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STRESS-LIMITING ANESTHESIA IN OPHTHALMOSURGERY

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ABSTRACT

Despite the significant advances made by modern anesthesiology in the perioperative management of patients, surgical interventions are still accompanied by a high proportion of complications and even deaths. At the same time, it is known that in 50% of cases mortality and serious postoperative complications could be prevented. After performing a thorough study of the factors affecting the increase in hospitalization and postoperative recovery (Kehlet H., 1997; Kehlet H., Wilmore D., 2002), it was determined that the surgical stress response is the most significant inducer of dysfunction of various organs. and systems. To date, it has been established that general anesthesia in its classical sense does not allow achieving complete protection of the patient from surgical trauma. More complete protection can be achieved by combining general anesthesia with regional blockages and adjuvant drugs with stress-protective properties. In the present study, we compared the severity of the surgical stress response and pain syndrome in patients operated on under conditions of multicomponent balanced general anesthesia (group K) with patients who received a stress-limiting anesthesia regimen (group DB). In both groups, multicomponent anesthesia was performed, in group K, sibazone was used for sedation, in group DB, dexmedetomidine was used. Also, patients of the DB group underwent regional blockade (blockade of the pterygo-palatine fossa) before surgery. The main criteria for evaluating the results were: hemodynamic stability, blood glucose, the level of venous blood leukocytes and the severity of pain according to the VAS in the postoperative period. Both schemes made it possible to avoid pronounced fluctuations in hemodynamic and gas exchange parameters at all stages of the study. When analyzing blood glucose and leukocyte counts, it was found that patients in the control group had a more significant deviation of both indicators from the preoperative level than in the stress-limiting anesthesia group. In the study of pain syndrome, it was determined that in the control group the level of pain according to the VAS was higher at all stages of the study compared to patients in the group of stress-limiting anesthesia.

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Introduction. Today, despite the fact that anesthetic science has reached significant development, surgical interventions are still accompanied by an unacceptably high rate of complications and even death. More than 230 million major surgeries are performed worldwide every year. Depending on the country and the hospital, about 4% of patients die before discharge from the hospital, 15% develop serious postoperative complications, and 5 to 15% of patients are rehospitalized within 30 days. It was calculated that in half of the cases, lethality and serious postoperative complications could have been prevented [1].

After a comprehensive study of the factors affecting the prolongation of hospitalization and rehabilitation (Kehlet H., 1997; Kehlet H., Wilmore D., 2002), it was determined that the surgical stress response is the most significant inducer of dysfunction of various organs and systems. (pain, metabolic disorders, pulmonary and cardiac dysfunction, gastrointestinal disorders, coagulopathy) [2, 3]. The stress response is hormonal and metabolic changes that occur after injury (including surgery) or injury. It is part of the systemic response to trauma, which includes a wide range of endocrine, immunologic, and hematologic effects. Although it seems that the stress response evolved to help the injured individual survive by catabolism of its own energy sources, it is now believed that such a response is not necessary in modern surgery [4]. The main links of the stress response are shown in Figure 1.

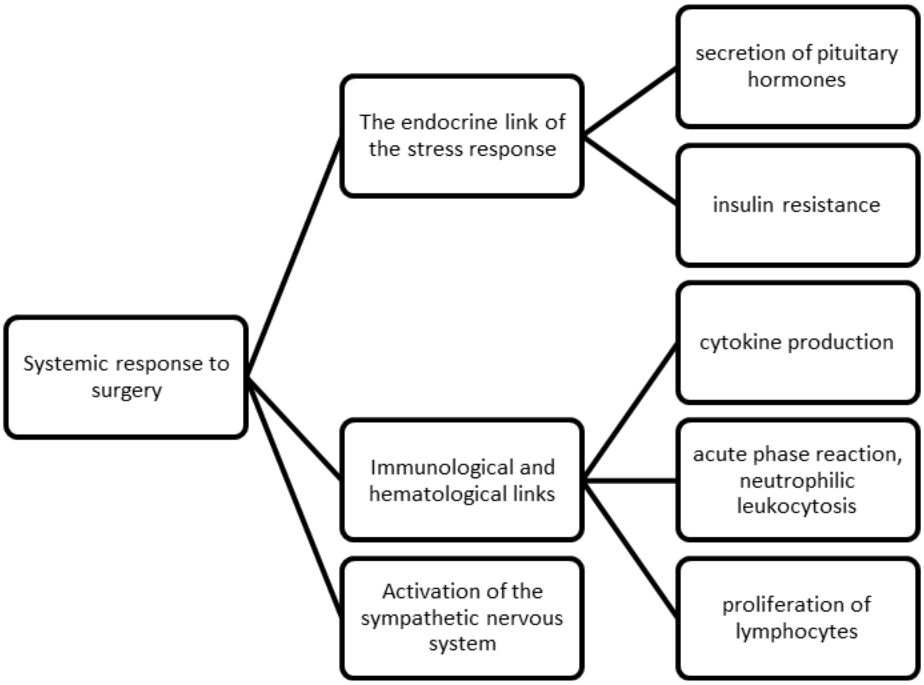

Fig. 1. The main links of the stress response. [4]

