ISSN 2545-4366
www.e-mja.com

MJA

Macedonian Journal of Anaesthesia

A Journal on Anaesthesiology, Resuscitation, Analgesia and Critical Care

Number 4. May 2018

Journal of the Macedonian Society of Anaesthesiologists
and Macedonian Society of Critical Care Medicine

Publisher:
Department of Anaesthesia and Reanimation, Faculty of Medicine,
"Ss. Cyril and Methodius" University, Skopje, Macedonia

Macedonian Journal of Anaesthesia

A Journal on Anaesthesiology, Resuscitation, Analgesia and Critical Care

Production Editor

Vanja Gievski

Publisher:

Department of Anaesthesia and Reanimation, Faculty of Medicine, “Ss. Cyril and Methodius” University, Skopje, Macedonia

Proofreading Daniela Nacevska Stojcevska

Printed by ASKOLOR

CONTENT

 ISSN 2545-4366 | UDC: 616-089.5(091)

EDITORIAL

Panta Rhei – Heraclitus
"Everything flows, everything changes"

One-hundred-seventy-and-two years have passed since the first officially administered anesthesia. Then, in Boston, the American dentist William Morton gave divinyl ether anesthesia to a 20-year-old patient, who at that time was underwent to a neck tumor surgery performed by the famous surgeon Collins Warren. This event was immediately reported in the newspapers at the time, while the news reached Europe quite rapidly thanks to the newly placed cable connection under the Atlantic. Here in the Balkans, only a year after, the Croatian dentist Ivo Bettini in Zadar extracted a tooth from a patient using general etheric anesthesia. However, already in 1848 the first death that had occurred from the use of general anesthesia was also reported.

Almost at the same time, local anesthesia started to be used in medical procedures ("anesthesia without sleep''). The first local anesthesia procedures were administered by surgeons and the first spinal anesthesia was performed by the German surgeon August Bier in 1898.

Since then, these two methods have been developing till this day as two parallel directions. There were times when one or the other was more popular, but in global terms, the dilemma whether general or regional anesthesia should be performed remains, of course in relation to surgeries where this type of choice is possible.

The first used general anesthetics consisted of gases or volatile liquids (ether chloroform, nitrous oxide, cyclopropane), thus, in people's collective memory the image of anesthesia as something that is inhaled through a mask which causes loss of consciousness has persisted. Today, with the exception of nitrous oxide, the anesthetics that introduced the era of anesthesia have become distant history. The contemporary inhalation anesthesia has reached its peak in 1956 when the use of Halothane was introduced and especially during the 80ties when Enflurane and Isoflurane were applied, while during the next decade Desflurane and Sevoflurane were introduced.

Intravenous anesthesia has bloomed during the World War II when Thiopentone was massively introduced in surgery, as a medication which was advertised that can be administered by the surgeon itself without the necessity of a different kind of a professional. However, due to this unserious approach, which was specially accentuated from the still unperfected techniques related to the maintenance of the airway, frequent incidents occurred that led to severe criticism by the professional public. Intravenous anesthesia had to wait for its next "golden age" for a long time, until the beginning of the 1980ies, when the combination of Fentanyl and Droperdol was massively being used together with the new relaxant at that time Pancuronum bromide, which produced the so-called neuroleptic anesthesia.

REVIEW ARTICLE ISSN 2545-4366 | UDC: 615.21.03:616-083.98

EVALUATION OF ANALGESIA, SEDATON AND AGITATION IN INTENSIVE CARE UNIT

Trojikj T[1]
[1] *University Clinic for Surgery "St. Naum Ohridski", Skopje, Macedonia*

