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INFLUENCE OF THE CHOSEN METHOD OF ANESTHESIA ON THE SEVERITY OF POSTOPERATIVE COGNITIVE DYSFUNCTION IN PATIENTS OF OPHTHALMOSURGERY PROFILE

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Ключевые слова: *послеоперационная когнитивная дисфункция, дексмедетомидин, шкала MMSE*

Abstract. Influence of the chosen method of anesthesia on the severity of postoperative cognitive dysfunction in patients of ophthalmosurgery profile. Dorofeeva G.S. *Reduction of cognitive functions in the postoperative period is gaining importance in the context of the insurance medicine introduction. Operational stress and anaesthetization are factors which increase the risk of deepening and developing postoperative cognitive dysfunction. The function of short-term memory, attention function, and the speed of psychomotor cognitive reactions are the most vulnerable to the action of general anesthetics. The influence of various methods of anesthesia on cognitive functions in ophthalmosurgery patients after end-to-end keratoplasty has been studied in this research work. Dexmedetomidine was used (the selective agonist of α-adrenoreceptors) as one of the components of multimodal anaesthetization. The sedative effect of this drug is explained by inhibition of neural activity in the blue spot of the brain stem. Dexmedetomidine is known to be used for sedation of patients. It allowed possibility to reduce the amount of fentanyl which was necessary for intra-and post-operative anaesthetization. Our research was conducted on the basis of ME "DRCOH". 78 patients at the age of 18 to 60 years were examined after end-to-end keratoplasty. Non-inclusion criteria: presence of concomitant pathology, neurological diseases, use of psychotropic substances and alcohol 6 months before the study. The study was conducted using neuropsychological testing: the Mini Mental State Examination (MMSE), the Frontal Assessment Battery (FAB), and Luria's test. Testing was performed before the operation, in 6, 24 hours, 7 and 21 days. Patients were randomized into two groups. The first group – group k (n_1=45) included patients who were provided with anaesthetic management according to the following scheme: premedication — ondansetron 4 mg, dexamethasone 4 mg, ketorolac 30 mg intravenously, sibazone 10 mg, fentanyl 0.1 mg intramuscularly 40 minutes before intervention. Induction of propofol – 2-2.5 mg/kg fractionally to achieve clinical symptoms of anaesthetization, fentanyl – 0.005% 0.1 mg tracheal intubation after relaxation on the background of atracuriumbenzylate – 0.3-0.6 mg/kg. Maintaining of anaesthetization: oxygen-sevoflurane mixture $FiO_2$50-55%, sevoflurane 1,4-1,8 vol.% on exhalation (1-1.5 MAC) with the flow of not more than 1 l/min. BIS indicators were kept at the level of 30-40, during the surgery, the bolus injection of 0.1 mg of fentanyl was used in the event of hemodynamic reactions. Anaesthetic support was performed using the infusion of dexmedetomidin for 40 minutes, ondansetron 4 mg, dexamethasone 4 mg, ketorolac 30 mg intravenously in the second group d (n_2=33). Induction, relaxation and maintenance of anaesthetization were performed as in the previous group. Intra-operative monitoring of patients in both groups included: non-invasive measurement of blood pressure (BP), heart rate (HR), pulse oximetry, determination of blood gases (oxygen, carbon dioxide and inhaled anesthetic on inhalation and exhalation). Control of the depth of anaesthetization was performed on the basis of BIS and ANI - monitoring. The use of dexmedetomidinu as the component of a multi-modal method of anaesthetizational allowed obtaining less pronounced POCD, due to the reduction in the number of used drugs. Further use of the combination of highly selective agonists of α2-adrenoreceptors with regional anaesthetization in ophthalmic surgery is the promising method.*

