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Comparative analysis of the impact of selected anesthesia methods on the cognitive function of patients undergoing ophthalmic surgery

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Background: *Anesthesiologists should not only save patient's life as a process, but also enable the patient to recover his/her social life after surgery, given increased longevity, high social activity throughout life, and increased use of technical equipment in everyday life.*

Purpose: *To assess central nervous system (CNS) changes in patients undergoing penetrating keratoplasty in order to optimize the choice of anesthesia technique, while taking into account the impact of general anesthesia on postoperative cognitive functions.*

Material and Methods: *We employed neuropsychological tests such as Mini-Mental State Examination (MMSE), Frontal Assessment Battery (FAB) and Luria's test to examine the cognitive function of patients before surgery and 6 hours, 24 hours, 7 days and 21 days after surgery.*

Results: *On the basis of comparative analysis of the impact of selected anesthesia methods on cognitive function of patients undergoing surgery (penetrating keratoplasty), we concluded that a combination of regional anesthesia (pterygopalatine fossa blockade), dexmedetomidine infusion (0.3 µg/kg) and general analgesia (maintenance in an oxygen/sevoflurane mixture) with exclusion of Sibazon 0.5% had the shortest and the least profound impact on the cognitive function.*

Conclusion: *On the basis of comparative analysis of the impact of selected anesthesia methods on cognitive function of patients undergoing penetrating keratoplasty, we concluded that a combination of regional anesthesia (pterygopalatine fossa blockade), dexmedetomidine infusion (0.3 µg/kg) and general analgesia (maintenance in an oxygen/sevoflurane mixture) with removal of Sibazon 0.5% from premedication and presence of a reduced amount of fentanyl used during anesthesia had the shortest (with a mean duration of a day) and the least profound impact on cognitive state in patients undergoing ophthalmic surgery.*

Keywords:

postoperative cognitive dysfunction, dexmedetomidine, MMSE scale, FAB scale, Luria test, pterygopalatine fossa blockade

Introduction

In the world today, one person in ten is aged 60 years or over. In this country, in 2010, one person in five was of that age group. Projections suggest that in 2050, people aged 60 years or over will account for 35% of the population in Europe.[1, 2] Because of an increase in the retirement age, anesthesiologists should not only save patient's life as a process, but also enable the patient to recover his/her social life after surgery. Loss of cognitive function results in increased difficulty performing tasks involving thinking, learning, rapid information processing and decision making, deterioration in other psychophysiological functions and the ability to perform activities of daily living, with gradual social disadaptation and deterioration in the ability to perform professional activities. This can be explained by the fact that intelligence itself is characterized by a set of cognitive functions, such as reasoning, perception, memory, problem solving, language use, and so on. Cognitive decline can lead to social disability.[3, 4] A combination of abilities (abilities to think and memorize, praxis, gnosis and intelligence) is vitally important given increased longevity, high social activity throughout life, and increased use of technical equipment in everyday life.[3] The anesthesiologist can impact the choice of anesthesia strategy, control of sedation depth, and prevention of inadequate analgesia during and after surgery. It is important to identify cognitive loss as early as possible, because early postoperative cognitive dysfunction (POCD) is a predictor of persistent POCD, with the latter increasing the risk of Alzheimer's disease.[1, 5, 6]

Prophylaxis of postoperative delirium aims to prevent the correctable risk factors of POCD.

The purpose of the study was to assess central nervous system (CNS) changes in patients undergoing penetrating keratoplasty in order to optimize the choice of anesthesia technique, while taking into account the impact of general anesthesia on postoperative cognitive functions.

Material and Methods

This study was conducted at the Dnipropetrovsk Regional Clinical Eye Hospital. Ninety-one patients of 18 to 60 years (mean age plus or minus standard deviation, 52.1 ± 2.0 years) underwent an examination before and after penetrating keratoplasty. Patients with the presence of ocular or systemic comorbidity, neurologic disease, or recent (< 6 month) history of use of psychotropics or alcohol were excluded from the study.

Mini-Mental State Examination (MMSE) and Frontal Assessment Battery (FAB) were utilized before surgery (time point 1) and 6 hours (time point 2), 24 hours (time point 3), 7 days (time point 4) and 21 days (time point 5) after surgery. Patients were randomly allocated to one of three anesthesia groups.