ABSTRACT

Most of the patients in the intensive care unit need sedation and analgesia in order to avoid pain, anxiety and to be able to have invasive procedures, mechanical ventilation and to reduce stress and oxygen consumption. Untreated patient increases stress response to invasive procedures such as intubation and central venous catheterization. The pain is the most common memory from intensive care unit and that can lead to agitation accidental extubation and removal of intravascular devices. Very often, patients in the intensive care are over sedated and that can prolong time of mechanical ventilation. Maintenance of light sedation, sufficient analgesia, early recognition and treatment of delirium, are imperatives in patients in the intensive care units. The Behavior Pain Scale (BPS), Richmond Agitation –Sedation Scale (RASS), Sedation Agitation Scale (SAS), Ramsey Sedation Scale are valid and reliable sedation assessment tools for measuring quality and depth of sedation in adults in ICU patients. Confusion Assessment Method (CAM) for the ICU as tool for early recognition of delirium is necessity for early and adequate treatment of delirium. Treatments according to these assessments of pain, sedation, agitation and delirium should be usual practice in intensive care unit. Protocols from literature and other hospitals may be initiative for preventing, prolonged sedation, ventilation and length of stay in intensive care unit.

Key words: agitation, critically ill patient, sedation.

Corresponding author: *Tatjana Trojikj, University Clinic of Surgery "St. Naum Ohridski", Skopje, Macedonia. E-mail: tanja.trojik@gmail.com*

Assessment of Pain in the Intensive Care Unit

Intensive care unit patients are not homogenous group of patients. However, all of them have sympathetic stress response due to increased endogenous catecholamine activity. Most of them are in pain during the whole period of intensive treatment. Pain and evaluation of pain is essential in treatment of these patients. In 35% to 55% ICU patients pain was underrate, furthermore 64% of ICU patients have procedures without receiving drugs for pain relief (1,2,3). The pain increases myocardial workload, which can lead to myocardial ischemia, or to splinting, atelectasis, and a cascade of events that in turn can lead to pneumonia (4). Pain and anxiety lead to agitation and delirium. This may also lead to significant physical and psychological stress, and long-term consequences (posttraumatic stress disorder (PTSD) and delirium). Analgesia and sedation, are administered to provide patient's comfort, safety by decreasing the stress response. Sometime patients in the ICU are oversedated. And that leads to prolongation of mechanical ventilation, greater need for radiological evaluations of mental status and developing brain dysfunction (5, 6). In order to avoid prolongation in ICU with all negative effects there must be a balance of analgesic and sedative drug administration. In order to have calm patient with adequate analgesia, we have to try to evaluate the pain. Which scale we should use depends on whether we have communicative or non-communicative patient. Numeric pain scale (NPS) is used to evaluate pain in communicative patient. In this scale 0 indicates that patient has no pain and 10 is the indictor that patient has worst pain that he has ever experienced. Most of the patients in ICU are unable to use this scale because they are on mechanical ventilation, sedated and even paralyzed from neuromuscular relaxants. Many patients are comatose or suffer from cognitive disorder. In these patients we have to focus on observation on behavioral and physiological indicators. In non-communicative patients, scales for evaluation of pain were developed from pediatric patients, newborns, and nonverbal toddlers etc., who were unable verbally to express pain. The first Adult Non-Verbal Pain Scale is modification of FLACC (face, leg, activity, cry, consol ability scale). In these days the most used scale for pain assessment is The Behavior Pain Scale (BPS), based on a sum score of three items: facial expression, movements of upper limbs, and compliance with mechanical ventilation. Each pain indicator is scored from 1 (no response) to 4 (full response) with maximum score of 12. Scores of each three domains are summed, with a total score from 3 to 12.

Table1. *Behavior Pain Scale (BPS)*

Item	Description	Score
Facial expression	Relaxed	1
	Partially tightened (for example, brow lowering)	2
	Fully tightened (for example, eyelid closing)	3
	Grimacing	4
Upper limbs	No movement	1
	Partially bent	2
	Fully bent with finger flexion	3
	Permanently retracted	4

Compliance with ventilation	Tolerating movement	1
	Coughing but tolerating ventilation for most of the time	2
	Fighting ventilator	3
	Unable to control ventilation	4

