THE ROLE OF THE MULTIMODAL ANALGESIA IN THE COMPLEX THERAPY OF GERONTOLOGY PATIENTS WITH TRAUMATIC DISEASE.

Yu. V. Volkova, A. A. Khyzhnyak, V. G. Poltoratskiy, M. A. Dolzhenko, E. A. ***Bausov***

Kharkov State Medical University

Summary. 90 geriatric patients with trauma was examined. We investigated the clinical and biochemical parameters, blood gases, and apoptosis markers of endothelial dysfunction, and pain intensity, quality of analgesia. It was revealed that the use of paracetamol in a complex of intensive therapy of traumatic disease in geriatric patients significantly reduced the severity of pain with the minimum daily dose and short term of forced needs for anesthesia. ***Keywords:*** *pain, trauma, gerontological patients.*

THE ROLE OF THE MULTIMODAL ANALGESIA IN THE COMPLEX THERAPY OF GERONTOLOGY PATIENTS WITH TRAUMATIC DISEASE.

Yu. V. Volkova, A. A. Khyzhnyak, V. G. Poltoratskiy, M. O. Dolzhenko, E. O. ***Bausov***

Summary. 90 geriatric patients with trauma was examined. We investigated the clinical and biochemical parameters, blood gases, and apoptosis markers of endothelial dysfunction, and pain intensity, quality of analgesia. It wad revealed that the use of paracetamol in a complex of intensive therapy of traumatic disease in geriatric patients significantly reduced the severity of pain with the minimum daily dose and short term of forced needs for anesthesia. ***Keywords:*** *pain, trauma, gerontological patients.*

THE ROLE OF THE MULTIMODAL ANALGESIA IN THE COMPLEX THERAPY OF GERONTOLOGY PATIENTS WITH TRAUMATIC DISEASE. ***Yu. V. Volkova, A. A. Khyzhnyak, V. G. Poltoratskiy M. A. Dolzhenko, E. A. Bausov***

Summary. 90 geriatric patients with trauma examined. We investigated the clinical and biochemical parameters, blood gases, and apoptosis markers of endothelial dysfunction, and pain intensity, quality of analgesia. It was revealed that the use of paracetamol in a complex of intensive therapy of traumatic disease in geriatric patients significantly reduced the severity of pain with the minimum daily dose and short term of forced needs for anesthesia. ***Keywords:*** *pain, trauma, gerontological patients.*

Address for correspondence: *Volkova Yulia Victorovna*
Candidate of medical sciences, senior lecturer
Kharkov State Medical University
61022, Kharkov, 4, Lenin str.

INTRODUCTION

In connection with the development of scientific and technological progress, modern medicine tends to reduce the number of postoperative complications, to reduce duration of stay in hospital and reduce the treatment expense [1].

Given that the course of traumatic disease is determined by the reactivity of the body that depends on the anatomical and physiological features of each patient, geriatric patients deserves special attention, cause their age-related changes and concomitant somatic pathology put forward some requirements to therapy.

The increased oxygen debt due to even minimal blood loss, which occurs in elderly patients on the background of the quantitative deficit “fully mature red blood cells”, as well as excessive activation of the sympathetic nervous system caused by pain with the consequent increase of myocardial oxygen demand and an increase of the catecholamine-procoagulant plasma level exacerbates the development of multicomponent hypoxia in geriatric patients, which has a negative impact on the prognosis of traumatic disease in general [2–4]. At the same time throughout the period of treatment of such patients a high probability of protopathic and visceral pain in the clinical presentation is an important factor that is directly related to the change in the oxygen regime of tissue - the development of oxygen deficiency is the energy equivalent of the structural deficit [5, 6].

Taking into account all the possible consequences of inadequate post-traumatic and/or postoperative analgesia in elderly patients with trauma, precisely gerontological group of patients require special attention because of their age-related changes of the body and the concomitant somatic pathology that put forward specific requirements for the prescription of analgesic.

That is why the aim of our study was to find the most rational approach to pain management in a hospital period of treatment of geriatric patients with trauma, focused on the most effective suppression of pain syndrome with the minimum possible adverse clinical effects. Main tasks of the study were determination of quality and duration of analgesic effect, as well as the frequency and nature of adverse effects of used analgesics.

