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THE EXPERIENCE OF USING DEXMEDETOMIDINE AS AN ADJUVANT OF ANESTHESIA IN OPHTHALMIC SURGERY

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Ключевые слова: *декседетомидин, мультимодальная аналгезия, послеоперационная боль*

Abstract. The experience of using dexmedetomidine as an adjuvant of anesthesia in ophthalmic surgery. Mynka N.V., Kobelyatskyy Yu.Yu. *Various techniques are applied to reduce the severity of postoperative pain and discomfort in patients. The purpose of this research work was to evaluate the effectiveness and safety of dexmedetomidine as an adjuvant of anesthesia in ophthalmic surgery. The study included 80 patients who underwent corneal transplantation on the basis of Dnepropetrovsk Regional Clinical Ophthalmologic Hospital. Patients were divided into 2 groups: control (group K) – 30 men and main (group D) – 50 ones. Multicomponent balanced anesthesia was applied in both groups. Sibazone was administered as the sedative medicine in the group K, Dexmedetomedin was administered in the group D. The main criteria for evaluating the research results were hallmarked: hemodynamic stability during surgery, the amount of administered opiates, the severity of intraoperative pain syndrome by evaluating the ANI index (ANI – analgesia nociception index), the severity of postoperative pain syndrome and the frequency of*

postoperative nausea and vomiting (PONV). Both schemes of anesthesia allowed avoiding pronounced fluctuations in hemodynamic parameters and gas exchange at all stages of the study. Analyzing the severity of intraoperative pain, we found that in group K pain relief could be considered insufficient during the first 7 minutes of the most traumatic stage of the surgery, while in group D the ANI index did not fall below 50. Statistically significant differences were obtained on minute 1, 2, 5, 6, and 7 of the surgery. The number of episodes of insufficient anesthesia during the most traumatic stage of the surgery in group K was statistically significantly higher than in group D. Analyzing the quality of pain relief in the postoperative period it was determined, that the level of pain on the Visual Analog Scale (VAS) after awakening in both groups was equal to 0. At the next three stages of the study (2 hours, 6 hours after surgery, and the next morning), the level of pain in group K was significantly higher than in group D. In addition, it was determined that the need for narcotic analgesics and the number of episodes of postoperative nausea and vomiting in group K was statistically significantly higher than in group D. These given data allow us to conclude that Dexmedetomedin is the effective adjuvant of the anesthesia for corneal transplantation.

Реферат. Опыт применения дексмедетомидина в качестве адъюванта анестезиологического обеспечения в офтальмохирургии. Мынка Н.В., Кобеляцкий Ю.Ю. *Для контроля послеоперационной боли у пациентов применяются различные техники, в том числе происходит постоянный поиск новых адъювантов анестезии. Целью исследования было оценить эффективность дексмедетомидина в качестве адъюванта анестезии в офтальмохирургии. В исследование было включено 80 пациентов, перенесших кератопластику. Пациенты были разделены на 2 группы: контрольная (группа К) – 30 человек и основная (группа Д) – 50 человек. В обеих группах была применена многокомпонентная анестезия, в группе К для седации использовали сибазон, в группе Д – дексмедетомидин. Основными критериями оценки результатов были приняты: гемодинамическая стабильность, количество затраченных опиатов, выраженность интраоперационной боли путем регистрации индекса ANI (ANI – analgesia nociception index), выраженность послеоперационной боли и частота развития послеоперационной тошноты и рвоты (ПОТР). Обе схемы позволяли избежать выраженных колебаний показателей гемодинамики и газообмена на всех этапах исследования. Анализируя выраженность интраоперационной боли, нами было установлено, что в группе К обезболивание может считаться недостаточным в течение первых 7 минут наиболее травматичного этапа операции, тогда как в группе Д показатели индекса ANI не опускались ниже 50. Статистически значимые отличия получены на 1, 2, 5, 6 и 7 минутах этапа. При анализе качества обезболивания после операции было установлено, что уровень боли по Визуальной аналоговой шкале (ВАШ) после пробуждения в обеих группах был равен 0, на последующих трех этапах исследования (через 2 часа, 6 часов после операции и на утро следующего дня) уровень боли в группе К был достоверно выше, чем в группе Д. Кроме того, было установлено, что в группе К потребность в наркотических аналгетиках и количество эпизодов послеоперационной тошноты и рвоты было статистически значимо выше, чем в группе Д. Вышеописанные данные позволяют сделать вывод о том, что дексмедетомидин является эффективным адъювантом анестезии при трансплантации роговицы.*