Management of the pain in the intensive care unit include regional and systematic analgesic therapy. In the ICU, these regional techniques likely have higher risk of failure, infection, bleeding, neuronal injury, pneumothorax, and hemodynamic compromise due to the patients critical illness and therefore they should only be performed by specially trained clinicians. Systemic therapies include acetaminophen and nonsteroidal anti-inflammatory drugs such as ketorolac, but the most commonly used analgesics in the ICU are opioids secondary to their analgesic and sedative properties. Negative effects of use of systematic pain therapy are: respiratory depression which is commonly seen and often enhanced by co-administration of additional sedative agents; and hypotension results from decreased sympathetic tone or vasodilation from histamine release. Other side effects are: decreased gastrointestinal motility, pruritus, flushing, urinary retention and delirium. Nonopioid analgesics should be considered for treatment of low acuity pain or as adjuncts to decrease opioid and to preserve mental status and pulmonary function. Morphine and hydromorphone are most often utilized as intermittent intravenous (IV) injections. Morphine dose is 2–5 mg IV every 5–15 minutes until the pain is controlled, followed by similar doses every 2–4 hours. Effects can be prolonged in patients with renal or hepatic impairment or obesity.

Fentanyl is a synthetic opioid with a rapid onset (5–15 minutes) and a short duration of action (30–60 minutes). Loading doses of 25–100 μg of fentanyl are given every 5–10 minutes until the pain is controlled, followed by infusion rates of 25–250 μg/h. It has a large volume of distribution, so significant drug accumulation and a prolonged half-life can occur with prolonged infusions.Fentanyl is the preferred opioid analgesic in hemodynamically unstable patients or those with renal insufficiency (1).

Remifentanil, a derivative of fentanyl, is an opioid that is utilized primarily as an infusion (0.05–2.00 μg/kg/min) and has an elimination half-life of less than 10 minutes regardless of the infusion duration. Dosing for the infusion should be based on ideal body weight or lean body mass, and hypotension and bradycardia are the most common side effects. Due to its ultra-short half-life, supplemental analgesic medications are required. Remifentanil provides better outcomes than morphine with regards to time at optimal arousal level, necessity of supplemental sedation, duration of mechanical ventilation, and extubation time in one randomized double blind study (7). Meanwhile, remifentanil and fentanyl have displayedequal efficacy in achieving sedation goals with no difference in extubation times. Patients receiving fentanyl required more breakthrough sedatives, but experienced less pain after extubation compared to the patients receiving remifent.

Sedation is necessary in intensive care patients. It facilitates mechanical ventilation, diminishes anxiety, leads to amnesia, and prevents self-mutilation, insomnia, and dyspnea. The appropriate

use of sedatives can facilitate patient care and contribute to patient's safety. Sometimes, appropriate sedation prevents psychiatric disorders delirium and leads to better cooperation with patient's family who likes to see that patient is peaceful and doesn't suffer.

However, the use of sedation is associated with negative patient outcomes, including prolonged mechanical ventilation and cognitive dysfunction (9,10,11). It is important, therefore, to define the indication for sedation, as this may affect the sedative selection and helps determine the endpoint for sedative utilization. There are many scales which are used to provide goal directed therapy individualized to the patient. When used appropriate, these scales can provide a therapeutic target, which can lead to decreased dosing of sedative medications and decreased time on mechanical ventilation (12). The most common sedative medications used within the ICU are propofol, dexmedetomidine and benzodiazepines, with other agents such as clonidine, ketamine, volatile anesthetics and neuromuscular blockers used as adjunct therapies. Importantly, the duration of sedative medication administration has shown to correlate with the duration of mechanical ventilation and the consistent theme throughout many sedation studies is that efforts should be made to minimize the total dose of sedative by using the minimum effective dose, daily interruption of sedation, and infusions for the shortest time required (13,14). Furthermore, there is increasing literature that favors the avoidance of benzodiazepines for sedation in the ICU in favor of propofol, dexmedetomidine or analgosedation regimens. Propofol is a diisopropylphenol anesthetic and a γ-aminobutyric acid (GABA) agonist. It has rapid onset (1–2 minutes) and short duration of action (2–8 minutes). It is typically given as a bolus injection of 40–100 mg IV, followed by an infusion of 25–75 μg/kg/min. Its volume of distribution is large with a short distribution half-life. Propofol side effects include hypotension due to vasodilation and myocardial depression, respiratory depression and hypertriglyceridemia. The hypertriglyceridemia may either be due to the intralipid carrier or altered hepatic lipid metabolism, which can be seen with the propofol infusion syndrome (PRIS) (15). PRIS is associated with increased dosage of propofol (doses >75 μg/kg/min or >5 mg/kg/h), pediatric sedation, critical illness, and prolonged infusions (>48 hours) and is characterized by severe lactic acidosis and rhabdomyolysis.