STUDY OBJECT AND METHODS

Given the suddenness of obtaining trauma by elderly patient, it should be noted that in the implementation of the pain syndrome involves all known components forming pain sensation in the body. So, tissue damage (injury) causes activation of pain receptors, and achievement of its critical mass triggers the formation of pain impulses [7]. Re-activation of these receptors causes changes in both central and peripheral nervous system [8]. Further the transfer of impulse in the posterior horns of the spinal cord occurs, where the perception of pain and its modification take place [9]. This is where information about pain is qualified by the degree of importance for the body and transferred to the numerous centres of the brain and spinal cord for the further formation of behavioural response with the formation of pain sensation in the brain [10].

Given the multicomponent nature of process of pain sensation formation, which in the elderly is exacerbated by factors such as the difficulty of contact with patient because of a violation of psycho-emotional state, post stroke speech changes, unwillingness to contact with treating physician, the use of large amounts of drugs for the treatment of concomitant somatic pathology, difficulty in food intake, associated with pathological processes in the oral cavity (missing teeth, periodontal disease), etc., on base of the Polytrauma Department of Communal Health Protection Institution “Kharkov City Clinical Hospital of Emergency Medical Care named after prof. A.I. Meschaninov" we carried out a long-term comprehensive clinical, instrumental and laboratory dynamic research of hemodynamic parameters, blood gases, full coagulation profile; TNF-a marker of systemic inflammatory response, interleukins 1 and 6, the apoptotic caspase cascade 3 and 8 by the enzyme immunoassay in geriatric patients with trauma.

Conditions for selection of patients in the study were: age over 60 years, the presence of trauma requiring hospital treatment (the maximum allowable blood loss 500-1000 ml), the possibility of a productive contact with the patient at the time of income, obtaining informed consent from of the patient to his/her inclusion in the study.

For proper stratification patients with scores less than 10 by the APACHE II scale, for whom the trauma correction was performed on a mandatory basis in the operating conditions (without the use of mechanical ventilation) were included in the study.

Patients were divided into 3 groups, No.1 (n = 38), No.2 (n = 32), No.3 (n = 20), who did not significantly differ by gender, age, anthropometric data, the nature of the damage, the time since getting trauma prior to admission to the hospital.

All patients during period of hospital treatment received identical treatment complex except pain management program. When we selected the complex of drugs for analgesia, we followed an accelerated rehabilitation program (Fast-track surgery), which allowed to reduce the number of post-hospital complications, to reduce economic costs, and this program involves performing of minimally invasive urgent manipulations, the optimal infusion of fluids, prevention of intraoperative hypoxia, a decrease in the number of cases of postoperative nausea and vomiting, an adequate nutritional support and early (as much as possible) immobilization of patients and balanced analgesia [11]. We also used modern principles of pain management according to the WHO [12]: the principle of individual approach, step principle, the principle of timely administration and the principle of the adequacy of administration method. Before selecting pain management schemes, we analysed the spectrum of opioid, non-opioid analgesics and adjuvants in relation to pharmacodynamic properties and their possible side effects. Taking into account the presence of factors limiting the use of opioid receptors agonists in elderly patients [13], as an alternative for analgesia in the early post-traumatic period (including in the operating room), we chose opioid receptors agonists-antagonists, in stimulated prescription of which we have sought to minimize the daily dosage for each of the examined patients. When prescribing drugs with non-steroidal anti-inflammatory effects, we also tried to minimize individual dosages because of the large number of negative effects in their prescription, including in geriatric patients groups. At the same time, the basic principles of the formation of analgesic program were: maximal strength of analgesia, maximal safety, minimization of the impact on platelet aggregation and blood clotting time, the minimal number of drug interactions.

Thus, the patients of group No.1 with the aim of analgesia received an inhibitor of cyclooxygenase (COX) + adjuvant, of group No.2 — inhibitor

(COX) + nalbuphine, group No.2 - from the moment of income - paracetamol + nalbuphine on demand.

Dosing of drugs was conducted based on the presence in patients of concomitant somatic pathology and carried out by the results of determination the intensity of pain on a visual analogue scale, Likert scale of analgesia quality with the mandatory definition of the minimum, average and maximum recorded needs for pain management. Clinical effects were assessed in order to prevent possible expansion of receptive fields and increasing the pain receptive of neuronal spinal cord structures that quite often leads to the formation of chronic neuropathic pain syndromes, which are based on plastic changes in the nervous tissue, since the frequency of their development is directly proportional depends from pain intensity and adequacy of analgesia in the first 72 hours after injury [14].