Now the issue of protecting the patient from surgical trauma and the adequacy of anesthesia are in the focus of attention of modern scientists [5,6]. Sometimes it seems that no technique can effectively block all aspects of the trauma response, and therefore the widespread use of the term stress-free anesthesia in surgery is invalid. So, at present, there is not a single drug or technique that can fully protect the patient from the occurrence of a stress response to surgical trauma [5].

In order to fully protect patients from surgical aggression, in different years, combined anesthesia, neuroplegia, potentiated, dissociative, antinociceptive and total intravenous anesthesia, polynarcosis, and NLA were proposed and used. However, they all have inherent, along with positive qualities, and certain disadvantages that do not allow to achieve ideal protection of patients. Thus, narcotic analgesics used in general anesthesia block nerve substrates that maintain a state of vigor, but leave intact or do not significantly affect the nociceptive sensory system and the processes of integration of pain reactions. Even with deep anesthesia, a certain part of nociceptive impulses from the surgical wound can enter the central nervous system and activate the autonomic apparatus, causing multiple unfavorable changes in the organism of the operated patients, which is regarded as “lack of anesthesia”.

At the beginning of the 20th century, the outstanding physiologist L. Orbeli said that the first link to which attention should be paid is the pain sensitivity apparatus itself. Limited data indicate that the quality of postoperative pain relief can affect the outcome of the operation, reducing cardiac, pulmonary and metabolic complications [7]. It is difficult to separate the contribution of postoperative pain per se from surgery-induced immunosuppression, and there is little empirical evidence on the effect of postoperative pain on immune function. In any case, it is obvious that the immune and nervous systems interact bilaterally and influence each other [8]; therefore, pain relief can affect the immune response in the postoperative period [9]. That is, if conditions are not created to exclude an irritating agent that causes pain, then stress protection cannot be achieved. However, in many cases this may not be enough, it is necessary to influence the sympathetic nodes. Only by applying an integrated approach can you achieve favorable results.

Thus, strong, selective and controlled analgesia is at the heart of anesthetic management, the key to protecting the structure and function of vital systems during and after surgery.

Analysis of numerous literature data allows us to assert that, once it has arisen, the pathological pain syndrome is not caused by an afferent influx from the irritation zone, but has much more complex mechanisms. The experience of neurosurgery also shows that by interrupting afferent conduction at any level of the ascending sensory pathways or by destruction of certain central structures associated with the integration of pain, it is impossible to fully achieve positive results. Therefore, blockade of nociceptive impulses and central analgesia alone is probably not enough to prevent overreaction of the sympathetic nervous system and adrenal glands, as well as adverse reactions from the organs and systems of operated patients. There is not, and probably will not be, a single drug that provides all the components of general anesthesia and adequate protection of the patient from surgical aggression. This is possible only when using multidirectional pharmacological agents. In this regard, it is considered expedient to block autonomic reactions additionally at the level of effectors. This explains the interest in the use of drugs that can selectively block efferent pathways and effectively prevent unwanted autonomic and neuroendocrine reactions to surgical trauma. More complete protection can be obtained by a combination of general, local anesthesia with stress-protective drugs [10]. Thus, using anesthesia, it is possible to influence the stress response of the body to surgical trauma by afferent blockade (various options for local anesthesia), central modulation (general anesthesia) and acting on the endocrine and autonomic nervous systems (various adjuvant drugs for anesthesia) [11]

The aim of this study was to assess the efficacy and safety of the proposed scheme of stress-limiting anesthesia in ophthalmic surgical patients with corneal transplantation.

Materials and methods.

The study included 76 patients who underwent corneal transplantation on the basis of the Dnepropetrovsk Regional Clinical Ophthalmological Hospital. The patients were divided into 2 groups: control (group K) - 45 people and the main (group DB) - 31 people. A description of the groups is provided in Table 1.

Table 1. Description of study groups (M ± m).

