of moderate to severe cerebellar and brainstem hypometabolism were in correspondence with previously published results by Gilman, S. (5), Otzuka, M. (9), and Worth, P. (14). In two patients, we also found a significant reduction in absolute values of regional glucose metabolism in the cerebral cortex. Wang, P. et al (13) showed similar variable patterns of sub- and supratentorial glucose metabolism in individuals with hereditary ataxias.

5. Conclusion

In the present study, (18F)-FDG PET showed abnormal patterns of glucose metabolism that corresponded to the picture of cerebellar impairment. Furthermore, this non-invasive diagnostic technique succeeded to document the influence of cerebellar disease on supratentorial neuronal function with relative sparing of the cerebral cortex. Based on our own clinical and neuroimaging findings, we supported the notion that brain FDG PET scanning may be useful as a complimentary diagnostic tool in evaluation of patients with adult-onset chronic cerebellar syndromes.

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Orbital pseudotumor and pituitary lesion with cavernous plexus and internal carotid artery deviation: clinical, MRI and (18F)-FDG PET findings

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Abstract

We present a 43-year-old man with three-month medical history of headache, diplopia, right eye conjunctival chemosis and exophthalmos. Endocrinological investigations revealed high level of serum prolactin (s-PRL). Magnetic resonance imaging (MRI) of the orbits showed right proptosis, homogenous retrobulbar infiltrate with minimal enlargement of the superior rectus muscle. Brain images demonstrated pituitary mass 8/6 mm, extending into the left cavernous sinus. (18F)-FDG PET scans revealed normal cerebral glucose metabolism.

We suggest that this case may represent an orbital pseudotumor and pituitary microadenoma - prolactinoma. The differential diagnosis from other cases of atypical and rare disorders will be discussed: orbital pseudotumor and hypophysitis with hyperprolactinemia, associated with IgG4-related systemic disease, orbital and pituitary lymphoma.

Key words: orbital pseudotumor, pituitary lesion, MRI, (18F)-FDG PET, differential diagnosis

1. Introduction

The most common causes of unilateral proptosis/exophthalmos in adults are thyroid orbitopathy; orbital lymphoma; orbital inflammatory pseudotumor - IgG4-related disease, presented as myositis, dacryoadenitis, anterior, apical, and diffuse orbital process; granulomatosis, orbital tumor: metastases, gliomas/meningiomas, hemangioma; vascular/venous abnormalities disorders: carotid-cavernous fistula, cavernous sinus thrombosis, aneurism. (2, 5)

Differentiation of sellar masses which induce neurological, ophthalmological, endocrine damage still creates diagnostic challenges. Pituitary lesions involve a heterogeneous group of cystic lesions (craniopharyngioma, arachnoid cyst), neoplasms (adenoma, meningioma, glioma, metastases, lymphoma), inflammation/infections (sarcoidosis, tuberculosis, pituitary abscess, lymphocytic hypophysitis, IgG4 hypophysitis), and empty sella syndrome (4, 7, 9, 11, 12).

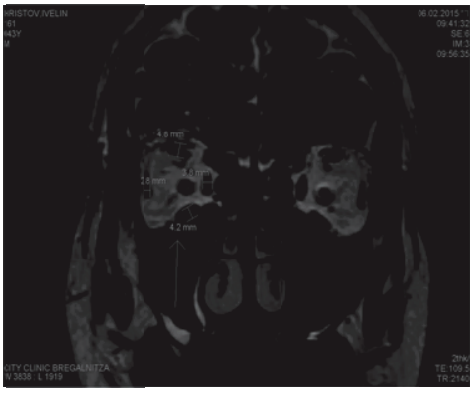
A presumptive accurate diagnosis of orbital and pituitary pathology can be made on the basis of clinical course, laboratory findings, and neuroimaging features, but a definitive diagnosis requires tissue biopsy (3). Evidence exists that magnetic resonance imaging (MRI) and positron emission tomography (PET) using 18F-FDG have been successfully applied in the diagnosis of neurological pathologies, including different vascular, neoplastic, inflammatory, autoimmune and degenerative central nervous system disorders (8, 10, 17). Respectively, we describe a case of right orbital proptosis and left pituitary lesion with cavernous plexus and internal carotid artery deviation, presenting with right eye exophthalmos, diplopia, headache, and hyperprolactinemia. An orbital pseudotumor and pituitary microadenoma/prolactinoma was suspected. A differential diagnosis for appropriate treatment was made.

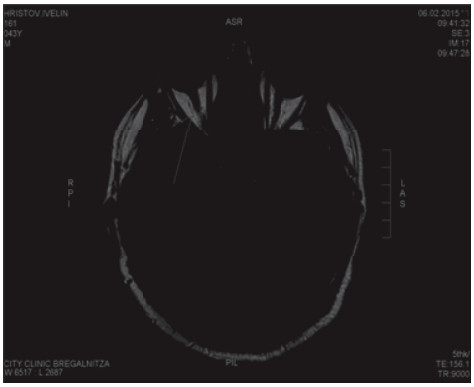
2. Case report

A 43-year-old man complained of one year headache. Initial laboratory findings and magnetic resonance imaging (MRI) were normal. The patient presented in our neuro-ophthalmological section with three months history of right eye exophthalmos and double vision. Neuro-ophthalmological evaluation revealed right eye proptosis, conjunctival chemosis, diplopia, normal visual acuity and visual field analysis.

MRI of the orbits showed minimal enlargement of the right superior rectus muscle, proptosis, and homogenous enhancing retrobulbar mass (Fig. 1).

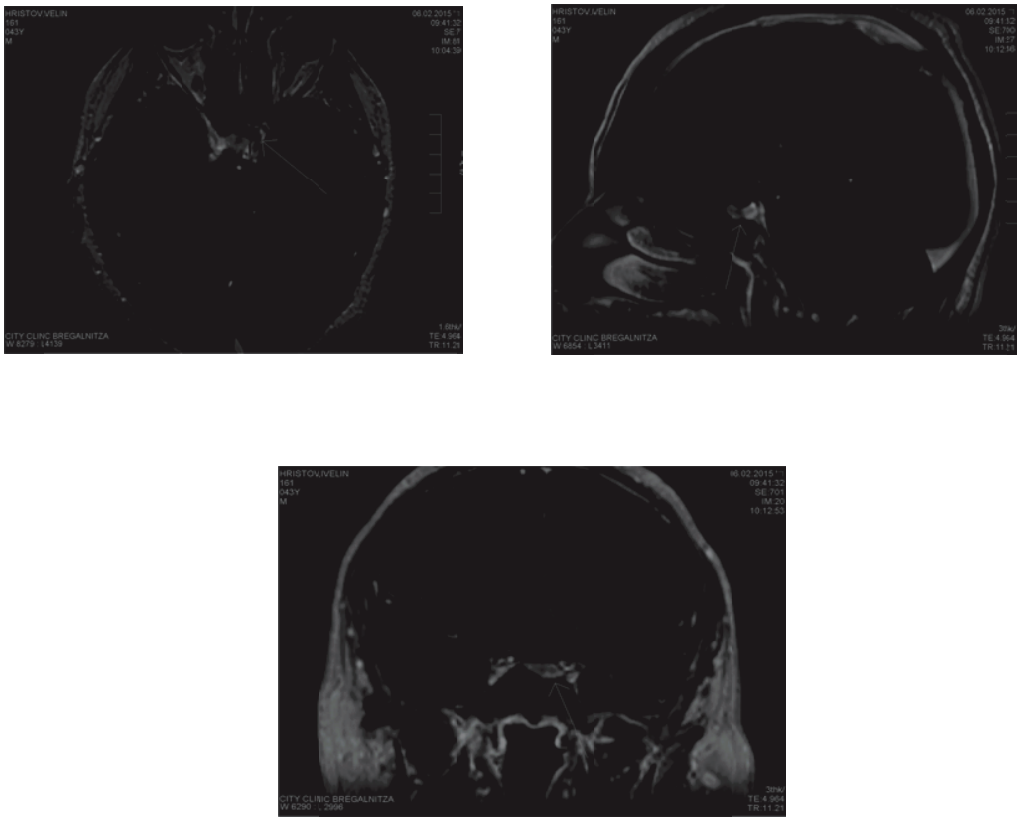
Figure 1





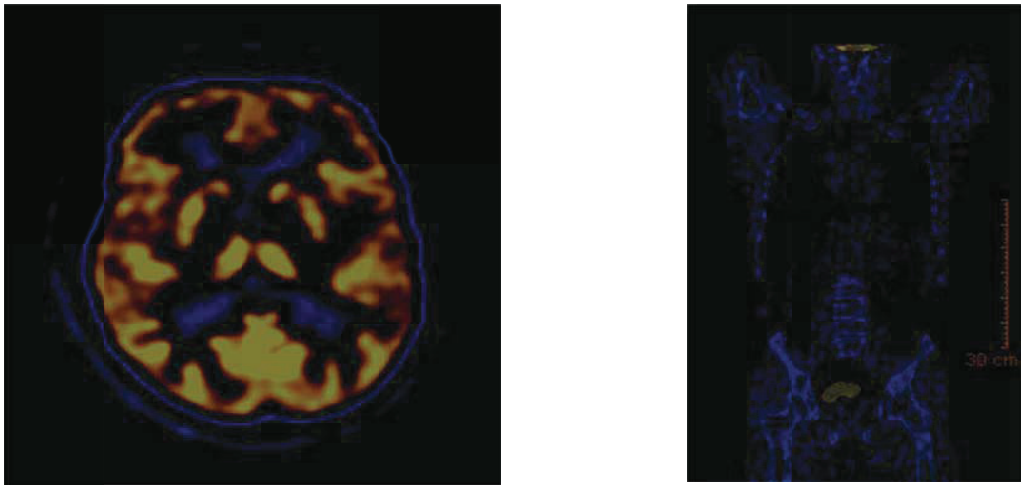
Brain MRI demonstrated pituitary mass 8/6 mm extending into the left cavernous plexus and left internal carotid artery deviation (Fig. 2).

Figure 2



(18F)-FDG PET revealed normal glucose metabolism of the pituitary gland, right orbital region and whole body (Fig. 3).

Figure 3



Physical (BMI 35 kg/m2), blood pressure 110/80 mmHg, pulse rate 60/min, and neurological examinations were normal. Level of serum prolactin (s-PRL) was significantly increased. A normal serum level of immunoglobulin G4 (IgG4) was observed. A routine blood test revealed normal parameters. Orbital and pituitary biopsy were not performed because the patient refused the examination. An orbital pseudotumor and pituitary microadenoma/prolactinoma were supposed. We initiated treatment with oral prednisone and cabergoline (Dostinex - 0.5 mg/twice weekly). Two months later, clinical improvement was observed – the exophthalmos and double vision decreased. Serum PRL was normalized. MRI revealed that the lesions persisted in the pituitary and the right orbit.

3. Discusssion

The differential diagnosis of orbital proptosis and pituitary lesions with hyperprolactinemia always challenges the correct therapeutic behavior, when neurological, ophthalmological and endocrine symptoms occur (2). Approximately 20-40% of patients with biopsy-proven IgG4-related autoimmune disease have normal IgG4 concentration at the time of diagnosis (5, 10). Respectively, despite the normal IgG4 level in our patient, we can discuss the presence of inflammatory orbital pseudotumor and hypophysitis with hyperprolactinemia.

According to the literature, the involvement of ocular, orbital, and pituitary structures is estimated to occur in patients with various neoplasms, including lymphoma. Metastases have also been known to cause a similar type of orbital and pituitary mass. In regards to previous reports, the anatomical and functional neuroimaging techniques are widely used for the detection and differentiation of brain lesions. Although, in our case MRI revealed simultaneous right orbit and sellar region abnormalities, supposing primary or secondary neoplasms, (18F)-FDG PET showed negative results for the presence of any kind orbital and cerebral malignancies. In context of earlier published review articles (1, 15, 18) and aforementioned results, here we also discussed the application of PET in differentiating inflammation from tumor.

In conclusion, this case report supports the notion that the distinction between IgG4 related disease, pituitary adenoma/carcinoma, lymphoma or metastasis is very difficult without a biopsy. Based on the literature review and our own observations, we suggest that brain MRI and (18F)-FDG PET in addition to the clinical and laboratory findings may serve as a useful diagnostic tool in patients with simultaneous orbital and pituitary lesions.

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Nursing Education and Practice: What Cultural Competency Can Teach Us

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Abstract

This manuscript begins with an overview of terminology and assumptions underpinning culture and cultural competence. Cultural competence education is explored from the perspectives of the recent growth of teaching-learning tools and identification of curricula grounded in the language of culture and cultural competence. Stereotyping, prejudice and discrimination are identified as contrary to the values and behaviors of culturally competent care. The transcultural nursing theories of Campinha-Bacote, Leininger, and Purnell, are detailed in relationship to nursing assessment, interventions and outcomes. Research evidence on the outcomes of cultural competency is identified, as are next steps in the process of improving nursing competence, expanding our knowledge of patient and family outcomes, and ensuring sustainability of this important determinant of health.

Key words: *competence; culture; ethnicity; transcultural nursing*

1. Introduction

Throughout human history, cultural differences have led to misunderstanding, lack of respect and conflicts between countries, communities and individuals. As communication, travel, and businesses rapidly expand worldwide, understanding culture and differences in life-experiences by different groups becomes more and more important. In healthcare, culture is widely considered to be an important but often overlooked determinant of health.

Culture has been defined in a number of ways. It is generally described as the learned and shared beliefs, values, and behaviors of a community of interacting human beings. While we frequently think of culture as being synonymous with ethnicity, culture also applies to other human communities such individuals with chronic illness or disabilities, generational groups, gender orientation groups, and even gangs. Culture determines what people think

causes health and illness, what healers are sought to prevent and treat disease, and what treatments are used. It also defines sick role behaviors, how long a person is sick, and when he or she has recovered.

This paper identifies fundamental assumptions about culture and addresses cultural competence from the perspectives of how it is learned and how it is practiced. Examples of culturally competent assessment and interventions across the lifespan are explored. Information grounded in transcultural nursing* theory is applied to nursing practice. In conclusion, research evidence demonstrating the impact of cultural competence on health outcomes is identified.

2. The Environment of Cultural Competence

2.1 Assumptions of cultural competence

An understanding of the assumptions underpinning culturally competent care creates a framework for teaching, learning, and practicing cultural competence. Learning to be culturally competent is an ongoing process that develops in a variety of ways, but primarily through cultural encounters. Cultural competence begins with self- and other awareness, an increased consciousness of the value of cultural diversity, and a willingness to learn about and provide culturally appropriate care.[4]

There are core similarities shared by all cultures as well as differences within, between, and among cultures. Cultural competence assumes one culture is not better than another. While there is more variability in culturally-based beliefs, values, and behaviors within ethnic groups than across ethnic groups, each individual has the right to be respected for his or her uniqueness and cultural heritage. Caregivers need both culturally general and culturally specific information in order to provide culturally competent care.

2.2 Cultural Competence Education (CCE)

Beach et al. authored a systematic literature review focusing on teaching cultural competence under the sponsorship of the Johns Hopkins Evidence-Based Practice Center and the Agency for Healthcare Research and Quality. Their review reported the following: (a) Programs and tools for CCE were appearing with increasing frequency in the literature; (b) CCE programs were gaining the attention of not only educators, but healthcare administrators as well;

*Transcultural nursing is a substantive area of study and practice focused on comparative cultural care (caring) values, beliefs, and practices of individuals or groups of similar or different cultures with the goal of providing culture-specific and universal nursing care practices in promoting health or well-being or to help people to face unfavorable human conditions, illness, or death in culturally meaningful ways. [14] [16]

(c) many different curricular methods and content areas had been evaluated; and (d) there was good-to-excellent evidence that cultural competence training impacts intermediate outcomes

such as the knowledge, attitudes, and skills of health professionals.[3] CCE programs and tools have continued to grow, populating scholarly literature and internet sites.

CCE program content ranges from anecdotes about international cultural immersion programs to rigorous Cochrane Collaboration reviews and updates.[5] [12] [20] Tools are available for specific healthcare populations,[2] [6] as well as for mid- and late-career health professionals.[9]

The American Association of Colleges of Nursing has identified culture competencies as a priority and developed CCE in the form of baccalaureate and graduate nursing tool kits for nurse educators to use.[1] The University of Washington (UW) School of Medicine developed a detailed CCE curriculum organized around four core competencies quite similar to those of Campinha-Bacote.[2][4] *Cultural Competency – Awareness* is expressed as sensitivity to one's own cultural heritage and respect of differences; ability to reflect on how one's own values and biases affect others; and comfort with differences of race, gender, sexual orientation, ability, spirituality/religion, and other socio-demographic variables. *Cultural Competency – Knowledge* includes having specific knowledge and information about the particular identity groups one is currently working with, including knowing how to obtain evidence-based information and data regarding social and behavioral determinants facing patients; and understanding the impact these have on decision-making and delivery of care for individual patients and their families. *Cultural Competency – Skills* signify effective verbal and non-verbal communication skills, appropriate cross-cultural conflict resolution and negotiation skills, and skills to assess patient literacy level. *Cultural Competency – Advocacy* focuses on the students' capacity to advocate for their patients in decision-making and to function as change agents.

2.3 Stereotyping, Prejudice, and Discrimination

A discussion about cultural competence would be incomplete without mentioning contradictory behaviors such as stereotyping, prejudice, and discrimination. Biases come in many forms, including race, age, gender, and ethnicity and can be universal or location specific. While stereotyping, prejudice, and discrimination are somewhat similar, they are also quite different. Each form of bias is carried out by one individual or group judging another, prior to obtaining factual knowledge of the individual or group. A stereotype is a widely held, oversimplified idea of a particular individual or group based on experience or hearsay. Stereotypes emerge from collective and/or individual experiences with different groups. Individuals behave in a prejudicial manner when they have an emotional reaction to another individual or group based on preconceived ideas about the individual or group. Discrimination is the denial of equal rights based on prejudices and stereotypes.[7] Prejudice and discrimination, whether manifested as racism, genderism or ageism, run counter to cultural competence.

3. Transcultural Nursing Theories: Applications in Practice

3.1 Campinha-Bacote's Model of Cultural Competence

The language of cultural competence is filled with a number of terms, which different authors and providers use differently. Campinha-Bacote identified a set of inter-related terms that incorporate cultural competence into assessment of patients' condition and needs.[4] *Cultural awareness* is the self-examination and in-depth exploration of one's own cultural and professional background. Without awareness of one's own beliefs, sensations, thoughts, and environment, the nurse risks *cultural imposition*, a term that describes the tendency of individuals to impose their own beliefs, values and patterns of behavior on another culture.[13] *Cultural knowledge* is the process of seeking and obtaining a sound educational foundation about diverse cultural and ethnic groups. *Cultural skill* is the ability to collect relevant cultural data regarding the patient's presenting problem as well as accurately performing a culturally-based health assessment. *Cultural encounter* is the process that motivates healthcare providers to engage in cross-cultural interactions directly with clients** from culturally diverse backgrounds. This theory largely framed the UW curriculum described above.

3.2 Purnell's Model of Cultural Competence

Purnell's Model of Cultural Competence provides twelve overlapping cultural domains that guide nursing assessment of relevant cultural data.[17] These domains begin with *Overview/Heritage*, which includes concepts related to country of origin, current residence, the effects of the topography of the country of origin and current residence, educational status and occupation, as well as economics, politics, and reasons for emigration. This concept also includes an understanding of the degree to which the patient and family adhere to a given cultural community's beliefs, values and practices about health and illness that are consistent with the values and behaviors of the dominant culture.

Communication plays an important role in culturally competent care. Key concepts include those related to the dominant language and dialects; contextual use of language such as use of names, voice volume, tone, and intonation; and willingness to share thoughts and feelings. Language differences, whether culturally specific or related to the language of medicine, require

** Patients and their families need culturally competent nursing care. Therefore, the term *client(s)* is used to include both patient and family.

the attention of the nurse. Medical terms and "lingo" often need to be explained by carefully selecting words and experiences that are familiar to the client. When the patient and family speak a language that is not known to the nurse, use of a trained interpreter is the preferred approach. This is not always possible and using nonverbal ways of communicating is of great value.

Nonverbal communication includes eye contact, facial expression, body language, special distancing practices, and acceptable greetings. Two important nonverbal means of communicating for nurses include temporality and touch. Temporality refers to the notion of "clock time" versus "social time" as well as whether the group has a past, present, or future worldview orientation. Touch can enhance both information exchange and comfort care. Holding a hand or gently squeezing or patting it can communicate comfort. Hands can say "stop" or they can ask, "may I go ahead with what I am doing for you?" Some cultures have norms about touch. Generally these are gender related (women may touch women and men may touch men), but can also relate to social status. Asking permission to touch is an especially important culturally competent behavior.

Family roles and organization include beliefs, values and behaviors related to family roles. Such roles include the head of household and who makes family decisions, gender roles, roles of aged family members and those of extended family members. Also included are matters of family and community relations, developmental tasks of children and adolescents, and child-rearing practices. Social status and views toward alternative lifestyles such as single parenting, sexual orientation, child-less marriages, and divorce are also included.

Workforce issues relate to autonomy, gender roles, ethnic communication styles, individualism, and health care practices of the country of origin. Workforce issues also include education, literacy, how knowledge is valued, and how information is accessed and by whom. The concepts of acculturation and assimilation are often linked to workforce issues.***

Bio-cultural ecology includes variation in ethnic and racial origins such as skin coloration and physical differences in body stature, genetics, and heredity, and endemic and topographical diseases. Bio-cultural ecology also includes how the body metabolizes drugs. It includes access to technologies ranging from high-level diagnostic equipment to roads, cars, and airplanes, as well as books, cell phones, television, clean water and the internet. Bio-cultural ecology also includes the many diseases that pose different risks to different ethnic groups. For example,

***The term *assimilation* describes the process by which immigrants give up their culture of origin for the sake of adopting the mainstream language and culture of their adopted country. The term *acculturation* describes the process of bi-directional change that occurs when two ethno-cultural groups come into sustained contact with each other.[18]

Sickle cell disease is most common among people whose ancestors come from Africa, Mediterranean countries, the Arabian Peninsula, India, and Spanish-speaking regions in Central and South America. Beta thalassemia occurs most frequently in people from Mediterranean countries, North Africa, the Middle East, India, Central Asia, and Southeast

Asia. Multiple sclerosis is more common in regions that are farther away from the equator, and lactose intolerance in adulthood is most prevalent in people of East Asian descent.[8]

High-risk behaviors manifest themselves in both active and passive behaviors. The use of tobacco, alcohol, recreational drugs, and high-risk sexual practices are examples of active high-risk behaviors. Lack of physical activity and non-use of road safety measure such as seatbelts and helmets are considered to be passive high-risk behaviors.

Nutrition includes having adequate food, the meaning of food, and food choices. Nutrition also includes food related rituals and taboos, and how food and food substances are used during illness, pregnancy, and for health promotion.

Pregnancy and childbearing includes fertility practices, methods of birth control, and views towards pregnancy. Prescriptive, restrictive, and taboo practices related to pregnancy, birthing, and postpartum treatment are also included.

Death rituals refer to how the individual and the culture view death, rituals and behaviors to prepare for death, care of the body, and burial practices. There may be bathing rituals, taboos against touch, or expectations about the opening or closing of windows. Bereavement behaviors are also included in this domain.

Spirituality includes religious beliefs and practices including belief in witchcraft, belief in a God who heals, or belief in a God who punishes. This domain also includes worship practices, rituals and holy items, holy days, religious activities, food restrictions, fasting, and care provided by a religious community. The use of prayer, behaviors that give meaning to life, and individual sources of strength are also included.

Health care practices include the focus of health care such as acute or preventive; traditional, magico-religious, and biomedical beliefs; individual responsibility for health; self-medication practices; and views towards mental illness, chronicity, and organ donation and transplantation. Barriers to health care and one's response to pain, and the sick role, are included in this domain.

Health care practitioner concepts include the status, use, and perceptions of traditional, magico-religious, and allopathic biomedical health care providers. In addition, the gender of the health care provider may have significance.

3.3 Leininger's Culture Care Diversity and Universality Theory

Madeleine Leininger is considered to be the "mother" of transcultural nursing. Her work as an anthropologist in the 1950s led the way to our understanding of the relationship between culture and health.[14] Leininger's *Culture Care Diversity and Universality Theory* identifies a set of factors designed to help members of the healthcare team assess the relevant cultural and social structures that support culturally congruent healthcare in a given situation.

Leininger's seven factors include technological factors, religious and philosophical factors, kinship and social factors, cultural values and lifeways, political and legal factors, economic factors, and educational factors.

Leininger's theory goes beyond assessment, to problem identification and intervention. Leininger places the nurse in a very central role in which she or he ensures that traditional (folk health) systems and professional (biomedical) systems are communicating with each other.[14] To this end, Leininger identifies three categories of nursing interventions:

Preservation and/or maintenance refer to those decisions that maintain, protect and save desirable and helpful values and beliefs. Examples include (a) encouraging direct care such as bathing, feeding, and other activities of daily living be performed by family members who wish to directly participate in the patient's care, and (b) encouraging the family to bring in foods they believe have healing properties that also fit with the patient's dietary restrictions related to medical diagnoses such as congestive heart failure or renal failure.

Accommodation and/or negotiation include helpful strategies when providing care that fit with the culture of the individual, family, or group. An example might be allowing clients to engage in religious practices while ensuring that the behaviors do not interfere with other patients' comfort or safety.

Repatterning and/or restructuring involve strategies the nurse employs through mutual decision-making with the patient to change or modify the plan of care in order to achieve better health outcomes. Examples include (a) the importance of avoiding homeopathic remedies known to be associated with harmful outcomes for vulnerable populations such as rubbing petrol or kerosene on children's scalps for the treatment of head lice or (b) putting butter or oil on a burn.

4. Research Evidence on Outcomes of Cultural Competency

Since the review by Beach et al., a collection of valid measures for examining the quality of research studies has emerged.[3] Horvat et al. published a Cochrane review on cultural competence education (CCE) for health professionals.[12] Healthcare providers demonstrated an increase in knowledge about culture, and client perceptions of health professional were significantly higher in the intervention groups. To assess effectiveness and consistency of educational programs, the team developed a conceptual framework for describing interventions. The framework was comprised of (a) educational content, (b) pedagogical approach, (c) structure of the intervention, and (d) participant characteristics.

The review included 337 healthcare professionals and 8400 patients, of which 41% were from culturally and linguistically diverse (CALD) backgrounds. Evaluation of patient-related outcomes following CCE for health professionals revealed low-quality evidence of improvements in the involvement of CALD patients. Conclusions focusing on future research asserted that measures of patient outcomes including treatment outcomes, health behaviors,

involvement in care and evaluation of care were needed targets for future research. They also highlighted the role of cultural competence in addressing health inequities.[12]

Truong et al. also published a systematic review examining interventions to improve cultural competency in health care, supported by the Australian National Health and Medical Research Council.[20] Inclusion criteria for the review required the participation of healthcare providers, health administrators, support staff and health service users (clients); and evaluation of CCE interventions and outcome measures at the individual level (surveys), organizational level (programs), and/or systems level (policy).

The search yielded 6,830 titles, of which 19 met overall inclusion criteria. Some studies examined outcomes of CCE for health providers and found some evidence of improvement in provider knowledge, skills and attitudes. Others looked at specific clients populations. Hawthorne et al., Sumlin and Garcia, and Whittemore developed culturally appropriate diabetes health education programs and found short-term effects (up to one year) for glycemic control and knowledge of diabetes and healthy lifestyles.[11] [19] [20] Whittemore studied only Hispanic populations; findings included significant improvements of selected clinical and behavioral outcomes and diabetes-related knowledge in the majority of studies. [21] Lu et al. and Harun et al. found mixed results in their reviews measuring patient/client satisfaction and hence were unable to generalize conclusions for patient participation in cancer screening.[15] [10]

Three aggregate reviews studied cost-effectiveness of interventions. It was noted in one review that fewer than 10% of the studies examined included costs of cultural competence, and in another that only rough estimates of costs were identified.[3] [11] [20] The conclusion by Truong et al. stated the majority of reviews found moderate evidence of improvement in provider outcomes and health care access and utilization outcomes, but weaker evidence for improvements in patient/client outcomes. [20]

This paper identified ways nursing can improve patient outcomes related to culture and culture care. Nurse educators, practitioners, and administrators are challenged to promote cultural competence through teaching, research, and practice.

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Degree education as an entry requirement for qualified nurses in Saudi Arabia: AnOverview

Abstract

AIM: This study aim is to provide an overview of the implications of Bachelor degree nurse education in Saudi Arabia (SA).

BACHGROUND: Ministry of Health (MoH) and other health care sectors in Saudi Arabia have stipulated the minimum requirement of a Bachelor's degree for entry into nursing practice in 2010, while the majority of nursing workforce was diploma holder. The implications of this requirement have not yet been investigated; therefore it is important to establish baseline information as a basis for future workforce planning and development.