An important aspect of modern anesthesiology is insufficient pain management. A large number of patients (up to 84%) after surgery complain of pain during the first 2 weeks after surgery [8, 11]. A survey of patients showed that in 87% of cases the intensity of postoperative pain is medium and high, and 17% of patients noted that its intensity exceeded expectations [4].

Insufficient postoperative analgesia has been shown to have physiological consequences: changes in the cardiovascular and respiratory systems, limited mobility, immunosuppression, sleep disorders, poor appetite, drug dependence, and an increased risk of prolonged chronic pain.

The complex pathological influence of postoperative pain on organs and systems is proved. Hypercatecholaminemia develops due to irritation of the hypothalamic-pituitary-cortical-adrenal system, which leads to the development of tachycardia, hypertension, arrhythmia and can end in acute myocardial ischemia. The vital capacity of the lungs decreases due to atelectasis, pneumonia develops. Vasospasm in the area of the splanchnicus leads to paresis of the intestine and translocation of the intestinal flora. The effect on blood clotting is accompanied by hypercoagulation with subsequent deep vein thrombosis, pulmonary embolism. The effect of postoperative pain on the CNS leads to the formation of chronic pain [6]. Despite the growing interest to the problem of postoperative analgesia, its quality remains unsatisfactory [4].

According to the definition of the International Association for the Study of Pain (IASP), pain is an unpleasant sensation and emotional experience associated with existing or probable tissue damage [5]. It is possible to approach the solution of the problem of adequacy of postoperative anesthesia only by implementing the concept of multimodal analgesia in the clinic [10]. Multimodal analgesia is the use of several drugs or techniques that

selectively affect the various physiological processes involved in the implementation of the nociceptive response. The concept of multimodal analgesia is implemented using two main techniques: a combination of drugs and local anesthesia or a combination of drugs from different pharmacological classes. According to data published by the American Society of Anesthesiology for the Treatment of Pain, the use of multimodal analgesia as a method of controlling perioperative pain is indicated in all cases in the absence of contraindications [9]. The combination of drugs of different classes as a part of multimodal analgesia is considered rational. To choose the right combination, it is necessary to have an idea of the main pharmacological features of each class of drugs. Careful selection of an effective analgesic regimen is based on the type and intensity of the expected perioperative pain syndrome, the ability to withstand stress and anxiety associated with severe pain.

There exist traditional analgesics and adjuvant analgesics. Among analgesic adjuvants, dexmedetomidine has recently been of great interest to anesthesiologists. There are more and more publications of research results that indicate a decrease in the concentration of inhaled anesthetic and the number of opiates used to ensure an adequate level of anesthesia when adding dexmedetomidine to anesthesia [3]. There are data confirming the presence of stress-protective, neuro- and nephroprotective properties of this drug [12]. Meta-analysis of G. Blaudszun et al. [2] showed a decrease in the number of opiates used, a decrease in the severity of pain and the incidence of PONV in the use of dexmedetomidine. Given the above effects of dexmedetomidine, it is rational to include this drug in the anesthesia regimen in patients with corneal transplantation.

The aim of the study was to evaluate the efficacy and safety of dexmedetomidine as an adjuvant of anesthesia in ophthalmic surgery.

MATERIALS AND METHODS OF RESEARCH

The study included 80 patients who underwent corneal transplantation on the basis of ME "DRCOH". Patients were divided into 2 groups: control (group K) – 30 people and the main (group D) – 50 people. The description of the groups is given in Table 1.