Indicator	**Group K**	**Group DB**
Age, years	49,6±2,4	55,5±3,3
Gender (m / f)	26/19	18/13
ASA class	1-2	1-2

Both groups were homogeneous in age and gender.

The applied method of anesthesia in group K was multicomponent balanced anesthesia according to the following technique: premedication - ondansetron 4 mg, dexamethasone 4 mg, ketorolac 30 mg, sibazone 10 mg, fentanyl 0.1 mg intramuscularly 40 minutes before the intervention. Induction with propofol 2-2.5 mg / kg fractionally until clinical symptoms of anesthesia are achieved, fentanyl 0.005% 0.1 mg. Intubation of the trachea after relaxation against the background of atracurium besylate 0.3-0.6 mg / kg. Maintenance of anesthesia: oxygen-sevoflurane mixture with FiO2 50-55%, sevoflurane 1.4-1.8 vol. % on exhalation (1-1.5 minimum alveolar concentrations of MAC) with a flow of not more than 1 l / min. The BIS values were maintained at the level of 30-40, during the operation, a bolus of fentanyl 0.1 mg intravenously was used when hemodynamic reactions appeared. Intraoperative monitoring of patients included: non-invasive measurement of blood pressure, heart rate, pulse oximetry, determination of the concentration of oxygen, carbon dioxide and inhalation anesthetic in the inhaled and exhaled air, registration of the bispectral index (BIS) in on-line mode. All patients underwent peripheral vein catheterization, the rate of intraoperative infusion did not exceed 3-5 ml / kg / hour. In the postoperative period, anesthesia was carried out by the planned administration of ketorolac 30 mg 2 hours after the intervention.

In the DB group, we applied the scheme of stress-limiting anesthesia. Multicomponent balanced anesthesia was supplemented with blockade of the pterygo-palatine fossa, and dexmedetomidine was used as an adjuvant. The introduction of the drug was carried out according to the following scheme: for premedication, instead of sibazon, dexmedetomidine was used intravenously in a stream at a dose of 0.5 µg / kg for 10 minutes, then the administration of the drug was continued during the operation at a maintenance dose of 0.5 µg / kg / h in the form of a continuous infusion.

The main criteria for evaluating the results of the study were: hemodynamic stability during surgery, the number of consumed narcotic analgesics, the severity of postoperative pain syndrome according to VAS and the incidence of postoperative nausea and vomiting (PONV), and blood was taken from a peripheral vein to study the parameters characterizing stress response (peripheral blood leukocytes and glycemia). The fixation of the results was carried out in 4 stages:

1. Beginning of the operation;
2. The most traumatic stage of the intervention ("open sky");
3. End of the operation;
4. 6 hours after surgery.

For statistical processing of the research results, the software package Microsoft Word, Microsoft Excel and Statistica v 6.1 (Statsoft Inc., USA) (No. AGAR909E415822FA) were used. The analysis of quantitative data was carried out taking into account the distribution law, assessed by the Shapiro-Wilk criterion. In the case of a normal distribution, the arithmetic mean (M), standard error (m), Student's tests for related (T) and unrelated samples (t) were used, in other cases, the median (Me), interquartile range (25%; 75%) were used., Mann-Whitney test (U). The difference between comparable values was considered significant at p≤0.050 [12].

Results and its discussion.

Table 2. Parameters of hemodynamics and gas exchange in patients in the study groups, (M ± m)

Stage/ indicator	**Start operations**		**Open skies stage**		**End of operation**		**After 6 hours after operation**	
	К	DB	К	DB	К	DB	К	DB
MBP Mm Hg	80,6±2,2	69,0±2,0	68,8±1,9	60,2±1,7	68,0±2,1	57,5±1,4	87,5±1,6	81,3±2,2
p	0,095		0,096		0,954		0,172	
HR beats/min	72,8±1,9	61,3±1,9	68,3±2,2	58,0±1,8	68,7±2,0	55,9±1,7	75,2±1,5	68,7±1,6
p	0,986		0,850		0,805		0,971	
SpO_2, %	98±0,2	98,7±0,2	98,7±0,2	98,5±1,8	98,4±0,3	98,2±0,3	-	-
p	0,943		0,860		0,994			
$EtCO_2$ мм рт.ст.	32,2±0,6	30,1±0,6	33,5±0,6	31,1±0,7	35,8±0,6	33,2±0,8	-	-
p	0,597		0,414		0,093			

The indices of hemodynamics and gas exchange at the stages of the study are shown in Table 2. Based on the data in the table, it can be seen that both schemes of anesthetic management allowed keeping the basic vital signs within the normal range.