METHODS: Data related to degree nursing education andthe nursing workforce in SA were extract from the local and global published literature identified through search of arrange of databases such as ProQuest, Medline, Science Direct, Wiley Inter Science, CINAHL via EBSCO, Pub Med and Google Scholar. Obtained information was evaluated for influence and order under thematic basis.

CONCLUSION: There are three major problems related to the nursing workforce in SA: which can be ordered under the headings of educational, ognisational and social.Firstly,the educational issues include many nursing personnel do not even have a degree of bachelors of Science in Nursing. Hence, this lack of education in the nursing staff is a hindrance in providing high quality of nursing care to the patients who need advanced level of nursing. Secondly, the organisationalissues involve the policy and regulations related to nursing along with the turnover and retention rate of nurses. Lastly, social issues include the working environment involving the gender ratio, long working hours, job dissatisfaction and low wages and these factors are a cause of the high turnover rate. Yet, all these issues need to be addressed in workforce planning to improve the Saudi nursing sector.

KEYWORDS

Nursing education, nursing workforce, qualified nurse, Saudi Arabia

Degree education as an entry requirement for qualified nurses in Saudi Arabia: An Overview

Introduction

A nursing career is a major need in all the countries but there is still a serious shortage of professional nursing staff in many nations (Al-Ahmadi, 2014). Due to this shortage, some nations are hiring unqualified nursing staff hence not giving patients the required level of need and care from the nursing staff (Alyasin and Doughlas, 2014).This paper provides an overview of the implications of Bachelor degree nurse education in Saudi Arabia (SA). It first explores the policy perspective; the scenario of shortage in global and local nurses and the high rates of turnover. It also examines current nursing education levels and entry requirements. Focus has been put on integrating knowledge with practical training in order to maximize the utility of the labour workforce.

An Overview of Policy Analysis

This policy summary illustrates the development of degree nurse education in the global context. There has been consideration of education delivery and entry requirement by nursing organisations globally, for example the International Council of Nurses (ICN) andSigma Theta Tau International(STTI). As yet within policy analysis there has been little consideration of workforce planning issues. Saudi Arabia has a wealth of information from the global nursing field to use to develop its own healthcare system and manage its workforce to make it fit for the 21st century. It has the advantage of looking at countries that have already implemented the policy making degree a minimum requirement for nursing and work with the outcomes of these to shape its own policy. In neighbouring Jordan, the first nursing baccalaureate was introduced in 1972 followed by a Masters' degree in nursing in 1986 and this has lead the way in nursing education in the Middle East. Jordan has 17 nursing schools and also offers doctorate level nursing degrees (Nabolsi, et al, 2014) whilst Saudi Arabia only recently made the degree in nursing mandatory. Jordan has long encouraged the professional development of nurses in obtaining degrees by supporting students with scholarships to study abroad to developed nations (e.g. USA, Canada, and UK). Where it was not possible for students to go abroad e.g. due to family commitments, Jordan responded with the development of its own high quality nursing education programmes at home and leads the way in the Middle East in the field of high quality nursing education (Shuriquie, et al, 2008) . Jordan is not without its problems though; the adoption of international standards to meet global requirements has meant there has been a gap in the delivery of services that are culturally and economically sensitive and need addressing (Shuriquie, et al, 2008); something for Saudi Arabia to consider when developing its nursing educational policies.

An increase in global ageing population is expected with better health care and increase in longevity therefore, Saudi will need to consider whether the policies it develops meets the need of this future population. Other aspects to cover includes covering training in predicted disease areas as there will be shift in the type of ailments seen with shift in time as seen historically. For example, according to WHO, there has been an increase in diseases

associated with life style in recent years in the Middle East; high on the list among these is coronary heart disease and diabetes. Acute Coronary Disease is one of the biggest killers in adult population in Saudi Arabia according to the WHO (2011) and coronary heart disease accounted for 23% of total deaths in Saudi Arabia (WHO, 2011). Training and resources to deal with such issues need to be addressed now to equip staff in readiness. Being prepared to deal with such issues will reduce financial and staff burden. The cost to the MoH in treating Saudi patients with heart condition is on average US$10,710 with average stay in hospital ranging from almost 8 days if patients do not have co-morbidities to 11 days if patients have co-morbidities (Alsultan, et al, 2011). The rising rate of obesity is likely to add to this problem in the future. A degree level education which deals with health promotion would cover these high need areas making policies and health care systems robust. Predicting and preparing for such issues would allow the MoH to allocate resources appropriately and manage the workforce to its full potential.

In contrast to Saudi Arabia, Kuwaiti Ministry of Health requires a nursing qualification (not necessarily a bachelor's degree) and one years' experience, however like Jordan; Kuwait does offer scholarships to encourage students to be educated at degree level in countries such as USA, UK, Australia and Ireland. Globally, the requirement for level of nursing qualifications varies. For example in India, there are many levels of nursing qualifications. The vocational courses are: Multi-Purpose Health Worker Female training, Female Health Supervisor training, General Nursing and Midwifery certifications. Degree level and above courses, in line with international standards, includes BSc in Nursing, MSc in nursing, MPhil and PhD – all of which are taught at universities (Nursing Education, 2013). The purpose of a policy offering such a wide range of courses in nursing is to meet the requirement of the society at different levels, which is socially and culturally incredibly diverse like the Middle East and has dealt with the issues overlooked in Jordan. India's varied approach to nursing education offers opportunities to all those who want to pursue a career in nursing at any level depending on personal circumstances and resource availability.

The need to reform nursing education as the world entered the 21st century drove the global impetus to reassess old policies and standardise education fuelled by the diversity of nursing roles and the global migration of nurses from one country to another. Furthermore, other health related fields were already one step ahead in offering and making degrees mandatory for practice e.g. physiotherapy, pharmacy and social care. The trend followed so that as one country made it mandatory to make degree in nursing the minimum requirement, soon after others followed, for example UK started the 'Project 2000' programme to move nursing education into university and allow nurses to acquire degrees. The reason for this shift includes many researchers demonstrating that education of nurses was directly linked to quality of patient care and patient mortality (Aiken, et al, 2014). There is a great shortage of nurses in the Middle East, majority of its nursing population are foreigners, therefore for the Middle Eastern countries to participate in the global nursing arena, and seen to be providing the same level of care, countries such as Saudi Arabia have also made it mandatory to make degree the minimum requirement for nurses recently following trends in other countries.

The change in the US policy on nursing education has actually seen an increase in the number of students taking up nursing (Aiken, 2002) despite the concerns from oppositions. As predicted, one of the reasons maybe that the nurses are given more autonomy, respect, and a wider range of transferable skills among others. The change in policy and the rise of uptake of nursing as a career will help ease the shortage of nurses globally. The ICN is an international body representing nurses from 130 countries aims to provide nursing guidelines to standardise nursing globally and unite the nursing community as one. The ICN identified a historical shortfall in the nursing profession i.e. nurses did not have a role in nursing policies, the ICN endorsed the need for more autonomy to nurses and their involvement in policy making on a global scale to help influence the profession as nurses are the individuals with front line hands on experience of the system. As part this initiative, the ICN recommends the improvement of education equivalent to degree level to help provide nursing services fit for the new millennium as degree education has been shown to enhance patient safety, quality, competency and service delivery (ICN, 2009; Aiken, et al., 2014).

Saudi Arabia offers both degree level and associated degree (diploma) level education in nursing. The Saudi Ministry of Higher Education (MoHE) has a policy to deliver high quality education to international standards in all fields including nursing (Alamri, 2011). It has taken steps towards achieving this in order to provide a nursing service equivalent to that of other developed nations; e.g. Saudi Arabia has also made it a policy to make degree the minimum requirement for nursing in the hope of addressing the previously poor nursing standards (Al-Homayan et al, 2013). Saudi Arabia has significantly increased its funding of student nurses, scholarships and encourages study-abroad programmes (Alamri, 2011). The feeling of political and social pressure to conform to standards of other developed nations in making degrees in nursing mandatory has driven the change in Saudi Arabia (Alamri, 2011). Until recently, the nursing policy only affected females as they were target group, and males were not offered nursing degrees. Males nurses are still not offered Masters' degree in nursing. The change in this has again been influenced by international standards and the need to increase home-grown nurses and widen the talent pool, an amendment to the policy that will have important positive impact on the workforce reaching out to another potential 50% of the population. Policies need to be implemented with the use of media as aid to reach a wide target audience. As previously mentioned, the change from diploma to degree level entry, may see a change in shift due to the prestige and accolade that comes with a degree and allow the profession to gain more respect and recognition in a country where nursing is seen as a low status job. There is great scope for any policies that are developed to shape the future of the country through changes in culture, education and social perception.

Although the Saudi government is trying to meet international standards when it comes to nursing degrees, it still has a lot of issues that need addressing; for example, the MoHE still does not have an established syllabus/learning outcomes and this is driven currently by the faculties themselves so that the standard of nursing varies according to the education of the head of the faculty (Alamri 2011). Furthermore, as the change in policy to degree level education is recent, nurses with associated degrees do not have any way of converting their associated degrees to a BSc equivalent and this is something that needs to be tackled in the

policy as it affects a large portion of the Saudi work force. As explained previously, there is a vast number of nurses within Saudi Arabia that are not currently employable due to the lack of bridging degree on offer to convert their nursing diplomas into Bachelor's degree. If Saudi wants to be a global participant, it also needs to address within its policy, offering these bridging degrees to foreign student to attract more staff and meet shortfalls in the current workforce and also deal with future predicted shortfalls in staff. Given Jordan has lead the way in nursing degrees in the Middle East, for Saudi Arabia to attract students away from competition, its policies need to cover incentives and welfare of foreign students and staff and not just the native population.

Associated degrees in nursing and funding for health care fall under the jurisdiction of the MoH, in order the bridge the gap above, there needs to be better communication and links between the two departments; or the policy needs to be transferred to one of the two departments for coherence e.g. MoHE. In Switzerland, due to the two different linguistic communities, the nursing education model has taken two separate pathways with high variability and inconsistency between them (Spitzer &Perrenoud, 2007) defeating the goals of organisations such as the WHO and the ICN in trying to standardise nursing education globally. Saudi Arabia could learn from the Swiss example in bettering its own nursing education system by merger or even the creation of a new department to help drive the initiative.

Nursing Workforce Challenge

The largest groups of health care professionals in the country are nurses; they delivered the high percentage of health care (Oulton, 2006). Despite the fact that being the largest group of health providers, the nursing profession has experienced an acute shortage of qualified nurses affecting the delivery of health care (Almalki et al, 2011; Chan &Marrison 2000; Fochsen et al. 2006). Saudi Arabia is challenged with a chronic shortage of qualified Saudi nurses, accompanied by high rates of turnover; in addition, the annual rate of Saudi graduate nurses is insufficient to meet the increasing health care demands (Gazzaz, 2009). Within the large numbers of Saudi students over the world, there is a low percentage of nursing students locally and internationally (Alamri, 2011). Recently, the admission level of entry into the nursing practice has been changed to baccalaureate degree (Alamri, 2011).

Today, according to Majeed (2014), above fifty percent of the workforce is comprised of nurses and other health care staff. The focal point and centre of the health care system are the nurses and the health care system without nurses will not be functional (Alyasin and Doughlas, 2014). In Saudi Arabia, the healthcare sector workforce mostly comprises of emigrant nurses; only 34% of the nursing workforce is Saudi nurses as stated by AlYami, (2014). A major portion of the emigrant nurses use the Saudi Arabian healthcare opportunities temporarily in order to get practice and knowledge. After gaining the required experience, they return to the healthcare sectors of the developed nations like USA, UK and Australia (Majeed, 2014).

The high rate of turnover among professional nurses in Saudi Arabia is adding to the worries such as management issues, organisational plan obstruction and bad service of

delivery thus affecting the workforce (Al-Ahmadi, 2014).The effectiveness of various healthcare systems is greatly threatened by such problems; for example, there is a constant need to replace and train staff. There are no reliable statistics related to this important problem but for the managers of the health care facilities, this emigrant movement is a big issue (AlYami, 2014). High turnover of nurses creates an unstable healthcare system where the burden of workload falls on the remaining staff. This inevitably has the potential to compromise the care given to patients, creates an environment of discontent and affects moral and motivation of remaining staff (Lamadah, et al., 2014). Lower staff turnover rates, higher staff retention and high level of nurse to patient ratio has been shown to be linked to higher quality of care and reduce in-patient stay (Collier and Harrington, 2008). High turnover of nursing staff also has a significant impact in the finances of a healthcare system. A survey of Jordanian nurses showed job satisfaction was a significant factor in retaining nursing staff (Alsaraireh,et al, 2014). Saudi nurses were happier when there was effective leadership shown by management and happier to stay in their jobs suggesting further need to address this at the policy level (AbuAlRub& Alghamdi,2012), therefore, Saudi MoH could retain staff through providing a better work environment to its employees, better leadership, and training programmes; these suggestions should be explored, for example offering incentives, facilities and rights, working conditions, and/or shorter working hours. Restructuring the education system to offer equal opportunities to men and women and offer higher degrees across various universities is more likely to allow recruitment and retention of nursing staff. According toAlmalki et al (2011)Saudi nurses make up a small percentage of the total nurse workforce; this percentage is even smaller in the private health sector where native nurses make up only 4.1% of the workforce (see Table 1). The lack of local nurses is a big problem due to various social, educational, and individual reasons.

Table (1.1): Nursing personal in the healthcare sectors in Saudi Arabia

Sector	*No.*	*Saudis*	*(%)*	*Non-Saudis*	*(%)*
Ministry of health	*55,429*	*24,689*	*(44.5)*	*30,740*	*(55.5)*
Other Govt.	*23,536*	*3,908*	*(16.6)*	*19,628*	*(83.4)*
Private Sector	*22,333*	*909*	*(04.1)*	*21,424*	*(95.9)*
Total	*101,298*	*29,506*	*(29.1)*	*71,792*	*(70.9)*

Source of the data: Annual Statistic book, MoH (2008).

Educational challenges

In Saudi Arabia, many nursing personnel do not even have a degree of bachelors of Science in Nursing (Al-Makhaita et al, 2014). Hence, this lack of education in the nursing staff is a hindrance in providing high quality of nursing care to the patients who need advanced level of nursing care (Al-Ahmadi, 2014). AlYami (2014) suggested that the increasing requirements of the Saudi healthcare sector are not being met by the low yearly induction of nursing graduates from Saudi Nursing schools. The effectiveness of various healthcare systems is greatly threatened by such problems and the Saudi MoH needs to address this to increase the uptake of nursing degrees by local people.

According to Jahan (2005), nurses with associate degrees have a lower status of professionalism than Bachelors of Science in Nursing (BSN); nurses and the education acquired by BSN nurses was linked with the social reciprocation on the funding in education. Al-Ahmadi (2014) gave three factors as to why associate degree nursing is not regarded as a professional and these are: nurses are not educated but trained; medics mainly control the nurses and ultimately, nurses do not have to answer for their actions. Majeed (2014) stated the training of people, forming their personality and preparing them for accountability is the responsibility of a university and this could be address with the introduction of the new policy in nursing education. It is widely believed that a Diploma is technical and a low level education (Aldossary et al, 2008); hence there is a need to eventually enhance the nursing education level to at least BSN level.

Almalki et al, (2011) stated that, all Nursing Colleges and health institutes were transferred from the MOH to the MoHE during 2008 as the first step to improve nursing education in the kingdom of Saudi Arabia. In addition, a Bachelor of Science in Nursing (BSN) is awarded following a five year curriculum at all the universities offering BSN programmes. The down side with a five year degree programme is that the length of commitment required before being able to practice and earn may hinder people from the profession, given nurses are already complaining of resource and time issues. Nevertheless, the Ministry of Health has been implementing the recommendation of the WHO that emphasis the bachelor degree as a minimum requirement for entry into nursing practice in 2010 (Almalki et al, 2011).

In the States, a historical review of the role of nursing shows that more and more nurses want to study for a degree in nursing as a way of increasing future career prospects, as a sign of prestige and achievement, as part of professional development (D'Antonio, N.D.). D'Antonio argues that the nurses should not be hindered socially or by policy and that this social upward movement should be supported and encouraged at government and policy level regardless ethnic background. Prior to the Civil Rights Movement in the 60's and 70's majority of the degree educated nurses in the States were white females but post movement, this has changed so that there are more African Americans nurses with degrees or equivalent as well as other ethnic minorities. Saudi has policies that are favourable to Saudi nationals or women only (e.g. Master's degree in nursing), perhaps broader policies may help recruit and retain staff.

A study on American nurses indicates that many nurses with diplomas or associated degrees did not pursue a Bachelors' degree because of lack of financial incentives and because of their own financial situation; other barriers in taking up degree courses included lack of flexibility in their current working situation, and family commitments (Romp et al., 2014). These are important issues that are likely to affect the Saudi nursing population and the results of Romp et al. (2014) study can be used to set up solutions before they cause a major problem in Saudi. For example, Saudi MoHE can offer scholarships to those wishing to complete an accelerated degree programme, or bridging degree. The government can offer paid study leave, distant learning opportunities and provide subsidised childcare facilities.

Organisational challenge

Al-Ahmadi (2014) examined anticipated turnover among nurses in the hospital of Saudi Arabia. The study included 5459 nurses in 80 hospitals who were randomly selected from the hospital database in The MOH. Al-Ahmadi observed in a survey that most of the individuals (interns, staff nurses, and senior nurses) mentioned education while serving and on-job training as reasons that affected their resolve to keep or quit the job at a specific organization. The participants considered the chance for uninterrupted education and advanced level training as key factors for their enthusiasm and contentment. For these individuals, their professional knowledge and practice is strengthened by in-service education and training. But on-the-job services differed significantly in various hospitals and fields. The nurses doing their jobs at government hospitals seem more annoyed and dissatisfied than the similar workers at other government sector jobs for getting fewer chances to be a part of such services (Al- Ahmadi, 2014).

Due to less nursing staff in Saudi Arabia, the Saudi governmental and private sector healthcare set ups are becoming more and more dependent on expatriate nurses serving to fill the void. According to Al- Ahmadi (2014), a large percentage of the nursing system is based on expatriate nursing. One of the implications of making a degree the minimum requirement for nursing in Saudi Arabia, which depends so heavily on foreign nurses, is that it may reduce its workforce considerably, if a country which supplies nurse to Saudi Arabia, does not offer nursing degrees or does not make it mandatory, meaning Saudi Arabia will start reducing its recruitment area from other countries.

The nursing care provided differs due to the diversity in educational and cultural backgrounds. Therefore, Adossary et al (2008) gave the following suggestion for the Saudi nursing department: *"The main challenge for Saudi Arabia, presently, is to develop Saudi national nursing staff in order to provide quality healthcare following the Saudi cultural and linguistic aspects. In the absence of such measures, it will be increasingly difficult to provide a high quality of healthcare to the Saudi nationals."*Aldossary (2008) predicted that the rising requirement of health care services for the elderly was expected to be even more in the coming years and the problem needs to be addressed immediately by the Saudi government and make necessary improvisations to the systems that facilitates and attracts more female workers (Majeed, 2014). Currently, training the nurses in departments such as gerontology needs to be practised at most to cater the growing percentage of the elderly people (Al-Ahmadi, 2014). It was stipulated that the Saudi kingdom must increase the count of nurses in the hospitals to meet the rising population percentage. This can only be achieved if the authorities break the cultural barriers that restrict women to opt into nursing as their profession (Aldossary, 2008).

Social challenge

Majeed (2014) asserted that Saudi Arabia needs to realise two things in their society. Firstly the current role and status of nurses in health care units and how it has evolved. Secondly, the realization of ways to improve the female nursing service for the public welfare and address the rising challenges (Al-Makhaita et al, 2014).For individuals who have selected the nursing

profession, nursing education seeks to provide knowledge, skills and attitudes (Tumulty, 2001). Nursing programmes started to be improved in Saudi Arabia, with the development of the curriculum, nursing education and practicing at graduate level programmes (Tumulty, 2001). Today, applications from female Saudi nationals with the right set of abilities, skills, intelligence and motivation for the study of nursing science are encouraged at Saudi universities (Almutair, et al, 2014). However, the universities considered in this study were exclusively developed for female students and therefore all respondents are females. This limitation of the study should be highlighted as previously mentioned.

The hospitals in Saudi Arabia are facing a new challenge owing to the rising rate of attrition of the female nurses. The reason of this deficiency in hospitals is due to averting attitude towards the profession (AlYami and Watson, 2014). The hospital management in Saudi Arabia needs to systemize their records and maintain them periodically. In spite of this, the hospitals in Saudi Arabia have not addressed this problem and increased their female nursing staff compared with other countries across the globe. The most affected are the elderly personnel in the country. The grave concern of the deficiency of competent nurses in the Saudi hospitals requires a profound scrutiny on the current and future nursing system which includes the training facilities (Almutair et al, 2014). This scrutiny should address the problem with special focus on elderly people.

Al-Ahmadi (2014) and Majeed (2014) asserted that with the policies attracting women to opt into this profession, the shift is seen by the kingdom's females. Although, this shift is quite slow and the experts claim it to be fully achieved with time. The reason for the delay is that women in Saudi culture face a lot of hindrances and the profession itself possesses an uncouth image in the society (Al-Makhaita et al, 2014). The apropos system for recruiting and training the nursing is inconsistent owing to the diversity of professionals working in these hospitals (Majeed, 2014). Another factor that contributes to this problem is the lesser percentage of female applicants when the recruitment programmes open (Al-Ahmadi, 2014). The prime reason lies in the social image of the nursing profession. Most often, females resort to take the administrative jobs owing to the high promotional chances (Almutairi, et al, 2014). Moreover, the female lots after acquiring the professional training are bound to marriage which forces them to leave the profession as per the social norms (Al-Makhaita et al, 2014). This creates a gap and affects the nursing education in the society.

All the issues above are related to female nursing; this is because whilst it is well known that nursing is a female dominated profession globally, it is more so in Saudi Arabia. Limited numbers of females want to go into the profession due to the social image and pressures, but even fewer men want to go into the profession. There are calls to overhaul to the policies affecting nursing in Saudi Arabia which are seen as inadequate with recommendation to enhance the status of nursing in Saudi Arabia to make it a worthwhile career, and this starts with dealing with some of the social stigma (Al-Omar, 2004; Al-Malki, et al. 2011). The Saudi government needs to use media to help engage with people and promote a positive image of the nursing profession to help with the shortfall in the local work force (Al-Malki, et al. 2011). The policy should not start out aimed at females and then be extended to men as it will enforce stereotypes and take longer to see changes. Instead, policies

should be aimed at both genders from the outset. Interviews conducted by the Saudi Gazette (N.D.) with health care workers in Saudi Arabia echoed some of the social stigma the health care workers have to face and overcome on a daily basis. For example, men and women equally feel that public perception of nursing is negative; opinions include a male should be in a role where his strength is required, for example, in the emergency department and not nursing the sick and frail. Those who go into nursing see it as a rewarding humanitarian job and have support from family meaning change in an individual's perception to get them into nursing may not be sufficient but the family/community need to be targeted. Saudi men avoid marrying female nurses due to the long hours of shifts and night work requirements. Family and social concerns aside, the long hours and night work also deters many from going into the profession. For those who are married and with children, they encounter difficulties with getting childcare; something resolvable through subsidised childcare.

Conclusion

The literature above indicates that the dire shortage of nursing staff in health care sector is compromising the quality of health care in Saudi Arabia. This is not only a phenomenon here but it is a global issue. Proper professional education and providing adequate job facilities to nursing staff is required in order to bring improvements. The universities need to improve their curriculums in order to cope with the changing and evolving needs of the nursing profession. The nursing staff promotional hierarchy should be revisited and improved as that is also a factor affecting the lack of professional nurses. The major nursing strategists have put their focus into combining knowledge with training to benefit the nursing profession and to improve its conditions. The issues of nursing staff, like lack of promotion, need to be carefully considered and resolved. There should be provided on job training and education in order to keep them up to date with the latest in the health technology and develop their skills as part of continuing professional development. These form the backbone of the healthcare sector, and their betterment is an imperative. Qualified nurses will be able to provide the required level of health care and a level of professionalism that is necessary with the job.

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Eating Disorders among Female Adolescents in Jeddah

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Abstract

Background: Adolescence period defined as a transitional stage that falls between childhood and adulthood. The Nutritional requirements are one of the most important aspects in this stage comparing to all life span due to achieving the optimal level of growth and development. Adolescents' concern about their body weight and shape can lead to disturbed eating behaviors such as starvation, fasting, frequently skipping meals, overeating and binge-eating followed by purging, also using of diet pills, laxatives, diuretics and excessive exercising. Eating disorder behavior is contributing to some risk factors which include age, genetics, pubertal status, pubertal timing and body mass index as biological factors. In addition, body image dissatisfaction, negative mood states such as depression and stress, low self-esteem and personality traits are contributed to eating disorders as psychological factors. There are also sociocultural factors such as peer pressure and influences by media to conform to an unrealistic standard of thinness, eating disorders in the family and bullying. Physical and sexual abuse considered plays a role in developing eating disorder. There is no specified study mentioned prevalence rate for eating disorder among female adolescents in Jeddah or any other place in Kingdom Saudi Arabia.

Objectives: The aim of the study is to assess eating disorders among female adolescents of secondary schools in Jeddah.

Methods: The study was conducted in 3 secondary schools in Jeddah. Cross sectional design was used. Four hundred twenty five female adolescents were recruited using non probability "Quota" Sampling in order to obtain a representative sample from the 3 levels in the secondary schools. The Arabic version of a self report Eating Attitude Test 26 questionnaire (EAT-26) was used. Total score and three subscales (dieting, bulimia, and oral control) are generated and a score of 20 and above indicates the risk for eating disorders.

Results: The findings of the current study revealed that 32.9% of the entire sample scored of 20 and above using Eating Attitude Test (EAT-26). This indicates that they are at risk for eating disorders. A significant relationship was found between the mean of participants' body mass index and their Eating Attitude total scale and the three subscales (dieting, bulimia, and oral control). Furthermore, a negative significant relationship was found between the mean participants' age and their Eating Attitude total scale.

Conclusion and Recommendation: In conclusion, the current study highlights the importance of eating disorders screening among adolescents to identify who have disturbed eating attitude and at risk for eating disorders. Further studies are needed either to modify the current

instrument or to develop a new culture specific instrument. Development of a community based preventive measures to help adolescent to have health eating attitude and habits is recommended.

Key words: Eating disorder, Female adolescents.

Introduction:

Adolescence period defined as a transitional stage that falls between childhood and adulthood. During this period, adolescents are undergoing of different dramatic changes and development of the physical, emotional and cognitive function. The Nutritional requirements are one of the most important aspects in this stage comparing to all life span due to achieving the optimal level of growth and development (Chin.Y and Mohod.N, 2009). It has been reported that irregular meals, snaking, eating out of homemade and following alternative dietary patterns happened frequently among adolescents (Washi S., Ageib M., 2010).

Unhealthy weight control behavior; such as fasting, vomiting on purpose after eating, taking diet pills, and use of laxatives can be used. (Gonsalves.D, Hawk.H, Goodenow.C, 2013). This kind of dieting behaviors may lead to develop a significant eating disorder which defined as anorexia nervosa, bulimia nervosa, binge-eating disorder (Gonsalves.D, Hawk.H, goodenow.C, 2013 and Coelho.G, Gomes.A, Ribeiro.B, Soaras.E, 2014). Adolescents' concern about their body weight and shape can lead to disturbed eating behaviors such as starvation, fasting, frequently skipping meals, overeating and binge-eating followed by purging, also using of diet pills, laxatives, and diuretics and excessive exercising.

Eating disorder behavior is contributing to some risk factors which include age, genetics, pubertal status, pubertal timing and body mass index as biological factors. In addition, body image dissatisfaction, negative mood states such as depression and stress, low self-esteem and personality traits are contributed to eating disorders as psychological factors. There are also sociocultural factors such as peer pressure and influences by media to conform to an unrealistic standard of thinness, eating disorders in the family and bullying. Physical and sexual abuse considered play a role in developing eating disorder (Coelho.G, Gomes.A, Ribeiro.B, Soaras.E, 2014).

Adolescents with eating disorder have high risk to develop anxiety disorder, cardiovascular symptoms, chronic fatigue and pain, depressive disorder, limitation in activity related to poor health, infectious diseases, insomnia, neurological symptoms, and suicidal attempts in their early adulthood as consequences for the disease (Johnson.J, Cohen.P, Kasen.S, Brook.J, 2002). There is no specified study mentioned prevalence rate for eating disorder among female adolescents in Jeddah or any other place in Kingdom Saudi Arabia so; the current study will assess eating disorders among female adolescents to set a base line data that will be used to build on in the future.

Aim of the Study:

The aim of the current study is to assess eating disorders among female adolescents in secondary schools in Jeddah.

Specific objectives:
1. To describe the prevalence of eating disorders among secondary school female adolescents in Jeddah.
2. To correlate between eating disorders and age, BMI of the participants.