Реферат. Влияние выбранного метода обезболивания на выраженность послеоперационной когнитивной дисфункции у пациентов офтальмохирургического профиля. Дорофеева А.С. *Снижение когнитивных функций в послеоперационном периоде приобретает значение в контексте внедрения страховой медицины. А операционный стресс и анестезия являются факторами, которые повышают риск углубления и развития послеоперационных когнитивных дисфункций. Наиболее уязвимой к действиям общих анестетиков является функция краткосрочной памяти, функция внимания, скорость психомоторных когнитивных реакций. В данной работе проведено исследование влияния различных методов анестезии на когнитивные функции у офтальмохирургических пациентов после сквозной кератопластики. Наше особое внимание привлекло использование методики мультимодального обезболивания с сочетанием блокады крыло-небной ямки. Как один из компонентов мультимодального обезболивания нами был использован дексмедетомидин (селективный агонист α-адренорецепторов). Седативное действие этого препарата объясняется ингибированием нейронной активности в голубом пятне ствола головного мозга. Также известно, что применение дексмедетомидина для седации пациентов позволило снизить количество использованного фентанила, необходимого для интра- и послеоперационного обезболивания. Наше исследование проводилось на базе КП «ДОКОЛ». Было обследовано 78 пациентов после операции по сквозной кератопластики возрастом от 18 до 60 лет. Критерии исключения из исследования: наличие сопутствующей патологии, неврологических заболеваний, употребление психотропных веществ и алкоголя менее чем за 6 месяцев до проведения исследования. Исследование проводилось с помощью нейропсихологического тестирования: шкала оценки психического статуса (MMSE), шкала лобной дисфункции (FAB). Тестирование проводилось накануне операции, через 6 часов, 24 часа, 7 дней и 21 день. Пациенты были рандомизированы на две группы. В первую группу – группа k (n_1=45) вошли пациенты, которым анестезиологическое обеспечение было выполнено по следующей схеме: премедикация – ондансетрон 4 мг, дексаметазон 4 мг, кеторолак 30 мг, сибазон 10 мг, фентанил 0,1 мг внутримышечно за 40 минут до вмешательства, индукция – пропофол 2-2,5 мг/кг фракционно до достижения клинических симптомов наркоза, фентанил 0,005% 0,1 мг интубация трахеи после релаксации на фоне атракурия безилата 0,3-0,6 мг/кг поддержка анестезии: кислородно – севофлурановая смесь $FiO_2$50-55%, севофлуран 1,4-1,8 об.% на выдохе (1-1,5 МАС) при потоке не более 1 л/мин. Показатели BIS удерживались на уровне 30-40, в течение оперативного вмешательства использовалось болюсное введение фентанила по 0,1 мг в/в при появлении гемодинамических реакций. Во второй группе – группа d (n_2=33) анестезиологическое обеспечение было выполнено с использованием инфузии дексмедетомидина за 40 мин., ондансетрон 4 мг, дексаметазон 4 мг, кеторолак 30 мг. Индукция, выполнение релаксации и поддержка анестезии выполнялись как в предыдущей группе. Интраоперационный мониторинг пациентов в обеих группах включал: неинвазивное измерение артериального давления (АД), частоты сердечных сокращений (ЧСС), пульсоксиметрию, определение газов крови: кислорода, углекислого газа и ингаляционного анестетика на вдохе и выдохе. Контроль глубины наркоза проводился на основании BIS- ANI-мониторирования. Использование дексмедетомидина, как компонента мультимодального метода обезболивания, позволяет получить менее выраженные ПОКД за счет снижения количества использованных наркотических средств. Дальнейшее использование комбинации высоко селективных агонистов α2-адренорецепторов в офтальмохирургии является перспективным методом.*

The study of cognitive dysfunction in the postoperative period in ophthalmosurgical patients is an important but little-studied topic [5]. This category of patients from the beginning has a decrease in cognitive function due to partial or complete loss of vision. Decreased cognitive functions in the postoperative period is gaining importance in the context of the introduction of insurance medicine [1]. Surgical stress and anesthesia are factors that increase the risk of deepening and development of postoperative cognitive dysfunction [2, 9]. The most vulnerable to the action of general anesthetics are the function of short-term memory, attention function, the speed of psychomotor cognitive reactions. According to L. Pengetal (2013), the level of intraoperative sedation is associated with the frequency of postoperative cognitive dysfunctions (POCD) [6, 10]. At the same time, there are conflicting data on the action of drugs used for this purpose, such as sevoflurane: according to X. Chenetal. (2001), it causes short-term depression with complete recovery within 6 hours, other authors, on the contrary, believe that this drug has no effect (G. Kadoi, F. Goto, 2007) and causes a neuroprotective effect (V.V. Likhvantseva, 2005, M.I. Neymark et al., 2007). Circadian dysregulation that occurs after surgery, especially in elderly patients, which causes sleep disorders and associated decreases in melatonin secretion contributes to the development of POCD as well [12]. Intraoperative infusion of dexmedetomidine significantly reduces the need for opioids, nausea, vomiting and itching compared with placebo within 48 hours after panhysterectomy (PHE) (Gurbetetal., 2006 Level II) [7, 11]. The combination of dexmedetomidine with morphine resulted in significantly better analgesia, reduced nausea, and a significant opioid-preserving effect (Linetal., 2009 Level II).