Table 1

Description of study groups

Indicator	Group K	Group D
Age, years (M±m)	48.6±2.9	49.9±2.4
Gender (male/female)	16/14	29/21
ASA Class	1-2	1-2

Both groups were homogeneous by age and gender. The method of anesthesia used in group K is multicomponent balanced anesthesia: premedication – ondansetron 4 mg, dexamethasone 4 mg, ketorolac 30 mg intravenously, sibazone 10 mg, fentanyl 0.1 mg intramuscularly 40 minutes before the intervention. Induction of propofol 2-2.5 mg/kg fractionally until clinical symptoms of anesthesia are achieved, fentanyl 0.005% 0.1 mg. Intubation of the trachea is 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 of minimum alveolar concentrations (MAC)) at a flow of not more than 1 l/min. BIS values were maintained at the level of 30-40, during surgery a bolus injection of 0.1 mg of fentanyl intravenously was used in case of hemodynamic reactions. Intraoperative monitoring of patients included: non-invasive measurement of blood pressure, heart rate, pulse oximetry, determination of oxygen concentration, carbon dioxide and of inhalation anesthetic in inhaled and exhaled air, registration of bispectral index (BIS) on-line, registrarion of ANI index. All patients underwent peripheral vein catheterization, the rate of intraoperative infusion did not exceed 3-5 ml/kg/h. In the postoperative period, anesthesia was performed by routine administration of ketorolac 30 mg intravenously 2 hours after the intervention.

In group D dexmedetomidine was used. The drug was administered according to the scheme: for premedication dexmedetomidine was used intravenously instead of sibazone at a dose of 0.5 μg/kg for 10 minutes, then the drug was administered during surgery at a dose of 0.5 μg/kg/h as an infusion. The main criteria for evaluating the results: hemodynamic stability, the amount of opioids consumed, the severity of intraoperative pain by registering ANI index [7], the severity of postoperative pain by VAS [4] and the frequency of postoperative nausea and vomiting (PONV) [7]. The results were recorded in 4 stages: the onset of the surgery, the most traumatic stage of the intervention ("open sky"), the end of the surgery, 6 hours after the surgery. For statistical processing the application package Microsoft Word, Microsoft Excel and Statisica v 6.1 (StatsoftInc., USA) (No. AGAR909E415822FA) was used The analysis of quantitative data was performed taking into account the distribution law estimated by the Shapiro-Wilk criterion. In the case of a normal distribution, we used the arithmetic mean (M), the standard error (m), the Student's criteria for bound (T) and unrelated (t) samples, in other cases – the median (Me), interquartile range (25%; 75%), Mann-Whitney test (U). The difference between the compared values was considered significant at $p \leq 0.050$ [1].

RESULTS AND DISCUSSION

Both schemes allowed to avoid the expressed fluctuations of indicators of hemodynamics and gas exchange at all stages. The measurement results are presented in Table 2.

The indicators shown in Table 2 indicate no statistically significant difference between the study groups.

The quality of intraoperative analgesia was assessed by recording the ANI index within 10 minutes from the onset of the most traumatic stage of corneal transplantation ("open sky" stage), and the number of episodes of insufficient analgesia (decrease in ANI index less than 50) was additionally recorded. The indicators of the ANI monitor are presented in Table 3.

The dynamics of the ANI index in the study groups is shown in Figure 1.