Research Question
What is the prevalence of eating disorders in female adolescents in secondary schools in Jeddah?

Methods:
Study Setting:
This study was conducted at three females secondary school in Jeddah (the 55th secondary school, the 18th secondary school and 28th)
Study Subjects/size:
The total sample of 425 female adolescents aged from, 15 – 18 years participated in the study. Female adolescents who have chronic diseases and those who are pregnant were excluded from the study.
Study Design:
Cross sectional design was used to answer the research question. "A cross sectional study examines data at one point in time, that is, data collected on only one occasion with the same subjects rather than with the same subjects at several time points."(LoBiondo-Wood and Haber, 2010).
Sampling Technique:
Non probability "Quota" Sampling was used in order to obtain a representative sample from the 3 levels in the secondary schools. "Quota sampling refers to form of non-probability sampling in which knowledge about the population of interest is used to build some representative into the sample. A quota sample identifies the strata of the population and proportionally represents the strata in the sample" (LoBiondo-Wood &Harber 2010).
Each stratum of the population was proportionately represented in the sample. A proportional quota sampling strategy was used and 30% of a population of about 1415 female adolescents (i.e., 425). Based on the proportion of each stratum (each educational level) in the population, 156 female adolescents from educational level 1inaddition to 146 female adolescents from educational level 2 and 123 female adolescents from educational level 3 were the quotas for the three strata. The researchers recruited subjects who met the criteria of the study until the quota for each stratum was filled.
Data Collection methods, instruments used, measurement
A self-administered questionnaire was utilized, the questioner includes two parts:-
Part I: includes age, level, weight, height, marital statues and BMI.
Part II: Eating Attitude Test 26 (EAT-26) was used. It is a widely used standardized self-report measure of symptoms and concerns characteristic of eating disorders. The original version of the EAT was published in 1979 (Garner &Garfinkel 1979). It was updated at 1982 by Garner and colleagues that describe a 26-item refinement of the original test (Garner DM. et al 1982). "The 26 items with three sub-scales including dieting scale items, bulimia & food preoccupation scale items and oral control scale items, Each item is responded to on a six-point

Likert scale ranging. To calculate the score of each item from 1 to 26 it scored as follows: Always = 3; usually = 2; Often = 1; other answers include 'Sometimes', 'Rarely' and 'Never' = 0. Only the item 25 is scored in the opposite direction, Never =3, rarely =2, Sometimes =3 other answers includes 'Always', 'usually' and 'often' =0. A total score of 20 and above was classified as at-risk of eating disorders (disordered eating)" (Jalali-farahani S. et al 2014). The EAT-26 was proved to be highly reliable and valid (Garner DM. et al 1982). The Arabic version has been used and valid by (Al-Adawi S., etal 2002).

Data Management:

Statistical package for social science software (SPSS version 18) was used for statistical analysis. Descriptive statistics was conducted to describe the demographic characteristics of the participators. In addition to this, the relationship between eating disorders and demographic variables was done using t- test. The significance level was at $P< 0.05$.

Ethical Considerations:

The proposal and the questionnaire were submitted to the research committee of the college of nursing in Jeddah, for audit and to get composed consent to conduct the study.

Female adolescents were informed about the natural of the study. They indicated their willingness to participate in the study by signing the informed consent. Confidentiality was ensured.

Results:

Table (1) presents the demographic characteristics of participants; four hundred and twenty five female adolescents participated in the current study, their age ranged from 15 to 18 with mean age of 2.5741±.97844, their weight ranged from 32.60-108.3 Kg with the mean weight of 52.37±11.1835 and their height ranged from 1.39-1.72 m with the mean height of 1.553±.0535. Furthermore, Participants' body mass index ranged from 13.76-40.76 with mean BMI is 21.6824±4.26108. As regards participants' educational level, 36.7 % of them from level 1 while 34.4 % of them from level 2 and 28.9 % of them from level 3 as in figure 1.

Table (2) presents the mean score of the first subscale: dieting subscale items. It was found that the highest mean (1.505±1.2759) was for "I Am terrified about being overweight" followed by "Think about burning up calories when I exercise" which has mean of 1.4753±1.3139 while the lowest mean (.2294±.6403) was for "I Particularly avoid food with a high carbohydrate content (i.e. bread, rice, potatoes, etc.)".

Table (3) presents the mean score of the second subscale: bulimia & food preoccupation scale items. It was found the highest mean (.7647±1.0777) was for "I Have gone on eating binges where I feel that I may not be able to stop" while the lowest mean (.0941±.43501) was for "I Enjoy trying new rich foods" .

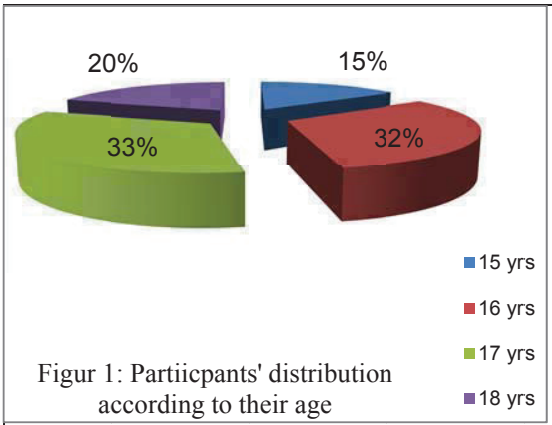
The mean score of oral control subscale items was presented in table 3. It found that the highest mean (1.718±1.2461) was for "Other people think that I am too thin" While the lowest mean (.2306±.5936) was for "I Avoid eating when I am hungry"

Table **(5)** presents the participants' total score of EAT-26. It was found that 32.9% get score of 20 and above while 67.1% get score lower than 20 with total mean score of 17.98 ±9.29. The

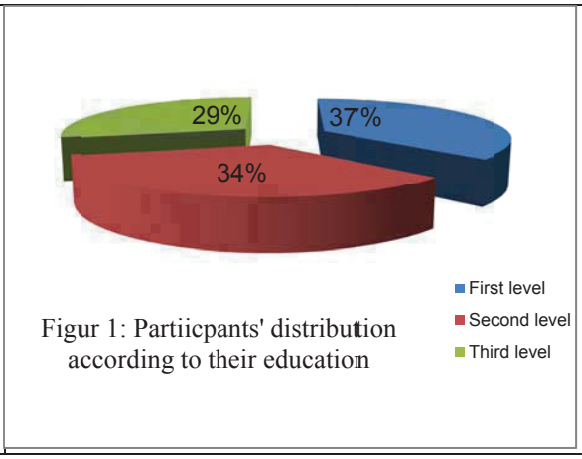
relationship between BMI and mean score of EAT-26 was presented in table **6**. It shows that there is a positive significant relationship between Body Mass Index and EAT-26 score. Furthermore, there is a negative significant relationship between participants' mean age and their mean score of EAT-26 scale and subscales of dieting and oral control as presented in table **7.**

Table (1) participants' distribution according to their demographic characteristics

	N= 425
Age : Min-Max	15-18
Mean±SD	16.5741±.97844
Weight: Min-Max	32.60-108.3
Mean±SD	52.37±11.1835
Height: Min-Max	1.39-1.72
Mean±SD	1.553±.0535
BMI: Min-Max	13.75-40.76
Mean±SD	21.6821±4.26108



Figur 1: Partiicpants' distribution according to their age



Figur 1: Partiicpants' distribution according to their education

Table (2) Participants' distribution according to dieting scale items

Dieting scale items	**Mean±SD**
I am terrified about being overweight.	1.505±1.2759
I aware of the calorie content of foods that I eat.	2824±.7862
I particularly avoid food with a high carbohydrate content (i.e. bread, rice, potatoes, etc.)	2294±.6403
I feel extremely guilty after eating.	5388±.9995
I am occupied with a desire to be thinner.	1.2306±1.3294
I think about burning up calories when I exercise.	1.4753±1.3139
I am preoccupied with the thought of having fat on my body.	6659±1.0646
I avoid foods with sugar in them.	2494±.6860
I eat diet foods.	3035±.7167

I feel uncomfortable after eating sweets.	4894±.9294
I engage in dieting behavior.	8071±1.1182
I like my stomach to be empty.	5388±.9948
I have the impulse to vomit after meals.	1.0635±1.1088
Total mean	9.3823 ± 7.045

Table (3) Participants' distribution according to Bulimia & food preoccupation scale items

Bulimia & food preoccupation scale items	**Mean±SD**
I find myself preoccupied with food.	5600±.94759
I have gone on eating binges where I feel that I may not be able to stop.	7647±1.0777
I vomit after I have eaten.	0847±.4032
I feel that food controls my life.	5247±.98334
I give too much time and thought to food.	4024±.82445
I enjoy trying new rich foods.	0941±.43501
Total mean	2.4304±3.0738

Table (4) Participants' distribution according to oral control subscale items

Oral control subscale items	**Mean±SD**
I avoid eating when I am hungry.	2306±.5936
I cut my food into small pieces.	8800±1.1252
I feel that others would prefer if I ate more.	9412±1.2733
Other people think that I am too thin.	1.718±1.2461
I take longer than others to eat my meals.	7435±1.0805
I display self-control around food.	1.1647±1.4766
I feel that others pressure me to eat.	1.0353±1.16804
Total mean	6.1671±4.3424

Table (5) Participants' total score of EAT-26

Participants' total score	**N=425**	**%**
Total score of 20 and above	140	32.9%
Total score of less than 20	285	67.1%
Total mean score of EAT -26 Mean ± SD	17.98 ±9.29	

Tables (6) Relationship between BMI and mean EAT-26

Mean EAT-26	t-test	P value
Dieting subscale	-19.598	< 0.0001
Bulimia & food preoccupation subscale	917	360
Oral control subscale	-16.733	< 0.0001
Total Scale	-3.095	0.002

Tables (7) Relationship between age and mean EAT-26

Mean EAT-26	t-test	P value
Dieting subscale	37.948	< 0.0001
Bulimia & food preoccupation subscale	77.104	<0.0001
Oral control subscale	44.409	<0.0001
Total Scale	7.826	<0.0001

Discussion:

Adolescence is a period of rapid growth in which the metabolic rate and the need for nutrients are increase (Stanfield, P. &Hui, YH. 2009). In this period, the adolescents make their food choices and their dietary attitude get affected by peer pressure (Dudek, 2010). Female adolescents especially are highly conscious about their weight that make them at risk for developing eating disorders (Wong et al., 2014). They have the desire to be thin and in order to be socially acceptable, they will resort to meal skipping which may lead to minerals deficiency, hair and skin problems and eventually eating disorders (Stanfield, P &Hui, 2009). So, the current study assesses the eating disorders among female adolescents.

Four hundred and twenty five female adolescents participated in the current study. It was found that 32.9% of participants scored above the cut off 20 and this indicated that they have a risk for eating disorders. This prevalence is higher than the prevalence of eating disorders in other countries using the same eating attitude test 26 (EAT 26). The result of study done in United Arab Emirates by Thomas,J., et al (2010) showed that 24.6% of respondents scored above the cut off 20. In addition, another study using the same scale (EAT-26) done by Jalali-Farahani,S., et al (2014) demonstrated that the prevalence of eating disorders in female adolescents was 26.4% and the sample age range was between 14-17 years old male and female adolescents. Furthermore, the result of study done in seven Arab countries which are Algeria, Jordan, Kuwait, Libya, Palestine, Syria and Sharijah, using EAT-2 by Musaiger,A., et al.(2013) showed that the prevalence of eating disorders was ranged from 16.2% to 42.7% in female adolescents aged form 15 to 18 years old. The study showed that the female Kuwaiti adolescents have a significantly high prevalence for eating disorders more than their peers in the other six countries.

The results of the current study revealed that the highest mean (1.505±1.2759) was for the item “I am terrified about being overweight” which is under dieting subscale. This indicates that female adolescents are highly conscious about their body weight. There are several reasons to justify why dieting concerns among female was the highest. Also, media shows the ideal

body of female models "the thinner the prettier" and the pressure to be accepted socially especially among peer group. This is supported by a study in South Africa that adolescents become conscious about their bodies and may perceive their weight in a negative way (Gitau et al., 2014). Another study had suggested that female adolescents are sensitive about their body size and may face a social pressure and associated body dissatisfaction with risk for eating disorders (Wong et al., 2014). The findings of another study by Tsai et. al. (2011) showed that there is association between adolescents being teased and disturbed eating behaviors.

In bulimia & food preoccupation subscale items, the current study revealed that the highest mean (.7647±1.0777) was for "I Have gone on eating binges where I feel that I may not be able to stop". This could be contributed to the attractive advertisement of food during the female adolescents favorite television show. In addition to food flavors in restaurants that hard to be obtained in the house which results into visiting the restaurant multiple times. Also, the psychological condition of adolescents can have an impact on their eating attitudes. This supported by a study revealed that disordered eating behavior was higher among female adolescents with depressive symptoms (Fortes et al., 2014).

It was found that the highest mean (1.718±1.2461) was for "other people think that I am too thin" under oral control subscale items. The findings suggest that female adolescents are under social pressure especially that they are maturing and nearing from marriage age. Parents especially will pressure their adolescent daughter to eat and comment about her body weight and shape. Also, societal pressure especially by the older generation who has an idea that the girl with thin body will not get married and the chubbier the girl the more beautiful the girl is.

There is a positive significant relationship between Body Mass Index and the mean of EAT-26 total scale and the three subscales. Similarly, high BMI of female adolescents was associated with risk for eating disorders in Brazil (Fortes et al., 2014). Another study, revealed that there is an association between obesity and eating disorders among adolescents (Musaiger et al., 2013) & (Tsai et al., 2011). The findings of previous studies had associated overweight with risk for eating disorders (Wong et al., 2014 & Tam et al., 2007).

The current study found a significant negative relationship between the mean participants' age and the mean of dieting subscale and oral control subscale. It means the younger participants are more at risk for eating disorders. On the other hand, Tam et al., (2007) found that eating disorders and age had no significant relationship and Wong et al., (2014) reported that age was not a causing factor for abnormal eating behaviors.

Conclusion / Recommendations:

In conclusion, the current study highlights the importance of eating disorders screening among adolescents to identify who have disturbed eating attitude and at risk for eating disorders. Further studies are needed either to modify the current instrument or to develop a new culture specific instrument. Development of a community based preventive measures to help adolescent to have health eating attitude and habits is recommended.

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Educational needs of families of children with Attention Deficit- Hyperactivity Disorder referred to Psychiatric Centers in Tehran

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Abstract:

Background and aim: According to changes in lifestyle cause by disease, identify the needs of families with sick children, is one of the main indicators of families' satisfaction with health care services. The aim of this study was to survey educational needs of families of children with Attention Deficit- Hyperactivity Disorder referred to Psychiatric Centers in Tehran.

Material and methods: This descriptive study was done on 200 parents of children with Attention Deficit- Hyperactivity Disorder who referred to Imam Hossein hospital and Rozbeh hospital. Parents were selected through a purposive sampling method. A researcher-made questionnaire was used to collect the data that was validated and made reliable. Data analyses were done via SPSS (ver.18) and descriptive and inferential tests.

Finding: According to this research finding, 69.5 percent of parents had high educational need. 23.5 percent of parents had moderate educational need .Seven percent of parents had low educational need. Mean of educational need was 79.64. Maximum mean of educational need was in child care scope (4.23±0.81). Minimum mean of educational need was in nature of the disease scope (3.65±1.10). There was no relationship between the parent's age, number of children, parents' education level, parents' gender, history of mental illness and chronic physical illness, and parents' jobs and scores of educational needs.

Discussion and conclusion: According to the results of this study that showed 69.5 percent of parents of children with Attention Deficit Hyperactivity Disorder have high educational needs, so it is recommended that training programs run through the mass media and health care centers for raising awareness and improving performance.

Key words: Educational need, Family, children with Attention Deficit- Hyperactivity Disorder.

Educational Intervention for Patients with Atrial Fibrillation

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Abstract

It is estimated that there will be more than 15.9 million people suffering from AF worldwide by 2050. To further explore the effectiveness of educational intervention with social support on lowering the uncertainty in illness, this article presents a proposal of a care program with phone follow up among patients with AF. The uncertainty of the illness is found to be appraised as a danger among individuals with AF which brought them anxiety. the effects of educational interventions were mixed and the effects might not persist. Studies also showed that specialized care for patients with AF resulted in less emergency department visit and less hospitalizations AF patients with greater social support experienced significantly less uncertainty in illness while their educational level was not associated with uncertainty. Nurses were recommended to maximize patients' perceived social support when intervening uncertainty in illness among AF patients. The proposed project concerning educational interventions with social support through group sessions and phone follow up should result in better patient outcomes.

Keywords: *atrial fibrillation; educational intervention; social support; uncertainty in illness*

1. Introduction

Atrial fibrillation (AF), being the commonest sustained cardiac arrhythmia, affects over 70,000 patients in Hong Kong [10]. From an epidemiological study, there are 4 millions Chinese suffering from AF in Mainland China [39]. With the aging population, it is estimated that there will be 5.2 million men and 3.1 million women aged over 60 with AF by 2050 in China [34]. It is also estimated that there will be more than 15.9 million people suffering from AF worldwide by 2050 [30]. AF can be existed in people who appear healthy but with lower than normal quality of life (QoL) [19]. The QoL of patients with AF was found to be significant worse than post-myocardial infarct patients and comparable to congestive heart failure [9]. Patients with AF also rated their QoL significant worse than patients with other arrhythmias [3]. AF increases the risk of ischemic stroke by about fivefold which also lead to

more severe stroke with greater disability. The risk of heart failure is also higher among patients with AF [20].

An international survey done by AF AWARE group found that one in four physicians experiences lack of time to educate the patients with AF. At least one-quarter of patients does not understand and cannot explain AF [1]. Many patients had fears of heart attacks or dying due to misunderstanding symptoms [8].The uncertainty of the illness is found to be appraised as a danger among individuals with AF which brought them anxiety [17]. The structural provider of social support and education in the proposed program with credible authority should help reducing patients' anxiety through adaptation of the uncertainty. This also improves patients' quality of life [31]. According to previous studies, the effects on patient's AF knowledge and clinical awareness through educational interventions were mixed [7, 21 25].
To further explore the effectiveness of educational intervention with social support on lowering the uncertainty in illness, this article presents a proposal of a care program with phone follow up among patients with AF.

2. History of Educational Interventions on AF Patients

As aforementioned, the effects of educational interventions were mixed [7, 21, 25] and the effects might not persist [15, 16, 24, 26, 29]. Studies also showed that specialized care for patients with AF resulted in less emergency department visit and less hospitalizations [12, 13, 33]. The patients also had a better time in therapeutic range of INR and a higher level of satisfaction [28].

2.1 Educational Intervention

Brief educational intervention with an information booklet did not significantly improved patient's knowledge of the risks associated with AF. It had little effect in increasing awareness of the benefit of stroke prevention and the bleeding risks associated with anticoagulants. It did not significantly affect the patient's perception on AF. However, the information booklet significantly improved patient's knowledge of the target INR range and factors that may affect INR levels. Further research is required to determine the patients' perceptions on and the optimum type of educational intervention required to educate patients about such complex conditions [21].

It was suggested that many patients, even highly educated ones, have considerable difficulty in understanding quantitative information. Study also showed that patient education with narrative evidence using patient anecdotes may be more effective than statistical evidence for some patient outcomes. A common example of narrative health messages are the sharing of health experiences from friends and family members. The mass media also provide the public health narratives through simplifying issues while increasing vividness, authenticity and audience interest. Narratives helped in facilitating information processing, reducing counter-arguing, facilitating observational learning, and influencing perceptions

susceptibility and social norms. AF patients may benefit from periodic education with narrative evidence [25].

According to the Canadian Cardiovascular Society Access to Care Working Group and the Canadian Heart Rhythm Society, the acceptable patient access time in out-patient clinic on management of AF should be less than 4-12 weeks, depending on the urgency of the need for consultation. A small scale trial on a model of AF clinic focused on initial contact and patient education by trained nurse clinicians showed that patient wait less time to have their AF managed. It also resulted in less emergency department visits and less hospitalizations [12].

Many patients had fears of heart attacks or dying due to misunderstanding symptoms [8]. Nurse-led AF clinic focusing on patient education, reassurance, prophylactic measures guided by electronic decision support based on the guidelines and the time spent with patients were the key of success in improving management of AF. Thereby decreased cardiovascular hospitalization and cardiovascular death [13].

The adherence to recommended management of AF often hindered with patients' poor knowledge of AF and its treatment. The TREAT trial aimed at improving patients' adherence to oral anticoagulant through educational intervention. The intervention involved one-off focus group session (1-6 patients) utilizing an "expert-patient" focused DVD, educational booklet, self-monitoring diary and worksheet. It is showed that a theory-driven educational intervention significantly improves time in therapeutic range of INR among AF patients taking warfarin. As patients had their knowledge of AF improved, the perception of treatment harm reduced. This in turn improved treatment compliance and reduced adverse clinical outcomes [7].

A multidisciplinary AF clinic, consisted of electrophysiologists and pharmacists, was designed in California aimed at reducing AF-related hospitalizations and stroke. The clinic involved individualized treatment plan, patient education, medication management and follow-up care. AF Patients were educated about the treatment options, anticoagulation therapy, dietary instructions, rate and rhythm control strategies, intervention options, dose titration, treatment of AF-associated risk factors, and management or prevention of common adverse drug effects. It was showed that managing AF patients in specialty clinics reduces AF-related hospitalizations and stroke [33].

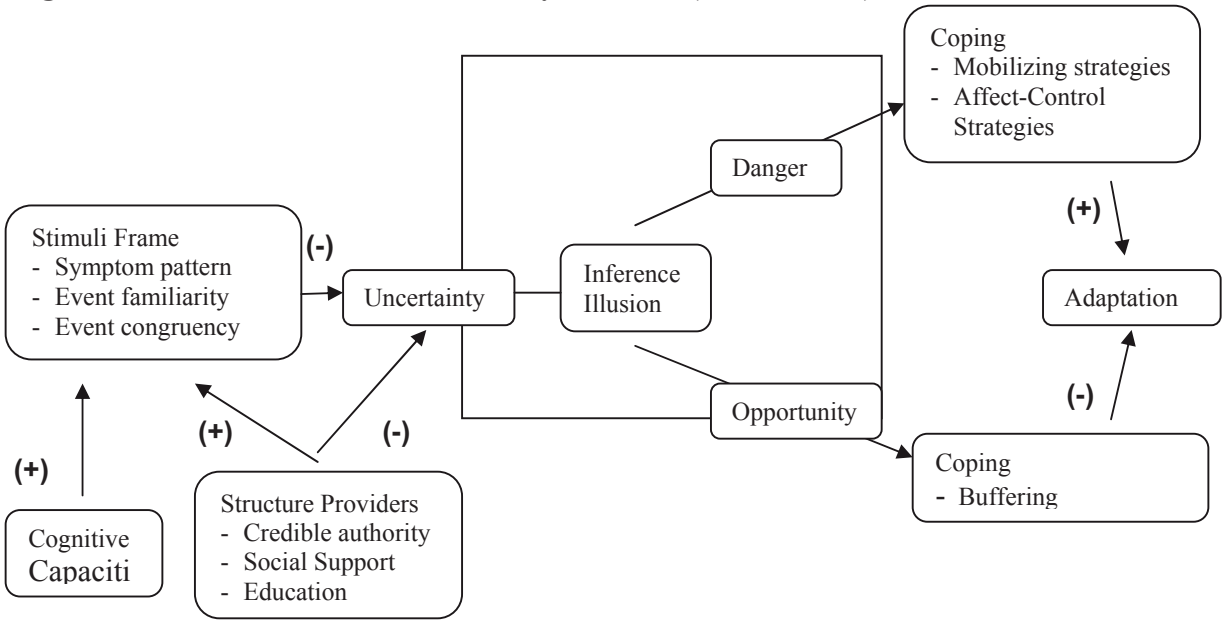
A structured nurse-led educational approach aimed at improving AF patients' knowledge on anticoagulant therapy was adopted in a regional hospital in UK. The use of an educational video and structured counseling significantly improved patients' knowledge at hospital discharge and at 3 months post discharge. The patients also had a better time in therapeutic range of INR and a higher level of satisfaction [28].

2.2 Uncertainty in Illness

According to a Korean study, AF patients with greater social support experienced significantly less uncertainty in illness while their educational level was not associated with

uncertainty. Nurses were recommended to maximize patients' perceived social support when intervening uncertainty in illness among AF patients [18].

Figure 1. Model of Perceived Uncertainty in Illness (Mishel, 1988)



3. Study Design

A prospective randomized controlled trial will be conducted. Individuals with non-valvular AF are randomised into two groups for clinical management by a cardiologist or physician (usual care group) or under educational interventional program led by nurse (intervention group).

3.1 Patient

Inclusion Criteria: Individuals diagnosed with non-valvular AF detected on electrocardiogram (ECG) or holter, age over 18 years and capable of providing informed consent who are literate in Chinese will be recruited.

Exclusion Criteria: Individuals with valvular heart disease or cognitive imparited are excluded.

3.2 Intervention

An educational intervention with group sessions on AF knowledge will be provided. Focused-group support and phone follow up will also be provided to the participants in the intervention group.

3.3 Outcomes

1. The frequency of cardiovascular hospitalization will be reduced among individuals with AF under interventional care.

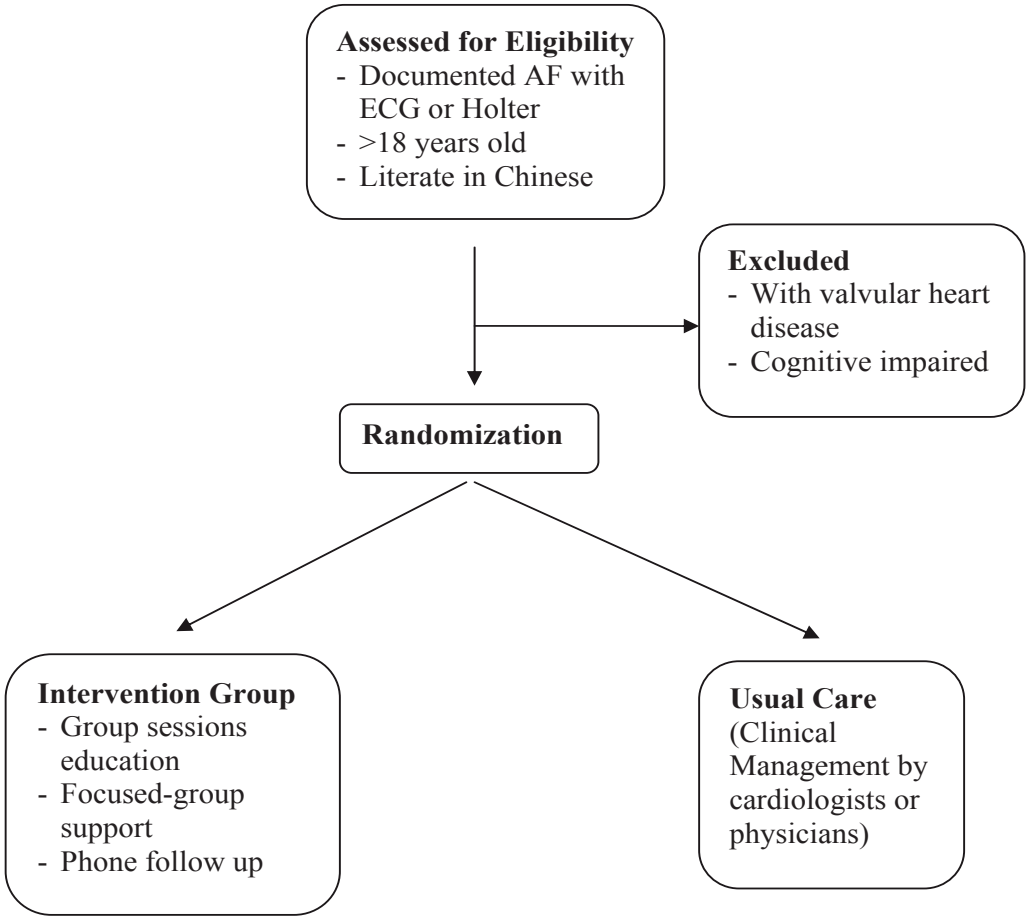
2. The QoL of individuals with AF under interventional care is higher than those under usual care as measured by AF-QoL questionnaire.

3. The knowledge on AF of individuals with AF under interventional care is better than those under usual care as measured by The AF Knowledge Scale.

4. The social support perceived by individuals with AF under interventional care is higher than those under usual care as measured by The Multidimensional Scale of Perceived Social Support.

5. The uncertainty level in illness of individuals with AF under interventional care is lower than those under usual care as measured by Mishel Uncertainty in Illness Scale.