The aim of our work was to study the effect of various methods of anesthesia, in particular the technique of multimodal anesthesia, on the cognitive functions in ophthalmosurgical patients after end-to-end keratoplasty.

MATERIALS AND METHODS OF RESEARCH

The study was conducted on the basis of ME "DRCOH". 78 patients were examined after end-to-end keratoplasty surgery aged 18 to 60 years (mean age 52.1±2.0 years). Exclusion criteria: presence of concomitant pathology, neurological diseases, use of psychotropic substances and alcohol less than 6 months before the study.

The study was conducted using neuropsychological testing: mental status assessment scale (MMSE), frontal assessment battery scale (FAB) [6]. Testing was performed before surgery (stage 1) and 6 hours (stage 2), 24 hours (stage 3), 7 days (stage 4) and 21 days (stage 5) after surgery.

Patients were randomized into two groups. The first group – group k (n_1=45) included patients who underwent anesthesia according to the following scheme:

- premedication – ondansetron 4 mg, dexamethasone 4 mg, ketorolac 30 mg intravenously, sibazone 10 mg, fentanyl 0.1 mg intramuscularly 40 minutes before the procedure;
- induction – propofol 2-2.5 mg/kg fractionally until clinical symptoms of anesthesia, fentanyl 0.005% 0.1 mg;
- intubation of the trachea after relaxation on the background of atracurium besylate 0.3-0.6 mg/kg;
- maintenance of anesthesia: oxygen-sevoflurane mixture FiO250-55%, sevoflurane 1.4-1.8 vol.% on exhalation (1-1.5 MAC) at a flow of not more than 1 l/min.

BIS values were kept at the level of 30-40, during surgery a bolus injection of fentanyl 0.1 mg iv was used in case of hemodynamic reactions. In the second group - group d (n_2=33) anesthesia was performed using an infusion of dexmedetomidine for 40 minutes, ondansetron 4 mg, dexamethasone 4 mg, ketorolac 30 mg intravenously. Induction, relaxation and maintenance of anesthesia were performed as in the previous group.

Both clinical groups were statistically comparable (p>0.05) by age and gender characteristics. In the control group (k) there were 26 (57.8%) men and 19 (42.2%) women, mean age – 49.5±2.5 years; in group d – 17 (51.5%) men and 16 (48.5%) women (p=0.583 by criterion χ^2), mean age – 55.5±3.2 years (p=0.142 per t-criterion).

Intraoperative monitoring of patients in both groups included: non-invasive measurement of blood pressure (BP), heart rate (HR), pulse oximetry, determination of blood gases: oxygen, carbon dioxide and inhalation anesthetic on inhalation and exhalation.

The control of anesthesia depth and level of analgesia was performed on the basis of BIS and ANI-monitoring [8].

Statistical processing of the study results was performed using the license package Statistica v.6.1 (StatsoftInc., USA) (N AGAR909E415822FA). The analysis of quantitative data was performed taking into account the distribution law, estimated according to the criteria of Liliefors and Shapiro-Wilk. In the cases of normal law, the arithmetic mean (M), its standard error (m), Student's criterion for independent samples (t) were used, in other cases the median (Me), interquartile range (25%; 75%), Mann's criteria were used, Whitney (U) and Wilcoxon (W). The probability of differences in relative indicators was estimated by the Pearson Chi-square criterion (χ^2). To assess the relationship between the various factors, a correlation analysis was performed by calculating Spearman's correlation coefficients (r). The value of p<0.05 (5%) was considered statistically significant [3].