Table 2

Indicators of hemodynamics and gas exchange in patients of study groups, Me (25%; 75%)

Stage/ indicator	Onset of surgery		Stage "open sky"		End of surgery		6 hours after surgery	
	K	D	K	D	K	D	K	D
Average BP mm Hg.	93 (84;113)	95.5 (85;107)	94 (67;117)	84 (64;99)	66 (57;81)	73 (56;82)	98 (78;113)	83 (75;113)
p	0.095		0.096		0.954		0.172	
HR beats/min.	76 (55;80)	80 (64;109)	70 (50;89)	72 (57;116)	69 (52;84)	66 (57;84)	77 (63;84)	76 (65;112)
p	0.986		0.850		0.805		0.971	
SpO_2 %	99 (97;100)	99 (95;100)	99 (96;100)	99 (95;100)	99 (97;100)	99 (97;100)	-	-
p	0.943		0.860		0.994			
$EtCO_2$ mm Hg.	32 (22;37)	26 (20;30)	33 (21;38)	27 (21;35)	39 (30;42)	30 (20;36)	-	-
p	0.597		0.414		0.093			

Note. Comparison of data of group K and D $p>0.05$ by U-Mann-Whitney test.

Table 3

ANI index in the study groups, Me (25%; 75%)

	Stage "open sky"									
hour	**1st minute**	**2nd minute**	**3rd minute**	**4th minute**	**5th minute**	**6th minute**	**7th minute**	**8th minute**	**9th minute**	**10th minute**
ANI gr. K	**46 (35;51)**	**39,5 (34;49)**	**43,5 (39;48)**	**46,5 (36;66)**	**48 (33;66)**	**48 (44;65)**	**49,5 (42;68)**	**53,5 (47;80)**	**60,5 (46;67)**	**62 (44;84)**
ANI gr. D	**66 (42;84)**	**64 (40;76)**	**54 (37;69)**	**56 (39;68)**	**62 (56;72)**	**67 (54;77)**	**64 (53;80)**	**72 (55;82)**	**74 (55;86)**	**73 (54;93)**
p	**0,05***	**0,02***	**>0,05**	**>0,05**	**0,04***	**0,05***	**0,04***	**>0,05**	**>0,05**	**>0,05**

Note. * – p≤0.05 between groups K and D by U-Mann-Whitney test.

The obtained data indicate an insufficient level of analgesia in group K during the first 7 minutes of "open sky", while in group D the index values during the whole time of the most traumatic stage did not fall below 50. Statistically significant differences were obtained at 1, 2, 5, 6 and 7 minutes of the stage.

The number of episodes of insufficient analgesia during the most traumatic stage of the operation in group K was 5.5 (4; 7) – Me (25%; 75%), while in group D only 2 (0; 2.5) – Me (25 75%) (p=0.001 according to the Mann-Whitney test), which is shown in Figure 2.

