ISSN 2545-4366
www.e-mja.finki.ukim.mk

MJA

Macedonian Journal of Anaesthesia

A Journal on Anaesthesiology, Resuscitation, Analgesia and Critical Care

Vol. 5 No 1, March 2021

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, R.N. Macedonia

Apotel® 1000mg/6.7ml

I.V. Paracetamol

БЕЗБЕДНА АНАЛГЕЗИЈА

менаџирање на болка кога сте загрижени за безбедноста

I.V. paracetamol за прв пат во Европа е применет во 2001 година, а денес поради неговата докажана безбедност и ефикасност е прв од избор **аналгетик и антипиретик.**

Предоперативна и Интраоперативна Аналгезија:
Предоперативна анелгезија е дефинирана како третман кој што започнува пред оперативниот зафат се со цел да се превенира воспоставувањето на централна сензибилизација на болка.
i.v. paracetamol е безбеден, добро толериран лек со докажана ефикасност како **предоперативна и интраоперативна анелгезија** за умерена до средна болка при оперативни зафати.
Голем број на клинички студии ја докажуваат ефикасноста на **i.v. paracetamol** како **преодоперативна и интраоперативна анелгезија**.

КЛИНИЧКА СТУДИЈА:
Ефект од **предоперативен i.v. paracetamol** за постоперативни аналгетски потреби кај пациенти кои се подлежни на оперативни зафати. A Sreenivasulu , R Prabhavathi, 2015
Цел: Да се утврди ефикасноста на **предоперативната употреба на 1000mg i.v. paracetamol** кај постоперативните болки и анелгетски потреби кај пациенти подлежни на хируршки зафати.
Метод: 60 пациенти беа поделени во две рандомизирани групи од по 30 пациенти.
На I. Група им беше администрирано **ампула од 1000mg i.v. paracetamol разредена 0,9%NaCl** р-ор 30 минути пред индукција **(ГРУПА П)**,
На II. Група им беше администрирано **i.v. 0,9% NaCl р-ор 100мл** 30 минути пред индукција **(ГРУПА НС)**
Сите пациенти беа индуцирани со i.v. thiopentone 5mg/kg, i.v. fentanyl 2µg/kg, i.v. vecuronium 0.1mg/kg
Постоперативниот резултат на болка беше мерен со **Визуелна Аналогна Скала (ВАС) од "0-10"**. Исто така беше забележувана и **постоперативната употреба на tramadol** како спасувачки аналгетик. Инциденцата на **постоперативно гадење и повраќање (ПОГП)** и други компликации исто така беа забележувани во пост оперативниот период.
Резултатот на постоперативната болка беше забележуван во интервали 15 мин, 30 мин, 1 час, 2 часа, и 6 часа.

Резултат:

Табела 1: *Споредба на средниот резултат на болка (ВАС) помеѓу двете групи*

Интервали	I Група П	II Група НС	*P вредност*
15 мин	2.06 ± 0.63	2.61 ± 0.56	0.0006
30 мин	2.35 ± 1.17	3.84 ± 1.55	0.0001
1 час	2.42 ± 1.12	2.87 ± 0.99	0.0989
2 часа	2.13 ± 1.06	2.52 ± 0.89	0.1219
6 часа	2 ± 0.52	2.52 ± 0.89	0.0549

Табела 2: *Споредба за потребите од tramadol помеѓу двете групи*

Интервали	I Група П	II Група НС	*P вредност*
До 1 час	4 (12.90%)	15 (50%)	0.0002
1-2 часа	3 (9.68%)	2 (6.45%)	0.64
2-6 часа	1 (3.23%)	3 (9.68%)	0.301
Вкупно	**8 (25.81%)**	**20 (64.52%)**	**0.002**

Табела3: *Споредба на ПОПГ помеѓу двете групи*

ПОГП	
I Група П	II Група НС
0	4

Заклучок: Предоперативна администрација на **1000mg i.v. paracetamol** кај пациенти подлежни на оперативен зафат обезбедува **статистички задоволителна анелегизија**, и ја **намалува постоперативната употреба на tramadol**. Оттука **1000mg i.v. paracetamol** може безбедно да се администитрира како превенција при оперативни зафати.

i.v. Paracetamol + јак опоид	МНОГУ ЈАКА БОЛКА
i.v. Paracetamol + слаб опоид	ЈАКА БОЛКА
i.v. Paracetamol + NSAID i.v. Paracetamol + rescue medicine	УМЕРЕНА БОЛКА
i.v. Paracetamol + rescue medicine	СЛАБА БОЛКА

Мултимодално менаџирање на постоперативна болка
I.V. Paracetamol е атрактивна компонента за мултиодално менаџирање на болка.