Figure 2. Recruitment Flow Diagram



4. Conclusion

The prevalence of AF is escalating worldwide especially among the Chinese populations. How AF worsen ones' cardiovascular well-being brings about uncertainty of the illness which further lowers the patients' QoL. To my best knowledge, there are scarce chronic care programs for patients with AF using educational intervention with focus group social support around the world. The research studies on social support and uncertainty of illness among patients with AF are also limited. The proposed project concerning educational interventions with social support through group sessions and phone follow up should result in better patient outcomes.

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THE ROLE OF A PSYCHIATRY NURSE IN A FIRST PSYCHOTIC EPISODE

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Abstract

A first psychotic episode is an unexpected and generally horrifying experience for the patients and their relatives. The patient and the family find themselves in a strange and alien environment which they are not prepared for and because of this scary, chaotic period they may exhibit irrational behavior. In this acute phase the psychiatry nurse who is an important member of the healthcare team assumes a key role in means of providing the patient and the family with care, counsel and education. Any intervention and education implemented by the psychiatry nurse before the illness progress into a chronic state add to the chance of preventing the relapses and lessens the frequency of the hospitalization.

Keywords: *first episode; psychosis; psychiatry nursing*

1. Introduction

A first psychotic episode is an unexpected and generally horrifying experience for the patients and their relatives. The young patient finds himself as a member of a group in which he has never identified before, a group marked and isolated by others (1). For the family of the patient, rejection of the illness, despair, uncertainty about the future, guilt caused by illness, and uncertainty of how to act toward the patient are the most common observable attitudes. (2). In this acute phase the psychiatry nurse who is an important member of the healthcare team assumes a key role in means of providing the patient and the family with care, counsel and education.

2. A first Psychotic Episode and Psychiatry Nursing

Contemporary specialist psychiatry nurses work together with the individuals, the family and the society in order to evaluate psychological needs, to diagnose and to implement nursing care. Protection of mental health, screening and assessment, management of therapeutic environment, helping patients with care activities, case management, psychological education, crisis intervention, and counseling are the main roles for the psychiatry nurses (3,4).

Patients with impaired ability to evaluate reality, with severe psychotic symptoms and severe introvert patients with deteriorating self care abilities, need support and help for all their responsibilities (5). These needs are addressed by the psychiatry nurses by evaluating the patient along with the family and his or her environment (4).

In the treatment of the first psychotic episode the main focus is to get rid of the symptoms rapidly and without much effect to the patient's life (6). In the acute phase, the main objectives of the psychiatry nurse are to take care of the basic needs of the patients like ensuring the safety of patients and his /her environment, nourishment, sleep, personal care, to implement the medication and taking patient's history (4). During the first psychotic episode an accurate diagnosis is said to be more important than choosing a treatment method. Psychotic mood disorders and other psychotic disorders caused by different reasons like substance abuse can be easily confused with schizophrenia (1,6). In this early stage a psychiatry nurse has a very important role in taking an accurate history of the patient. At the same time, it is stated that psychosocial treatments for the patients and education for the patient and the family are at least as important as medication. It is observed that in the psychotic disorders, early stages of the illness are the most appropriate time for the early interventions that affect the long term course of the disease (7,8).

Studies show that in the treatment of mental disorders, treatments that exclude the family are insufficient (2,9). Identification of the difficulties of the patient's family as well as the difficulties of the patient and providing support are the main purpose of the psychiatry nurse. When caregivers feel supported, they can deal more easily with the problems which are created by the patients or with the problems that they think are created by the patients. Only working with patients without providing family support, produce limited results (10).

Various methods can be used by the psychiatry nurse when approaching patients and their families. These include home visits, meeting with the families of the hospitalized patients, individual family meetings, family therapy and family education. Among the psychosocial treatments one of the methods that can be used by the psychiatry nurse is psychoeducation (3). Psychoeducation is an educational program for patients and their families that focus on the disease etiology, clinical features, treatment, and outcome of the illness and the transfer of contemporary knowledge and experience (7). When encountered first time with the illness, the health education needs of the patient and the family are very important because it affects the long term course of the illness. Studies indicate that most patients and their relatives need health education on the subjects about general information about the illness, recognizing the signs of illness and coping with these symptoms, communication and social relations (7,8,11). Early interventions by way of education at the first stage of the illness are very effective at changing the variables that affect the prognosis of the illness. The level of expression of emotions, interaction between family members and the role of the patient in the family are some of the examples of these variables (12,13).

The goals of psychoeducation for the patient and the family are: to decrease the relapse, to improve patient functionality, to improve family functionality, to ensure compliance with co-operation and treatment. With psychoeducation family members can recognize the early symptoms of the illness, they can form a treatment plan and implement it, and also they can regulate family interaction (14).

The most appropriate time to take the family into psychoeducational family gatherings is reported to be the acute phase of the illness. When the patient's condition is serious families are more motivated to build relationships, to continue relationships, gather information, search trust and ask questions. It is easier to solve the problems if the education of patient and the family includes: definition of the illness, causes of the illness, treatment options, specifics of the medication, communication and relation building skills, coping methods and stress management and support systems (8,12). The psychiatry nurse should be aware of the fact that faster and more positive response to treatment in the first period of the illness is important and act accordingly. It is possible that the patient may fail to continue his/her medication properly or stop it altogether. It is especially important that the

patient and the family should be informed about the duration of the drug treatment (7).

Studies show that families who receive education better accept the illness, provide social support for the patient, and they are more in harmony with the patient. As a result, hospitalization frequency and duration lessens (15,16).

3. Conclusion

A first psychotic episode is a serious crisis for the patient and the family (1.11). In the psychotic disorders loss of mental faculties generally occurs and it extensively affects in material and moral ways not only the patient but the family too (17). It is obvious that any intervention at the early stages of the illness without the illness getting chronic affects the course of the illness. Any explanation coming from the psychiatry nurse may have life-changing consequences for the patient. Implementation of intervention and education by the psychiatry nurse in this stage, where the chance of success for treatment is maximal, are very important at preventing the relapses and lessening the frequency of the hospitalization.

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THE EXPERIENCES WITH NURSES TRAININGS CONCERNING PREVENTION OF VIOLENCE IN THE CZECH REPUBLIC IN YEARS 2010-2013

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Abstract

The aim of this paper is to analyze the results from the implemented projects and trainings which were aimed to minimize violence in health care area in CR (the Czech Republic) in years 2010-2013. The paper describes the results and experience from the communication trainings which were gained within the projects: CR lacks the support of government agencies so as employers and research on the issue, medical staff are not professional enough in communication, there are more requirements for the quality of lecturers; there is no existing general system of monitoring of violent incidents; there is no relevant education at schools. The article contains also new general ways how to resolve mentioned problems. These results include the special mini project where were educated 550 staff members in the health care area in a short time period and to teach them key skills for how to approach the aggressive patients—50.6% respondents used successfully the gained skills in their practice (negotiation with patients, aggressive related); 42.7% respondents also used successfully the gained skills in their private life. It was find out that with the used skills the courage by conflict resolution was created.

Keywords: *violence, CR (the Czech Republic), communication, training, prevention.*

1. Introduction

CR (the Czech Republic) has a problem with violence in the health care area. CR lacks the support of government agencies, employers and research on the issue. Gradually, however, efforts have begun to emerge, aiming to minimize violence in health care. In the CR, several projects have been undertaken to minimize violence and the experience from the projects suggest deficiencies in staff training and the importance of educating employees and trying to minimize violence in health care. The aim of this paper is to analyze the results from the implemented projects and trainings. The author is a medical employee and communication lecturer. He prepares improvements for staff members in the health care and their patients in the CR on the basis of an analysis and comparison of the relevant projects. The research on violence is mostly focused on psychiatric hospitals and ICU (Intensive Care Units) and these data are transferred to non-psychiatry wards automatically (general wards, non-intensive wards). Likewise, the preventive and strategic arrangements are transferred from the ICU and psychiatry wards to the general wards and non-intensive wards. But the general wards are specific in a different way (1). The violence seen most often in the general wards is based on escalated negative emotions which get out of control. This type of violent behavior could be de-escalated by proper communication and specific approaches. The health care workers in CR are not trained and skilled enough in such approaches. This is due to the fact that the education at schools is not sufficient (2). Three projects (2010-2013) have been implemented in CR for education and prevention of violence in the health care area. The paper describes the results and experience from the communication trainings which were gained within the projects.

2. Methodology

Data analyze of existing surveys in CR on the topic violence in the framework of provision of care in health and social system. The subchapters show the evolution in concrete periods.

2.1 Period 2004 - 2010

In 2004, research organized jointly by the Ministry of Health and IHPE (Institute of Health Policy and Economics) set out to determine any facts concerning violence in the Czech health care system. The research was planned to continue to the year 2009, but the IHPE was closed down, and so it took place for only two years. During those two years, an empirical quantitative research was carried out among 675 employees in the health care in the CR (3).

The study found that violence in the healthcare system in the CR is a serious problem. 42% of staff members had experience of verbal violence and 13% staff had

experience of physical violence. The incidence of physical violence was the highest in comparison with other countries (Thailand, Bulgaria, Brasil, Libanon, and Portugal). The study contained also qualitative interview with patients who were victims of violence to the

medical staff, such as patients who were coming for operations were attacked by medical staff

via verbal violence (non-professional communication, arrogant behavior) (4).

This fact was confirmed by means of another qualitative study in 2006 which was aimed to the violence in the emergency medical services in CR. Interviews were performed with the managers of emergency medical services in the CR. The findings are as follows: The verbal aggression is present in every third intervention; physical violence is present in 13% of all interventions; and 15% of violent incidents were due to the behavior of the staff of emergency medical services in the CR (when the staff provoke potential aggressors to the attack due to non-professional communication) (5). Within the above-mentioned time, other studies about violence in the health care system in the CR were carried out. Unfortunately, these research undertakings failed to contain valid data and the numbers of respondents were too few.

We can determine the general points in researches in the years 2004-2010:

(1) Violence is a serious problem in the healthcare system in the CR;

(2) Verbal violence prevails over physical violence;

(3) Absence of both central and local data on violence in the healthcare;

(4) The last surveys included a low number of respondents;

(5) Violent incidents are partly caused by medical staff via their non-professional behavior;

(6) An absence of education in schools.

2. 2 Period 2010-2013

Czech-Moravian Confederation of Trade Unions started the project called Prevention of Violence in Health and Social Systems in the CR in 2010. It was a quantitative study covering 1,500 employees, which found that violence in the workplace was experienced by 31% of employees (health and social workers) in the previous year. The physical violence was

admitted in 17% and the psychological violence was admitted in 41% (mobbing, sexual harassment, bossing, and racial harassment). The numbers of violent verbal attacks was similar to the numbers of violence attacks shown in the projects of the year 2004. The incidence of physical violence was even higher. The changes were also in the approach of the management of hospitals and social areas—60% managers adopted the measures against the occurrence of violence at their premises (measures associated with the safety and occupational health screening and patient). Unfortunately, there were still persisting deficiencies in the work environment, human resources development, increasing staff numbers, or staff training in communication skills. Even though six years passed from a similar project, the main problems remain the same: That is overworked staff, non-professional communication, and unawareness (6).

Unlike in the first project in 2004, the medical staff wasn't educated practically. Generally, 1,004 staff members in this project, so-called key people for violence in the health care, were educated. Every person was educated during five days: one day in the management of violence, two days in communication skills, and two days in physical self-defense. In this project, an idea to create 14 violence prevention teams who should try to minimize violence in individual regions. Unfortunately, this activity currently works only in one region (Pilsen). As time went on, it was found that the education in this project was not effective. The selection of so-called key people did not have any criteria and the five educating days were not effective because many of the 1,004 persons didn’t repeat the knowledge gained. The lecturers weren’t experts. The lecturers were people from different workplaces and departments, minimum of them worked in the immediate contact with patients. Some educating days were aimed to prevent violence a lot but some educating days weren‘t aimed at violence at all. Despite the criticism, this project was coming to a greater offer of communication trainings for health care professionals throughout the country, especially in the health care area. Most of the courses were unfortunately one-off, and if they are not repeated, the knowledge and training aren’t beneficial for practice.

In the years 2011-2013, another big educational project for medical staff in CR was performed. The organizer of the project was the Ministry of Health plus Aesculap Academy. The project was unique in its practical approach. It was the only educating project without quantitative research, but a great emphasis was placed on the quality and experience of the lecturers. One of the topics of education was the safety of staff members in the health care area. 1,948 staff members in the health care were educated in 26 seminars and nine conferences in total. A mini project was included in this project. 550 health staff members

from the hospital in the town of Jihlava were educated in the approach and communication with aggressive patients or their relatives (7). Nurses were educated during 14 seminars (One seminar was for max; 40 staff members and took 120 minutes). The main goal of this mini project was whether is possible to educate staff members in the health care area in a short time period and to teach them key skills for how to approach the aggressive patients. The evaluation was done after 12 months from start of the mini project. Seminars were unique not only because of evaluations but also with the own contain (impact by experiences, influence by emotions and infinite number of real situations). The feedback of questionnaires was 42%. Main results: 50.6% respondents used successfully the gained skills in their practice (negotiation with patients, aggressive related). 42.7% respondents also used successfully the gained skills in their private life. It was find out that with the used skills the courage by conflict resolution was created. 70% respondents plan to use the skills in the future.

The development of violence prevention in the Czech Republic in the year 2010-2013 (based on the projects):

(1) The researchers are focused on a greater number of respondents;

(2) The frequency of violent incidents stays the same;

(3) Medical staff are not professional enough in communication;

(4) Conferences and seminars are more focused on the professionalism in communication;

(5) There are more requirements for the quality of lecturers;

(6) There is no existing general system of monitoring of violent incidents, the medical staff aren't motivated to report any possible incidents;

(7) There is no relevant education at schools;

(8) There is no continuous repetition of the knowledge and skills gained;

(9) If the communicational education is aimed to presentation model situations with real facts then influence of educational course impacts positive experience and to enable change of our behavior.

2. 3 The Planned Research

Currently, a small project is running in CR which is targeted only on Prague. Prague wasn’t included in previous projects. The project is targeted on TPV (the third party violence) (medical staff, patients, and relations). The main coordinator of project is the Trade Union, and the project takes place with a considerable support by Norway. The main aim of this project is to train 200 medical staff. These people should be educated to become lecturers and

educate other people after the project will be finished. The project should be realized without deficiencies shown in previously projects. There was created a five member team of experts—a psychologist with experience in TPV, a lecturer of communication and researcher TPV in CR, a lecturer of self-defense, and the trade union representatives. The psychologist and an expert of TPV are incessantly supervising the preparation of trainings for 200 medical staff (includes 10 organizations provide health or social care). The project started in September 2013 and will end in October 2014. The training will be organized like the interactive seminars. These seminars will prepare medical staff for managing violence incidents in the future. The aim of the project is to train 200 medical staff which should be well-orientated in the problematic of TPV and they should help to deal with the violence incidents at their workplace. Organizer of the project currently plans to create the interventions teams which will be specially educated (Two members from ever organization will be educated in approach of monitoring incidents in their own department and of provide effective feedback after violence incidents).

Medical staff in the project will be trained during five days:

(1) Three days: communication—verbal self-defense, victimology, analysis of TPV incidents;

(2) One day: management of TPV;

(3) One day: physical self-defense —defensive approach, light techniques.

The preparations for this project have revealed several shortcomings that exist in the TPV situation in CR:

(1) Deficiency of experts and explorers in this field;

(2) Absence of an institution for TPV;

(3) Ignorance of procedures for dealing with TPV at departments;

(4) Low level of national monitoring of TPV;

(5) Measures for TPV are often only temporary.

2. 4 New General Way?

Another great contribution for the improvement of mentioned situation should be a dissertation work on this topic. Since 2004, the violence in health care in the CR occurs only in the context of short studies or final reports of the projects. Most of the reports are only for informative purposes—the number of attacks and forms of attacks. An elaboration attacks

lack in the studies, also missing test cases and ways how to solve of them. There is an absence of reflection about training days for TPV, many of them have a design such a one day course. A major drawback is the establishment of a center for the capture of violent incidents—their subsequent analysis by experts and draw conclusions. All of these shortcomings will saturate dissertation, which aims to create a manual for management violence in the health sector in the CR.

Based on the analysis of the foreign literature and practical experience of relevant experts, recommended procedures will be produced to monitor and minimize the problem. There will be also created how to make an effective research, and how to make an effective education for medical staff in this problematic area. We try currently to create system for monitoring violence incidents via special website (currently is under construction) in CR. This is the main point for the optimal start in this problematic. We can present the case interpretation from this system and then we can give several solutions for preventing and solving the situations.

3. Conclusion

The violence in CR is a serious problem. There were seen many situations of non-professional behavior on the side of the medical staff. There is an absence of effective education in approach to aggressive patients and their relations in CR. The professional staff lacks professional approach, the members of the management avoid solving violent situations, and the examples from foreign countries are rarely followed. The projects offered brought forward temporary solutions only and serve as a plaster on the wound rather than a cure. The researches over the past 20 years have shown a positive contribution of education and communication skills training for health professionals. The courses have measurable results and nurses themselves considered them as beneficial. Acquired behavioral skills increase the patient‘s satisfaction with how the patients learn and understand health care.

As it turns out that any form of repression does not provide qualitative and expected changes, the only possible way to cope with violence is to re-seek practical training in communication with patients and colleagues. An essential part of such trainings must, however, provide feedback, medical personnel must be aware of how to “see” his patient.

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REFLECTING ON THE DEVELOPMENT OF A LOGIC MODEL FOR AN 'EARLY YEARS' PROGRAM TO REDUCE HEALTH INEQUALITIES IN NHS LANARKSHIRE, SCOTLAND[1]

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Abstract

A simple logic model was developed as a planning and evaluation tool for a program to reduce health inequalities in NHS Lanarkshire in Scotland. The logic model developed was a comprehensive and graphic way to identify the relationships among the resources available to operate the program, plan activities, and identify the changes or results hoped to achieve in the short, medium and long terms. This paper presents the purpose and functions of the logic model, the planning and development of the logic model and reflects on the usefulness of the process in team building, partnership working and communication within the 'early years' team. Limitations perceived included the speed of implementation in practice, the number of ongoing activities, the format of the logic model and the changing priorities for resources.

Keywords: *logic modelling, logic model benefits, logic model limitations, evaluation tool*

[1] UWS/NHS Lanarkshire collaboration.

1. Introduction

Health inequalities exist across the world and are often closely linked with degrees of social disadvantage. The fundamental drivers of health and health inequity relate to where people are born, grow, live, work and where they age [10,19]. This exists both between and within countries and leads to premature death and people living restricted lives [2,19,20]. In Scotland, health inequalities remain a major challenge with every generation, past and present, having experienced poverty and inequalities [7,11,13]. Scotland has now set a clear challenge to reduce poverty, and social and health inequalities across Scotland. The key theme is to tackle and reduce inequalities to ensure that every child and young person has equal access to opportunities and health improvements [11,12,13]. This is supported by a series of national guidelines and policy drivers to focus the development of relevant 'early years' services [14-18]. In October 2012, NHS Lanarkshire, in collaboration with the University of the West of Scotland, launched an innovative program to address health inequalities in the 'early years'. This has been the most challenging and ambitious approach in the redesign of service provision across Lanarkshire. The magnitude of the approach was recognized by the team who anticipated a long-term commitment to changes in behavior and outcomes.

The program team developed a simple logic model as a planning tool to evaluate the effectiveness of the program. This paper presents an overview of the development of the logic model and reflects on the usefulness of the process in team building, partnership working and communication within the 'early years' team.

2. The Logic Model

The Logic Model is a tool that has been commonly used for several decades to clarify and describe the effectiveness of a program, project or initiative within an organization [1,5,8,9,21]. It is rooted within theories of change and is a relatively simple graphic plan reflecting how and why a program will work [1,4]. It is defined as being a systematic, and visual way to present and share understanding of the relationships among the resources available to operate a program, plan the activities, and the identify the changes or results hoped to achieve [1,5,8,9]. The visual step by step plan is often supported with additional narrative to provide further explanation of the components of the plan [1,4].

The logic model is often described as a road map showing the route travelled to reach a destination. At various points on the map, progress needs to be reviewed with adjustments made as necessary. In this respect the logic model is a flexible live tool. Most importantly, a logic model keeps participants moving in the same direction by providing a common language and point of reference. There are many types of logic models with versions used for different purposes with the most common formats being flow charts, maps, or tables. The different range of formats can be located on the NHS Scotland website [21]. NHS Scotland encourages regional health boards to construct logic models for major health outcome objectives to ensure that objectives contribute to the ultimate improvements in national Health Goals.

3. Functions of Logic Models

The logic model has three key functions including effective communication, clarification of logical connections, and the identification of performance measures [6]. The tool can be used effectively to systematically convey the often complicated relationships among services and other contributing factors. It is also a succinct way to keep all of the health services committed to the ultimate health status goals for the population [6]. The

graphics often used in logic models are useful for *reducing* an overwhelming volume of information down to relevant and critical 'bite-size' chunks of information necessary for a particular purpose [6]. Individuals in health using this model, keep focused on both their own immediate achievements and also the ultimate goals. In addition to communication, other key uses of the logic model reported include clarification, management, evaluation planning, the determination of evaluation questions, documentation, as well as problem solving [3-8].

Team working is enhanced through developing logic modeling [3]. Both program developers and program evaluators need to be engaged in the process with this effective team involvement having the outcome of promoting collaborative learning [3,6]. This learning evolves when team members are engaged in discussions about development of the model, respective meaningful definitions and coming together in a consensus about the building process of the model [3,6]. Timing is also important [3]. It has been argued that while early development of a logic model may be beneficial, further contribution is also important at any time, if it is relevant, well thought through and that all individuals involved understand the iterative nature of the logic modeling process [3,6]. The logic model should always be revisited and revised as program demands irrespective when the model was initially developed [3-8]. This ongoing revisiting the model pays specific attention to the fidelity of program implementation, progress toward goal achievement, and outcome assessment.

4. Planning Process

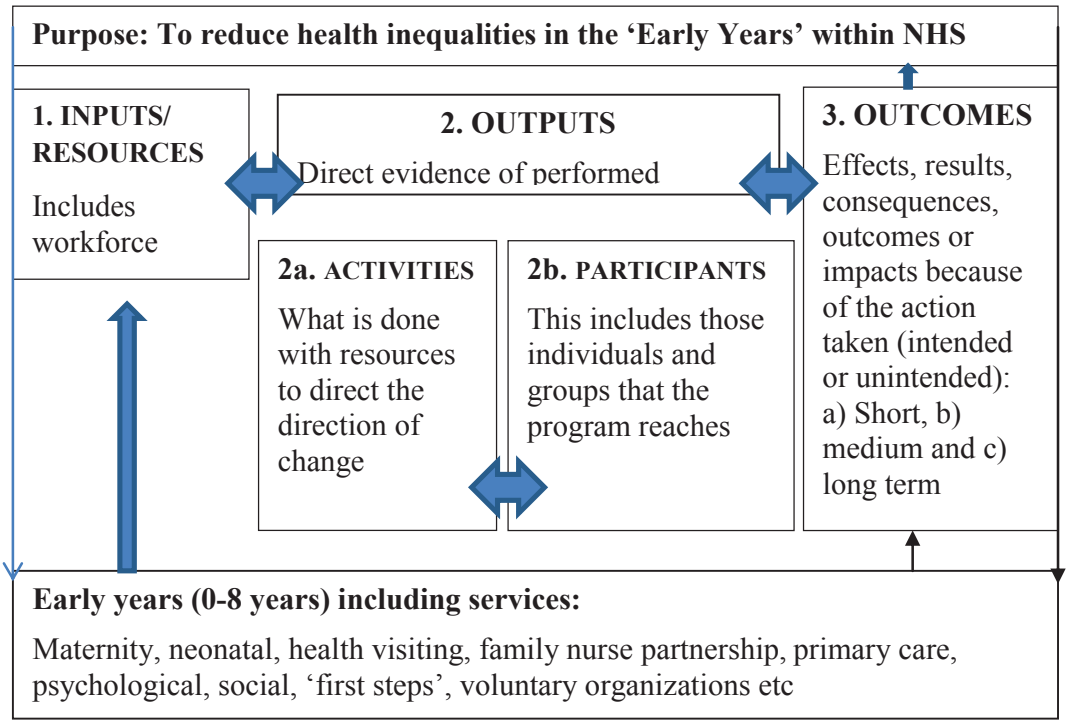
Initially the team had to spend time to determine the implications of meeting the aims of the program. This included the resources available, workforce issues to provide the redesigned services planned and overall an explicit understanding of the challenges ahead. This initial process helped the team to focus on the full scale of the program in hand as well as the component parts. Following initial training, the team proceeded to construct and develop a simple linear and graphic logic model. This process involved a series of meetings of discussion, commitment, and reflection with the tool revisited on a regular basis.

The basis of the logic model was to provide a succinct plan of activities, outcomes and evaluation for the program to reduce health inequalities in babies and children (0-8 years) in line with the guidance from the national 'early years' policies and guidelines [14-18]. One of the benefits of logic modeling is that it allowed the program team to question 'the logic' and to identify things that might go wrong. An impact assessment was also conducted on the final program with input from the NHS Lanarkshire Equality and Diversity Officer.

Assumptions and external factors were all carefully considered in the planning phase. This related to the following aspects - the program; the size, relevancy and significance of the problem; the availability, reliability and sustainability of the resources; the outcomes as whether they were realistic, measurable and achievable; and the potential risk factors occurring over the duration of the program for the short term goals and beyond for the medium and long term outcomes.

The basic elements of the logic model as a structured, framework for the evaluation adopted for this 'early years' program is presented in Figure 1. Reading the logic model from left to right provides the chain of reasoning and the connection amongst 1) inputs/resources, 2) activities/participants- outputs and 3) outcomes. Two alternatives include context and impact and relate to intended or unintended changes occurring at various levels.

Figure 1 Basic elements of the logic model used for the 'Early years' program



The following issues were addressed in the early planning stages.

- Clear identification of the scope of the program's influence and determine the current situation where the impact of the program was intended.
- Setting logical and related short, medium and long term outcomes reflecting the changes required at designated time periods by considering what the situation will look like when the desired situation or outcomes are achieved.
- Identification of the services and behaviors needed to change for the range of outcomes to be achieved.
- Identification and mapping of the knowledge or skills that people need before the services and behavior would change.
- Identification of the range of activities (minor to major) needed to be performed to cause the necessary learning and situational changes.
- Determining the resources required to achieve the desired outcome which also took account of the adequacy of resources available and what would be required to proceed as planned by the Organization.
- Ongoing review and validation of the logic model by the Program Steering group.

5. An Overview of Building this 'Early years' Logic Model

Reading left to right along 6 columns:

Column 1: Inputs → Activities → **Column 2 Outputs** → Participants → **Column 3 Outputs** → **Columns 4-6** Short, medium and long term outcomes

Inputs: this included everything invested in the program or will be brought to the program.

- Details of NHS Lanarkshire workforce, input from the university, primary care, local authorities, third sector (Voluntary).
- Funding streams though Best Possible Start, the Refreshed Framework for Maternity Services, Maternal and Infant Nutrition, Family Nurse Partnership etc.
- National strategies for maternity, health visiting and maternal and infant nutrition [14-18].
- Parenting strategy, Scottish Government targets for antenatal access to services and evidence based practice.

Outputs: Activities related to what the program does and who it reaches.

- Develop safe and effective person-centred universal and vulnerable families pathways from preconception to age 8 years.
- Implementation of the 27-30 month universal child health review [18].
- Implement GIRFEC practiced model appropriate clinical intervention / requests for assistance and notification of concern [17].
- Provision of tailored, accessible, and asset based support, information and advice to affect behavior changes.
- Implementation of the Family Nurse Partnership Programme.
- Expand and develop the First Steps Programme.
- Review and develop workforce knowledge, skills and capability*.
- Develop and implement appropriate IT and data collection systems to facilitate regular and systematic measurement of improvement and outcomes.
- Undertake research to further develop the midwifery/neonatal and public health nursing professions.

Outputs: Participants- Who do we reach?

- Women of child-bearing age / Pregnant women.
- Parents/carers of babies, infants and children.
- Children from 0-8 years.
- All health and key agency staff working in the early years.
- Communities / Employers / Third sector.
- 'Early Years' Programme Board.

**The programme has a particular focus on targeting hard to reach/high risk groups including those experiencing: Deprivation/Poverty, Substance Misuse, Obese Parents and Children, Mental Health issues, Domestic Abuse, Homeless, BME communities, Teenage Parents, Looked after Children.*

Figure 2 presents the three columns depicting the short term, medium term and long term outcomes of the 'Early Years' program.