Choice of injection form of paracetamol Infulgan (”YURiA-PHARM”, Ukraine) as an alternative to COX inhibitors has been made in view of its pharmacodynamic properties. As you know, paracetamol inhibits COX I and II only in the central nervous system by acting on centers of pain and thermoregulation. Cellular peroxidase neutralizes the effect of paracetamol on COX in the inflamed tissues, that explains the almost complete absence of anti-inflammatory effect. Absence of the influence on prostaglandin synthesis in peripheral tissues causes lack of preparation adverse effect on the water-salt metabolism (sodium and water retention) and on the digestive tract mucosa [15], which is a beneficial effect in gerontological group patients. Given the anatomical and physiological features of the aging organism, in group No.3 patients Infulgan was administered from the moment of admission to hospital in dose of 500 mg 3 times a day (interval 8 hours), on the 2nd and 3rd day of treatment - 500 mg per day.

Taking into account all the known negative effects of acute pain, especially in patients with a high risk (gerontology group, co-morbidities) we have created a list of diagnostic tests chosen for the statistical comparison of examined patients groups. So in all patients a full range of clinical laboratory tests was carried out with the additional definition of 1, 3, 7 hemodynamic parameters by the method of integral tetrapolar rheography by Tishchenko using "Rheograph" P4-02 No. 05562 with the use of ECG device ЭК1Т-03М, parameters of blood gas composition using BMS-2 MK2 "Radiometer", full coagulation profile, activity of lipid peroxidation (LPO) by chemiluminescence method using the device ХЛМЦ-01, TNF-a marker, markers of the apoptotic caspase cascade 3 and 8, intragastric pH-metry with 3-electrode pH-probe. The registration of indices was carried out daily from 8 a.m. Separation of the blood into fractions was carried out using the "lab centrifuge" ЦЛК-1 No.8173, blood platelet count - by phase-contrast microscopy method in a Goryaev chamber in oxalate environment, the induced platelet aggregation by method of turbidimetry with adrenaline induction. Screening tests for evaluation of plasma hemostasis included the definition of an activated partial thromboplastin time (aPTT) by manual method with kaolin, prothrombin time by Quick method, international normalized ratio (INR), thrombin time, fibrinogen concentration in plasma by Clauss method, protein C by coagulation method, antithrombin III by hardware method using the reagent "Antithrombin-tehplastin", euglobulin clot lysis time (XIIa dependent fibrinolysis) by addition of calcium chloride, plasminogen by method of hydrolysis of the chromogenic substrate, soluble fibrin monomer complexes (SFMC) with the orthophenanthroline test. The concentration of tumor necrosis factor (TNFa) was determined using ELISA analysis with reagents "TNF-Vector Best", the level of caspase in the blood by ELISA. Preparation of test material to perform the methods was carried out by blood sampling from peripheral veins in patients during admission to hospital on the beginning of therapy and thereafter each control day of hospital and ambulatory observation at 8 am. The blood was centrifuged for 10 minutes at 2000 round per minute. In the separation of blood into fractions 500 - 1000 µl of serum was taken using 1 ml pipette (GOST 29227-91), and, if necessary, frozen at -20 °C, keeping to the conducting of the study. In order to assess reliability of the differences the Student's t-test with Bonferroni correction for multiple comparisons was used.

Study results and their discussion

In the course of the study in order to achieve its main goals a very important point was to prove the lack of significant differences between the groups, i.e. a proof of their representativeness, which underlines the dependence of possible changes in the studied parameters on the type of pain managment scheme.

In conducting a comparative analysis of clinical and biochemical parameters, blood gases, and apoptosis markers and endothelial dysfunction throughout the examination period no significant differences were detected between the groups, which excludes significant impact of clinical and pathological aspects of pain

on their dynamics in the examined patients.

In the analysis of hemodynamic parameters in patients group No.1 a significant (p <0.05) increase in peripheral vascular resistance was revealed on the 1st and 3rd day of treatment, compared with groups No.2 and No.3 (Fig.1).

luminescence (Max) in all examined patients were (306.4 34.7) cps, and the light sum (S) for 180 sec - (29429,3 1137,4) cts. Mean value of the angle, which reflects the ability of antioxidant systems of the body was (67.3 ± 3.9) °.