RESULTS AND DISCUSSION

Analysis of indicators characterizing the depth of anesthetic sleep (BIS index) and the level of analgesia and nociception (ANI index) showed their similarity (p>0.05) in both study groups during surgery (Table 1). At the same time, taking into account the ability of dexmedetomidine to potentiate the action of narcotic analgesics, in group d the average amount of analgesic used (fentanyl) was 1.4 times less – 3.82±0.24 ml against 5.26±0.26 ml (p<0.001).

The indicators of ANI-and BIS-monitoring were within the optimal values in patients of both groups. Hemodynamic values and parameters of blood gases also did not differ significantly in the groups. The state of cognitive functions was assessed using neuropsychological testing on scale FAB and short scale of mental status assessment (MMSE) before surgery and at certain intervals after surgery (6 hours, 24 hours, 7 and 21 days) . The dynamics of cognitive function depending on the stage of the study in clinical groups are presented in Table 2.

The data in Table 2 show that the indicators of neuropsychological testing on both scales (MMSE and FAB) showed a more pronounced decrease in

the postoperative period using the "standard" method of analgesia (group k). Thus, in the first hours of the postoperative period in group k the median score of mental status on the MMSE scale decreased by 7 points, or 29.2% (p<0.001), on the FAB scale – by 6 points, or 42, 9% (p<0.001) from baseline. The next day after the intervention there was a partial recovery of cognitive impairment – the difference in score with baseline was already 4 points on the MMSE and FAB scales (p<0.001) with complete recovery of functions (p>0.05) only up to 21 day of the survey.

Table 1

Comparison of the average number of used narcotic analgesics, BIS and ANI indicators during surgery in groups k and d (M±m)

Group	Number of used narcotic analgesics, ml	ANI indicator, relative units	BIS indicator, relative units
k (n_1= 45)	5.26±0.26 *	60.6±6.8	36.4±1.9
d (n_2= 33)	3.82±0.24 *	58.0±4.7	36.2±1.7

Note. * – p<0.001 between groups, in other cases p>0.05 (t-test).

In group d, the decrease in cognitive functions in the early postoperative period was less pronounced – the median indicator on the MMSE scale decreased by 3 points, or 12.0% (p<0.001), on the FAB scale – by 2 points, or 12.5% (p<0.001) from baseline. Restoration of the state of cognitive functions to the initial level in this group occurred the next day after surgery (p>0.05 compared to baseline). In the subsequent observation periods (in 7 and 21 days) there was a further improvement in cognitive function compared with the data on the eve of surgery (Table 2). This phenomenon can be explained both by the properties of dexmedetomidine and by the improvement of vision due to the performed surgical intervention.