- **Синергистичко делување**
- **Зголемување на аналгетски ефект**
- **Значително намалување на болка**
- **Редукција на дозата на опоидни лекови за - 40% во првите 24 часа**
- **Намалување на несаканите ефекти поврзани со монотерапија на NSAID и опоидни лекови**
- **Ублажување на акутна и хронична болка**

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FARMA TREJD

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CONTENT

PANCREATIC CANCER: WHERE DO WE STAND?

Meri Trajkovska, MD, PhD
University Clinic of Gastroenterohepatology, Faculty of Medicine, "Ss. Cyril and Methodius" University, Skopje, North Macedonia

Less than 5% of patients diagnosed with pancreatic cancer (PC) survive for five years, and the average lifetime following the diagnosis is no more than 5 months. Although pancreatic cancer across Europe is on seventh place according to incidence rates with 100,000 new cases, every year, it is the third leading cause of cancer-related death, claiming the lives of 95,000 citizens per year. According to the data of European Cancer Information System, last year in our country pancreatic cancer was on the 6th place with incidence of 16.7 in 100,000 people. Despite these horrifying facts, there has been a little advancement in patient outcomes last five decades, and pancreatic cancer remains a disease which has been "staked" in the past. The silent killer shows no signs of conceding either, with the morbidity and mortality rates estimated to grow up to 40% by 2035 as stated by European Parliament Interest group on Digestive Health. Forecast is similar in United States, with projections disclosing that "pancreatic carcinoma will be the second cause of cancer related deaths by 2030".

Pancreatic cancer is hard to recognize in its initial phase, due to non-specific presenting symptoms. Although scientists are trying to come upon the molecular mechanisms leading to malignant transformation of healthy pancreatic cells and discover new biomarkers that can signify the presence of the disease in its early stage when is still treatable, in Europe pancreatic cancer research has limited funding of less than 2% of overall cancer funding. This actuality, in conjunction with the therapeutic resistance of pancreatic cancer, is the main reason of lowest survival rate among "the cancers" and steadily increasing incidence (1 – 9).

The Facts

Predominant part of pancreatic carcinoma, more than 80% are caused by sporadic mutation, and minor proportion is due to germ-line mutations in BRCA2, p16, ATM, STK11, PRSS1/PRSS2, SPINK1, PALB2. Aetiology still remains unrevealed, nonetheless, a vast majority of well-known risk factors do exist like: cigarette smoking, heavy alcohol drinking, chronic pancreatitis, diabetes (especially recent onset, or longstanding diabetes with unexplained instable hyperglycaemia), obesity (central type with BMI>30), hereditary pancreatitis and hereditary pancreatic carcinoma (having two first degree relatives with PC doubles the risk of developing cancer). Lifestyle risk factors are modifiable, which offers enormous mode of prevention, if public awareness is developed. Regarding hereditary pancreatitis/ carcinoma, genetic cancer screening is recommended by International Cancer of the Pancreas Screening (CAPS) consortium in all patients with Peutz-Jeghers syndrome, all carriers of CDKN2A mutation, carriers of a germline BRCA2, BRCA1,

Some interesting data come from the latest publications showing no significant difference in ICU admissions, the need and duration of intubation between patients with and without PE development. Almost two thirds of the patients with diagnosed PEs did not require treatment in the ICU, which is quite opposite to the actual published study that underlines that PE is associated to ICU hospitalization and invasive ventilation (9). Our case is an example of PE as a first manifestation of COVID-19 infection, which lead to severe hemodynamic compromise. Fibrinolytic therapy leads to hemodynamic stabilization. Our patient did not require ventilatory support and he had good short-term outcome.