Figure 2 'Early Years' Program Outcomes: short term, medium term and long term

Short term results: *(0-2 years)*	***Medium term results:*** *(2-5 years)*	**Long term results:** *(10+ years)*
Reduction in self-reported smoking during pregnancy	Reduction in self-reported smoking during pregnancy	Reduced maternal, infant and child morbidity and mortality
Reduction in self-reported alcohol consumption during pregnancy	Reduced harm to children from exposure to second hand smoke	Reduction in still births
Reduction in self-reported drug use during pregnancy	Reduction in self-reported alcohol consumption during pregnancy	Reduced inequalities** in maternal, infant and child health
Improved nutrition in pregnancy	Reduced harm to infants from maternal alcohol consumption	***Inequalities in physical, mental, and social health and wellbeing*
45% of babies are breastfed at birth	Reduction in self-reported drug use during pregnancy	****Capability goes beyond competence: it includes the ability to apply knowledge, skills and attitudes across a range of complex and changing settings*
35% of babies are breastfed at 10 days	Reduced harm to infants from maternal drug use	
Early assessment of pregnant women and children using GIRFEC practice model	28% of babies are breastfed at 6-8 weeks	
At least 80% of pregnant women in each SIMD quintile will have booked for antenatal care by the 12th week of gestation by March 2015	Improved parenting capability***	
Integrated care planning and integrated service planning	Improved parent-child attachment	
Improved engagement of vulnerable women and their families	Women have improved control of their reproductive health	
Increased LARC in vulnerable patient groups	Reduced maternal obesity	
Recognition and management of psychosocial need in pregnancy, labour and in the postnatal period	Reduced child obesity	
Every woman is seen by no more than three midwives during planned antenatal care	More infants have healthy birth weight	
Women and their families use information and services to support positive behaviours	Improved mental health and wellbeing during pregnancy and postnatally	
Electronic patient records are in place in maternity, NNU and public health nursing	85% of all children reach all of the expected developmental milestones at the time of the child's 27-30month review by end 2016	
Parents delay weaning to stage of appropriate developmental readiness	Positive experience for women and their families	
More parents choose healthy food and drinks for all the family		
Increased play and physical activity for children		
1:1 care during labour		
Person centred, safe and effective care is provided to all women and families		

6. Planning of Evaluation

An evaluation framework was developed format to assess the program in line with the outcomes of the logic model. The evaluation framework was in three distinct phases:

1) A minimum data set was agreed. This was derived from the key health outcomes and behavior changes identified from the national strategies and guidelines. In total 56 distinct measurable data were identified and where this data could be directly sourced was noted. A data quality officer was seconded from the Quality Assurance department to collate, monitor and report on this data.
2) A program of research related activity was implemented to gain insight into more qualitative data. This included person-centred care, strength based approaches to care, positive parenting, motivational interviewing of professionals to promote lifestyle changes etc. A further stream of activity focused on workforce perceptions and views on support and preparation for implementation of the service redesign.
3) Describing outputs allowed the program team to establish and monitor linkages between the problem or situation identified and the impact of the program on the planned outcomes. Dissemination included: launch events, conference presentations, poster presentations briefing workshops, annual reports and published reports on activities and progress, DVDs, fact sheets, publications and other forms of dissemination. As a result of the program, the good practice of influencing leadership and building research capacity has been monitored and published. Further planned activity is to review the effectiveness of the collaboration and any external situations that affected the program.

7. Reflections on the benefits and limitations of using the logic model

The numerous meetings to tease out the inputs, outputs and program outcomes did stimulate indepth discussion and debate. Several benefits highlighted through this process included further clarity around issues, putting these into context within the whole picture of what the program was trying to achieve, and getting consensus with colleagues and others involved around the intended short. It was important to develop a user-friendly and comprehensive logic model for the program. The logic model was approved by the program steering board. Once approval was obtained then the model became a tool to communicate the plan or road map of activity with others involved in the program.

There is no doubt that team building, and communication was enhanced through this planning process. This included strengthening partnerships with other professions and services. The program's team perceived benefits of developing and applying the logic model are summarised in Figure 3. Many of these benefits support the well-established findings previously highlighted from similar papers on using logic models [1,3-6]. The logic model also acted as a learning tool. A range of activities had to be implemented in clinical areas to set the course of action to meet short term outcomes. This involved the workforce developing new skills and knowledge, promoting opportunities for leadership, and building research capacity to both integrate evidence based practices from prior research and to contribute new findings from studies. The logic model has already been clearly recognized as being a powerful tool for learning, critical thinking, and problem-solving.

It was also found that the logic model was consistently used as a reference document to keep the program team focused and reminded of the initial agreement with managers and stakeholders. The tool was revisited and refined several times over the duration of the

program in light of issues arising that influenced the plan. Revisiting the tool was a worthwhile and essential process. Further financial resources were successfully negotiated to support the development of the workforce and test out new ways of working within the services. The logic model is a live working tool and should always be revisited, refined and updated in line with changing resources, allocation of resources, and internal and external factors influencing the status of the program.

Figure 3 Benefits of using a logic model

Benefits	The process of building the model improved clarity and focused thought processes
	Contributed to effective team building
	Connected inputs, activities and effects
	Mapped out resources and inputs and highlighted areas that needed to be addressed
	Highlighted where data was already available to measure outcomes and areas to be addresed
	Defined shared vision, direction and terminology
	Enhanced collaboration. interprofessional working and partnerships with agencies including communication
	Enhancde accountability by keeping the team focused on outcomes
	Built research capacity for evidence based practice

Figure 4 presents some perceived limitations and challenges of this ambitious program. One key challenge related to the speed at which the program was implemented within practice with numerous levels of activity required to prepare the workforce and services. This resulted in time constraints for the team to revisit and refine the logic model. Another limitation related to the changing priorities for resources.

Figure 4 Limitations of using a logic model

Limitations	Pace of program implementation versus time to review logic model
	Challenges presented when dealing with multilevels of staff, wide range of services and external agencies
	Changing priorities for resources
	Lack of familiarity with the format of the logic model used

8. Conclusion

The logic model has been an important and valuable tool in sharing information, facilitating the planning of the 'early years' program and providing direction to process and outcome evaluations. The time spent in the planning stage demystified and brought clarity to the purpose of the program for the team and stakeholders. This included defining the shared vision, direction and terminology for use across all services. Detailed planning was useful in teasing out the elements of the program most likely to produce meaningful and relevant evaluation data. In turn, this enhanced the development of realistic and measurable outcomes.

Reflections on the development of the logic model reinforced and contributed to the existing body of knowledge on the benefits and usefulness of logic models. This included influencing team building, partnership working, workforce development, leadership opportunities and building research capacity. The development of the logic model was also a powerful learning tool generating learning through critical thinking and problem-solving. Limitations perceived included the speed of implementation in practice, the number of ongoing activities, the format of the logic model and the changing priorities for resources.

The logic model is a live working tool regularly updated to reflect changing resources, and influencing internal and external factors. This provided leverage to successfully negotiate further financial resources to contribute to achieving the outcomes of the program. There is no doubt that revisiting and refining the logic model tool was an essential and worthwhile process.

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STIGMATIZATION IN MENTAL HEALTH PROBLEMS AND PSYCHIATRIC NURSING

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Abstract

Mental health problems, are known to race and seen in every socioeconomic level, in every cultural group, in the developed and developing countries. Mental disorder label reveals the stereotypes which represent the common idea of the society in the individual. Stereotypes are effective information structures which enable defining or perceiving a social group. As indicated in many studies, “mentally ill stereotype” in the society is the “dangerous” and “unpredictable” stereotype. This conclusion causes that a standing prejudice is revealed. Nurses, who constitute more than half of the mental health professionals, are responsible for rehabilitation, organizing the hospital environment and most of the services provided. Positive and negative attitudes adopted towards individuals with mental disorders are revealed most clearly in the relationship between the patient and the nurse Nurses' attitudes regarding prevention of labeling, is important to build bridges between people all health professionals for mental disorders.

Keywords: *mental health problems, stigmatization, psychiatric nursing*

1. Introduction

Mental health problems, are known to race and seen in every socioeconomic level, in every cultural group, in the developed and developing countries (T.C. Ministry of Health, 2007). Mental problems are quite important for society as they are frequent and may result in disabilities and cause economical loss (Ocaktan et. All. 2004). Prejudices regarding the fact that individuals with mental disorders are considered as dangerous as they are unpredictable and their actions cannot be understood and these prejudices are established and generalized by mass media. It is seen in researches that these individuals are alienated and subjected to negative attitudes which cause stigmatization (Bahar, 2007; Fink et. All. 1992; Star, 1955).

2.1. Stigmatization

Stigma concept is defined as a black mark which endangers the respectability of an individual or a group, causes objection by others or hesitation and devalues; the existence of a circumstance which should be ashamed of or the indication of not being accepted by others (Challenging Stigma, 2005; Alptekin et. all., 2007; Mak et. all. 2006; Schulze et. all. 2003; Porter, 1998; Byrne, 2000). According to Erwing Goffman (Goffman, 1963), stigmatization "is a situation which causes a deep shame, devalues the individual and reduces respectability". Stigmatization concept is the body of attitudes which involves society's adopting a particular attitude against and alienating certain patient groups. In that respect, individuals with mental disorders constitute the most affected group in many societies (Kocabaşoğlu et. all, 2003; Demiralp et.all, 2005).

Mental disorder label reveals the stereotypes which represent the common idea of the society in the individual. Stereotypes are effective information structures which enable defining or perceiving a social group (Watson, 2001). Studies identified four stereotypes for mental disorders; individuals with mental disorders are dangerous and they should be avoided, the weakness or deficiency in their character is responsible for their disability or incapability. Individuals with mental disorders are not responsible for their actions and behaviours due to their mental condition and it requires experts to make a decision about them, these individuals look like children and they need someone as protector like parents (Watson, 2001).

As indicated in many studies, "mentally ill stereotype" in the society is the "dangerous" and "unpredictable" stereotype. This conclusion causes that a standing prejudice is revealed (7). For a member of a social group, prejudice is a judgment generated on some previous judgments and stereotypes just because of being a member of that group (Kırel et.all, 2004). Prejudices strengthen stereotypes and cause emotional reactions such as fear and therefore discriminative and alienating behaviours occur (Watson, 2001). Loss of social status also occurs in the socially alienated person in which negative ideas are developed as a result of "not being one of us, different" label (Corrigan, 2001; Gonzalez et. all, 2007).

2.2.Impact of Stigmatization on the Patients

Reintegration of the mentally ill individual in the society and gaining their previous functionality are closely related to the society's general attitude towards mental disorders (Taşkın et. all, 2006). It can be seen in various studies that the society has labelling attitudes towards individuals with mental disorders and do not want to be in close connection with such

people as the society considers individuals with mental disorders as “dangerous” and “unpredictable”. In addition, there are many studies which indicate that mental disorder label causes negative and rejectionist attitudes (Taşkın et. all, 2006; Özmen et. all,2004). Stigmatization for mental disorders may be as bad and harmful as the symptoms of the disorders (Feldman et. all, 2007), because labelling causes social isolation, limited living opportunities and delayed call for help in patients. Due to negative evaluations by the society, insulting discrimination and internalized stigmatization, self-confidence of the individuals is damaged, their self-respect decrease and their quality of life deteriorates in time (Kocabaşoğlu et. all, 2003; Çam et.all, 2009; Switaj et.all,2009; Corrigan, 1998; Gaebel et.all, 2003, Link et. all, 2006). Stigmatization individuals devalues themselves, suffer from the fear of being rejected and lose their hope (Sirey et. all, 2007). Negative labeling of the mentally ill leads to serious difficulties in many areas of their lives. They experience housing and job discrimination, and they also suffer isolation, friendship and relationship failures, parental conflict, income loss, an increase in their depressive symptoms and a decline in their social skills (Corrigan et.all, 2004; Gingerich, 1998; Bostancı, 2005; Switaj 2009; Corrigan, 2005; Hocking, 2003).

2.3.The role of the nurse in fighting with stigmatization

Nurses, who constitute more than half of the mental health professionals, are responsible for rehabilitation, organizing the hospital environment and most of the services provided. Positive and negative attitudes adopted towards individuals with mental disorders are revealed most clearly in the relationship between the patient and the nurse. Attitudes of nurses who are close and long term contact with the patients directly affect the patients and their attitudes may also influence the therapeutic environment of the clinic (Bahar, 2007).

Psychiatry nurses, who have roles such as therapist, advisor, trainer, consultant, researcher, clinician and case manager, also have an identity of policy maker in the field of social psychiatry. Primary precaution in accordance with social psychiatry involves determining and preventing some factors which deteriorate mental health. Secondary precaution is reducing the illness rate of individuals who are under high risk with early diagnosis and treatment of acute and preclinical diseases. Tertiary precaution is determined as minimizing the impacts of mental illness on the individual with rehabilitation and care. The nurse in the social psychiatry team works with healthy and risky groups and the population diagnosed with psychiatric diseases. When providing services to the population diagnosed with psychiatric diseases, the case manager is in the position of the team member who implements care and rehabilitation. Within the scope of the tertiary precaution, social

psychiatry nurse evaluates the patient and his/her family in their own environment by the help of home visits. The nurse evaluates the possibility of familial and social medical crisis of the patient and his/her family and makes attempts for coping with and resolving such crises. Determines training requirements in relation with the disease, symptoms of the disease, treatment options, communication skills, stress and coping with the stress, solving problems, assertiveness, sources and use of social support and provides training. Implements therapy in terms of increasing insight, recognizing feelings, organizing behaviours and managing the disease. Evaluates opportunities in meeting the needs of the individual such as accommodation, employment, social security and nutrition and provides financial and social support if necessary (Çimen, 2009).

Protectiveness is an important step in mental disorders. Prevention of mental disorders aims decreasing the frequency and prevalence of mental disorders, preventing or delaying the recurrence of the diseases and reduce the impact of the disease on the individual, his/her family and the society. Prevention of mental disorders is one of the effective ways to reduce the burden of the diseases on the country. When making mental health policies, preparing laws and making decisions, the countries and societies which want to reduce the medical, social and economic burden of the mental disorders are expected to pay more attention to prevention and improvement in mental health (Gültekin, 2010).

Various studies show that acquiescent, supportive and tolerant attitudes influence the patient in a comforting and reintegrative manner and enable their participation in treatment and care; on the contrary insulting, rejecting, restrictive and abstractive attitudes alienate the patient and influence the treatment and care in a negative manner. For that reason, regardless of their field of study, nurses are expected to diagnose the underlying causes of emotions and behaviours which may occur in case of diseases and plan and implement care accordingly. When doing so, it is important to be free from social prejudices and not to lose objectivity being aware of their own emotions and attitudes (Kayahan, 2009). In their study in which they evaluate the attitude and behaviours of the nurses towards individuals with mental disorders, Bostancı and Aştı (Bostancı, 2004) concluded that the psychiatry nurses exhibited more positive attitudes than other nurses and stated that having psychiatry knowledge and skills will be effective in preventing prejudices and fallacies. Psychiatry nurses who can provide medical training and consultancy in protection from mental diseases, can understand the psychological condition of the healthy individuals and patients and evaluate their behaviours, have good skills to perceive psychological needs, can provide necessary care, consultancy, rehabilitation and support to the patient and have knowledge and skills in interpersonal relationships should

be at the front row in studies aiming for decreasing labelling and discriminating against individuals with mental disorders (Psikiyatri Hemşireleri Derneği,2014). They should improve themselves in the light of the advanced technology and science and carry out the roles of advocating patients and protecting the mental health of the society.

3. Conclusion

Protection, development and maintenance of mental health of individual, family and community is carried out by a multidisciplinary team approach with the functioning of health services. Nurse is also one of the members of this team. Nurses' attitudes regarding prevention of labeling, is important to build bridges between people all health professionals for mental disorders. Nurses often facilitate communication among various healthcare disciplines, they can use this skill to facilitate dialogue to reduce stigma.

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Russelioside B from *Caralluma quadrangula* improved hepatic glucose metabolism in diabetic rats

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Abstract

Background: Diabetes mellitus (DM) has emerged as a global epidemic, which is predicted to worsen in the coming decades, particularly in developing countries. An alternative strategy to treat diabetes is the use of various natural agents possessing hypoglycemic effect.

Ethnopharmacological relevance: *Caralluma quadrangula* the source of russeliosid B has been used by Bedouins of Saudi communities in cases of thirst and hunger and for the treatment of diabetes, vitiligo, melasma and freckles.

Objective: The present study was aimed to evaluate the improving effect of russelioside B (RB), a major pregnane glycoside isolated from *Caralluma quadrangula* on glucose metabolism in the liver of streptozotocin (STZ)-induced diabetic rats.

Study design: Extraction and isolation of the major pregnae glycoside RB was carried out using chromatographic techniques. RB was identified by comparing its spectral data (^{1}H- and ^{13}CNMR) and melting point with those reported in the literature. The efficacy of RB was investigated on glucose utilization pathways and on hepatic glucose production in STZ-induced diabetic rats, since both of them contribute significantly to plasma glucose level.

Methods: Diabetes was induced by a single intraperitoneal (i.p.) injection of STZ. The rats were assigned in the following groups: **Group 1**: served as normal control group. **Group 2** animals received STZ were served as diabetic group. **Group 3**: this group received daily oral dose of RB in a dose of 50 mg/kg body weight for 30 days, and served as RB-treated group. At the end of the experimental period, levels of glucose, insulin, and lipid profile including serum total cholesterol (TC), high density lipoprotein-cholesterol (HDL-C) and triglyceride (TG) were assayed in the blood serum. On the other hand, a heparinized blood portion was used for the estimation of glycated hemoglobin percentage (HbA1c%). The liver tissue was used to measure glycogen contents, glucose metabolism related enzymes and mRNA expression levels of glucokinase (GK) , Glucose-6-phosphatase (G-6-Pase), glycogen

synthase (GS) and glycogen synthase kinase -3β (GSK-3β). Body weights of all the animals were recorded prior to the treatment and sacrifice.

Results: The results showed that RB improved the fasting serum glucose level, glycated hemoglobin percent, serum insulin level and lipid profile. The altered activities of the key enzymes of carbohydrate metabolism such as glucokinase, glucose-6-phosphatase, glucose-6-phosphate dehydrogenase, and glycogen phosphorylase in liver of diabetic rats were significantly improved by the administration of RB. Further, RB administration to diabetic rats reverted gene expression of glucokinase, glucose-6-phosphatase, glycogen synthase and glycogen synthase kinase-3β to near normal levels.

Conclusion: To the best of our knowledge, this is the first mechanistic study of the antidiabetic activity of RB glycoside or related pregnane glycosides in animal model. Since, RB exhibited anti-hyperglycemic and anti-hyperlipidemic potential, which acts by improving insulin secretion and the alterations in the carbohydrate and lipid metabolism. We can conclude that administration of RB isolated from aerial parts of *Caralluma quadrangula* may represent a potentially useful strategy for the management of diabetes. Further clinical investigation in human will be undertaken in future study.

Key words: *Caralluma quadrangula*, Russelioside B, Streptozotocin, Diabetes, Rat, Carbohydrate metabolizing enzymes

COST EFFECTIVENESS ANALYSIS OF FILGRASTIM *versus* PLACEBO IN POST ALLOGENIC BONE MARROW TRANSPLANTATION

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Abstract

Filgrastim is used to accelerate hematopoietic recovery after allogeneic bone marrow transplantation (ABMT). Its impact on the total cost of patient care remains to be explored.
We therefore undertook a cost effectiveness analysis in the context of a randomized clinical trial of Filgrastim versus placebo in post ABMT.
A primary endpoint, duration of myelosuppression, and three secondary end points (number of days of fever, length of hospital stay, survival at one hundred days) were used to assess efficacy. Direct costs were evaluated and allowed the calculation of the incremental cost-effectiveness ratios (ICER) for the major endpoints of the trial.
Sixteen patients were included in the study. The duration of myelosuppression was significantly decreased in the Filgrastim arm with medians of 15 days vs. 19 days in the placebo arm ($p<0.05$). Cost analysis showed no statistically significant difference between the two arms. According to the calculation of ICER, Filgrastim was more costly and more effective than placebo for the number of days of aplasia avoided and the number of days with fever avoided. Placebo strictly dominated filgrastim for days of hospitalization avoided.
Filgrastim has proven effective in reducing the duration of aplasia without increasing costs.

Keywords: *Filgrastim; placebo; cost; effectiveness; Allogeneic Bone Marrow Transplantation;*

1. Introduction

Allogeneic bone marrow transplantation (ABMT) remains, until the development of gene therapy, the only curative treatment of a number of constitutional deficit disorders of the hematopoietic tissue. It remains the eradicator treatment of a number of malignant hematological diseases and keeps this place in the therapeutic arsenal. However, the success of this therapy is not always guaranteed and depends on several factors such as patient age, post-transplant immunological complications, adverse reactions of the conditioning treatment, the

occurrence of infections associated with neutropenia caused by myeloablation and / or myelosuppression and the duration of the neutropenia (1).

The Filgrastim, a granulocyte colony-stimulating factor analog, is used to reduce the duration of neutropenia in patients undergoing myeloablative therapy followed by bone marrow transplantation (2). Hence it represents an additional cost of drug spending in the care of patients undergoing ABMT. Widespread use should be based on a rational assessment of cost effectiveness in a context where health expenditures are increasing (3).

We intend to conduct a cost-effectiveness analysis of Filgrastim (Neupogen ©) *vs.* placebo in reducing the duration of neutropenia in patients undergoing myeloablative therapy followed by ABMT.

2. Patients and methods

This pilot study is part of the evaluation of the effectiveness and cost of Filgrastim after geno-identical ABMT. It concerns adult patients hospitalized in the sterile unit of the Hematology / Bone Marrow Transplantation service in the *Centre National de Greffe de Moelle Osseuse*-Tunisia. Patients were randomized to belong to one of two groups (Filgrastim or placebo) in a single blind conducted trial. We had the agreement of the ethics committee for the conduct of this trial.

Filgrastim is used in primary prevention on the regimen of 5µg / Kg once daily by intravenous infusion. The administration begins on day 7 of the allograft and is maintained 72 hours after the absolute neutrophil count (ANC) stabilizes above 1000 elements / microL.

Data collection has been done by means of a table including patient characteristics and different clinical parameters used to assess efficacy. The study covered a period of one hundred days from the day of the transplantation.

2.1 Effectiveness

The primary endpoint was the myelosuppression period defined by an ANC <500 /microL. The secondary endpoints were the number of days of fever, the number of days of hospital stay and survival at 100 days.

2.2 Cost data

Direct costs were calculated for both arms of the study and are expressed in euros. It includes cost of laboratory tests, cost of medical imaging, drug Costs (divided into anti-

infectives, parenteral nutrition, oral decontamination, hematopoietic growth factors and other medicines), cost of therapeutic drug monitoring (TDM) and cost of labile blood products.

2.3 Cost-effectiveness analysis

Incremental cost-effectiveness ratios (ICER) expressing the additional cost of one unit of outcome gained/avoided by one strategy compared with another, were calculated for the mainly endpoints of the trial. This is the ratio of the difference in costs between the two arms of treatment (Filgrastim and placebo) to the difference in effectiveness (4).

2.4 Statistical analysis

A statistical analysis was performed through SPSS (Statistical Package for the Social Sciences) Version 21.

Quantitative variables were described as median, mean and standard deviation. Qualitative variables were described as percentages.

The efficacy endpoints and the different costs were compared between the two independent samples (Filgrastilm arm and placebo arm). Quantitative variables were analyzed using the Mann-Witheney U test. The Fisher exact test was used to compare categorical variables. The difference was considered statistically significant when the p value was less than 0.05 in a bi-tailed test.

3. Results

3.1 Patient characteristics

A total of sixteen patients (nine in the Filgrastim arm and seven in the placebo arm) aged 17 to 37 years (Table 1) participated in the study. All underwent génoidentical ABMT and received a GvHD prophylaxis based on ciclosporin and methotrexate.

Table 1 Patient caracteristics

	Filgrastim (N=9)	**Placebo (N=7)**	***p***
Age [a] (years)	24.78 ± 7.31	25 ± 6.53	0.98
Sex ratio (males : females)	4 : 5	6 : 1	0.15
Body Mass Index (Kg/m^2) [a]	20.16 ± 1.88	24.86 ± 5.21	**0.02**
Diagnosis [b]			
Acute leukemia	5 (55.6%)	2 (28.6%)	
Aplastic anemia	4 (44.4%)	5 (71.4%)	0,36
Standard risk [b]	7 (77.8%)	6 (85.7%)	
High risk [b]	2 (22.2%)	1 (14.3%)	1
Sex Mismatch			
Present [b]	6 (66.6%)	3 (42.9%)	
Absent [b]	3 (33.3%)	4 (57.1%)	0,62
ABO compatibility			
Compatible [b]	7 (77.8%)	2 (28.6%)	
Incompatible [b]	2 (22.2%)	5 (71.4%)	
Major	1	2	0,13
Minor	1	1	
Mixed	0	1	
Mononuclear cells infused ($\times 10^8$/kg) [a]	1.89 ± 0.59	2 ± 0.75	0.78

[a] *moyenne ± standard deviation*
[b] *n (%)*

3.2 Effectiveness

The duration of myelosuppression was shorter in the Filgrastim arm relative to the placebo arm (median of 15 days vs. 19 days) ($p < 0.05$) (Table 2).

Table 2 Efficiency measured according to the treatment group

Endpoints	Filgrastim (N=9)			Placebo (N=7)			p
	Median	Mean	Standard deviation	Median	Mean	Standard deviation	
Duration of myelosuppression*	15	15,44	1,24	19	19,57	4,39	**0,03**
Number of days of fever	4	6,33	5,7	4	7,57	6,85	0,90
Duration of hospitalization*	24	26,22	6,78	25	24,43	4,86	0,98
Survival at 100 days*	100	100	0	100	87,85	32,13	0,44

**days*

3.3 Cost data

The total cost was measured higher in the Filgrastim arm but the difference between the two groups was not significant (Table 3).

Table 3 Mean total costs per patient (in 2015 euros)

Costs	Filgrastim (N=9)		Placebo (N=7)		p
	Mean	Standard deviation	Mean	Standard deviation	
Anti infectives	2347,8	1098,5	3880,5	1783,0	0,83
Growth Factors	1753,2	254,1	0,0	0,0	$< 10^{-4}$
Parenteral Nutrition	321,1	147,9	262,4	120,5	0,75
Oral Decontamination	91,8	85,3	79,9	36,7	0,75
Other medicines	608,8	160,0	1149,9	528,3	1
Total (medicines)	5122,8	1051,3	5372,5	2468,5	0,53
Therapeutic Drug Monitoring	517,0	70,7	397,0	182,4	0,12
Blood Derivatives	873,0	361,9	1016,6	467,1	1,00
Biological analyzes	3387,9	1802,1	2138,3	982,5	0,09
Medical imaging and anatomopathological analyzes	170,8	260,3	73,1	33,6	0,45
Total	10071,6	2145,4	8997,5	4134,1	0,35

3.4 Cost effectiveness analysis

The calculation of ICER (Table 4) showed that the amount to be paid to avoid a day of myelosuppression was 260 €. The amount to be paid to avoid a day of fever was 866.2 €.

The Filgrastim was less effective and more expensive than placebo in reducing the number of hospitalisation days (ICER = -600) as shown in Table 4.

Table 4 Incremental cost-effectiveness ratios (ICERs) of Filgrastim versus placebo

	Filgrastim	Placebo	difference	ICER
Mean cost (€, 2015)	10071,6	8997.5	1074.1	
Effects : mean days				
Myelosuppression	15,44	19,57	4,13	260.1[a]
Fever	6,33	7,57	1,24	866.2 [a]
Hospitalisation	26,22	24,43	-1,79	-600.1[b]

[a] *Filgrastim more effective and more expensive*
[b] *Placebo dominates*

4. Discussion

Our study shows that filgrastim reduces the duration of myelosuppression from 19 days (placebo group) to 15 days ($p<0.05$) as shown in Table 2. This was found in several studies, including that of Bishop et al and that of Ernst et al. (11 days and 15 days repectively for Filgrastim and 15 days and 19 days respectively for placebo (5, 6)

The acceleration of medullar engraftment by Filgrastim does not seem significantly affect 100 days survival even if it is increased in the filgrastim group *vs.* placebo group in our study. This was also found in the two studies cited above (5, 6). Due to some controversies, the real impact on survival of G-CSF still seems unclear (7, 8).

The Filgrastim is not an additional expense compared to placebo, at least among the costs measured in our study (Table 3). The ICER in reducing myelosuppression is about 260 euro. This figure should be compared to the threshold values of ICER depending on social, economical and political factors. The placebo strictly dominated filgrastim for the duration of hospitalization. Several alternatives seeking to improve the cost-effectiveness ratio of myeloid growth factors, have turned to pegfilgrastim (a covalent conjugate of Filgrastim characterized by a greater half-life (7)) and found it more efficient and cheaper (9). The pegfilgrastim has also been proposed as an alternative in some of the recommendations to Filgrastim (2, 7). The cost-effectiveness of G-CSF mimetic (second generation products) remains to be explored.

This study presents multiple bias. It is based on a reduced cohort of sixteen patients. This pilot study should be continued with a larger number of patients. The body mass index was significantly different between the two arms of treatment. This could be a source of bias such in the assessment of the cost of medicines or if it causes some comorbidities.