Table 2. *Richmond agitation sedation scale*

Score	Term	Description
+4	Combative	Overtly combative or violent, immediate danger to staff
+3	Very agitated	Pulls on or removes tubes or catheters or exhibits aggressive behavior toward staff
+2	Agitated	Frequent nonpurposeful movement or patient-ventilator dyes-synchrony
+1	Restless	Anxious or apprehensive but movements not aggressive or vigorous
0	Alert and calm	
-1	Drowsy	Not fully alert, but has sustained (>10 seconds) awakening, with eye contact, to voice
-2	Light sedation	Briefly (<10 seconds) awakens with eye contact to voice
-3	Moderate sedation	Any movement (but no eye contact) to voice
-4	Deep sedation	No response to voice, but movement to physical stimulation
-5	Unarousable	No response to voice or physical stimulation

Table 3. *Ramsey scale*

Response	Level
Awake and anxious, agitated, or resless	1
Awake, cooperative, accepting ventilation, oriented, or tranquil	2
Awake, responds only to commands	3
Asleep, brisk response to light, glabella tap or loud noice	4

Table 4. *Sedation agitation scale*

Score	State	Behaviors
7	Dangerous-agitation	Pulling ET tube, climbing over bedrail, striking at staff thrashing side to side
6	Very agitated	Does not calm despite frequent verbal remaining, requires physical restrains
5	Agitated	Anxious or mildly agitated attempting to sit up, calms down to verbal instructions
4	Calm and cooperative	Calm awakens easily, follows commands
3	Sedated	Difficult to arouse, awakens to verbal stimuli or gentle shaking but drifts off
2	Very sedated	Arouse to physical stimuli but does not communicate or follow commands
1	Unarousable	Minimal or no response to noxious stimuli, does not communicate or follow commands

Table 5. *CAM in ICU (Confusion Assessment Method for the ICU)*

RASS ABOVE -4		STOP REASSESS LATER SCORE AS UNABLE TEST
↓ YES		
ACUTE ONSET FLUCTUATING COURSE ACUTE CHANGE IN MENTAL STATE OR CHANGE IN RASS GCS LAST 24 H	NO	STOP NO DELIRIUM
↓ YES		
INNATTENTION SQUIZZE HAND WHEN HEAR LETTER A ABRACADBRA	< 3 ERRORS	NO DELIRIUM
↓ YES ≥ 3 ERRORS		
ALTERED LEVEL OF CONSIUOUSNESS RASS=0?	NO	STOP DELIRIOUS
↓ YES		
DISORGANISED THINKING 1. WILL STONE FLOTE ON WATER 2. DOES 0NE KG WEIGHT MORE THEN TWO 3. ARE THERE FISH IN THE SEA	→	> 1 ERROR =DELIROUS ≤ 1 ERROR NO DELIRIUM

Delirium in Intensive Care Unit

Delirium is an acute fluctuating change in mental status. It is characterized by inattention and altered levels of consciousness. Delirium now is considered to be a presentation of brain organ dysfunction. Patients in ICU suffer up to 80% from some form of delirium (hyperactive, hypo-active or mixed form) and it can lead to long-term cognitive dysfunction.

The pathogenesis of delirium is not fully appreciated, and there are many proposed hypotheses including inflammatory changes, impaired oxidative metabolism, neurotransmitter disturbances, and alterations in amino acid precursors (16-18).