Conclusions

Hospitalized patients with COVID-19 infection are population with increased risk for thrombotic events. Sudden worsening of respiratory function accompanied with high D-dimers values should raise clinical alert for pulmonary embolism as a first manifestation of the disease which requires prompt diagnosis and proper management. In hemodynamically unstable patients with massive PE, fibrinolytic therapy is lifesaving treatment option.

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ORIGINAL ARTICLE

UDK: 616.24-002-085.216.2:[616.98:578.834
616.98:578.834]:616.24-002-085.216.2

EVALUATION OF THE EFFECT OF THE NEBULIZED LOCAL ANESTHETIC FOR INHALATION IN PATIENTS WITH CONFIRMED COVID-19 PNEUMONIA IN SERIES OF CASES

Markovska Z[1], Malinovska-Nikolovska L[2], Meshkova I[1], Mijakoski D[3,4], Troic T[1], Kuzmanovska K[5]

[1] Department of Anesthesiology, City General Hospital "8mi Septemvri", Skopje, Republic of North Macedonia

[2] Department of Pediatric Cardiac Surgery, Acibadem Sistina Hospital, Skopje, Republic of North Macedonia

[3] Institute of Occupational Health of RNM, WHO CC, Skopje, Republic of North Macedonia

[4] Faculty of Medicine, "Ss. Cyril and Methodius" University in Skopje, Skopje, Republic of North Macedonia

[5] Department of Anesthesia and Intensive Care, City General Hospital Strumica, Republic of North Macedonia

ABSTRACT

The aim of this study was to evaluate the data in 12 patients with Covid-19 pneumonia and different types of hypoxemia (mild, moderate and severe) in whom nebulized lidocaine was given and to analyze the efficiency of the lidocaine in the improvement of the oxygenation.

Material and Methods

12 patients with confirmed COVID-19 pneumonia aged between 22 and 72 years (mean age 53), who had dyspnea admitted to the City General Hospital "8th of September", Skopje, Macedonia were enrolled in the study. In all patients nebulized lidocaine was given at doses of 2.85 mg/kg via inhalation, four times daily. Patients' demographic, clinical data, body mass index and average number of days between illness and inhalation were collected for each of the patients.

We analyzed the level of the partial pressure of oxygen (Pao2) and level of blood saturation 5 minutes before the treatment and 30 minutes after inhalation.

Results

12 patients with COVID-19 pneumonia have been enrolled in this study: 9 patients (75%) were male and 3 (25%) were female. Most of the patients presented with shortness of breath (50%), 9 patients (75%) have co-morbidities and 66.7% were obese. 9 (75%) patients had opacity while 3 (25%) patients had pattern on radiological findings. At the time of presentation, the hypoxemia was mild (85-90%) in 4 patients, 3 patients had moderate hypoxemia (75-85%) and 5 patients had severe hypoxemia (50-75%). The average number of the days was 6.5 days.

Conclusion

We observed improvement in oxygen saturation after inhalation in all patients.

Key Words: *hypoxemia, lidocaine, nabulisator, oxygenation.*

Introduction

Large number of studies show that local anesthetics and, among them, lidocaine have effects that prevent cellular damage caused by inflammation of the lungs (1). Based on John Hopkins University Report on COVID-19 for Macedonia, there were a total of 586 new confirmed cases until November 16, 2020 (2). Since the start of the pandemic, many medicaments, even older ones, have been researched and tested for possible efficacy against COVID-19 (3). Accumulating data suggest that local anesthetics possess a wide range of anti-inflammatory effects, due to their effects on cells of the immune system (4). Additionally, lidocaine has shown beneficial role in reducing cytokine storm (5).

The aim of this study was to evaluate the data in 12 COVID-19 positive patients with interstitial pneumonia and different types of hypoxemia (mild, moderate and severe) to whom nebulized lidocaine was given in a dose of 2.85 mg/kg via inhalation, and to analyze the efficiency of the lidocaine in the improving of the oxygenation.