5. Conclusion

The Filgrastim shows an interesting effectiveness in reducing the duration of myelosuppression in allograft patients, without any significant change in the number of days of fever, length of hospital stay or survival. It does not present a significant additional cost in return compared to placebo. These data are to be discussed at the risk of an increase in graft versus host disease. Larger studies are needed to confirm our results. We mention that the cost effectiveness of filgrastim may be significantly improved by the adoption of biosimilars.

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Optimization of Vancomycin Dosing Regimens in Critically Ill Patients: Focus on Early Individualization

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Abstract

Background: Despite the current clinical guideline recommendation, the optimal dosing regimen of intravenous vancomycin remains controversial. Achievement of therapeutic trough early in the course of illness may be beneficial.

Objective: Our objective was to assess and validate the effectiveness of first dose adjustment in achieving target recommended goal in critically ill patients.

Methods: Twenty critically ill patients with sepsis received loading dose of 25 mg/kg of vancomycin and then randomly assigned to 2 groups. Group 1 received maximum empirical doses of vancomycin as 15 mg/kg every 8 hours for a maximum of 24 hours. In the group 2, the doses were individualized based on serum concentrations of vancomycin. First dose non-steady state sampling was used to calculate pharmacokinetic parameters of the patients within 24 hours. Vancomycin doses were adjusted to achieve AUC=400−600 mg·hr/L and avoiding peak serum concentration higher than 40 mg/L.

Results: Significantly more patients in group 2 had a trough higher than 15mg/L in day-3 and day-5, compared with group 1 (P=0.043, P=0.015). Also trough serum concentrations in day-3 was significantly higher in group 2 (19.4 ± 4.4) comparing group 1 (14.4 ± 4.3) respectively while it was not statistically significant in day-5 between two groups (12.3 ± 5.6 vs. 17.1 ± 1.8). AUCs in day-3 were significantly higher in group 2 (665.9 ± 136.5) comparing group 1 (490.7 ± 101.1) while it was just marginally higher in day-5 (606.1 ± 76.0 vs. 484.0 ± 130.4).

Conclusions: With early individualized dosing (within 48 hours) significantly more patients achieved peak and trough steady state concentrations without additional venous sampling. Also in the context of pharmacokinetic/pharmacodynamic goal of AUC/MIC ≥400, it seems if pharmacokinetic goal is achievement to trough serum concentration ≥15 mg/L and AUC ≥400 mg.hr/L, maximum empirical doses of vancomycin can be used to achieve these goals. However, according to the differences of MIC in various centers, it is necessary to individualize doses of vancomycin in critically ill patients if pharmacokinetic target is to obtain trough serum concentration of vancomycin of ≥15 mg/L and AUC ≥600 mg.h/L.

Keywords: Vancomycin, Critical Care, Therapeutic Drug Monitoring, Pharmacokinetic, Early Individualization

Introduction

Infections in intensive care unit (ICU) continue to be one of the main causes of mortality and morbidity in critically ill patients [1-2]. Sepsis is defined as a life-threatening infection which has ability to damage multi organ systems and cause to fail them. Optimizing effective antimicrobial therapy as soon as possible is necessary in order to prevent multiple organ failure disorder and bacterial resistance [3-4]. Recent studies have emphasized on the increasing prevalence of gram-positive microorganisms, especially methicilin-resistant Staphylococcus aureus (MRSA)[5-7]. Due to the increase in prevalence of antimicrobial

resistance, efforts to treat gram-positive microorganisms led to reconsidering traditional antibiotics regimens like vancomycin. Vancomycin is a large glycopeptide antibacterial agent that inhibits bacterial cell wall synthesis by blocking glycopeptide polymerization through binding tightly to D-alanyl-D-alanine portion of cell wall precursor. It has been wildly used for treatment of serious gram-positive infections involving MRSA[8]. In the absence of consequences about the indication of vancomycin initiation in sepsis, depending on center base guidelines, it can be used as a first line of treatment for septic patients with un-known etiology, sepsis associated with un-stable hemodynamic, ventilation associated pneumonia (VAP), high clinical suspected for skin soft tissues or abdominal source of infection and catheter related infection [9-11]. Despite the vital role of vancomycin in the treatment of MRSA infections, a complete consensus has not been reached to the recommended dose adjustment of this antibiotic in critically ill patients. Traditional therapeutic regimens of vancomycin was administrated 1 g every 12 hours or 15 mg/kg every 12 hours in order to set trough serum concentration of vancomycin in the range of 5-10 mg/L[12]. Following the reports of increase in incidence of vancomycin-resistant S.aureus strains (VRSA) and germs with higher minimum inhibitory concentrations (MICs) for vancomycin, a large number of studies have performed to identify the determinants that influence bacterial resistance against vancomycin. Optimum area under the time concentration curve/minimum inhibitory concentration (AUC/MIC) and variety of trough concentration ranges has been studied. Finally the studies concluded that AUC/MIC ≥400 of vancomycin is the best factor in the success of treatment and prevention of vancomycin-resistant [13-14]. Considering that implementation of AUC/MIC in the setting of therapeutic drug monitoring requires expertise clinicians to adjust the dose regarding calculated volume of distribution and clearance of the drug, a shift in the identified target trough concentrations of vancomycin of 5-10 mg/L to 15-20 mg/L has been recommended. American Society of Health-system Pharmacists (ASHP) therapeutic guidelines recommend that "For a pathogen with an MIC of 1 mg/L, the minimum trough serum vancomycin concentration would have to be at least 15 mg/L to obtain the target AUC/MIC ≥400" [14]. It seems that majority of fixed dose regimens of vancomycin have not been successful in achieving these goals. On this basis, we planned a randomized two-arm prospective study to assess the role of therapeutic drug monitoring (TDM) in dose adjustment of vancomycin following maximum fixed doses and individualized therapeutic regimens in tailoring vancomycin dosing regimen in maintaining recommended targets of pharmacokinetic/pharmacodynamic (PK/PD) parameters in critically ill patients.

Methods

Study design and participants

This study was designed as a randomized clinical trial. It was performed in two phases. In the first phase (cross sectional), in order to ensure avoidance of toxic serum concentrations following maximum empirical dosing of vancomycin and finding standard clinical laboratory to assay vancomycin levels, serum concentrations of vancomycin measured without any intervention in 10-bed ICU patients. Patients admitted to general and emergency ICU ward of

"Sina" Hospital affiliated to Tehran University of Medical Sciences (TUMS), Tehran, Iran, from October 2012 to August 2014 were screened for the study eligibility during ICU stay. In all cases informed consent was obtained from patients or their closest relatives. The study procedure and protocol were approved by the ethical committee of TUMS. Our clinical trial has been registered in Iranian Registry of Clinical Trials with code number of (IRCT201209291497N2).

Inclusion in the study required that the patients to be older than 18 years old, normal renal function (defined as eGFR ≥60 ml/min estimated with Cockcroft-Gault equation), evidence of sepsis following systemic inflammatory response syndrome (SIRS) (body temperature less than 36_C or greater than 38_C, heart rate more than 90 beats per minute, respiratory rate more than 20 breaths per minute or an arterial partial pressure of carbon dioxide less than 32 mmHg, white blood cell count less than 4000 cells/mm^3 or more than 12000 cells/mm^3), survival prognosis more than 72 hours, recent onset of vancomycin administration and no vancomycin sensitivity. Patients with the following conditions were excluded from the study: patient died within first 72 hours, acute renal injury development during the study (according to the criteria of RIFLE[15]), adverse reaction of vancomycin, change in treatment of vancomycin during the first 72 hours, discontinuation of vancomycin during the first 72 hours of treatment, loss of the samples of the first 48 hours and failure of individualization due to pharmacokinetic, physicians and nurses miscommunication. In the second phase (clinical trial) 20 patients who had indication of treatment with vancomycin following sepsis, received loading dose of 25 mg/kg based on actual body weight at a rate of 1000 mg/hr and then maximum empirical doses of vancomycin as 15 mg/kg every 8 hours was administrated for all patients. Then the patients wererandomly divided into two groups and depending on the group, treatment was continued. One of the groups (group 1) received the same maximum empirical doses of vancomycin as 15 mg/kg every 8 hours for a maximum of 24 hours. In the other group (group 2), the doses were individualized based on serum concentrations of vancomycin.

Demographic and clinical data were obtained from the medical notes of patients. These included sex, age, body weight, height and estimated glomerular filtration rate (eGFR) upon initiation of vancomycin. Sepsis workup and SIRS criteria exploration was performed for every patient at the baseline. All relative routine critical care laboratory tests are followed and documented by daily visits.

Patients were blinded to antibiotic regimen during the experiment. Serum concentrations of vancomycin in patients receiving fixed doses regimen were not available for the medical team for dose adjustment of vancomycin. Serum concentrations of vancomycin were taken at 6 times included: 1- 1 hour after the end of first dose infusion, 2- 4-6 hours after the first sample, 3- 1 hour after the end of fifth dose infusion (fifth dose peak), 4- 1 hour before the sixth dose infusion (fifth dose trough), 5- 1 hour after the end of ninth dose infusion (ninth dose peak) and 6- 1 hour before the tenth dose infusion (ninth dose trough), within during 5-days of study. After centrifugation, plasma samples were analyzed within 2 hours by means of fluorescence polarization immunoassay (Siemens Healthcare Diagnosis, United Kingdom, EMIT).

Pharmacokinetic calculation and early individualization

By measuring both of trough and peak serum concentration of first dose of vancomycin, we calculated pharmacokinetic parameters such as elimination rate (K_{el}), volume of distribution (V_d), half-life ($t_{1/2}$), clearance of vancomycin (Cl_{vanco}) and AUC individually for each patient. These parameters were calculated based on Andrew DeRyke et al., methods [13]. Early individualization of vancomycin was performed with dose adjustment to achieve AUC=400−600 mg·hr/L while avoiding peak serum concentration higher than 40 mg/L, within first 24 hours in divided doses of every 6 to 12 hours daily. Calculations were performed by the clinical pharmacists but the results were not communicated to the ICU physicians.

According to doses of 15 mg/kg every 8 hours as usual empirical doses of vancomycin in our center, we frequently observe patients with AUC less than 400 mg.hr/L. Regarding the pharmacokinetic goal of AUC ≥400 mg.hr/L, we estimated that less than %70 of patients may achieve AUC ≥400 mg.hr/L. Considering the study power %80 and level of significance of 0.05, the sample size of study calculated to be 42 patients (21 patients in each groups).

Data analysis

Trough and peak serum concentration of vancomycin and AUC were compared in two groups during 5-days of study. The AUC/MIC was calculated based on the assumption that MICs were 1−1.5 mg/L for all cases. Goal target of pharmacokinetic was defined as AUC/MIC ≥400. All the analyses were performed using SPSS statistical package, version 20 for windows. All variables were tested for normality of distribution with Kolmogorov-Smirnov test. Levene's test for equality of variances was used to compare the means and the results were analyzed based on Independent t-test. Pearson chi square test or Fisher's exact test was used for ordinal and nominal data. Odds ratio was used when results were statistically significant or marginally significant. P-value of <0.05 was considered statistically significant for all tests.

Results

In the middle of the study due to achievement of significant differences in our primary outcome of frequency of patients who failed achieve to AUC ≥400 mg.hr/L on 20 patients (10 patients in each group), we stopped the study to avoid wasting of resources. 108 samples of vancomycin serum concentrations were assayed. A total of 25 patients were assigned to the second phase, 5 cases excluded based on the exclusion criteria. Demographic information and pharmacokinetic parameters of the included patients are shown in table 1. The difference between study groups was not significant regarding gender, age, body weight and eGFR at the baseline.

Trough serum concentrations in day-3 was significantly higher in group 2 (19.4 ± 4.4 mg/L) comparing with group 1 (14.4 ± 4.3 mg/L) (P=0.029) while it was not statistically significant in day-5 between two groups (12.3 ± 5.6 mg/Lvs. 17.1 ± 1.8 mg/L) (P=0.137).AUCs in day-3 were significantly higher in group 2 (665.9 ± 136.5) comparing with group 1 (490.7 ± 101.1)

respectively (P=0.008) while it was just marginally higher in day-5 (606.1 ± 76.0 vs. 484.0 ± 130.4) (P=0.054). There are no significant differences regarding average vancomycin dosage between two groups in day-3(44.9 ± 3.8 mg/kg vs. 49.4 ± 13.1 mg/kg) and day-5 (46.3 ± 3.3 mg/kg vs. 47.1 ± 12.5 mg/kg)respectively (P=0.33, P=0.87).

Table 2 describes frequencies of patients who failed to achieve pharmacokinetic goals of trough serum concentrations of more than 15, 12.5 and 10 mg/L and AUC of less than 400 and 600 mg.hr/L. Frequencies of trough serum concentration less than 15 mg/L in day-3 and day-5 were significantly lower in group 2 (%10, %0) comparing with group 1 (%62.5, %66.7) respectively (P=0.043, P=0.015). Frequencies of AUC less than 400 mg.hr/L in day-3 and day-5 were significantly lower in group 2 (%0, %0) comparing with group 1 (%14.3, %40) respectively (P=0.041, P=0.012) while frequencies of AUC less than 600 mg.hr/L in day-3 and day-5 did not differ between two groups (P=0.05, P=1).

According to serum concentrations of vancomycin, %80 of patients in group 2 required individualization. It means the need to increase or decrease the dose of 250 mg or to change in dosing interval from 8 hours to 6 or 12 hours. There are no significant differences in frequencies of patients with vancomycin toxicity regarding trough and peak serum concentrations more than 25 and 40 mg/L respectively between two groups during the study (P=1, P=1) (Table 3).

Discussion

This study describes the evaluation of dose adjustment of vancomycin in critically ill patients. The results demonstrate that an individualized regimen of vancomycin is more likely to result in PK/PD targets of AUC/MIC ≥400. Patients received individualized regimen, are 14 and 15 times more likely to have AUC ≥600 and trough serum concentration ≥15 mg/L than patients received maximum empirical doses regimen respectively.

According to consensus review of ASHP, IDSA and SIDP guideline, empirical doses of vancomycin as 15-20 mg/kg every 8-12 hours can be used for most patients with normal renal function to achieve therapeutic serum concentration of 15-20 mg/L and AUC/MIC ≥400 when MIC is less than 1 mg/L [14]. But the results of present study show that considerable percentage of patients treated with almost fixed doses of vancomycin of 15 mg/kg every 8 hours fails to achieve these goals, while individualized regimen of vancomycin could put the patients in achieving therapeutic serum concentrations.

Recommendations of individual pharmacokinetic adjustments and verification of achievement of target serum concentrations is recently highlighted by IDSA led to improve clinical outcomes of patients [16].Unlike the methods of individualization of vancomycin noted in clinical guidelines that recommend to measure serum concentration at steady state conditions [13-14], we found that early individualization and first dose monitoring of vancomycin let the patients to achieve therapeutic serum concentrations earlier. The results in 3th and 5th day of study show that the first dose monitoring of vancomycin within the first 24 hours of initiation of treatment has been effective in achieving pharmacokinetic goals in less than 48 hours. In other words, by calculation of pharmacokinetic parameters at non-steady state conditions,

there is no need for waiting to reach steady state and delaying interventions for at least 72 hours, especially in terms of MIC ≥1 mg/L. Crumby et al. [17]performed a similar study in 108 patients and compared nomogram-based and individualized vancomycin regimens in neonates. Significantly more patients achieved peak and trough steady state concentrations after first dose pharmacokinetic dose adjustment. This study also confirmed the benefits of early individualized dosing without additional venous sampling.

Nephrotoxicity associated with vancomycin monotherapy is uncommon, but recent studies demonstrate that excessive serum concentrations can led to nephrotoxicity [18-19]. Lodis et al., [20] concluded that high doses regimens of vancomycin of more than 4 g/day are related to higher incidence of nephrotoxicity exacerbated by some factors including ICU residence. In other hand another study showed that vancomycin doses greater than 2 g/dose did not show a significant increase in serum creatinine [21]. Therapeutic monitoring of serum concentrations would allow interventions that reduce toxicity[13-14]. The results of present study did not show a statistically significant in toxic trough and peak serum concentrations between two groups. In other words maximum empirical doses vancomycin as did not show increase in toxicity. Therefore due to the lack of efficacy of fixed dose regimens to achieve targets of pharmacokinetic and the risk of vancomycin toxicity with higher empirical doses, individualized regimens are necessary for patients to achieve specific pharmacokinetic goals.

Due to MICs of vancomycin against S.aureus were commonly 1 mg/L or less, trough serum concentrations of vancomycin of 5-10 mg/L were considered acceptable [22]. These results show that patients who receive maximum empirical doses of vancomycin may almost achieve this trough serum concentration. However according to increased vancomycin MICs and guidelines suggestion of trough serum concentration of 15-20 mg/L, it seems that individualized regimens are preferred. Lodise et al. [23]found vancomycin MIC ≥1.5 mg/L to be associated with a 2.4-fold increase in treatment failure in MRSA bacteremic patients when compared with patients isolate with MICs of ≤1 mg/L (%36.4 vs. %15.4 respectively, P=0.049). In addition, failure or success did not correlate with attainment of primary trough of at least 15 mg/L irrespective of MIC[13].

Conclusion

Although maximum empirical doses of vancomycin have low risk of toxicity and can be used in all septic patients with normal renal function under therapeutic drug monitoring, PK/PD targets of AUC/MIC ≥400 may not to be achieved in terms of relative antimicrobial resistance. Therefore according to the increase in the incidence of VRSA and germs with higher MICs, it is necessary to individualize doses of vancomycin in critically ill patients. In addition delay in pharmacokinetic parameters calculation to reach the steady state condition may put the patients in the risk of under-treatment for at least 72 hours. In summary, our study suggests that first dose pharmacokinetic monitoring and early individualization of vancomycin should be considered for critically ill patients in order to achieve pharmacokinetic goals of trough serum concentration more than 15 mg/L and AUC ≥400 mg.hr/L.

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Table 1. Patients' demographics and pharmacokinetic parameters in two groups.

	Measures	Group 1	Group 2	Sig. (2-tailed)
		Mean ± **S.D**	Mean ± **S.D**	
	Number of patients	10	10	–
	Sex (male/female)	8/2	8/2	0.610
Baseline	Age (year)	48.5 ± 18.3	47.7 ± 20.9	0.933
	Body weight (kg)	66.0 ± 12.1	73.0 ± 12.2	0.245
	Height (cm)	170.1 ± 9.1	171.5 ± 13.9	0.784
	eGFR (ml/min)	99.8 ± 49.8	112.4 ± 45.7	0.586
	Number of patients	8	10	–
	eGFR (ml/min)	111.1 ± 57.2	113.2 ± 45.9	0.933
	Total dose (mg/kg)	44.9 ± 3.8	49.4 ± 13.1	0.328
	Trough (mg/L)	14.4 ± 4.3	19.4 ± 4.4	0.029
Day-3	Peak (mg/L)	28.1 ± 6.0	33.7 ± 6.7	0.076
	V_d (L/kg)	0.65 ± 0.12	0.68 ± 0.10	0.609
	Cl_{vanco} (ml/min)	45.1 ± 54.8	79.3 ± 53.7	0.202
	AUC (mg.hr/L)	490.7 ± 101.0	665.9 ± 136.5	0.012
	Number of patients	5	8	–
	eGFR (ml/min)	115.5 ± 72.3	125.2 ± 51.2	0.764
	Total dose (mg/kg)	46.3 ± 3.3	47.1 ± 12.5	0.873
	Trough (mg/L)	12.3 ± 5.6	17.1 ± 1.8	0.137
Day-5	Peak (mg/L)	21.8 ± 2.7	31.4 ± 4.9	0.002
	V_d (L/kg)	0.97 ± 0.58	0.68 ± 0.11	0.330
	Cl_{vanco} (ml/min)	111.2 ± 39.9	103.6 ± 32.0	0.712
	AUC (mg.hr/L)	484.0 ± 130.4	606.1 ± 76.0	0.054

eGFR: Estimated Glomerular filtration rate, AUC: Area Under the Curve, Cl: Clearance, V_d: Volume of distribution, Vanco: Vancomycin.

Table 2. Frequencies of patients who have sub therapeutic levels regarding specific pharmacokinetic goals.

	Frequencies	Group 1	Group 2	Sig. (2-sided)	Odds Ratio
		%	%		
	Number of patients	8	10	–	–
	Trough <15 (mg/L)	62.5	10	0.043	15
	Trough <12.5 (mg/L)	50	0	0.023	–
Day-3	Trough <10 (mg/L)	12.5	0	0.444	–
	AUC <400 (mg.hr/L)	14.3	0	0.041	–
	AUC <600 (mg.hr/L)	85.7	30	0.050	14
	Number of patients	5	8	–	–
	Trough <15 (mg/L)	66.7	0	0.015	–
	Trough <12.5 (mg/L)	50	0	0.055	–
Day-5	Trough <10 (mg/L)	50	0	0.055	–
	AUC <400 (mg.hr/L)	40	0	0.012	–
	AUC <600 (mg.hr/L)	80	62.5	1	–

AUC: Area Under the Curve.

Table 3. Frequencies of patients who have toxic levels regarding specific pharmacokinetic goals during the study.

Frequencies	Group 1	Group 2	Sig. (2-sided)	Odds Ratio
	%	%		
Trough >25 (mg/L)	12.5	20	1	–
Peak >40 (mg/L)	0	10	1	–

Preparation and Clinical evaluation of Finastride gel in the treatment of idiopathic Hirsutism

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Abstract:

Objective:

Hirsutism is the presence of excess terminal hairs in females in a male-like pattern. The most accepted hypothesis for the development of hirsutism is increased 5-α reductase activity in hair follicles of hirsute women. Finasteride partially blocks the conversion of testosterone to dihydrotestosterone through inhibition of 5α - reductase in hair follicles. This study was designed to determine the efficacy of finasteride gel 0.25% in management of idiopathic hirsutism and treatment of hirsutism with topical finasteride to lessen the side effects.

Methods:

Women after puberty that have idiopathic hirsutism criteria are divided randomly in 2 groups; treatment and control. The number of patients in each group is 15 and received finasteride and placebo gel once a day on their skins. The patients were visited every month by dermatologist and the amount of response to the treatment and the patient satisfaction was recorded. Ferriman–Gallwey score of the treated area was determined.

Results:

After 6-month, mean thickness hairs in treating group were decreased from 102.00 ± 9.58 μm to 86.4±11.4 μm ($p < 0.05$),this difference was statistically significant. Gel application did not indicate any type of side effects.

Limitations:

Inclusion and exclusion criteria

Conclusion:

Finasteride partially blocks 5α - reductase. Because of the good absorption through the skin and good solubility of this medicine, the prepared gel formulation applied on the hirsutism area showed a significant decrease in hair growth locally, so finasteride gel is an efficient and harmless therapy in patients with idiopathic hirsutism.

Keywords:

Finastride, Idiopathic hirsutism, Testosterone

1. Introduction

Hirsutism is the presence of excess body or facial terminal hair growth in females in a male-like pattern, and affects 5–15% of women depending on definition[1]. Hirsutism is often regarded as a purely aesthetic problem but its medical importance is highlighted by the high prevalence of androgen excess disorders reported among hirsute women[2]. Although there are objective methods of assessing the extent of hirsutism, the perception and impact of excess body hair in an individual woman depends not only on its extent and severity but also on social and cultural influences[3]. Quality of life studies have indicated that severe hirsutism has a serious adverse effect on social interactions and that affected women have a high incidence of depressive symptoms[4-6]. A commonly used method to grade hair growth is a modified scale of Ferriman and Gallwey. A score of eight or more has been considered to represent hirsutism[7].Sex steroids and a number of local and systemic factors can act directly and indirectly on the dermal papilla to regulate hair growth. In response to the increased levels of androgens at puberty, vellus follicles in specific areas develop into terminal hairs[8, 9]. Androgens increase hair follicle size, hair fibre diameter, the proportion of time terminal hairs spend in the anagen phase and sebum secretion. Therefore, not only androgen action alters the type of present hair, but also they will increase the oiliness of skin and hair[9, 10].

Hirsutism is a sign of increased androgen action on hair follicles, from increased circulating levels of androgens (endogenous or exogenous) or increased sensitivity of hair follicles to normal levels of circulating androgens. The severity of the hirsutism does not directly correlate with the level of androgen plasma concentration, because the response of the androgen-dependent follicles to excess amount of androgen was considerably varies between individuals[8, 11].

The term idiopathic hirsutism has been used to describe the circumstance in which hirsutism is present with circulating androgen levels within the normal range[9]. Nearly all hirsute women have an increased in androgens, usually testosterone, but the increase may not be sufficient to raise the serum total testosterone concentration above the normal range because the carrier protein for testosterone, sex hormone-binding globulin, is suppressed when androgen production is increased. In the remaining women, the hirsutism may be due to increased conversion of testosterone to dihydrotestosterone by the enzyme 5α-reductase in peripheral tissue, including hair follicles which this metabolite is more potent than testosterone [12-17]. Thus, elevated 5a-reductase activity has been demonstrated in the hair follicles of women with idiopathic hirsutism, and excess hair growth is likely to be due to an exaggerated response of the hair follicle to normal androgen levels[18]. Nearly all circulating testosterone is bounded to sex hormone binding globulin and albumin, with free testosterone being the most biologically active form[11].

Different medical therapies, alone and in combination have been used to treat idiopathic hirsutism. Oral contraceptives and antiandrogen therapy such as spironolactone, cyproterone acetate and flutamide inhibits ovarian or adrenal androgen production and androgen activity either by blocking androgen cytochrome P450 receptors or by inhibiting 5α- reductas activity. In addition cosmetic hair removing procedures (camouflage by bleaching and various mechanical ways such as shaving, plucking and using depilatory creams) achieve the desired result for only a brief period [19, 20].

Finasteride is a 5α-R inhibitor which can be used systemic or local. Finasteride decreases hair growth by causing less exposure of hair follicles to androgen stimulation[21, 22]. Although the efficacy of systemic finasteride has been reported in different studies, there is a few articles in which the efficacy and tolerability of topical gel of finasteride has been evaluated. The aim of this study was to examine the efficacy and tolerability of topical finasteride in female with idiopathic hirsutism.

2. Materials and Methods

2.1. Materials

Hydroxy propyl methyl cellulose (HPMC) and sodium carboxy methyl cellulose (CMC) were purchased from Pastor chemical company (Japan). Sodium hydroxide (NaOH), potassium dihydrogen phosphate (KH_2PO_4), methyl paraben and propylene glycol were purchased from Merck (Germany). Finasteride was provided by Iran hormone pharmaceutical company (Tehran, Iran), ethanol and dialysis membrane were purchased from Touba azma (Tehran, Iran).

2.2. Clinical study

A double blind and randomized study which is controlled by dermatologist in comparison to placebo gel have been done for 6 months

The inclusion and exclusion criteria for the subject selection are presented at the following:

1. Ferriman-Gallwey Score > 8 [7]
2. Normal serum androgen (total testosterone, free testosterone, androstenedione and DHEA-S)
3. Normal serum level of thyroid hormone, prolactin and cortisol.
4. No chemical or biochemical evidence of polycystic ovarian syndrome which is ruled out by regular menstrual cycles, normal ultrasound exam, and serum LH/FSH ratio < 1 and normal serum SHBG.
5. Normal basal and ACTH-stimulated serum 17-hydroxyprogestrone level.
6. Absence of chronic renal disease, diabetes mellitus and hepatic disease.
7. The subjects that did not use any other drugs for treatment of hirsutism

The selected women after signing a written consent are divided randomly in 2 groups; treatment group (with finasteride) and control group (with placebo). The number of patients in each group was 15.

This study was approved by the ethical committee of Kermanshah University of medical sciences. All the patients were informed consent for their participation in our study after reading the protocol of this experiment. They were informed that finasteride could affect a male fetus and consequently pregnancy was contraindicated during the treatment and so effective contraceptive must be used. They were also informed that potential side effects of finasteride were unknown in women and they should report any possible side effects during the medication. The patients were explained not to use any other drug for idiopathic hirsutism at the same time. Moreover electrolysis, waxing and plucking were not permitted during the treatment whereas shaving was permitted for subjective evaluation of hair growth by patients. The degree of hirsutism in the skin area was determined by Ferriman-Gallwey score. The scale is from 0 (absence of terminal hairs) to 4 (extensive terminal hair growth). Premature scores were determined by 2 examiners and mean scores were calculated for each patients.

Three hairs of the skin area were plucked from each patient. Each hair was then fixed on a slide with a transparent resin that solidifies with air and was covered with another slide. Hair caliber was measured with a micrometer applied to an optical microscope (x 10 magnificence). Then they received finasteride gel 0.25% on their skins once a day for 6 months. They were explained to clean the skin area before usage and to avoid using powder, lotions, and sprays three hours after gel.
The patients were seen in consultation at 1 month's intervals. Questions were asked about the side effects, menstrual abnormalities and also patients self-evaluation of the clinical effects of the treatment. After six months rate of hair growth of the skin area, the mean caliber of three plucked hairs and the Ferriman-Gallwey score of the skin area was evaluated.