Group 1 (group b, n1 = 28) received multicomponent balanced anesthesia with addition of pterygopalatine fossa blockade as a component of multimodal analgesia. Lidocaine 2% (2 ml) and naropin 5 mg/ml (2.0 ml) were used for regional anesthesia. Premedication consisted of intravenous ondansetron (4 mg), dexamethasone (4 mg), and ketorolac (30 mg), and intramuscular Sibazon (10 mg) and fentanyl (0.1 mg), which were given approximately 40 minutes before the intervention. Induction was performed with propofol (2-2.5 mg/kg) given in fractions until clinical signs of narcosis were observed and fentanyl 0.005% (0.1 mg). The trachea was intubated after relaxation with atracurium besilate (0.3-0.6 mg/kg). Anesthesia was maintained with sevoflurane (1.4–1.8% end-tidal concentration, 1.0–1.5 minimal alveolar concentration (MAC)) in an oxygen/sevoflurane mixture (FiO2 50–55 %) at a flow ≤ 1 l/min. Bispectral Index (BIS) values were maintained between 40 and 50.

Perioperatively, boluses of intravenous fentanyl (0.1 mg) were administered if hemodynamic responses were observed.

In group 2 (group d, n2 = 32) premedication consisted of dexmedetomidine infusion (0.3 μg/kg), and intravenous ondansetron (4 mg), dexamethasone (4 mg), and and ketorolac (30 mg) given 40 minutes before the intervention. Anesthesia induction, relaxation and anesthesia maintenance strategies were similar to those used in group 1.

Patients in group 3 (group db, n4 = 31) received regional anesthesia (pterygopalatine fossa blockade) and dexmedetomidine infusion (0.3 μg/kg) before surgery.

All three groups were statistically comparable (p > 0.05) in terms of age and sex. Group b consisted of 16 (57.1%) men and 12 (42.9 %) women (mean age plus or minus standard deviation, 55.8 ± 3.4 years). Group d consisted of 17 (51.5%) men and 16 (48.5 %) women (p = 0.583, as assessed by chi-square test) with a mean age plus or minus standard deviation of 55.8 ± 3.4 years (p = 0.142, as assessed by t-test). Group db consisted of 18 (58.1%) men and 13 (41.9%) women (p = 0.583, as assessed by chi-square test) with a mean age plus or minus standard deviation of 54.9 ± 3.1 years (p = 0.142, as assessed by t-test).

Perioperative monitoring included non-invasive measurement of blood pressure, heart rate, oxygen saturation, and inspired and end-tidal concentrations of oxygen, carbon dioxide, and inhalation anesthetic agent in blood. Depth of sedation was controlled by Analgesia Nociception Index (ANI) monitoring, and depth of anesthesia was controlled by BIS monitoring. We aimed for an ANI level of 50 to 70 and a BIS level of 40 to 60.[7]

Statistical analysis was performed using Statistica v.6.1 software (StatSoft Inc, Tulsa, OK; license number, AGAR909E415822FA). Quantitative data was assessed for normality by using the Shapiro-Wilk test and Lilliefors test. Normally distributed data are expressed as mean plus or minus standard deviation (SD) and analyzed by the Student's t-test for independent samples. Non-normally distributed data are expressed as median (interquartile range) and analyzed by Wilcoxon signed rank test or Mann-Whitney U-test, as appropriate. Pearson chi-square test (χ 2) was used to assess statistical significance of differences in age and sex. Spearman correlation coefficients were calculated to assess associations between variables. The level of significance p ≤ 0.05 was assumed.[8]

Results

Analysis of perioperative analgosedation showed that mean ANI and BIS scores were statistically comparable among the three groups and score values were within the target ranges during surgery (Table 1).

Of note that the amount of narcotic analgetic required was larger in the group with the use of dexmedetomidine than in other groups. The amount of narcotic analgetic required was 15.9% smaller in the db group and 4.5% smaller in the b group compared to the d group. Therefore, the amount of narcotic analgetic required was smaller in the db group than in the two other groups, with sedation and analgesia levels maintained and no substantial difference (p < 0.001) in these levels among the groups.