Delirium occurs when there is impaired pattern of sending and receiving signals from the brain.

Delirium is associated with the use of sedative medications and contributes to increased mortality, morbidity, hospital length of stay.

The presence of delirium is evaluated by Confusion Assessment Method for the ICU. Early recognition and early treatment are essential for patients in delirium. Haloperidol (Haldol) 2-5mg per os or intravenous every 8h. If patients are older than 60 years then the dose is 0,5 -2mg every 8 hours. Maximum dose is 20 mg. Olanzapine can be used in delirium 5 mg per os in 24 hours or in patients older than 60 years 2,5 mg in 24 hours.

Conclusion:

Evaluating pain mental status, level of sedation, is imperative for treatment of patients in the intensive care unit (ICU). There are many protocols for sedation and analgesia in the intensive care unit (18-20). Namigar et al. made compression of Richmond and Ramsey scale for sedation in critically ill patients in order to prevent over sedation and complication of sedation (21). Curtis N Sessler and Wolfram Wilhelm were evaluating the long-term effects of analgesic and sedative drug management on neuropsychological function in recovering period (22). Elliott R, McKinley S, Aitken LM, Hendrikz J. evaluated the effect of sedation on prolonged mechanical ventilation (23). Sedation and treatment of delirium is evaluated in pediatric patients as well (24, 25). In all these articles there is necessity for exact protocols for sedation. In Cochran library there is an article by Aitken and coworkers whether protocol directed sedation has better results in di-minishing the duration of mechanical ventilation in intensive care patients (26). However, the necessity of evaluating the sedation pain and delirium by numerous scales, is evident (27-29). Everyday implementation of these scales should be routine among doctors residents and nurses in the intensive care units.