Material and Methods

12 patients with confirmed COVID-19 pneumonia, aged between 22 and 72 years (mean age 53), who had dyspnea and difficult breathing and have been admitted to the City General Hospital "8th September" Skopje, Macedonia were enrolled in the study. All patients regardless of the type of disease who were admitted for hospitalization, were inhaled with lidocaine. The Ethical Committee of the hospital approved this report according to the situations for emergency infected diseases. We included patients with different stages of illness (4 patients had mild type, 3 were with moderate type of COVID-19 pneumonia and in 5 patients COVID-19 pneumonia was severe). All patients had clinical symptoms for respiratory failure with hypoxemia and supplementary oxygen requirement at the time of presentation. One patient required life support with inotropic medicaments from the first day of hospitalization. All patients had hypoxemia with partial pressure of oxygen between 25 and 89 mmHg when nebulized lidocaine was given. Ventilation support was ongoing from the first day of admission in all 12 patients. Out of the 12 cases, 3 patients were intubated immediately after hospitalization, and noninvasive ventilation with cpap mask was ongoing in the other 9 patients. Out of the 12 cases, only one had preexisting respiratory complain before the COVID-19 pneumonia and only one was smoker. All patients had therapy with antibiotic (Beta lactam antibiotic in dose 1 gram every 8 hours), corticosteroids (methylprednisolone in dose 4 mg/kg/daily), anticoagulant (nadroparin calcium administered on a daily basis according body weight and hemostasis), vitamins and antihistaminic ha2 receptor antagonist for intravenous use in dose 40 mg two times daily.

In purpose to improve oxygenation in all 12 patients nebulized lidocaine was given as supportive drug. In all patients nebulized lidocaine was given in a dose of 2.85 mg/kg, diluted as a 1% solution, via inhalation, four times daily. Inhalation was performed using a ventilator with nebulizer. We analyzed the level of the partial pressure of oxygen (PaO2) measured by the gas analyzer Gem premier 3000 from the radial artery blood 5 minutes before the treatment and 30 minutes after nebulized lidocaine was given. Level of blood saturation measured by pulse oximeter put on point finger was also analyzed, 5 minutes before the inhalation and 30 minutes after nebulized lidocaine was given. Patients were analyzed at hospital admission for demographics data (gender, age), presence of clinical anamnestic data for symptoms (temperature, shortness of breath, dyspnea, cough, fever, pain, renal problems, general weakness), the present co-morbidities (diabetes mellitus, hypertension, chronic renal failure, chronic obstructive pulmonary disease, chronic cardiomyopathy, stenting), x-ray specificities (opacity, pattern) and degree of hypoxemia (mild, moderate, severe). Body fat assessment was performed within 48 hours of admission using measures of height and weight. For each patient, we calculated body mass index (BMI). BMI was calculated by using on-line calculator (htts://www.calculator.net/bmi-calculator.html) entering patients' weight and height. Patients were classified, according to World Health Organization Classification, in correlation to BMI, into following groups: normal BMI (18.5-24.9), overweight (25-29.9), obesity class (>30) (6).

Average number of days from the beginning of the symptoms to the introduction of inhalation was filled latter after admission, using medical records.

Results

12 patients with COVID-19 pneumonia have been enrolled in this study. Patients' demographics characteristics are shown in Table 1.

Out of them, 9 patients (75%) were male and 3 (25%) were female. Most of the patients presented with shortness of breath (50%), dyspnea (41.6%) and cough (41.67%), and 9 patients (75%) had co-morbidities. Among the various co-morbidities, hypertension has been the most common disease.

Table 1. *Patient's demographic and clinical characteristics*

Characteristics	**N (%)**
Gender	
Male	9 (75%)
Female	3 (25%)
Symptoms	
Shortness of breath	6 (50%)
Dyspnea	5 (41.67%)
Cough	5 (41.67%)
Fever	4 (3.34%)
Pain	2 (16%)
Anuria/oliguria	1 (8.33%)
General weakness	1 (8.33%)
Co-morbidities With comorbidities Without comorbidities	 9 (75%) 3 (25%)
Diabetes mellitus	3 (25%)
Hypertension	6 (50%)
Chronic renal failure	2 (16%)
Chronic obstructive pulmonary disease	1 (8.33%)
Cardiomyopathy chronic heart failure	1 (8.33%)
Stenting on coronary arteries	1 (8.33%)

Examination with x-ray showed that all patients had radiological findings and opacity was found in 9 (75%) patients and 3 (25%) patients had pattern.