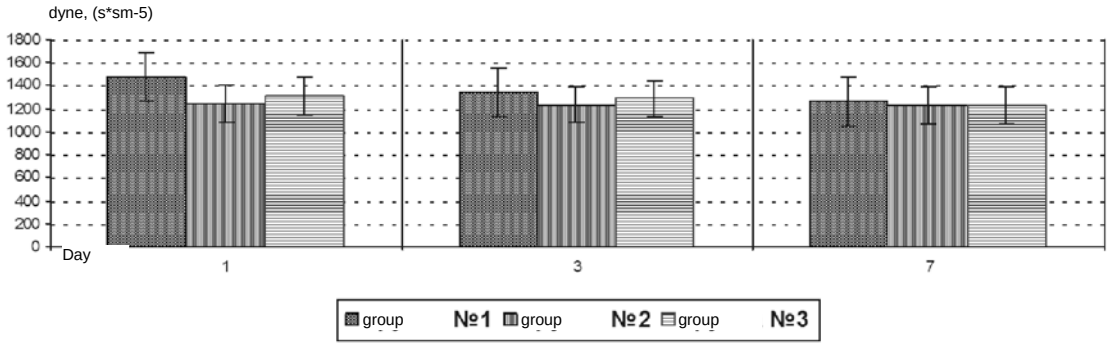

Fig. 1 Dynamics of peripheral vascular resistance in examined patients.

In comparative analysis of the respiration rate a tendency to increase was detected in patients of group No. 1. Similar trend was observed when assessing the level of oxygen saturation in the blood.

In conducting a statistical evaluation of the indicators of vascular-platelet hemostasis in patients of group No.1 a significant (p < 0.05) tendency to coagulate were detected on the 3rd day of the examination (APTT — (42.1 ± 3.4 sec.); antithrombin III (2.21 ± 0.27) mg/l) compared with patients in groups No. 2 and No. 3.

In comparative data analysis of blood plasma chemiluminescence during first 24 hours of hospitalization (Table 1) an increased intensity of activation of the LPO was revealed. Mean indicators of induced maximum

In further analysis of the dynamics of chemiluminescence parameters a significant decrease in the maximum induced luminescence on the 3rd and 7th day in patients of groups No.2 and No.3, a reduction of the light sum indicator on the 3rd day in groups No.2 and No.3 and an increase of the angle induced with the flash of weakest luminescence on the 7th day of treatment also in patients of groups No.2 and No.3, compared with the group No.1 were revealed, that is the evidence of a more active antioxidant action of drugs from the complex therapy of patients of groups No.2 and No.3.

In conducting an express pH-meters for patients on the 5th day of examination, we recorded the time of response beginning (from the time of preparation administration to the beginning of raising the pH), alkaline time (from the beginning of raising the pH to the return to

Table 1

Dynamics of chemiluminescence parameters of plasma in examined patients

Day		Max, cps/s	
	Group No.1	Group No.2	Group No.3
1	331.2 ± 41.6	284.1 ± 33.4	328.2 ± 36.1
3	315.4 ± 36.2	246.1 ± 25.9*	275.8 ± 37.2*
7	258.6 ± 33.1	228.4 ± 26.9*	223.1 ± 31.4*
Day		S, cts	
	Group No.1	Group No.2	Group No.3
1	30245.4 ± 1608.22	28784.2 ± 1465.52	31213.1 ± 1685.29
3	29667.2 ± 1521.44	24341.2 ± 1338.41*	25877.6 ± 1426.12*
7	24539.2 ± 1382.34	24132.1 ± 1255.41	24596.7 ± 1412.16
Day		τ, °	
	Group No.1	Group No.2	Group No.3
1	66.9 ± 4.1	68.7 ± 4.4	66.1 ± 3.2
3	69.2 ± 3.7	67.8 ± 3.1	68.4 ± 2.6
7	67.5 ± 4.1	73.7 ± 2.7*	71.3 ± 2.6*

Note. * - significant difference in parameters between the groups (p <0.05).

baseline, t), the time of maximum pH (tmax) in the antrum or corpus. In a comparative analysis of the results the mean time of the response beginning was the lowest in patients of group No.1, the largest - in patients of group No.2. At the same time the mean duration of alkalizing effect was maximal in the group No.3, minimal - in the group No.1. The analysis of a pH-grams revealed the mean maximum pH values, with no significant differences in the groups No.1 and No.2, data from group No.3 was significantly ($p < 0.05$) different from those in the groups No.1 and No.2.

