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BLOCKERS 5-HT3 SEROTONIN RECEPTOR IN THE COMPLEX OF INTENSIVE THERAPY OF TRAUMATIC DISEASE IN PATIENTS WITH POLYTRAUMA

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БЛОКАТОРИ 5-НТ3 РЕЦЕПТОРІВ СЕРОТОНІНУ В КОМПЛЕКСІ ІНТЕНСИВНОЇ ТЕРАПІЇ ТРАВМАТИЧНОЇ ХВОРОБИ У ПАЦІЄНТІВ З ПОЛІТРАВМОЮ

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У рамках дослідження проведено комплексне клініко-лабораторне обстеження пацієнтів з множинною травмою. Ми описали роль рецепторів серотоніну 3-го типу (5-НТ3) в патогенезі травматичної хвороби. Виявлено позитивний ефект від застосування блокаторів 5-НТ3 в комплексній інтенсивній терапії у пацієнтів з краніо-абдомінальною травмою.

Ключові слова: множинна травма, серотонінові рецептори, інтенсивна терапія.

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In the investigation we performed complex clinical and laboratory examination in patients with multiple trauma. We described the role of the 3rd type serotonin receptors (5-HT_3) in the pathogenesis of traumatic disease. We found a positive effect of using of 5-HT_3 blockers in complex intensive therapy in patients with cranio-abdominal injury.

Key words: multiple trauma, serotonin receptors, intensive therapy.

Introduction.

It has been proven that the course of a traumatic illness determines the reactivity of the organism, which is manifested by the features and types of both nervous and humoral regulation of functions [1]. One of the important pathogenetic mechanisms of the development of complications in patients with polytrauma is the effects caused by irritation of both nerve fibers located directly in the tissues and receptor formations. In this case, there is intense afferent impulses along the conductors of various kinds, which, outside the use of therapeutic measures, persists for a long time during and after injury [2]. In turn, damage to specific cells leads to the release of various kinds of active

substances and disruption of the corresponding functions. For example, the violation of the integrity of the connective tissue is accompanied by the destruction of mast cells, which leads to massive resorption of proteinogenic amines [3], some of which are peptide synaptic mediators.

As a result of the search for new directions in the treatment of various kinds of functional disorders in patients with polytrauma, the study of the action of peptide hormones is promising. It is known that their biological effect is realized by binding to specific receptors of the postsynaptic membrane, as a result of which the conductivity of the latter increases with the final result – excitation or inhibition, which depends solely on the properties of the ion channel [4]. The number of receptors is in a dynamic state. It is regulated physiologically and changes in diseases or under the influence of therapeutic agents [5], in particular, the so-called antagonists of synaptic transmission. By binding to the receptor, they do not cause changes in conductance, since they interfere with the action of mediators or their agonists [6].

It is known that 5-hydroxytryptamine (5-HT) – serotonin is essential in the formation of pain syndrome [7]. According to its chemical structure, it belongs to the group of indolylalkylamines and is formed in the body as a result of the conversion of the amino acid L-tryptophan. Serotonin is found in various organs and tissues, including platelets, intestinal enterochromaffin cells, and adrenal medulla cells. It realizes its action through a system of serotonin receptors located on different types of neurons of the enteric plexus, on smooth muscle and epithelial cells of the gastrointestinal tract and brain cells [8].

Currently, 7 types of serotonin receptors have been identified. Drugs that have an affinity for 5-HT – receptors are able to influence the transmission of nerve impulses at the receptor and interneuronal levels, to regulate impaired motility of the gastrointestinal tract. A large number of serotonergic receptors are located in the structures of the brain, and serotonergic fibers are part of the descending antinociceptive structures. A decrease in serotonin levels leads to a decrease in the pain threshold and increased pain [9].

Taking into account the peculiarities of the course of traumatic illness, it is interesting from a pathogenetic point of view to use antagonists of type 3 serotonin receptors (5-HT3) in the period of acute reaction to trauma and its early period. These receptors in the gastrointestinal tract are localized in afferent sensory fibers and postsynaptic enteral neurons of the intermuscular and submucosal plexuses. In addition, they are found in neurons in the dorsal horns of the spinal cord, which transmit sensory impulses from the distal intestine. In the central nervous system, 5-HT3 – receptors are expressed in the cortex and limbic system, in the vomiting center, found in the nuclei of the vagus nerve.

Antagonists of 5-HT3-receptors are divided according to the dominant effect on the central and peripheral structures. They are able to control the motor activity of the small and / or large intestine, reduce the frequency of bowel movements and urge, reduce the perception of pain in response to distension of the colon, and suppress the gag reflex [10].

The aim of the study was finding the most rational choice of drugs that have an antiemetic effect in patients with polytrauma in the acute and early periods of traumatic illness.