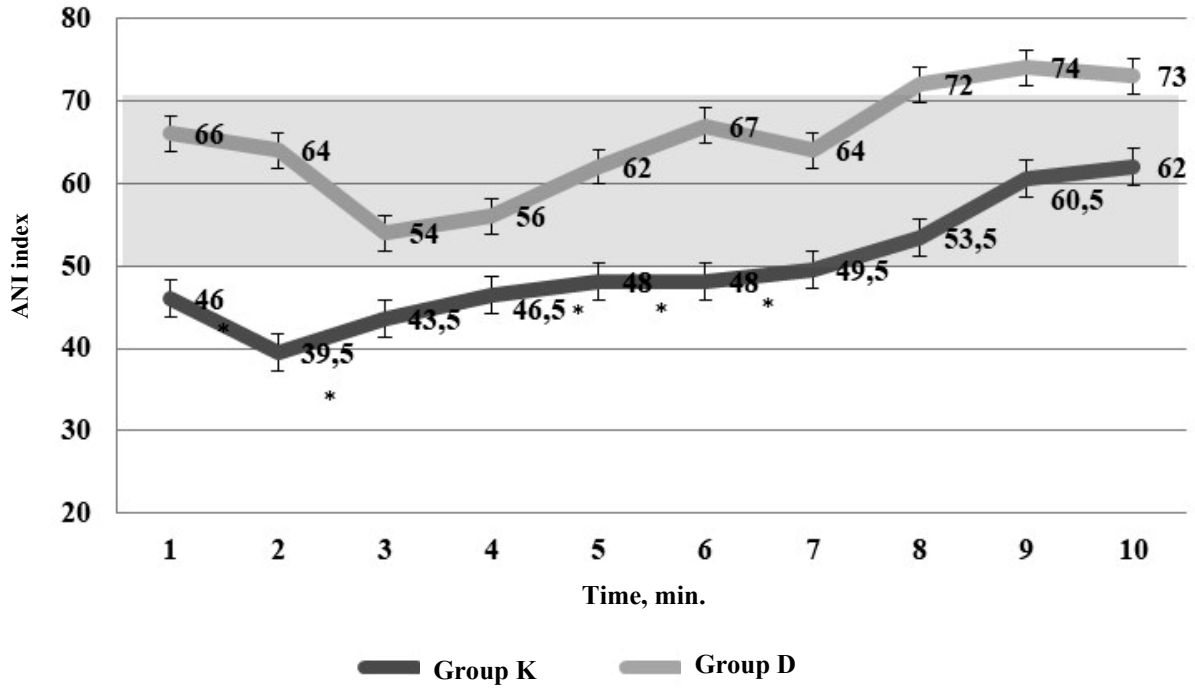

Fig. 1. Dynamics of ANI index in the study groups

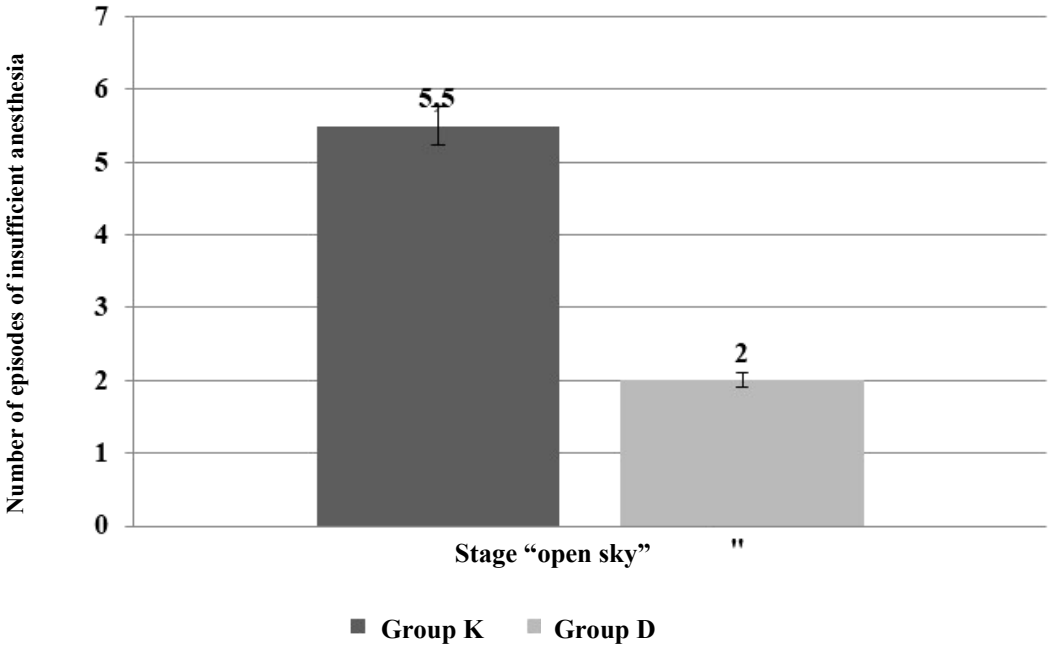

Fig. 2. Number of episodes of insufficient analgesia (within 10 minutes of the most traumatic stage of surgery)