Before and at the beginning of surgery (stages 2 and 3), the glucose level in both groups was practically the same, glucose 2 in group K was 5.36 ± 0.2, in the DB group 5.27 ± 0.09 (p = 0.750 Mann-Whitney test), glucose 3 - 5.64 ± 0.23 and 5.57 ± 0.09, respectively (p = 0.819 according to Mann-Whitney test). However, at the “open skies” stage (stage 4), the glucose level in the control group was higher than the glucose level in the stress-limiting anesthesia group, 6.37 ± 0.27 versus 5.71±0.12 (p = 0.043 according to Mann's test). Whitney). A similar trend persisted 6:00 after the end of the operation, when the glucose level in the control group was statistically significantly higher than in the DB group, 7.72 ± 0.6 versus 5.86 ± 0.17 (p = 0.005 according to Mann's test -Whitney). This may indicate a more pronounced tension of the endocrine-metabolic link of the surgical stress response in group K compared with group DB. Figure 3 shows the dynamics of the level of leukocytes.

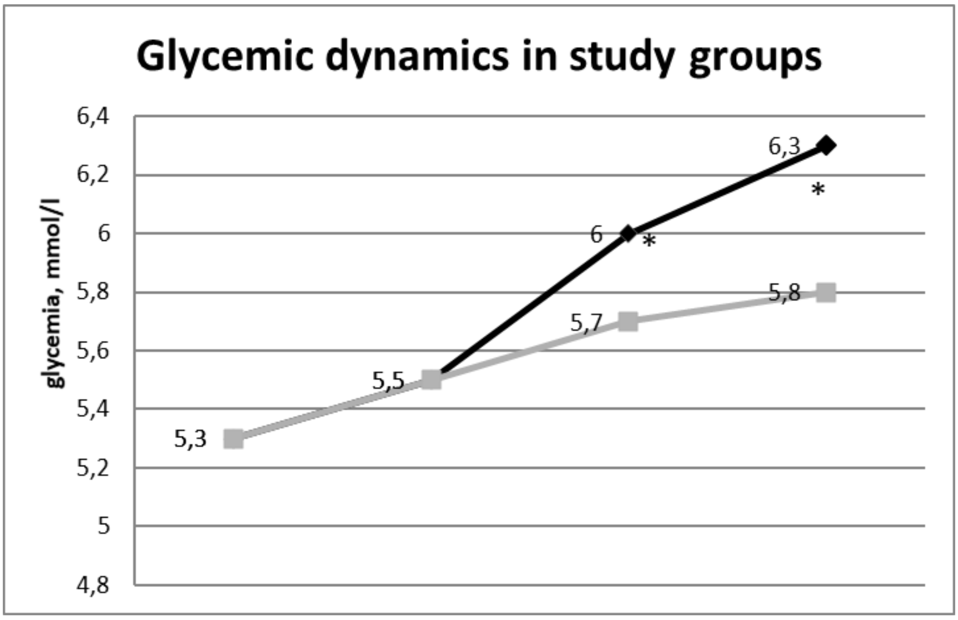

Fig. 2 shows the dynamics of blood glucose levels in the studied groups.
*Note: * - p<0.05 according to the Mann-Whitney test.*

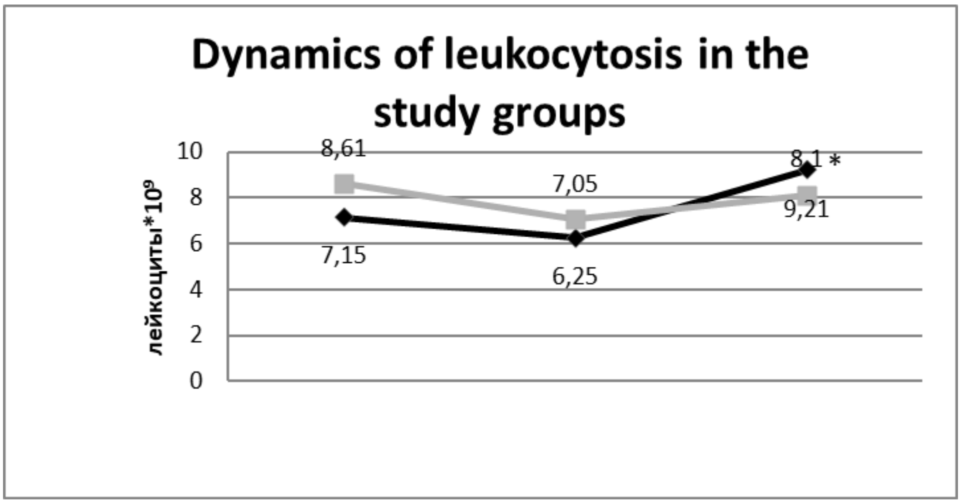

Fig. 3. Dynamics of the level of leukocytes in the study groups
*Note: * - p<0.05 according to the Mann-Whitney test.*