2.3. Statistical analyses
Data are presented as mean ± SD or percentage. Statistical analyses were performed using spss software version 16:0:0 and paired T-Test for comparison of quantitative variables was used to compare the hair caliber before and after medication. P values less than 0.05 were statistically significant.

2.4. Preparation of Finastride gel
According to previous studies related to clinical effect of finasteride on hirsutism, for preparing finasteride gel 0.25%, pure finasteride was used. hydroxy propyl methyl cellulose and sodium carboxymethyl cellulose as Polymers gel formulations was used by the specified amount. Propylene glycol as wetting agent and ethanol as cosolvent for finasteride and methyl paraben as a preservative agent was used.15 gr aluminum tube was selected as an appropriate package. The placebo gel consisted of the derma base alone in the same size and type of tube. No difference in color or texture was evident between the placebo and medication containing gels.

2.5. Physicochemical and microbial stability tests
To study the chemical and physical stability of the formulation, pharmaceutical products was placed at 40 ° C and 70% humidity in the germinator and each month for viscosity, color, and amount of drug was studied. Microbial and preservative effectiveness testing was based on the United States Pharmacopoeia guidelines.

2.6. In vitro Evaluation of drug release
2.6.1. Preparation of solutions
Isotonic phosphate buffered saline pH 5.75 (PBS-buffer) was prepared by dissolving 1.36 g KH_2PO_4 and 0.028g NaOH in 200 ml distilled water. PBS-buffer was used as the receptor solution.

2.6.2. Experiments with Franz diffusion cells
Franz diffusion cell with a volume of 78 ml was used for the drug release evaluation. The Franz diffusion cell consisted of a donor and receptor compartment .The membrane was mounted between the cell compartment and an O-ring was used to position the membrane. The two cell compartments were held together with a clamp. The temperature of Franz diffusion cell chamber was adjusted to

37°C by a water bath circulation and 1g of gel was applied to the cell that was put on dialysis membrane. The receptor solution was continuously stirred by means of a spinning bar magnet, at 200rpm. 2.0 ml aliquots were withdrawn through the sampling port of the receptor compartment at specified time intervals. The cells were refilled with receptor solution to keep the volume of receptor solution constant during the experiment. The experiments were run for 3 hours. Sample absorbance was read by a spectrophotometer at a wavelength of 210 nm. The linearity of calibration curve with concentration range from 0.6125-10 µg/ml and linear equation "y = 0.1669x – 0.0196" has been verified. The drug release profiles of the drug formulations were plotted according to the calibration curve.

3. Results

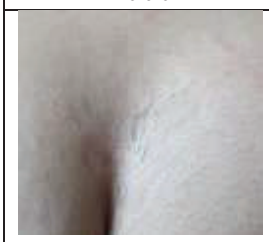
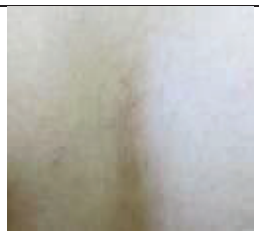
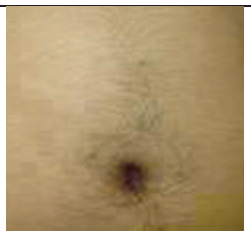
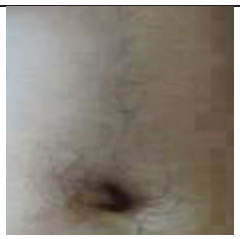
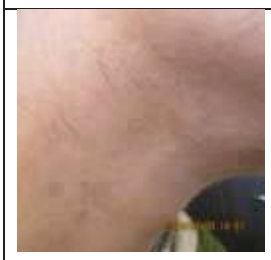
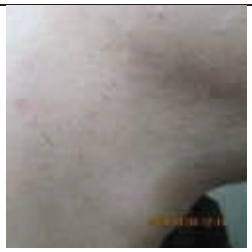
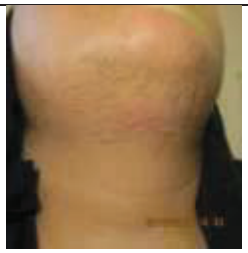
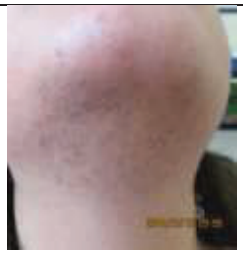
3.1. Patient compliancy

None of the women reported any problems with irregularity of menstrual periods, changes in libido, and changes in energy level, nausea, vomiting, diarrhea, abdominal pain, or headache. Allergic reaction to the medication or skin eruption in the areas in which the gels were applied was observed in one patient. All of the patients showed a good compliancy related to the finasteride gel application and there were no incompliance report about the viscosity, odor, color and filling during remaining time of gel on the skin.

3.2. Clinical effects

All of the patients in treating group noted a considerable diminished rate of hair growth on the areas in which the gel were applied (at least fewer times needed for shaving) and hair follicles became looser and easier to pluck, but patients in placebo group didn't mention any difference rate of hair growth. The pictures of some patients before and after treatment are showed in figure 1.

Severity of hirsutism after 6 months treatment with 0.25% finastride gel

Before	After	Before	After
			
			

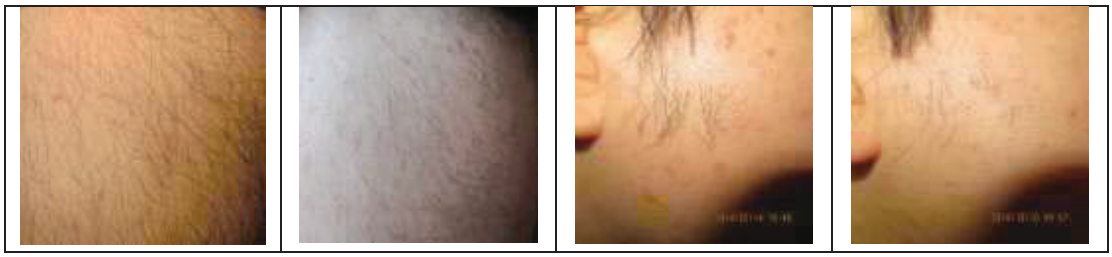


Fig. 1: Severity of hirsutism after 6 months treatment with 0.25% finastride gel

Hair thickness in treating group, before and after treatment are showed in table 1 and table 2 and hair thickness in placebo group, before and after treatment are showed in table 3 and table 4. Comparison Chart for mean thickness hairs before and after six months in both groups are shown in Figures 2 and 3.

Tab 1. Hair thickness (mm) – before treatment in treating group

Hair thickness (mm)						
Number	**Hair 1**	**Hair 2**	**Hair 3**	**Average**	**SD**	**% CV**
1	0.07	0.1	0.09	0.086667	0.015275	17.62529
2	0.11	0.11	0.11	0.11	0	0
3	0.08	0.07	0.07	0.073333	0.005774	7.872958
4	0.12	0.11	0.11	0.113333	0.005774	5.094267
5	0.08	0.1	0.09	0.09	0.01	11.11111
6	0.1	0.08	0.08	0.086667	0.011547	13.32347
7	0.12	0.11	0.1	0.11	0.01	9.090909
8	0.1	0.1	0.13	0.11	0.017321	15.74592
9	0.12	0.11	0.1	0.11	0.01	9.090909
10	0.1	0.11	0.11	0.106667	0.005774	5.412659
11	0.11	0.11	0.11	0.11	0	0
12	0.08	0.08	0.1	0.086667	0.011547	13.32347
13	0.08	0.08	0.07	0.076667	0.005774	7.530656
14	0.12	0.1	0.11	0.11	0.01	9.090909
15	0.11	0.12	0.08	0.103333	0.020817	20.14515
Average				0.102	0.00958	14.05297

Tab 2.Hair thickness (mm) –after treatment in treating group

Hair thickness (mm)						
Number	**Hair 1**	**Hair 2**	**Hair 3**	**Average**	**SD**	**% CV**
1	0.06	0.05	0.05	0.0533	0.0058	10.8253
2	0.09	0.1	0.11	0.1000	0.0100	10.0000
3	0.06	0.06	0.06	0.0600	0.0000	0.0000
4	0.1	0.13	0.07	0.1000	0.0300	30.0000

5	0.09	0.09	0.08	0.0867	0.0058	6.6617
6	0.06	0.08	0.1	0.0800	0.0200	25.0000
7	0.09	0.1	0.11	0.1000	0.0100	10.0000
8	0.06	0.08	0.07	0.0700	0.0100	14.2857
9	0.1	0.1	0.1	0.1000	0.0000	0.0000
10	0.08	0.08	0.11	0.0900	0.0173	19.2450
11	0.07	0.09	0.11	0.0900	0.0200	22.2222
12	0.11	0.13	0.09	0.1100	0.0200	18.1818
13	0.1	0.1	0.09	0.0967	0.0058	5.9726
14	0.12	0.11	0.11	0.1133	0.0058	5.0943
15	0.08	0.09	0.11	0.0933	0.0153	16.3663
Average				0.0896	0.0117	12.9237

After 6-month, mean thickness hairs in treating group were decreased from 102.00 ± 9.58 µm to 86.4±11.4 µm ($p < 0.05$),this difference was statistically significant.

After 6-month, mean thickness hairs in placebo group were decreased from 98.22 ± 22.32 µm to 96.88±20.75 µm ($p < 0.05$),this difference was not statistically significant.

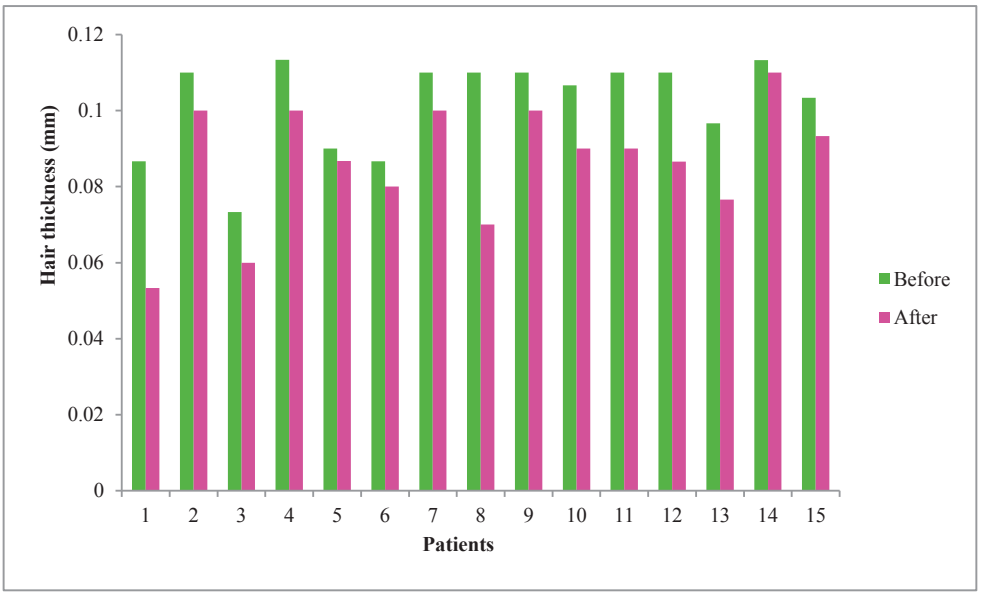


Fig 2. Comparison Chart for mean thickness hairs before and after six months in treating group

Tab 3. Hair thickness in placebo group, before treatment

Hair thickness (mm) - Before						
Number	**Hair 1**	**Hair 2**	**Hair 3**	**Average**	**SD**	**% CV**
1	0.03	0.03	0.02	0.026667	0.005774	21.65064
2	0.11	0.1	0.14	0.116667	0.020817	17.84285
3	0.1	0.09	0.1	0.096667	0.005774	5.972589
4	0.08	0.09	0.09	0.086667	0.005774	6.661734
5	0.11	0.1	0.11	0.106667	0.005774	5.412659
6	0.1	0.08	0.09	0.09	0.01	11.11111
7	0.12	0.12	0.1	0.113333	0.011547	10.18853
8	0.1	0.09	0.13	0.106667	0.020817	19.51562
9	0.11	0.11	0.09	0.103333	0.011547	11.17452
10	0.1	0.08	0.11	0.096667	0.015275	15.80199
11	0.1	0.11	0.13	0.113333	0.015275	13.47816
12	0.12	0.09	0.1	0.103333	0.015275	14.7825
13	0.08	0.9	0.11	0.093333	0.015275	16.36634
14	0.14	0.11	0.12	0.123333	0.015275	12.38534
15	0.09	0.12	0.08	0.096667	0.020817	21.53448
Total average				0.098222	0.02232	22.72441

Tab 4. hair thickness in placebo group, after treatment

Hair thickness (mm) - After						
Number	**Hair 1**	**Hair 2**	**Hair 3**	**Average**	**SD**	**% CV**
1	0.03	0.03	0.03	0.03	0	0
2	0.12	0.11	0.1	0.11	0.01	9.090909
3	0.11	0.09	0.1	0.1	0.01	10
4	0.08	0.1	0.09	0.09	0.01	11.11111
5	0.11	0.1	0.12	0.11	0.01	9.090909
6	0.08	0.08	0.07	0.076667	0.005774	7.530656
7	0.08	0.13	0.12	0.11	0.026458	24.05228
8	0.11	0.1	0.12	0.11	0.01	9.090909
9	0.1	0.12	0.09	0.103333	0.015275	14.7825
10	0.11	0.09	0.11	0.103333	0.011547	11.17452
11	0.12	0.08	0.11	0.103333	0.020817	20.14515
12	0.1	0.11	0.08	0.096667	0.015275	15.80199
13	0.08	0.1	0.11	0.096667	0.015275	15.80199
14	0.12	0.11	0.11	0.113333	0.005774	5.094267
15	0.08	0.12	0.1	0.1	0.02	20
Total average				0.096889	0.020758	21.42466

After 6-month, mean thickness hairs in placebo group were decreased from 98.22 ± 22.32 μm to 96.88±20.75 μm ($p < 0.05$),this difference was not statistically significant.

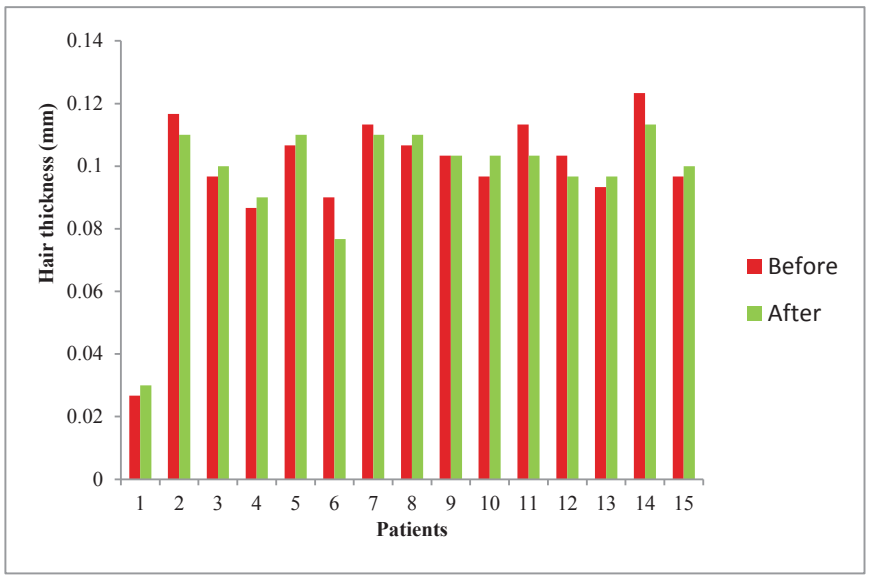


Fig 3. Comparison Chart for mean thickness hairs before and after six months in placebo group

3.3. In vitro drug release

Sample absorbance was read by a spectrophotometer at a wavelength of 210 nm. The linearity of calibration curve with concentration range from 0.6125-10 µg/ml has been proved. The drug release profiles of the drug formulations were plotted according to the calibration curve. The percent of drug release can be seen in table 5 and figure 4.

Tab 5. The percent of drug release from finastride gel

Time (min)	Absorbtion	Concentration (µg/ml)	Q* in 78 cc (µg)	Release (%)
15	0.068	5.248	409.39	16.37
30	0.203	13.337	1040.31	41.61
45	0.254	16.393	1278.65	51.14
60	0.294	18.789	1465.59	58.62
75	0.315	20.047	1563.73	62.54
90	0.348	22.025	1717.96	68.71
105	0.360	22.744	1774.04	70.96
120	0.385	24.242	1890.88	75.63
135	0.403	25.321	1975.00	79.00
150	0.411	25.799	2012.39	80.49
165	0.414	25.979	2026.41	81.05
180	0.417	26.159	2040.43	81.61

* The amount of drug

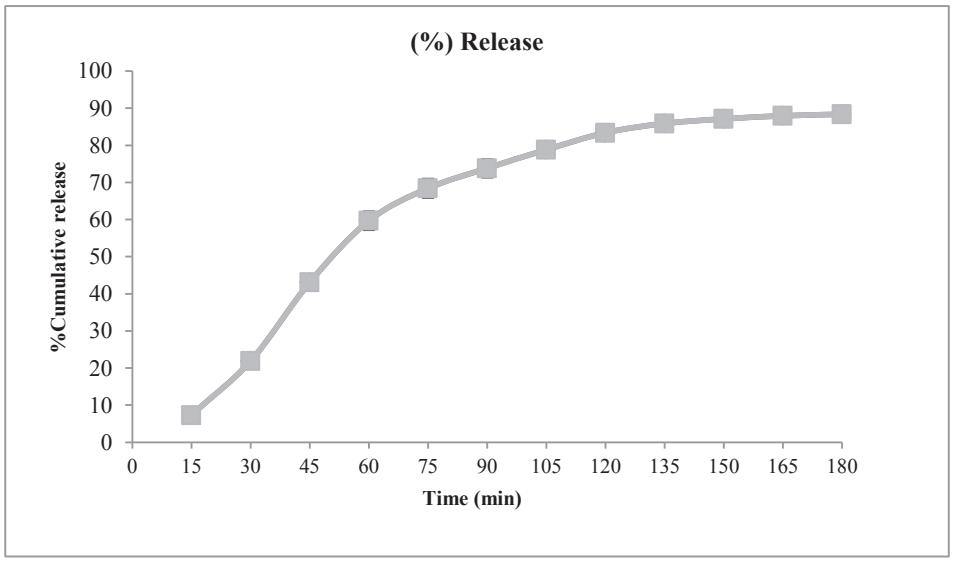


Fig 4. Curves of cumulative percentage drug release

4. Discussion

Hyperactivity of 5α- reductase in the skin is considered a major mechanism of excessive hair growth in hirsute women with normal levels of serum androgens. Androgens increase hair follicle size, hair fiber diameter, the proportion of time terminal hairs spend in the anagen phase and sebum secretion. Therefore, not only androgen action alters the type of present hair, but also they will increase the oiliness of skin and hair, since finasteride is a 5α- reductase inhibitor, with no androgenic, anti-androgenic, steroid hormone-related properties and affinity for androgen receptors, the use of finasteride for the treatment of hirsutism is rational because of its specific effect on 5α - reductase, the enzyme responsible for sensitizing the hair to testosterone [22-26]. In previous studies, orally administered finasteride has been successfully used in the treatment of hirsutism but have major side effects [27-29]. Notably there have been fewer investigations about topical application of finasteride. In fact its effects as a topical drug in the treatment of hirsutism are still debated, so this study was designed to determine the efficacy of finasteride gel 0.25% in management of idiopathic hirsutism and treatment of hirsutism with topical finasteride to lessen the side effects. Because the majority of patients with hirsutism have oily skin, oily base used for production pharmaceutical formulations may cause unpleasant feeling on the skin and can even lead to acne. So usage of the water-based gel formulations, in addition to the lack of acne it is more suitable for washing and cleansing of the skin, and have greater acceptance by patients. *Heydari et al*, Forty women with idiopathic hirsutism received finasteride cream 0.25% twice a day for 6 months on their chins and reported that acne was reported by 8 patients (20%) during the therapy[30], while in this study gel application, acne was not reported by patients. In a previous study, *Lucas* showed a significant reduction in mean hair counts and the thickness of the hairs in eight women with hirsutism that treated with finasteride cream 0.25%

[22], in other study *Heydari et al* indicated that mean hair thickness and mean *Ferriman –Gallwey* score were decreased [30] and Our study confirms the results of these two studies.

5. Conclusions

The current study, designed to assess the clinical effects of finasteride gel on hirsutism, showed significant improvement in the area treated by topically applied finasteride.

In our study no adverse effect except rash in one person was reported. This indicates that topical finasteride is a promising therapy for idiopathic hirsutism with less side-effect in comparison with orally administered one.

In this study, hair follicles became looser and easier to pluck. These effects helped the patients to have fewer problems with their hirsutism, as they managed to pluck hairs in longer intervals. One of the most important reasons for patient satisfaction from this dosage form was reduction in shaving time.

6. Acknowledgment

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Medulloblastoma and CNS-PNET Subtypes: Molecular basis to Histopathological features to Clinical Outcome

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Abstract:
Subtypes of central nervous system (CNS) primitive neuroectodermal tumors (PNET) were recently described. Two of them were found to have clinical significance and carry significant weight on prognosis. Between 1980 and 2014 more than 300 cases of CNS-PNET are identified in the hospital pathology archives. These tumors, like the medulloblastoma (as they are usually called when localized in the cerebellum) are usually composed of undifferentiated small blue cells, with areas showing tendency for glial, neuronal, melanocytic, myoblastic, and other mesenchymal differentiation. One of these CNS-PNET subtype is called lipidized medulloblastoma or medullocytoma. It is characterized by typical features of medulloblastoma with areas of "lipomatous differentiation", low proliferative potential, manifestation in adults, and apparent better prognosis. Another CNS-PNET subtype is called atypical teratoid/rhabdoid tumor (ATT/RT). ATT/RT is characterized by the presence of fields of primitive neuroecdtodermal tumor typical of medulloblastoma and areas of rhabdoid cell differentiation. ATT/RT is usually positive for a triad immunohistochemical analysis of epithelial membrane antigen (EMA), vimentin, and smooth muscle actin (SMA).

Introduction:
Central nervous system primitive neuroectodermal tumors (CNS-PNET) are the most common malignant brain tumors in children, and they are most commonly located in the cerebellum, where they are known as "medulloblastomas". The histogenesis of this tumor had been debated since the original description of the medulloblastoma in 1925 [(1)]. It is generally regarded as an embroyonal tumor with well-defined clinical and histological features [(2,3)]. This tumor is usually composed of morphologically undifferentiated small blue cells. It may show a tendency for neuronal [(4,5)], glial [(6)], melanocytic [(7,8)], myoblastic, and other mesenchymal differentiation [(9,10)].

Recently, two subgroups of CNS-PNET have been identified, namely medullocytoma [(11)] and atypical tetratoid/rhabdoid tumor [(12)]. To date, only 12 cases of medullocytoma (lipidized medulloblastoma) [(11,13-18)], and approximately 133 primary CNS atypical teratoid/rhabdoid tumors (ATT/RT) [(12,19-29)] had been reported. Medullocytoma is a new clinical pathologic entity characterized by typical features of medulloblastoma with areas of lipomatous differentiation, low proliferative potential, manifestation in adults, and apparent favorable clinical prognosis [(11)]. In contrast, the ATT/RT are most common in infants less than 2 years of age. They contain rhabdoid cell differentiation and fields of typical primitive

neuroectodermal tumor with unique immunohistochemical profile, including epithelial membrane antigen (EMA), vimentin, and smooth-muscle actin (SMA), and they are immunohistochemically negative for germ cell tumor markers [12]. Molecular genetic studies demonstrated that these tumors are also characterized by the cytogenetic finding of monosomy 22, while the classical medulloblastoma has isochromosome 17q [29].

The aim of this study is to identify these two newly recognized subgroups of CNS-PNET, namely medullocytoma and atypical tetratoid/rhabdoid tumor, in the hospital pathology archive.

Materials and Methods:

Cases: Between 1980 and 2014 more than 300 cases of CNS-PNET were identified in the hospital pathology archive.

Immunohistochemical studies: In this project the labeled Streptavidin-Biotin method was used to demonstrate the presence of epithelium membrane antigen, cytokeratine, vimentin, desmin, smooth-muscle Actin, S-100 protein, neurofilament protein, glial fibrillary acidic protein, synaptophysin, alpha fetoprotein, placental alkaline phosphatase, and human chorionic gonadotropin using antibodies on paraffin imbedded tissues. Briefly, after rehydration of the sections, an antigen retrieval method was utilized (microwaving), and followed with antibody incubation overnight. LSAB kit was used to localize the reaction and DAB chromogene to visualize it. Slides were cover-slipped and evaluated by light microscopy.

Results:

More than 300 cases of CNS-PNET were identified in the hospital pathology archive. These malignant cerebellar tumor are more common in children (82%, peak age 3-7 years). They made 19% of CNS tumors in children. They also can be seen in adults (18%, median 28 years). They made 1% of CNS tumors in adults. Despite these differences they had same 5 year actuarial survival of 50%. Long-term survival in adults was observed in two situations. One when surgical resection followed by radiotherapy to the posterior fossa and spinal cord are carried out, and the other when histological diagnosis of lipidized medulloblastoma (medullocytoma) is recognized. The lipidized medulloblastoma (medullocytoma) is seen in adults with cerebellar neoplasm exhibiting mature-type adipocytes in PNET background with low mitotic activity. These features are found to be associated with favorable prognosis. Immunohistochemistry of these neoplasms shwed positivity for GFAP (also in adipocytes), synaptophysin, neurone specific enulase, S-100, and vimentin. The *p*53 is negative and MIB-1 labling index is usually < 5%. Teratoid/rhabdoid tumors (ATT/RT) was usually misdiagnosed as PNET-MB, because it has PNET-like histology. It was seen in infants and children (1 - 14.9 years), and it carried grim prognosis. This type was seen in the cerebellum and cerebellopontine angles in 75%, in the cerebrum in 20%, in the pineal gland region in 6%, and in multiple sites in 10%. The histology of these ATT/RT showed rhabdoid cells in 100% of the cases (11% were purely composed of rhabdoid cells), PNET histology in 67%, mesenchymal features in 31%, and epithelial elements in 25%. Immunohistochemistry of

these ATT/RT neoplasms shwed positivity for EMA and vimentin in all cases (100%), SMA in 97%, GFAP in 73%, keratin in 66%, NFP in 38%, and desmin in 9%. Cytogenetics of ATT/RhT ahowed monosomy 22 in a third of cases and partial deletion of 22q11 in another third, while "typical" PNET showed i(17q) in half of the cases.

Discussion:

Identification of important parameters to use prospectively for the routine evaluation of primitive neuroectodermal tumors. This study will be valuable in identifying those laboratory evaluations which are of most benefit in providing accurate diagnoses. This will allow more effective and individualized treatment modalities to be applied in certain cases. Immunohistochemical analysis of a subset of primitive neuroectodermal tumors called "medullocytoma". The objective of this study is to identify this newly recognized subset of primitive neuroectodermal tumors, which is thought to carry a better prognosis than the classical primitive neuroectodermal tumor. This will be useful in providing more informed knowledge about this group of tumors to patients affected by this type of brain tumors. Evaluation of these cases and identification of this subset of primitive neuroectodermal tumors will enable us to perform correletion between the histological features and immunohistochemical analysis on one hand, and the clinical outcome and follow-up on the other hand.

Immunohistochemical catheterization of the atypical teratoid/rhabdoid tumors, which (by some investigators is considered a separate tumor misdiagnosed as PNET) form another subset of the primitive neuroectodermal tumors occurring in children of two years of age or younger. These tumors carry a grim prognosis and analysis of these cases will again enable us to estimate a more informed clinical outcome in terms of prognosis.

The study contributes to the following developmental issues: 1) To better understand the disease process in patients developing this type of brain tumor, namely primitive neuroectodermal tumors. 2) To delineate further the specific features of the subtypes of these neuroectodermal tumors, namely the "medullocytoma" and the atypical teratoid/rhabdoid tumors, in patients in terms of their morphological presentations. 3)To classify the "subtypes" of these neuroectodermal tumors of the brain in our patient population. 4) To identify those "subsets" of tumors in our patients for appropriate treatment modalities.

In conclusion, it is obvious that primitive neuroectodermal tumors have been well known, though their histogenesis raised tremendous debate. Fairly recently two "subtypes" of these tumors have been characterized. One carry a grim prognosis and occurs in children of two years of age or younger, and the other has a better prognosis than the usual primitive neutroectodermal tumor and usually occurs in adults. This retrospective study made use of more than 300 cases archived since 1981, and enabled us to identify these two main "subsets" of the primitive neutroectodermal tumors of the brain to help predict more accurately their histologic behaviour and their clinical outcome. In turn this will be used prospectively to better evaluate primitive neuroectodermal tumors and make us better informed about the prognosis of these tumors, based on their morphological and immunohistochemical profiles.