Based on the evaluation of VAS data and Likert scale by comparing them with the results obtained in the analysis of other indicators, it was found that the use of paracetamol in early posttraumatic period in geriatric patients with trauma significantly ($p < 0.05$) reduced the severity of pain on the background of the average daily dosage of 500 mg (~ 10 mg/kg) and non-durable period of forced need for anesthesia, minimization of negative effects on the cardiovascular system, hemostasis, and pH of the stomach taking into account the age stress rate of examined patients, which improves the emotional state of the patients and the minimization in prescribing of drugs with a full and/or partial opioid agonism.

So it should be noted that for patients aged over 60 years with trauma a combination of paracetamol and agonist-antagonists, the latter of which are prescribed on demand (in our study - 36% of patients) is optimal to deal with pain syndrome.

CONCLUSIONS

- In gerontological group of patients the age-related changes of the body and the concomitant somatic pathology put forward specific requirements for the use of analgesics focused on the most effective suppression of pain syndrome with the minimum possible adverse clinical effects.
- For geriatric patients with trauma a combination of paracetamol and agonist-antagonists is optimal to deal with pain syndrome.

The use of the proposed scheme of pain management allowed to reduce the severity of negative effects on the hemostasis, cardiovascular and digestive systems, and improve the emotional state of patients.

REFERENCES

1. Травматическая болезнь и ее осложнения Текст / под ред. Селезнева С. А., Багненко С. Ф., Шапота Ю. Б., Курыгина А. А. – СПб.: Политехника, 2004. – 414 с.
2. Чеснокова, И. Г. Изменения в иммунной системе при травматической болезни (клинико-патогенетическое, прогностическое значение и коррекция) Текст / И. Г. Чеснокова // Иммунология. – 2000 . - №6. – С.39–42.
3. Калинкин, О. Г. К патогенезу травматической бо лезни Текст / О. Г. Калинкин, А. О. Калинкин // Проблеми військової охорони здоров’я. – 2002 . - С. 34–43.
4. Еременко, А. А. Оценка кислородного статуса у больных в критических состояниях Текст / А. А. Еременко // Неотложная медицина в мегапо лисе: Научные материалы международного фору ма. – М., 2004. – С. 76–77.
5. Геріатрична анестезіологія та реаніматологія Текст / Л. П. Чепкій, Л. В. Усенко // К: Здоров’я, 1994. - 256 с.
6. Котельников, А. В. Проницаемость гистогематического барьера органов и тканей при старении Текст / Котельников А. В., Теплый Д. Л // Клиническая геронтология. – 2006. – № 3. – С.21–25.
7. Асанов, Е. О. Вікові особливості реакції організму на гіпоксичний стрес: механізми та шляхи підви- щення стійкості до гіпоксії Текст : Автореферат дис... д. мед. н.. Ін-т геронтології АМН України. - Київ, 2008. – 36 с
8. Fioramonti, J. Centrally acting agents and visceral sen sitivity Text / J. Kioramonti, L. Bueno. // Gut. – 2002 . – V. 51, –5. – P. 191–195.
9. Адаптация, стресс и профилактика Текст / Ф. З. Меерсон. – М: Наука, 1981. – 278 с.
10. Овечкин, А. М. Боль в Европе. Обзор материалов 2-го Конгресса Европейской ассоциации по изуче нию боли Текст / А. М. Овечкин, А. В. Гнездилов // Анестезиология и реаниматология. – 1998. – №5. - С. 64–71.
11. Postoperative Pain Management Text / F. M. Ferrante, T. R. VadeBoncouer. – М.: Медицина, 1998. – 640 с.
12. Wind, J. Systematic review of enhanced recovery pro grammes in colonic surgery Text / J. Wind, S. W Polle // Br. J. Surg. – 2006 . – V 93. – P. 800–809.
13. Opioid analgesics Text / H. B . Gutstein, H. Akil // In: Hardman J.G., Limbird L.E., editors. Goodman & Gilman’s The pharmacological basis of therapeutics. 10th ed. New York: McGraw-Hill. – 2001 . – P. 569–619.
14. Malinovsky, J. M. Nalbuphine reverses urinary effects of epidural morphine: a case report Text / J. M. Malinovsky, J. Y .Lepage, G. Karam, M. Pinaud. // J. Clin. Anesth. – 2002 . – V. 14. – P. 535–538.
15. Современные аспекты рационального обезболива ния в медицинской практике Текст / Л. В. Яковле ва, О. Н. Шаповал, И. А. Зупанец. – Киев «Мори он», 2000. – С. 6–12.