Table 2. *Chests' x-ray findings*

CHEST X RAY	N (%)
Opacity	9 (75%)
Pattern	3 (25%)

Out of 12 patients, 16% had normal BMI, 16.67% were overweight and 66.67% were obese.

Table 3. *Body mass index in patients*

BODY MASS INDEX	N (%)
Normal 18.5-24.9	2 (16.67%)
Overweight 25-29.9	2 (16.67%)
Obesity class 1 (>30)	8 (66.66%)

Table 4 showed type of ventilator support according the type of disease. 3 patients were on mechanical ventilation. Non-invasive ventilation was ongoing in 4 patients with mild type of disease, in 3 patients with moderate and in 5 patients with severe type.

Table 4. *Type of ventilation support according the type of disease*

	Mild type of disease N (%)	Moderate type of disease N (%)	Severe type of disease N (%)
Invasive ventilation	/	/	3 (25%)
Non-invasive ventilation	4 (33.33%)	3 (25%)	5 (41.67%)

Level of oxygen saturation shows hypoxemia at the time of presentation in each patient. The hypoxemia was mild (85-90% of oxygen saturation) in 4 patients, 3 patients had moderate hypoxemia (75-85%) and severe hypoxemia (50-75%) was noticed in 5 patients (Table 5). The average number of days from the beginning of the disease to the introduction of our therapeutic strategy with lidocaine was 6.5 days. Seven patients had experienced a rapid improvement of hypoxemia from the day of admission to the day of treatment.

Table 5. *Oxygen level on admission, before and after inhalation*

	Oxygen saturation (SaO_2) on admission	Oxygen saturation (SaO_2) before the treatment with lidocaine	Partial pressure of oxygen (PaO_2) before the treatment with lidocaine	Oxygen saturation (SaO_2) after the treatment with lidocaine	Partial pressure of oxygen (PaO_2) after the treatment with lidocaine
Case 1	87%	49%	30 mmHg	87%	60 mmHg
Case 2	65%	25%	18 mmHg	80%	48 mmHg
Case 3	60%	66%	45 mmHg	99%	162 mmHg
Case 4	87%	84%	64 mmHg	100%	96 mmHg
Case 5	83%	80%	32 mmHg	100%	90 mmHg
Case 6	60%	61%	30 mmHg	69%	36 mmHg
Case 7	85%	60%	50 mmHg	80%	90 mmHg
Case 8	60%	85%	48 mmHg	87%	90 mmHg
Case 9	80%	61%	33 mmHg	69%	35 mmHg
Case 10	82%	79%	52 mmHg	100%	246 mmHg
Case 11	86%	89%	83 mmHg	99%	102 mmHg
Case 12	68%	86%	54 mmHg	87%	60 mmHg

In all 12 patients who had mild (4 patients) or moderate hypoxemia (5 patients) at admission, we observed significantly improvement in oxygen saturation after inhalation. Even in severe group with 5 patients we noticed improvement in all of the 5 patients.

Discussion

COVID-19 patients can experience respiratory failure associated to profound hypoxemia (7). Clinical indicators of respiratory failure include increase in respiratory rate, decrease of oxygen level or increasing supplementary oxygen requirement (8). The main goal of dealing with respiratory failure is to improve oxygenation. Our study reported twelve patients with mild, moderate and severe hypoxemia in whom nebulized lidocaine was used as additional therapy for the improvement of oxygenation. After inhalation with nebulized lidocaine SaO2 and PaO2 have higher values. In comparison to the moderate and severe group of patients, the group with mild hypoxemia had the most significant improvements.

Lidocaine has been continuously used for decades, and it has a long history of practice (9). Recently lidocaine has been shown to reduce cytokines storm and suppresses the development of netosis as a form of cell death (10). It was confirmed that cytokines are involved in viral propagation to respiratory failure (11). Another mechanism of acting of lidocaine is blocking the voltage of Na and Ca channels (12).