Material and methods. We examined 82 patients with polytrauma, 62 men and 20 women. The age of the patients varied from 19 to 50 years. For a comparative analysis, 2 groups of victims were selected, control and main, 36 and 46 people, respectively, which did not significantly differ in gender, age, anthropometric data, the nature and severity of injuries, and the timing from the moment of injury to admission to the hospital. The severity of polytrauma was comparable in both groups and when assessed on the ISS scale was 24.50 ± 4.32 and 25.12 ± 5.08 points, respectively, the prognosis on the TS scale was 10-13 points. When choosing patients for the study, particular importance was attached to the combination of injuries, the various variants and the number of which have a direct impact on the course of the traumatic disease (Table 1). Trauma: TBI – cranial, A – abdominal, T – thoracic, S – skeletal.

Table 1

Distribution of patients by type of injury

	Groups		
Type of injury	**Control (n = 36)**	**Main (n = 46)**	**Total**
TBI + A + S	15	15	30
TBI + A + T	16	22	38
TBI + A + T + S	5	9	14

At the same time, preference was given to victims with the presence of combined cranio-abdominal injuries, one of the clinical manifestations of traumatic disease in whom vomiting of various etiologies was one of the clinical manifestations of traumatic disease.

The level of consciousness of patients on admission according to the Glasgow coma scale was 13.24 ± 1.76 points with no significant difference between the groups ($p > 0.05$).

Under the conditions of programmed intravenous anesthesia with mechanical ventilation against the background of the administration of muscle relaxants, all patients underwent laparotomy with a full volume of surgical correction. In stages, the victims with traumatic brain injury underwent surgical intervention in the presence of intracranial pathology, primary surgical treatment of wounds; for patients with injuries of the musculoskeletal system – traumatological correction for severe injuries in a reduced volume using a minimally invasive method, in other cases – metal osteosynthesis, application of the Ilizarov apparatus. In the presence of a thoracic injury, puncture or drainage of the pleural cavity according to Bulau.

The duration of the patients' stay in the operating room averaged 161.2 ± 25.7 minutes. After being transferred to the intensive care unit, all victims were extubated during the first 24 hours of hospital stay.

Patients with hemodynamic disorders who required correction with adrenaline were excluded from the study. At the same time, in the postoperative period 61.1% of patients in the control group needed additional administration of ß-dosages of dopamine, α-dosages – 13.9%. In the main group of patients, these figures were 58.7% and 15.2%, respectively.

Taking into account the peculiarities of the management of patients with polytrauma, such as urgency, the inability to fully collect anamnestic data and often

forced polypharmacy, due to the selection of drugs taking into account an individual approach, in addition to premedication in order to prevent possible dyspeptic syndrome, patients in the control group were injected metoclopramide 0.14 ± 0.02 mg / kg body weight. After transfer to the department, its daily dosage was 0.41 ± 0.05 mg / kg of body weight in one ampoule (10 mg) mode intravenously every 8 hours for 5 days. In turn, the patients of the main group received premedication of sturgeon (ondansetron hydrochloride dihydrate) 0.06 ± 0.01 mg / kg body weight. In the postoperative period, its daily dosage was 0.11 ± 0.01 mg / kg of body weight in the mode of one ampoule (4 mg) intravenously every 12 hours for 5 days. In all the victims in the first 5 days of hospitalization, the clinical manifestations of dyspeptic sidroma, the intensity of peristalsis in points on the Orel V.V. scale were studied. (2002), the intensity of pain on the VAS scale against the background of the administration of non-steroidal anti-inflammatory drugs (narcotic analgesics were not used in the postoperative period).

To achieve representativeness between the groups, the degree of blood loss was determined based on the amount of blood in the abdominal and pleural cavities, using the calculation method according to the formula F.D. Moore and on the basis of the data in the table G.A. Barashkov, P. Kazal. Hemodynamic parameters were determined by the method of integral rheography according to M.I. Tishchenko, blood pressure – using the resuscitation-surgical monitor «UTAS-300M».

To assess the significance of differences, we used the Student's t test. At $p < 0.05$, the differences were considered statistically significant.

Research results. The research results have proved that the use of sturgeon in patients with polytrauma in premedication and in the postoperative period is the most optimal. From the first hours of the postoperative period, the patients of both groups underwent a point assessment of the intensity of peristalsis (Fig. 1).

When conducting a comparative analysis of the data in Figure 1, it can be seen that against the background of complex intensive therapy in all patients, peristalsis tended to increase and by the end of the acute period of traumatic illness reached 2 points in the absence of a statistically significant difference between the groups ($p < 0.05$).

The study of pain intensity using the VAS scale (Fig. 2) revealed a persistent tendency to its decrease in all victims, more pronounced in patients of the main group in the absence of a statistically significant difference between the groups ($p < 0.05$).