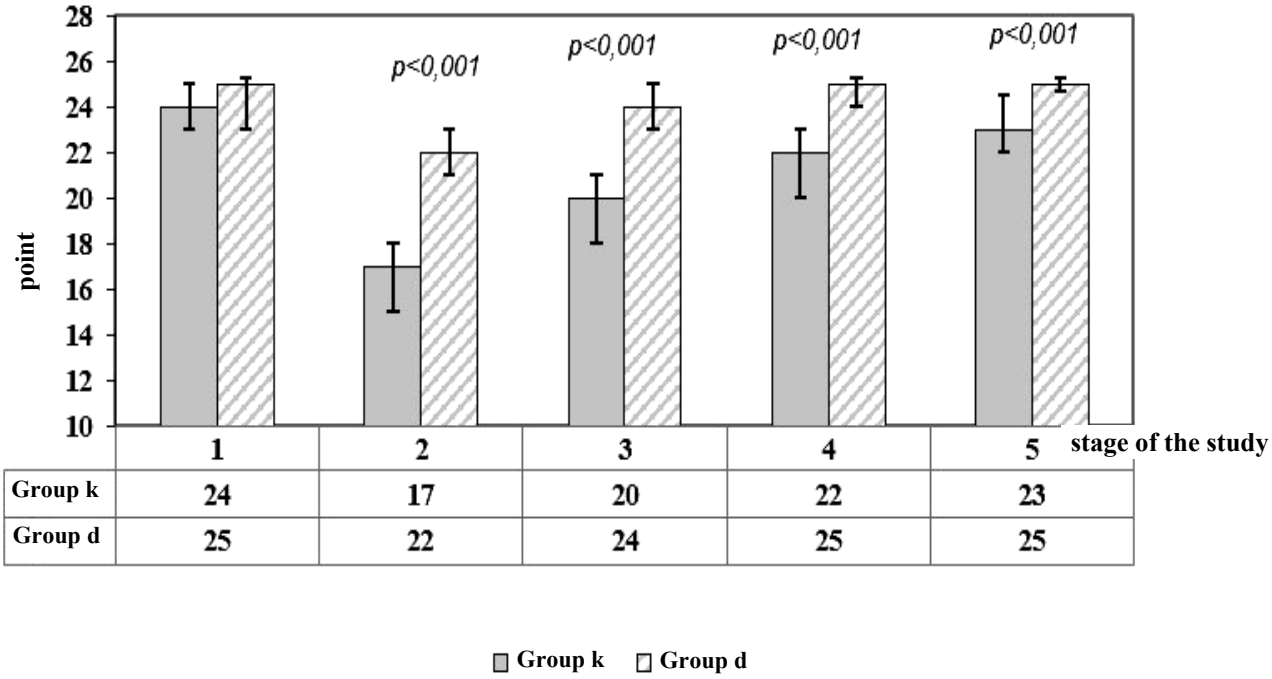
Table 2

Dynamics of cognitive functions depending on the stage of the study in groups k and d

Етап/ метод	MMSE, points, Me(25%;75%)		FAB, points, Me(25%;75%)	
	group k	group d	group k	group d
On the eve	24 (23; 25)	25 (23; 25)	14 (13; 15)	16 (15; 16)
In 6 hours	17 (15; 18) **; ''	22 (21; 23) **; ''	8 (7; 10) **; ''	14 (13; 14) **; ''
In 1 day	20 (18; 21) **; ''	24 (23; 25) ''	10 (9; 12) **; ''	16 (15; 17) ''
In 7 days	22 (20; 23) **; ''	25 (24; 25) *;''	13 (11; 14) **; ''	16 (16; 17) *; '
In 21 days	23 (22; 25) ''	25 (25; 25) *	14 (13; 16) ''	17 (16; 18) **; '

Notes: probable differences as compared to the initial level: * – p<0.05; ** – p<0.001; probable differences as compared to the previous stage: ' – p<0.05; '' – p<0.001 (according to W-test Wilcoxon).

Figure 1 clearly shows that when dexmedetomidine is used as a component of multimodal analgesia, there is a short-term and less pronounced decrease in cognitive function than when using "standard" anesthesia.



	1	2	3	4	5
Group k	24	17	20	22	23
Group d	25	22	24	25	25

The average score of cognitive functions by the MMSE method in groups k and d at different stages of the study: given Me (25%; 75%); stages of the study: 1 – on the eve of the surgery, 2 – in 6 hours, 3 – in 24 hours, 4 – in 7 days, 5 – in 21 days after surgery; p is the level of statistical significance of the difference between the groups

Thus, based on the assessment of cognitive functions on the scale FAB and the short scale of mental status, MMSE, it can be argued that the percentage of reduction and rate of recovery of cognitive function in ophthalmic patients depended on the chosen method of analgesia. In cases where the number of narcotic analgesics (fentanyl) was less, then the decrease in cognitive function was less. This is confirmed by the inverse correlations between the amount of analgesic used and the score of cognitive functions at different stages of the study: on the MMSE scale – $r= -0.28$, $p<0.05$ in 1 day, $r= -0.23$, $p<0.05$ in 7 days after the intervention; on the FAB scale – $r= -0.40$, $p<0.001$, $r= -0.38$, $p<0.001$, $r= -0.33$, $p<0.01$, $r= -0.34$, $p<0.01$ in 6 hours, 1, 7 and 21 days after the intervention, respectively.

Thus, cognitive functions underwent minor changes with multimodal analgesia using dexmedetomidine. The recovery of the central nervous system was faster (on average in 1 day after surgery), and in some patients (30.3% on the MMSE scale and 66.7% on the FAB scale) we observed an increase in indicators.