The figure above shows that the preoperative level of blood leukocytes in the stress-limiting anesthesia group slightly exceeded the level in the control group, 8.61 ± 0.50 versus 7.25 ± 0.52, but no statistically significant difference was found (p = 0.960 by Mann-Whitney test). At the most traumatic stage of the intervention, there was a decrease in the level of leukocytes in both groups: group K - 6.25 ± 0.52, group DB - 7.05 ± 0.47 (p = 0.790 according to the Mann-Whitney criterion), which is possibly associated with exposure to on the body of general anesthesia. 6 hours after the operation, the level of leukocytes in the control group crossed the normal limit and amounted to 9.21 ± 0.65, while in the stress-limiting anesthesia group, the level of leukocytes remained within the normal range (8.1 ± 0.47) and even decreased in compared with the preoperative level (p = 0.026 according to the Mann-Whitney test). Such changes in the leukocyte formula may indicate a greater severity of the inflammatory component of the operational stress response in the control group compared to the stress-limiting anesthesia group.

When analyzing the severity of postoperative pain, it was found that immediately after awakening, patients in both groups did not experience any discomfort associated with pain. 2 hours after surgery, patients in both groups experienced minor pain within 1-2 points according to VAS, which is quite acceptable in the postoperative period. However, already 6 hours after the intervention, despite the planned administration of ketorolac, the control group patients complained of severe pain, on average

6 ± 0.41 points on the VAS, which could indicate insufficient pain control in the postoperative period and required local blockade anesthetics, and in some cases even the introduction of narcotic pain medications. Whereas in the stress-limiting anesthesia group, pain remained mild and no additional anesthesia was required. The next morning, in the control group, the pain level decreased to 4 points, while the patients in the main group no longer experienced any discomfort associated with postoperative pain.

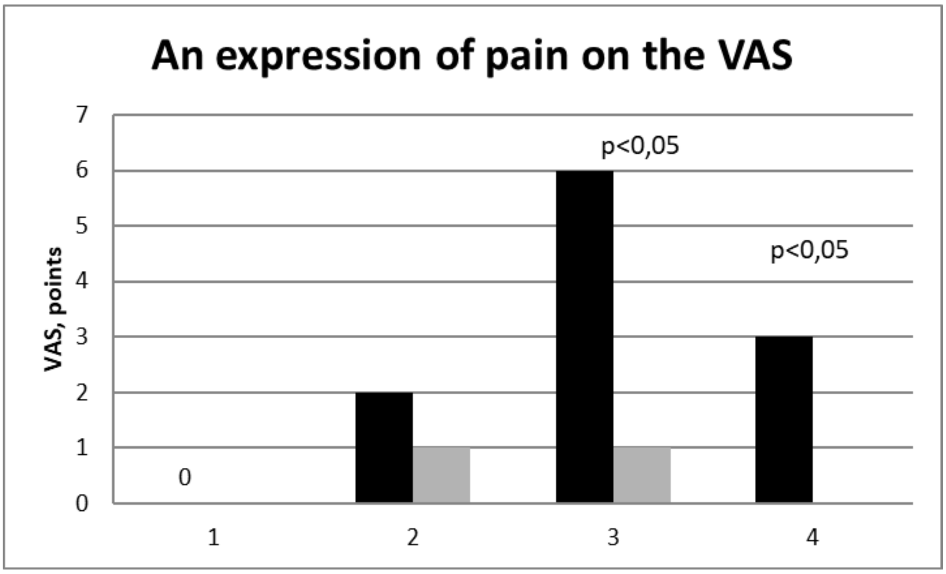

Fig. 4. The severity of pain according to VAS in the study groups
Note: $p<0.05$ according to the Mann-Whitney test.

Conclusions.

1. The use of stress-limiting anesthesia in patients with corneal transplantation is safe and does not cause pronounced fluctuations in hemodynamic and gas exchange parameters in the intraoperative period.

2. The addition of the pterygo-palatine fossa block and the drug dexmedetomidine to the anesthesia scheme allows more reliable control of the operational stress response in ophthalmic surgical patients.

3. The scheme of stress-limiting anesthesia allows to control postoperative pain without additional use of narcotic analgesics and blockades in the postoperative period.

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