Table 2 compares groups in terms of glycemic levels (presented as median (25%, 75%)) before surgery, in the early perioperative period, during the most traumatic phase of surgery, and in the late perioperative period. Glycemic levels in groups varied during surgery, with median (25%, 75%) values for groups b, d and db being 5.68 (5.01; 6.14), 5.7 (5.16; 6.2), and 5.58 (5.25; 6.08), respectively (p < 0.05). No significant difference (p > 0.05) was observed between groups in terms of glycemic levels in the early perioperative period and during the perioperative period. Median glycemic levels of db, d and b groups increased insubstantially during surgery, by 0.5 mmol/l, 0.9 mmol/l and 0.4 mmol/l, respectively. Therefore, glycemic level as a marker of perioperative stress in patients changed

Table 1. Amounts of narcotic analgetic useed and Analgesia Nociception Index (ANI) and Bispectral Index (BIS) values (expressed as mean value plus or minus standard deviation) during surgery

Group	Amount of narcotic analgetic required (ml)	ANI (conventional units)	BIS (conventional units)
b (n_1= 28)	4 ± 0.21*	59.5 ± 3.0	30.0 ± 1.3
d (n2= 32)	4.52 ± 2.18	56.2 ± 3.2	33.3 ± 1.6
db (n_3= 31)	3.82 ± 0.24*	58.0 ± 4.7	36.2 ± 1.7

Note: *, significant difference between groups (p < 0.01) as evaluated by Student t-test for independent samples

Table 2. Glycemic levels (presented as median (25%, 75%) mmol/l) before surgery, in the early perioperative period, during the most traumatic phase of surgery, and in the late perioperative period

Group	Time points			
	Before surgery	Early perioperative period	The most traumatic phase of surgery	Late perioperative period
	Glycemic levels (presented as median (25%, 75%) mmol/l)			
b (n_2= 28)	5.4(4.9;5.9)	5.7(5.1;6.3)	5.8(5.25;6.25)	5.8(4.8;6.1)
d (n_3= 32)	5.2(4.8;5.8)	5.5(4.95;6.1)	6.0(5.5;6.4)	6.1(5.4;6.5)
db(n_4= 31)	5.3(4.9;5.7)	5.5(5.2;5.9)	5.7(5.5;6.3)	5.8(5.4;6.4)

Note: For all comparisons between groups, P-value was above 0.05 as assessed by chi-square test, Student t-test and Mann-Whitney test for independent samples

with time during surgery, with the least changes observed in the group with the regional anesthesia combined with preoperative dexmedetomidine infusion. Analysis of hemodynamic characteristics of study patients showed that at baseline, groups were comparable in terms of blood pressure and heart rate (p < 0.001).

Figure 1 shows mean perioperative blood pressure values for the groups. Group d showed the highest mean SBP (103.1 ± 3.6 mmHg), with mean SBP values in groups db and b being 94.1 ± 2.7 mmHg and 96. 5 ± 2.9 mmHg, respectively, which was 9 mmHg and 6.6 mmHg, respectively, lower than that in group d. There was no substantial difference in the change in heart rate during surgery between groups.

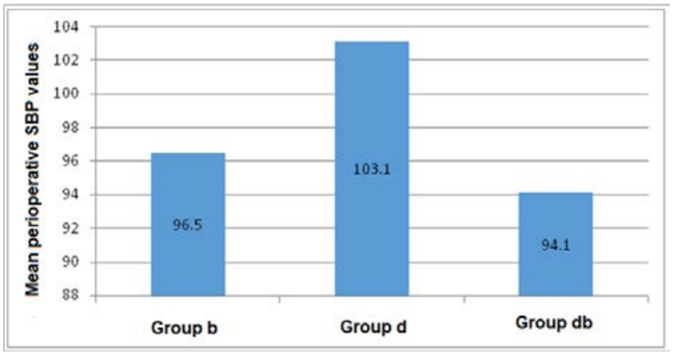

Fig. 1. Mean perioperative systolic blood pressure (SBP) values for groups

The groups exhibited changes in the state of the CNS. At baseline, the groups were comparable with no substantial differences in terms of cognitive functions as assessed by MMSE, FAB and Luria test. The reductions in MMSE scores in the group with the regional anesthesia combined with preoperative dexmedetomidine infusion tended to be less profound and durable than those in the two other groups.