CONCLUSIONS

1. The use of dexmedetomidine, as a component of a multimodal method of analgesia allows to obtain less pronounced POCD by reducing the number of drugs used by 1.4 times.
2. Dexmedetomidine, due to its ability to potentiate the action of narcotic analgesics (fentanyl), makes it possible to maintain the quality of anesthesia with less number of used narcotic analgesic. Indicators for assessing the depth of anesthesia and the level of analgesia (using BIS- and ANI- monitoring) remained within normal limits.
3. Further use of highly selective α2-adrenoceptor agonists in ophthalmic surgery is a promising method. This is clinically appropriate.

Conflict of interest. The author declares no conflict of interest.

REFERENCES

1. Akimenko TI, Zhenilo VM, Zdiruk SV, Alexandrovich YuS. [Reducing the incidence of postoperative cognitive impairment after uterine amputation with inhalation anesthesia with sevoflurane]. Almanac of Clinical Medicine. 2018;46(7):699-707. Russian. doi: https://doi.org/10.18786/2072-0505-2018-46-7-699-707

2. Aleksandrovich YuS, Akimenko TI, Pshenisnov KV. [Postoperative cognitive dysfunction – is it a problem for an anesthesiologist-resuscitator?]. Bulletin of anesthesiology and resuscitation. 2019; 16(4):5-11. Russian.
doi: https://doi.org/10.21292/2078-5658-2019-16-4-5-11

3. Antonomonov MYu. [Mathematical processing and analysis of biomedical data]. Kyiv; 2017:578. Russian.

4. Avezov AM, Panteleeva MV, Knyazev AV, et al. [Cognitive dysfunction and general anesthesia: from pathogenesis to prevention and correction]. Neurology, psychiatry, psychosomatics. 2016;3:101-5. Russian.

5. Kolesnikov VG. [The results of the assessment of cognitive impairments in the early period of surgery in cardiac patients with arterial hypertension, operated in the minds of a piece blood circulation]. Medicine of emergency conditions. 2020;16(2). Russian. doi: https://doi.org/10.22141/2224-0586.16.2.2020.203142

6. Krishtafor AA, Yovenko IA, Chernenko VG, Klimenko KA, Krishtafor DA. [Features of cognitive impairment in wounds received in combat conditions]. Emergencymedicine. 2018;2(81).
doi: http://dx.doi.org/10.22141/2224-0586.2.81.2017.99701

7. Melanie Varin, Marie-Jeanne Keroat, Sylvie Belleville, et al. Age-Related Eye Desease and Cognitive Function. Ophtalmology; 2019 okt. 09.

8. Ayvardgi AA, Kobeliatskyy YuYu. ANI-monitoring in assessing the effectiveness of the anesthetic management for plastic surgery of the nose.Emergency medicine. 2018;1(88):103-7.
doi: https://doi.org/10.22141/2224-0586.1.88.2018.124975

9. Srivastava VK, Agrawal S, Kumar S, et.al. Comparison of Dexmedetomidine,propofol and midazolam for short-term sedation in postoperatively mechanically ventilated neurosurgical patients. J Clin. Diagn. Res. 2014;8(9):GC04-7.
doi: https://doi.org/10.7860/JCDR/2014/8797.4817

10. Emery N, Kara J Pavone, Marusa Naranjo, Multimodal General Anesthesia: Theory and Practice. Anesth Analg. 2018 Nov;127(5):1246-58.
doi: https://doi.org/10.1213/ANE.0000000000003668

11. Nalini Kotekar, Anshul Shenkar, Ravishankar Nagaraj, Postoperative cognitive dysfunction – current preventive strategies. Clin Interv Aging. 2018;13:2267-73. doi: https://doi.org/10.2147/CIA.S133896

12. Neda Mansouri, Kobra Nasrollahi, Hamidreza Shetabi. Prevention of Cognitive Dysfunction after Cataract Surgery with Intravenous Administration of Midazolam and Dexmedetomidine in Elderly Patients Undergoing Cataract Surgery Adv Biomed Res. 2019;8:6. doi: https://doi.org/10.4103/abr.abr_190_18