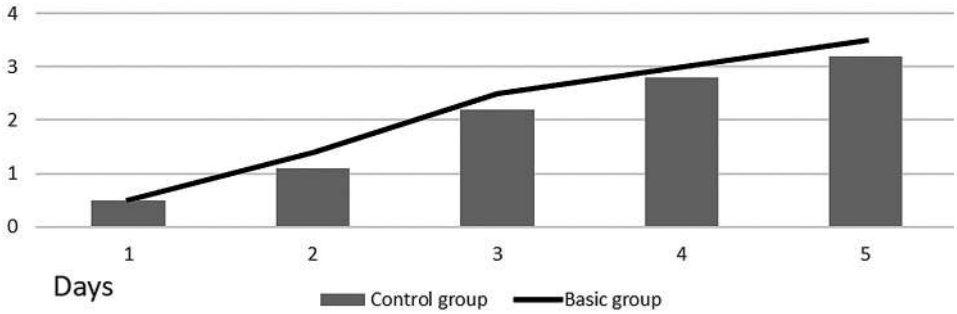

Figure 1. Dynamics of the intensity of peristalsis in points in victims of both groups, points

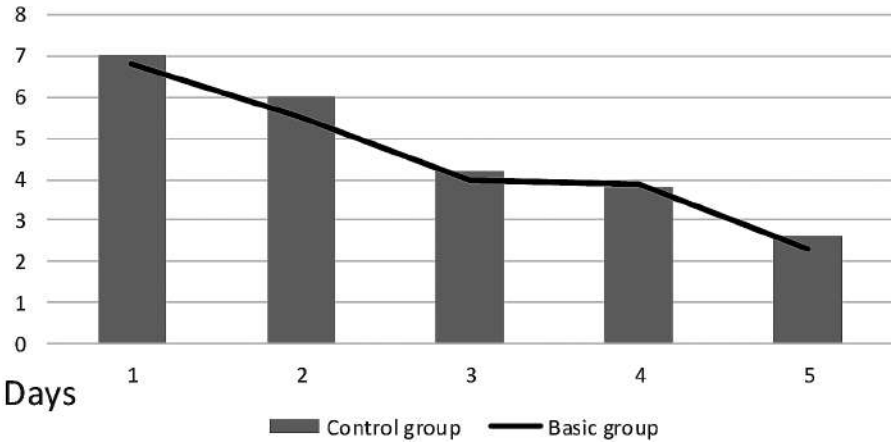

Figure 2. Dynamics of pain intensity according to VAS in victims of both groups, points

In a comparative analysis of hemodynamic parameters, we did not reveal a significant difference between their indicators in both groups (Table 2).

However, it was interesting to identify the fact of a persistent increase in the dosage and the time required for exogenous dopamine administration in patients of the control group. In our opinion, this may be due to the blocking of dopamine D2 receptors by metoclopramide and requires a special study.

When metoclopramide was used in the prevention and treatment of vomiting in victims of the control group, the full antiemetic effect was achieved in 72.4% of patients. At the same time, such possible side effects of this drug as extrapyramidal disorders and impaired concentration made it difficult to differentiate the clinical condition of patients.

When used in the prevention and treatment of vomiting in the victims of the main group of sturgeon, the full antiemetic effect was achieved in 96.3% of patients. At the same time, it was determined that such a clinical effect of this drug as a decrease in peristaltic activity does not aggravate postoperative intestinal paresis, but, on the contrary, is an element of prevention of irritable bowel syndrome and diarrhea against

Table 2

Dynamics of hemodynamic parameters in victims of both groups

Indicator	Group	1 day	2 day	3 day	5 day
MAP, mmHg	Control	101,3±7,4	106,6±11,5	100,1±9,6	93,5±5,8
	Basic	98,8±5,9	108,2±9,4	99,7±10,2	96,1±10,3
SV, ml	Control	48,7±7,2	58,4±6,2	58,5±2,7	66,1±7,1
	Basic	55,4±5,6	58,1±3,1	62,7±3,2	68,4±8,5
MVBC, l/min	Control	5,4±0,2	5,4±0,9	5,5±0,2	6,2±0,6
	Basic	5,5±0,7	5,7±0,3	6,0±0,4	6,3±0,2

* $p > 0,05$

the background of dysbiosis caused by massive antibiotic therapy. In turn, such effects of sturgeon as anxiolytic effect without sedation and impaired coordination of movement, relief of somatic and psychopathological symptoms in alcohol-toxic withdrawal syndrome contributes to the correct interpretation of the clinical manifestations of traumatic illness, which makes it the drug of choice in the clinic of polytrauma.

Conclusions.

1. An important component of the complex treatment of traumatic illness in patients with polytrauma is the use of drugs with an antiemetic effect.
2. Interesting from the pathogenetic point of view is the use of antagonists of serotonin receptors type 3 (5-HT3) in the treatment of traumatic disease.
3. In patients with polytrauma with cranio-abdominal injuries, the most rational from the pathogenetic point of view is the use of type 3 serotonin receptor antagonists.

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