The level of pain was assessed by a visual-analog scale (VAS). Assessment of pain by VAS was performed for the first time on the operating table (immediately after the patient's recovery of consciousness), then – in 2, 6 hours and in the morning the day after surgery. Interpretation of data by VAS: 0 points – no pain; 1-3 points - mild pain; 4-6 points – moderate pain; 7-9 points – severe pain; 10 points – unbearable pain. The level of pain by VAS after extubation in both group K (n=30) and group D (n=50) was 0. Anesthesia at this stage in both groups can be considered satisfactory. However, 2 hours after the surgery the level of pain in group K (n=30) was 3 (1; 5) – Me (25%; 75%), which is statistically significantly more than in group D (n=50) – 1 (1; 1) – Me (25%; 75%) ($p<0.001$ according to the Mann-Whitney test). 6 hours after the intervention, the gap in the indicators of pain levels in the groups differed even more and in the group K (n=30) was – 6 (3; 7) – Me (25%; 75%), which is statistically significantly larger than the group D (n=50) – 2 (1; 3) – Me (25%; 75%) ($p<0.001$ according to the Mann-Whitney test). At this stage, analgesia in group K can not be considered satisfactory, while patients in group D experienced only mild pain. The above dynamics was observed the morning after surgery. The level of pain by VAS was statistically significantly higher in group K – 3 (1; 4) – Me (25%; 75%), while in group D (n=50) – 0 (0; 1) – Me (25%); 75%) ($p<0.001$ according to the Mann-Whitney test).

The dynamics of pain level by VAS are presented in Figures 3a, b, c.

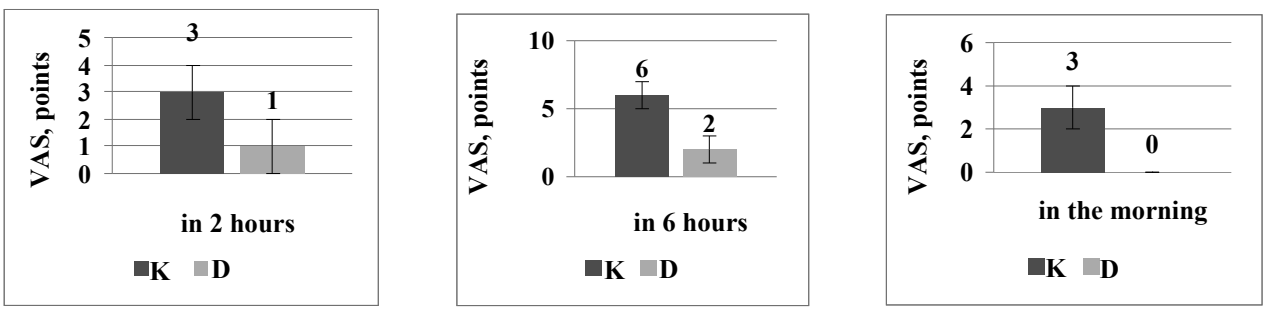

Fig. 3a, b, c. Pain level by VAS in study groups in 2, 6 hours and in the morning the day after surgery

The average level of need for fentanyl (ml) during surgery in group K (n=30) was 5 (4; 6) – Me (25%; 75%), which is statistically significantly higher than in group D (n=50) – 4 (4; 6) – Me (25%; 75%) (p=0.03 according to the Mann-Whitney test). PONV was observed in group K (n=30) in 9 patients, which was 30%, while in group D (n=50) – in 4-8%.

CONCLUSIONS

1. The use of dexmedetomidine in ophthalmic surgery is safe and allows to achieve a high level of postoperative comfort by reducing the need for opioids, reducing the number of episodes of PONV, improving the quality of analgesia.
2. The addition of dexmedetomidine can reduce the severity of intraoperative pain, as evidenced by the values of ANI monitor, being above 50 within the whole "open sky" stage. The number of episodes of insufficient analgesia was 2.5 times higher in the control group compared with the dexmedetomidine group.
3. When analyzing the level of pain by VAS in the postoperative period, it was found that pain was significantly more pronounced in the control group compared with the dexmedetomidine group at all stages of the study.
4. The need for fentanyl and the number of episodes of PONV were also significantly higher in the control group compared to the dexmedetomidine group.

Conflict of interests. The authors declare no conflict of interest.

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