13. Chen C, You M, Li Z, Nie L, Zhao Y, Chen G. Study of Feasibility and Safety of Higher-Dose Dexmedetomidine in Special Outpatient Examination of Pediatric Ophthalmology. J. Ophthalmol. 2019 Apr 8;2560453. doi: https://doi.org/10.1155/2019/2560453

СПИСОК ЛІТЕРАТУРИ

1. Акименко Т. И., Женило В. М., Здирук С. В., Александрович Ю. С. Снижение частоты послеоперационных когнитивных нарушений после ампутации матки при ингаляционной анестезии севофлураном. *Альманах клин. медицины*. 2018. Т. 46, № 7. С. 699-707. DOI: https://doi.org/10.18786/2072-0505-2018-46-7-699-707

2. Александрович Ю. С., Акименко Т. И., Пшениснов К. В. Послеоперационная когнитивная дисфункция – является ли она проблемой для анестезиолога-реаниматолога? *Вест. анестезиологии и реаниматологии.* 2019. Т. 16. № 4. С. 5-11. DOI: https://doi.org/10.21292/2078-5658-2019-16-4-5-11

3. Антомонов М. Ю. Математическая обработка и анализ медико-биологических данных. Киев. 2017. 578 с.

4. Когнитивная дисфункция и общая анестезия: от патогенеза к профилактике и коррекции / А. М. Авезов и др. *Неврология, психиатрия, психосоматика.* 2016. № 3. С. 101-105.

5. Колесников В. Г. Результати оцінки когнітивних порушень у ранній післяопераційний період у кардіохірургічних пацієнтів з артеріальною гіпертензією, оперованих в умовах штучного кровообігу. *Медицина неотложных состояний*. 2020. Т. 16, № 2. DOI: https://doi.org/10.22141/2224-0586.16.2.2020.203142

6. Особенности когнитивных нарушений при ранениях, полученных в условиях боевых действий / А. А. Криштафор и др. *Медицина неотложных состояний.* 2018. Т. 81, № 2.
DOI: http://dx.doi.org/10.22141/2224-0586.2.81.2017.99701

7. Age-Related Eye Desease and Cognitive Function / Melanie Varin et al. *Ophtalmology*. 2019. 09.

8. Ayvardgi A. A, Kobeliatskyi Yu. Yu. ANI-monitoring in assessing the effectiveness of the anesthetic management for plastic surgery of the nose. *Emergency medicine.* 2018. Vol. 88, No. 1. P. 103-107. DOI: https://doi.org/10.22141/2224-0586.1.88.2018.124975

9. Comparison of Dexmedetomidine,propofol and midazolam for short-term sedation in postoperatively mechanically ventilated neurosurgical patients / V. K. Srivastava et al. *J Clin. Diagn. Res*. 2014. Vol. 9, No. 8. P. GC04-7.
DOI: https://doi.org/10.7860/JCDR/2014/8797.4817

10. Emery N. Brown, Kara J. Pavone, Marusa Naranjo, Multimodal General Anesthesia: Theory and Practice. *Anesth Analg*. 2018. Vol. 127, No. 5. P. 1246-1258. DOI: https://doi.org/10.1213/ANE.0000000000003668

11. NaliniKotekar, Anshul Shenkar, Ravishankar Nagaraj, Postoperative cognitive dysfunction – current preventive strategies. *Clin. Interv Aging*. 2018. Vol. 13. P. 2267-2273. DOI: https://doi.org/10.2147/CIA.S133896

12. Neda Mansouri, Kobra Nasrollahi, Hamidreza Shetabi Prevention of Cognitive Dysfunction after Cataract Surgery with Intravenous Administration of Midazolam and Dexmedetomidine in Elderly Patients Undergoing Cataract

Surgery Adv Biomed Res. 2019. Vol. 8, No. 6. DOI: https://doi.org/10.4103/abr.abr_190_18

13. Study of Feasibility and Safety of Higher-Dose Dexmedetomidine in Special Outpatient Examination of Pediatric Ophthalmology / C. Chen et al. *J. Ophthalmol*. 2019. 8. Apr. Vol. 2019. P. 2560453. DOI: https://doi.org/10.1155/2019/2560453

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