Virus induced disruption in Epithelial Sodium Channel (ENAC) or amiloride-sensitive sodium channel which is selective permeable to the sodium ions. This ion channel modulation regulates the alveolar fluid clearance (13). Thus, decreasing in this ion-channel function leads to accumulation of fluid across already inflamed lung epithelium. By using lidocaine and by blocking the voltage of Na and Ca channel, the progression of fluid accumulation across ENAC may be stopped, even in the patients with severe conditions. However, there have been identified some risk factors for poor outcomes, such as preexisting co-morbidities, obesity, and male gender (14). In our study we identified some risk factors for poor outcomes.

Extent of radiology changes is also negatively associated to prognosis (15) and this was also presented in our patients. Many studies demonstrated improvement in airway obstruction and oxygenation when asthmatic patients were treated with nebulized lidocaine (16). In our data nebulized lidocaine was also associated to increasing level of partial pressure of oxygen and oxygen saturation. But, there are limited studies for the use of nebulized lidocaine and the most of them hypothesize the role of lidocaine in COVID-19. Searching in the literature for the nebulized lidocaine, many studies showed a promising efficacy in improving pulmonary function and reducing cough in asthmatic patients (17). Additional investigation is warranted for the beneficial effects in COVID-19.

These results are obtained from one day application. Secondly, the number of the patients is small, although the role of nebulized lidocaine in improving the oxygenation was our focus.

Conclusion

In this case series, we used nebulized lidocaine as a supportive drug. In all 12 patients who had different types of hypoxemia (mild, moderate, severe) we observed improvement in oxygen saturation after inhalation.

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CASE REPORT

UDK: 616-007.41:[616.98:578.834
616.98:578.834]:616-007.41

SITUS INVERSUS TOTALIS: PATIENT WITH POST COVID-19 INFECTION

Chabukovska-Radulovska J[1], Petrovska T[1], Poposka A[2], Shosholcheva M[1], Chabukovska E[3]

[1] PHIUniversity Clinic of Surgery "St. Naum Ohridski" – Skopje

[2] PHI University Orthopaedic Clinic – Skopje

[3] PHP Psychiatric Hospital – Skopje

ABSTRACT

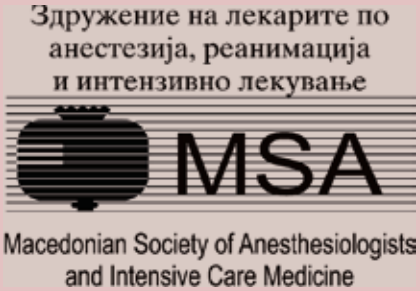
Situs inversus totalis (SIT) is an especially rare congenital condition with complete reverse location of the thoracic and abdominal organs. People with situs inversus totalis sometimes are unaware of their unusual anatomy condition until the moment they need some medical diagnostic procedures or some surgical interventions. We present the case of the 41-years-old female, with post COVID-19 infection in November 2020, with long lasting cough for two months, who was referred to the Radiology Department for CT examination of the lungs. CT scan without contrast was performed. We discovered a situs inversus totalis, where the heart was located on the right side of the thorax, the stomach and spleen were situated on the right side of the abdomen and the liver, gallbladder and duodenum were on the left side. CT scans of the lungs showed normal lung density, without sign of the consolidation, pulmonary fibrosis or pleural effusion. The thoracic and abdominal organs and the viscera were complementary inversed, as a mirror image of the normal position of the internal organs. All laboratory tests were normal. No previous radio diagnostic exams of the thorax or abdomen existed. Patient had the pregnancy and she gave a birth in 2018, with no evidence of the situs inversus totalis. It is very important to make an evidence and inform the patient and medical professionals of the diagnosis of situs inversus totalis in the direction to prevent future complications which can arise from patient's assessment and care, especially in cases of the accidental abdominal or thoracic organs trauma or in cases with acute infection condition as cholecystitis, appendicitis.

Key Words: *Situs Inversus Totalis (SIT)*

CONFLICT OF INTERESTS: None declared.

Introduction

Situs inversus totalis (SIT) is a rare condition of congenital anomaly, which are characterize by the transposition of the thoracic and abdominal organs, viscera and vascular structures, with the incidence of the 0,01% of the population, or about 1 person in 10,000 births. The term situs inversus derives from the Latin phrase: "situs inverses viscerum", which means "inverted position of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