References

1. Hamill-Ruth RJ, Marohn ML. Evaluation of pain in the critically ill patient. Crit Care Clin. 1999;15:35–54. doi: 10.1016/S0749-0704(05)70038.
2. Puntillo KA. Pain experiences of intensive care unit patients. Heart Lung. 1990;19:526–533.
3. Puntillo K. From Theory to Practice: Preventing Pain After Cardiac Surgery *Am J Crit Care* March 1, 2003 12:136-143 Am J Crit Care. 1997;6:259–260.
4. Kapfhammer HP, Rothenhausler HB, Krauseneck T, et al. Posttraumatic stress disorder and health-related quality of life in long-term survivors of acute respiratory distress syndrome. Am J Psychiatry. 2004;161(1):45–52.
5. Agarwal V, O'Neill PJ, Cotton BA, et al. Prevalence and risk factors for development of delirium in burn intensive care unit patients. J Burn Care Res. 2010;31.
6. Watson PL, Shintani AK, Tyson R, et al. Presence of electroencephalogram burst suppression in sedated, critically ill patients is associated with increased mortality. Crit Care Med. 2008;36(12):3171–3177.
7. Dahaba AA, Grabner T, Rehak PH, et al. Remifentanil versus morphine analgesia and sedation for mechanically ventilated critically ill patients: a randomized double-blind study. Anesthesiology. 2004;101(3):640–646.
8. Muellejans B, López A, Cross MH, et al. Remifentanil versus fentanyl for analgesia based sedation to provide patient comfort in the intensive care unit: a randomized, double-blind controlled trial [ISRCTN43755713].
9. Kollef MH, Levy NT, Ahrens TS, et al. The use of continuous i.v. sedation is associated with prolongation of mechanical ventilation. Chest. 1998; 114(2):541–548.
10. Pandharipande P, Shintani A, Peterson J, et al. Lorazepam is an independent risk factor for transitioning to delirium in intensive care unit patients. Anesthesiology. 2006;104(1):21–26.
11. Nelson BJ, Weinert CR, Bury CL, et al. Intensive care unit drug use and subsequent quality of life in acute lung injury patients. Crit Care Med. 2000; 28(11):3626–3630.
12. Botha JA, Mudholkar P. The effect of a sedation scale on ventilation hours, sedative, analgesic and inotropic use in an intensive care unit. Crit Care Resusc. 2004;6(4):253–257.
13. Kollef MH, Levy NT, Ahrens TS, et al. The use of continuous i.v. sedation is associated with prolongation of mechanical ventilation. Chest. 1998; 114(2):541–548.
14. Kress JP, Pohlman AS, O'Connor MF, et al. Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. N Engl J Med. 2000;342(20):1471–1477.
15. Diedrich DA, Brown DR. Analytic reviews: propofol infusion syndrome in the ICU. J Intensive Care Med. 2011;26(2):59–72.
16. Cerejeira J, Firmino H, Vaz-Serra A, et al. The neuroinflammatory hypothesis of delirium. Acta Neuropathol. 2010;119(6):737–754.
17. Hshieh TT, Fong TG, Marcantonio ER, et al. Cholinergic deficiency hypothesis in delirium: a synthesis of current evidence. J Gerontol A Biol Sci Med Sci. 2008;63(7):764–772.
18. Babamohamadi, Hassan and Tangestani, et al. (2017) Effect of a sedation guideline on the duration of mechanical ventilation and length of stay in intensive care unit. Koomesh. pp. 380-390.
19. Kayir S, Ulusoy H, Dogan G. The Effect of Daily Sedation-Weaning Application on Morbidity and Mortality in Intensive Care Unit Patients. Muacevic A, Adler JR, eds. *Cureus*. 2018;10(1):e2062. doi:10.7759/cureus.2062.
20. Sessler CN, Wilhelm W. Analgesia and sedation in the intensive care unit: an overview of the issues. *Critical Care*. 2008;12(Suppl 3):S1. doi:10.1186/cc6147.
21. Namigar, Turgut, et al. "The correlation among the Ramsay sedation scale, Richmond agitation sedation scale and Riker sedation agitation scale during midazolam-remifentanil sedation." Brazilian Journal of Anesthesiology (English Edition) 67.4 (2017): 347-354.
22. Sessler CN, Wilhelm W. Analgesia and sedation in the intensive care unit: an overview of the issues. *Critical Care*. 2008;12(Suppl 3):S1. doi:10.1186/cc6147.
23. Elliott R, McKinley S, Aitken LM, et al. The effect of an algorithm-based sedation guideline on the duration of mechanical ventilation in an Australian intensive care unit. Intensive Care Medicine2006;**32**(10):1506-14.
24. Keogh SJ, Long DA, Horn DV Practice guidelines for sedation and analgesia management of critically ill children: a pilot study evaluating guideline impact and feasibility in the PICU BMJ Open 2015.
25. Stephen D. Playfor; Analgesia and sedation in critically ill children, *Continuing Education in Anaesthesia Critical Care & Pain*, Volume 8, Issue 3, 1 June 2008, Pages 90–94.
26. Aitken LM, Bucknall T, Kent B, et al. Protocol-directed sedation versus non-protocol-directed sedation to reduce duration of mechanical ventilation in mechanically ventilated intensive care patients. Cochrane Database of Systematic Reviews 2015, Issue 1. Art. No.: CD009771. DOI: 10.1002/14651858.CD009771.pub2.6.
27. Pandharipande PP, Morandi A, Adams JR, et al. Plasma tryptophan and tyrosine levels are independent risk factors for delirium in critically ill patients. Intensive Care Med. 2009.
28. Brook AD, Ahrens TS, Schaiff R, et al. Effect of a nursing-implemented sedation protocol on the duration of mechanical ventilation. Critical Care Medicine1999.
29. Bucknall TK, Manias E, Presneill JJ. A randomized trial of protocol-directed sedation management for mechanical ventilation in an Australian intensive care unit. Critical Care Medicine 2008;36(5):1444-50.

Здружение на лекарите по
анестезија, реанимација
и интензивно лекување

MSA

Macedonian Society of Anesthesiologists
and Intensive Care Medicine

КБП

Здружение на лекари за
критично болни пациенти