The most substantial changes in the median cognitive function score were observed at 6 hours after surgery, with five-point (20.8 %) reductions for group b and three-point (12 %) reductions for groups d and db. At 21 days after surgery, the cognitive function as assessed by the MMSE, did not change compared to baseline in 35.7% (n = 10), improved in 50 % (n = 14) and did not restore to baseline in 14.3 % (n = 4) of the patients of group b. In addition, in group d, the percentages and numbers of patients showing improvement, deterioration and restoration in the cognitive function compared to baseline as assessed by the MMSE were 12.5 % (n = 4), 9.4 % (n = 3) and 78.1 % (n = 25), respectively. Moreover, in group db, the percentages and numbers of patients showing restoration and improvement in the cognitive function compared to baseline as assessed by the MMSE were 74.2 % (n = 23) and 25.8 % (n = 8), respectively.

In group b, the median FAB score reached the baseline value earlier than 7 days after surgery, and improved compared to baseline in 23/28 (82.1%) patients by day 21. In addition, in group d, the percentages and numbers of patients showing improvement, deterioration and restoration in the cognitive function compared to baseline as assessed by the FAB were 68.7 % (n = 22), 3.2 % (n = 1) and 28.1 % (n = 9), respectively. Moreover, in group db, the percentages and numbers of patients showing

Table 3. Cognitive state (as assessed by median MMSE score (interquartile range) of patients of groups b, d and db, before surgery, and 6 hours, 24 hours, 7 days and 21 days after surgery

Time point	Groups		
	group b	group d	group db
	Median MMSE score (25%;75%)		
Before surgery (baseline)	24 (22; 24)	25 (24; 25)	25 (23; 25)
6 hours	19 ** (17; 20)	22 (22; 23)	22 (21; 23)
24 hours	22 * (20; 23)	24 (23; 25)	24 (23; 25)
7 days	24 (22; 25)	25 (24; 25)	25 (24; 25)
21 days	25 (24; 25)	25 (24; 25)	25 (25; 25)

Note: Significant difference compared to baseline as assessed by the Wilcoxon signed rank test: *, p < 0.05; **, p < 0.001

Table 4. State of the central nervous system (as assessed by median FAB score (interquartile range) of patients of groups b, d and db, before surgery, and 6 hours, 24 hours, 7 days and 21 days after surgery

Time point	Groups		
	group b	group d	group db
	Median FAB score (25%;75%)		
Before surgery (baseline)	14 (13; 15)*	16 (15; 16)**	16 (15; 16) **
6 hours	10 (9; 12)*	14 (12; 15)**	14 (13; 14) **
24 hours	13 (11; 15)*	16 (15; 17)**	16 (15; 17) **
7 days	16 (14; 17)*	17 (16; 18)**	16 (16; 17) **
21 days	16 (15; 17)*	17 (16; 18)**	17 (16; 18) **

Note: *, significant difference (p < 0.05) as assessed by Kolmogorov-Smirnov test; **, significant difference (p < 0.01) as assessed by Kolmogorov-Smirnov test

restoration and improvement in the cognitive function compared to baseline as assessed by the FAB were 32.3 % (n = 10) and 67.7 % (n = 8), respectively.

No change in verbal short-term memory deficit as assessed by the Luria test by day 21 after surgery was found in only two elder patients (7.1 %) in group b (p < 0.05) and three patients (9.4 %) in group d. By day 21, an improvement in verbal short-term memory compared to baseline as assessed by the Luria test was seen in 15/31 (48.4%) patients in group db.

Discussion

To our best knowledge, this is the first study on the comparative assessment of the impact of selected anesthesia methods on the cognitive function of patients undergoing ophthalmic surgery. On the basis of comparative analysis of the impact of aforementioned anesthesia methods on cognitive function of patients undergoing penetrating keratoplasty, we concluded that a combination of regional anesthesia (pterygopalatine fossa blockade), dexmedetomidine infusion (0.3 µg/kg) and general analgesia (maintenance in an oxygen/sevoflurane mixture) with removal of Sibazon 0.5% from premedication and presence of a 1.4-times reduction in the amount of fentanyl used during anesthesia compared to controls (p < 0.05) had the shortest (with a mean duration of a day) and the least profound impact on CNS cognitive state in patients undergoing ophthalmic surgery.

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Disclosures

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Abbreviations: *bp, blood pressure; CNS, central nervous system; DBP, diastolic blood pressure; FAB, Frontal Assessment Battery IOP, intraocular pressure; MAC, minimal alveolar concentration; MMA, multimodal analgesia; MMSE, Mini-Mental State Examination; POCD, postoperative cognitive dysfunction; PPGB, pterygopalatine ganglion blockade; SBP, systolic blood pressure*