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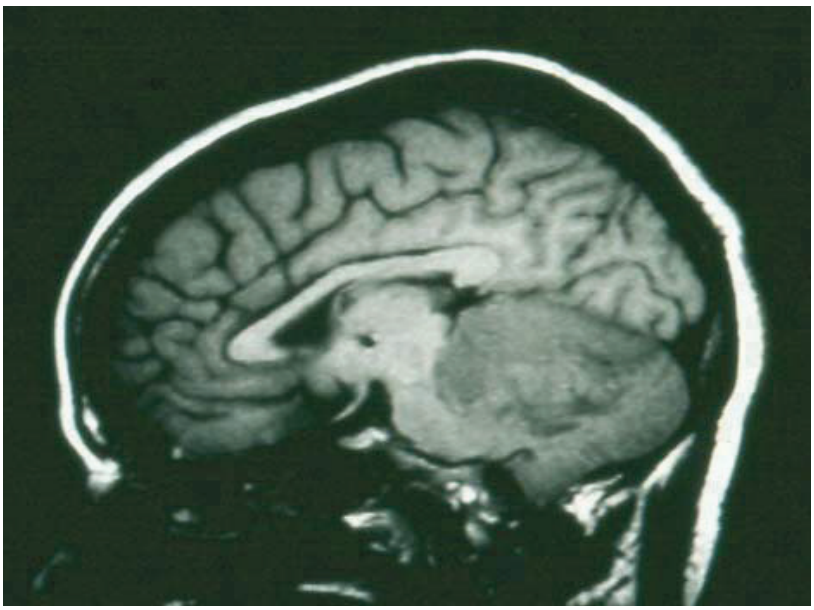

Figure 1. “Typical” medulloblastoma MRI.

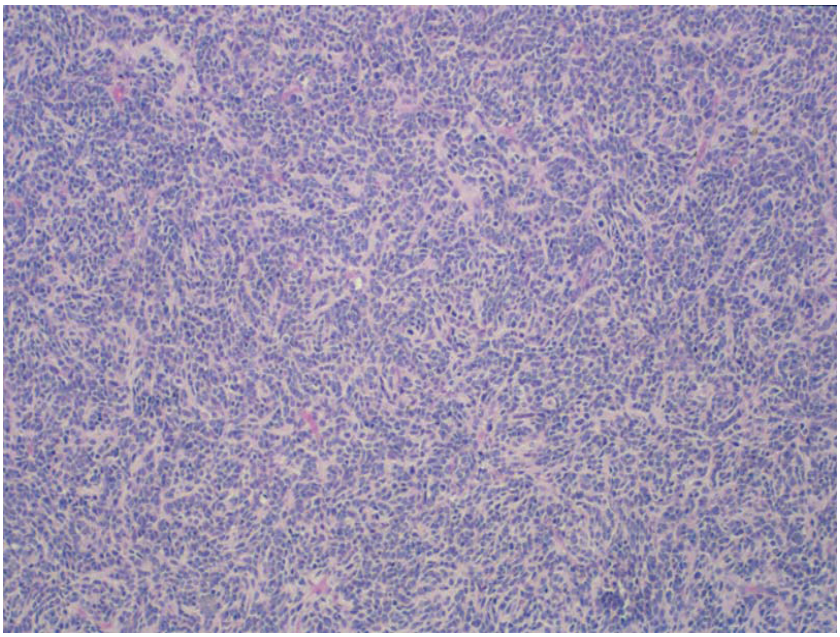

Figure 2. “Typical” medulloblastoma. Histology.

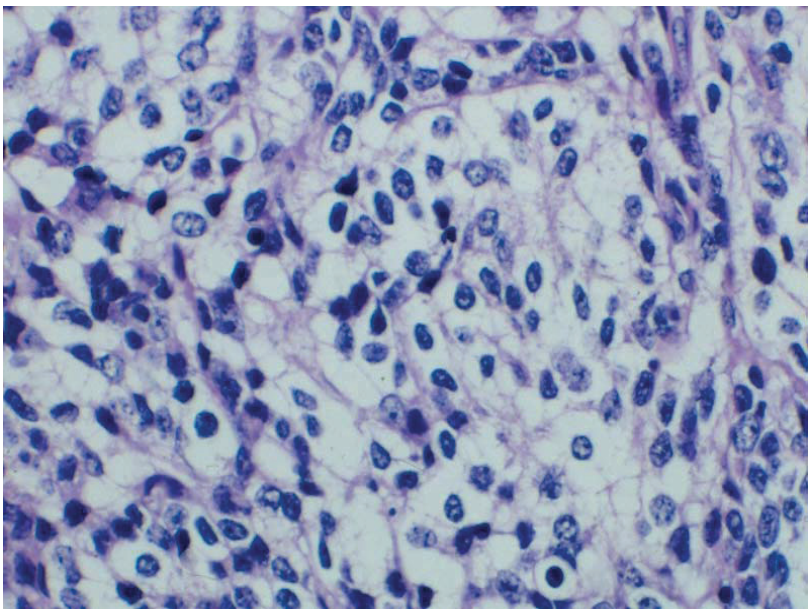

Figure 3. Medullocytoma (lipidized medulloblastoma). Histology.

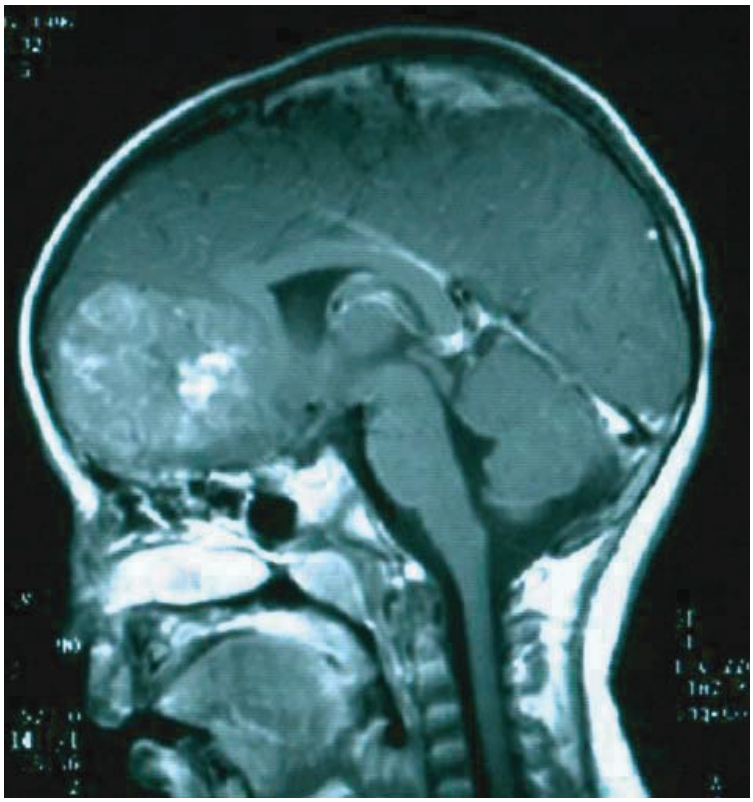

Figure 4. Atypical teratoid/rhabdoid tumors (ATT/RT). MRI.

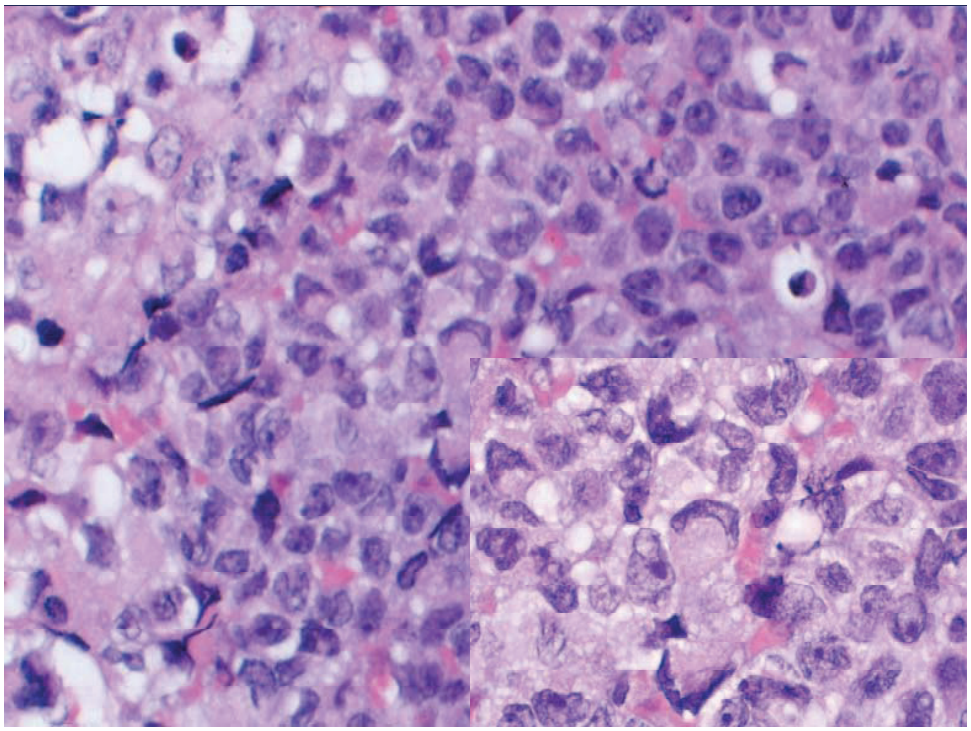

Figure 5. Atypical teratoid/rhabdoid tumors (ATT/RT). Histology.

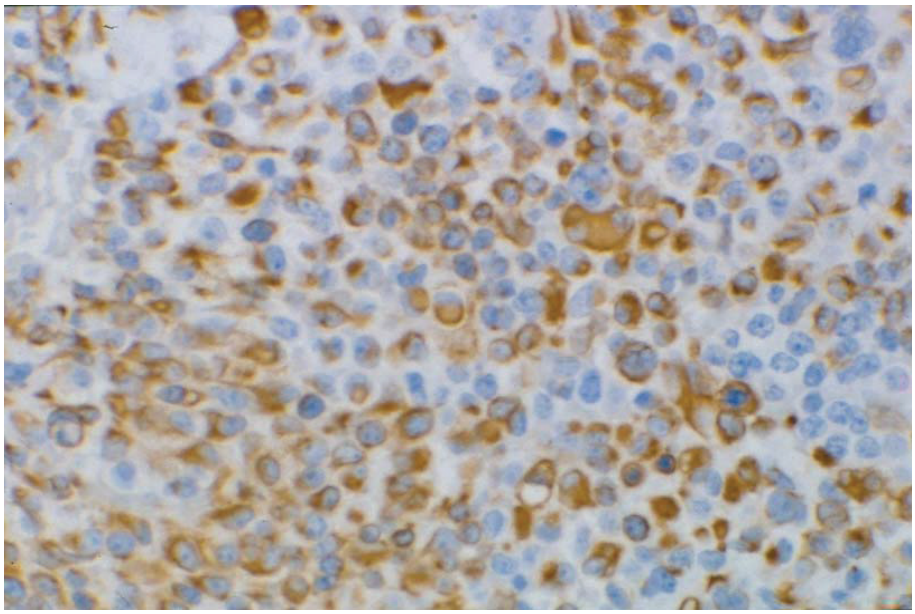

Figure 6. Atypical teratoid/rhabdoid tumors (ATT/RT). EMA Immunohistochemistry.

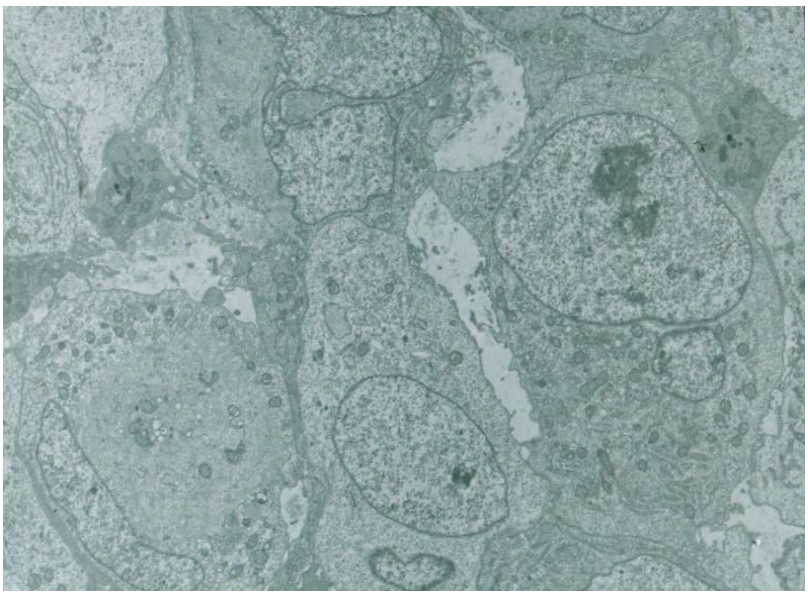

Figure 7. Atypical teratoid/rhabdoid tumors (ATT/RT). Electron microscopy.

Performance assessment of the X-rays imaging system fabricated in King Saud University[1]

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Abstract

All imaging system and especially X-rays should possess excellent image quality. Which is linked with accuracy and the superior performance of the X-ray tube itself to investigate the imaging performance and the commissioning tests. The accuracy requires the holder for the X-ray imaging system is good enough to withstand the weight of the imaging system and allows it to move and rotate in all directions. Therefore, an approach for design and analysis of mechanism frame using advanced computer aided engineering (CAE) tools will be applied for shielded fabricated holder as well as locally reassembled with a collimator. In addition, most standard, commissioning and acceptance tests (reproducibility, kVp accuracy, stability with change in tube voltage, half value layer and tube output) have been applied to the SB-80-250 X-ray imaging system to assess its performance. The stress values and reported results were within the international standards.

Keywords: *X-ray tube, performance, reproducibility*

1. Introduction

X-ray radiography imaging system offers the potential of providing opportunities for early detecting of diseases and thus considered the most important technique for diagnose. However, it is always a problem to carry the X-ray to scan a patient in which the stability and accuracy are the major role for fine scanning results. Therefore, it must possess both excellent spatial resolution and optimum contrast. The image quality from such system is intimately linked to the precise and accurate acquisition of information from the X-ray beam attenuated from the patient [1].

[1] This work was supported by the NSTIP strategic technologist program number (MED_1827) in Kingdom of Saudi Arabia.

The main aim of this study is to make the SB-80-250 X-ray tube geometrically suitable for use in imaging application, then performance assessment of the X-rays imaging system.

This is obtained throughout the initial implementation we were unable to move the X-ray system at any angle or at any direction, i.e. on six axes of movement, Consequently, the system motion will be in x, y, z directions. This is allowed movement in forward/backward, up/down and left/right directions. , the tube can be used in all geometrical set-ups. Then, we can determine how is a SB-80-250 X-ray tube easy achieve any experimental test, such use it for 3D-imaging of the uncompressed breast. The test methods and standards applied in performance test, are mainly derived from safety report series NO.39 [2] and radiation protection NO.91 [3] and the Canadian Guidelines [4].

2. Materials and Methods

Figure 1 shows the SB-80-250 X-ray tube possesses a 35-80 kVp, 10-250μA, stability 0.5% [5]. The system was fabricated and locally reassembled with a collimator. The collimator is a British made and its model is Picker international limited. It characterized by having a small light that can be used to determine the centre point of the area being imaged. Two dosimeters was used to commissioning and acceptance testing of the X-ray imaging system. Unfors RaySafe Xi whose possesses 0.05 – 9999 mAs, reproducibility < 0.5 %, dose range 10 μGy-9999 Gy and 35-160 kVp. In addition Fluke TNT 12000 with 0-999.9 mAs, with reproducibility of ±0.5 %, dose range from 5 mGy upto 999 Gy, and kVp from 22 up to 150 kVp [6]. For design [7] a good model. an arm with six full rotation holders for holding the X-ray detector. It has to operate safely. In addition, it needs to be made of material of high mechanical properties to resist fracture, deflection, buckling and corrosion. The holder should be able to sustain the weight of the X-ray and its accessories which is about 40kg. Also, it should be relatively light so that it can be moved easily. The material of the base metal used in this work is austenitic stainless steel (AISI 304) sheet with 1.00 mm thickness. The mechanical properties of this material are found to be: Modulus of Elasticity 193.7GPA; Poisson's ratio 0.3; Yield Stress 277.3MPa and; Ultimate Stress 737MPa. These are the average values obtained from the standard tensile tests performed on three standard samples of this material according to ASTM standard E8-81 [8].

Figure 1 The SB-80-250 X-ray tube

3. Results and Discussions

3.1 SB-80-250 X-ray tube geometric development

For using SB-80-250 X-ray tube to imaging at different positions and angles. it needs to be held on a mechanism that provides six degrees of freedom motion. Therefore, a holder is designed locally on site so that it can give a full six degrees of freedom motions. Three translation in x, y, z directions, and three rotations about x, y, z axes.

This mechanism has the following four degrees of freedom: move up/down (z-axis), forward/backward (x-axis), left/right (y-axis), and rotate about z-axis (yaw axis). The other missing two degrees of freedom are: rotate about the x-axis (roll axis) and rotate about y-axis (pitch axis). To add these two missing degrees of freedom, an additional parts need to be manufactured. These parts are first designed using CAD software as shown in Figure 2. Part one is the base, part two is the connecting holder, part three is the bolt. As seen in Figure 3 the new model of x-rays device after add these parts were manufactured locally.

It is very important to isolate the sides of the X-ray machine from all sides except the focal point to insure that no X-ray radiation getting outside from all sided except the focal point. Therefore, a shielding material made of lead with a thickness of 2 mm is used. radiation leakages were counted by the survey device and the measured value found to be zero. To collimate the beam of the X-ray device a filter device to the x-ray beam such as collimator is added. Finally, the X-ray device on a long standing holder for the thyroid to make it negotiable to lift and reduction to use it at any source to image distance as shown in Figure 4.

Figure 2 The CAD models of the required parts (1-3)

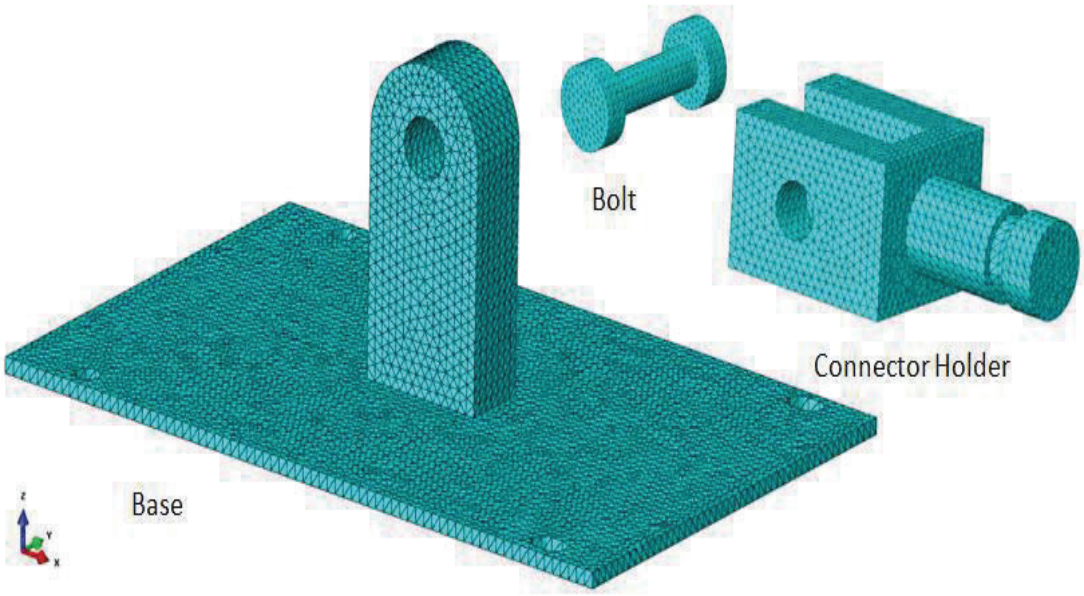
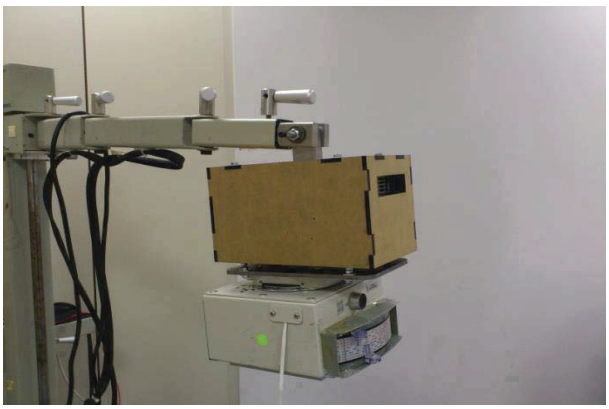


Figure 3 Assembling all the locally manufactured parts to the X-ray (SB-80-250) device

Figure 4 The imaging system showing the placement of lead shied on the SB-80-250 X-ray tube joined with the collimator and thyroid holder



3.2 Performance testing and commissioning of the SB-80-250 X-ray tube

Before using the X-ray tube for imaging it is necessary to test the performance of the tube to obtain accurate assessment with minimum dose to patients and staff. Therefore, Initially we confirmed the tube voltage is constant over time and the current. To start investigate the performance assessment and commissioning tests of a SB-80-250 X-ray tube. Most standard, commissioning and acceptance testing of the X-ray imaging system will be reported. This includes, tube output, reproducibility, kVp accuracy, stability with change in tube voltage and half value layer. The radiation scattered and leakage were measured using both Radcale and Fluke detectors. Then, we have performed the acceptance for the X-ray source used for our study as follows:

3.2.1 Radiation leakage

We found that the leakage radiation from the X-ray tube housing, with all the shutters closed, not exceed 2.5 mR/hr at 5 cm from the surface as recommended [3].

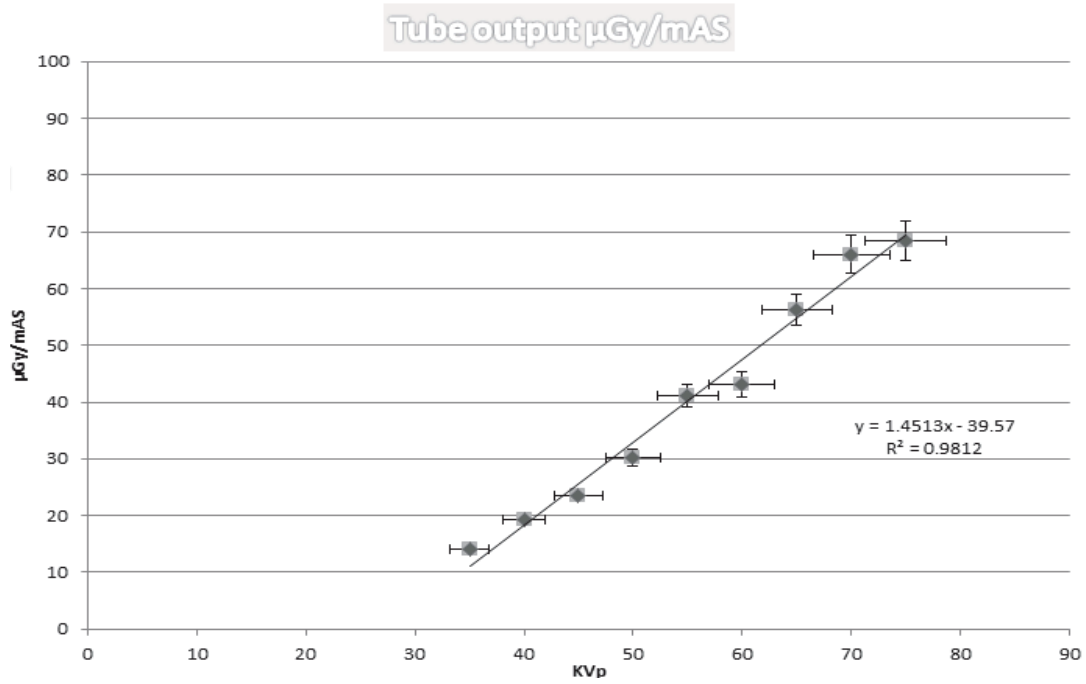
Then, we measured the radiation leakage to the SB-80-250 X-ray at 80 kVp and 250 μAs for 10 sec by applying a lead sheet stopper to discard the primary radiation beam using Radcal 2026C, was 0.1584 mGy/h at 0.3m, 0.014256 mGy/h at 1 meter, much less than 1mGy during 1 hour of exposure at 1 meter distance from the source according to international recommendations [2].

3.2.2 Tube output

Figure 5 give an overview of the tube output measurements for every voltage. Such output was within the desirable interval that reported [9].

The tube output of an X-ray system is the dose generated at 1 m distance of the focus, per unit of mAs. At focus to detector distance FDD=600 mm, the tube output was measured for different kVp settings from 35 to 80 kVp, ten dose measurements were taken by Fluke dosimeter detector TNT 12000 DoseMate at 250 μAs settings and 10 sec. The average exposure was found to be between 39.31-239.36 μGy/mAS as in the table 1, consequently the specific tube output at a distance of 1 meter was between 14.15-86.16 μGy/mAS .

Figure 5 Overview of the tube output to the SB-80-250 X-ray tube



Source: Author's calculation

Table 1 Tube output to the SB-80-250 X-ray tube

	Dose	***Dose***	***Tube output***	***Tube output at 1 m***
KVp	***mR***	***µGy***	***µGy /mAS***	***µGy/mAS at 1m***
35	*11.17*	*98.296*	*39.3184*	*14.15462*
40	*15.23*	*134.024*	*53.6096*	*19.29946*
45	*18.63*	*163.944*	*65.5776*	*23.60794*
50	*23.89*	*210.232*	*84.0928*	*30.27341*
55	*32.45*	*285.56*	*114.224*	*41.12064*
60	*34*	*299.2*	*119.68*	*43.0848*
65	*44.4*	*390.72*	*156.288*	*56.26368*
70	*52.1*	*458.48*	*183.392*	*66.02112*
75	*54*	*475.2*	*190.08*	*68.4288*
80	*68*	*598.4*	*239.36*	*86.1696*

Source: Author's calculation

3.2.3 Reproducibility

At fixed tube voltage of 35and 80 kVp, the reproducibility was evaluated by repeating the measurement 10 times for each KVp, using the kVp meter. The measured kVp was within the range of (35.1 – 35.3 kVp) and (80 – 80.2) respectively , fulfilling the recommendation to be within ± 0.5 kV [3].

3.2.4 Accuracy

The accuracy was assessed by applying a number of tube voltages, covering all the range of KVp used settings (35 - 80 kVp) and the results were all cases within a ± 1 kV error interval [3].

3.2.5 Half value layer

For many years medical physicists had been using half-value layer (HVL) in order to specify the quality of X-ray beams [10]. By used different KVp and 250 μA an accurate measurement of the half value layer (HVL) is required to many of the experiments. Such parameter were obtained by adding Aluminium filters of density 2.7 g/cm3 and purity of 99.59 % to the X-ray beam and measuring the attenuation effect according to the following equation (1) [4]:

$$HVL = \frac{X1 \times Ln\left(\frac{2Y2}{Y0}\right) - X2 \times Ln\left(\frac{2Y1}{Y0}\right)}{Ln\left(\frac{Y2}{Y1}\right)} \quad (1)$$

Where Y1 and Y2 are the exposure readings, with added aluminium thickness of X1 and X2 respectively and Y0 correspond to the primary exposure. We found a HVL in the Table 2 as recommendation [4] to be as the following equation (2):

$$HVL \geq \frac{KVp}{100} + 0.03 \quad (2)$$

Table 2 HVL amusement to the SB-80-250 X-ray tube

X-Ray tube voltage	***HVL***	***Accepted***
KVp	***Al mm***	***HVL ≥***
35	*0.926*	*0.38*
40	*1.024*	*0.43*
45	*1.090*	*0.48*
50	*1.296*	*0.53*
55	*1.674*	*0.58*
60	*1.505*	*0.63*
65	*1.299*	*0.68*
70	*1.454*	*0.73*
75	*1.654*	*0.78*
80	*1.352*	*0.83*

Source: Author's calculation

4. Conclusion

An approach for design and analysis of mechanism frame using advanced computer aided engineering (CAE) tools was applied. All stress values were compared to the elastic limits of the materials used in the study. An arm with six full rotation holders for holding the X-ray detector was design. It operates safely. The configuration model is able to sustain the weight of the X-ray and its accessories which is about 40kg.

Then, most of the commissioning and performance tests were performed on such system. The obtained results of all tests were within the international standards. The commissioning and performance testing of SB-80-250 X-ray tube includes tube output, reproducibility, kVp accuracy, stability with change in tube voltage and half value layer.

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