INFLUENCE OF ANESTHETIC TECHNIQUES ON OCCURRENCE OF POSTOPERATIVE COGNITIVE DYSFUNCTION IN ELDERLY PATIENTS UNDERGOING GYNECOLOGICAL SURGERY

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Postoperative cognitive dysfunction (POCD) is a disorder that develops in the early postoperative period, persisting for several days or weeks and leading to decrease in higher cortical functions (speech, memory, attention, etc.). POCD is often associated with anesthetic techniques and drugs. This paper studied the effect of general, neuraxial and combined anesthesia on POCD development in elderly women undergoing gynecological surgery. The study featured 43 patients (mean age 65,0 ± 2.2 years). There were 12 women in the general anesthesia group, 23 in the neuraxial anesthesia group, and 8 women in the combined anesthesia group. Intraoperative monitoring included electrocardiography, non-invasive blood pressure measurement, determination of blood oxygen saturation level (rSO_2) and determination of bispectral index (BIS monitoring). A day before surgery and on the 5th day after the surgery, neuropsychological tests were carried out through tracking test, Mini-Mental State Examination and frontal assessment battery. All intraoperative indicators were normal in all the patients. POCD was diagnosed in 3 women who were under general anesthesia, in 7 women under neuraxial anesthesia and 2 under the combined group (25, 30 and 25 % relative to the total number of patients in the groups, respectively). The average rSO_2 value was below the initial level in all groups: below by 6 % in the general anesthesia group, by 15 % in the neuraxial group, and by 10 % in the combined group. However, the differences were statistically insignificant (p >0.05). The study found no relationship between anesthetic techniques and POCD.

Keywords: postoperative cognitive dysfunction, cognitive impairment, general anesthesia, neuraxial anesthesia, combined anesthesia, elderly age

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ВЛИЯНИЕ МЕТОДА АНЕСТЕЗИИ НА ВОЗНИКНОВЕНИЕ ПОСЛЕОПЕРАЦИОННОЙ КОГНИТИВНОЙ ДИСФУНКЦИИ У ПАЦИЕНТОВ ПОЖИЛОГО ВОЗРАСТА ПРИ ОПЕРАЦИЯХ В ГИНЕКОЛОГИИ

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Послеоперационная когнитивная дисфункция (ПОКД) — расстройство, развивающееся в ранний послеоперационный период, сохраняющееся в течение нескольких дней или недель и проявляющееся снижением высших корковых функций (речи, памяти, внимания и др.). Возникновение ПОКД часто связывают с методом анестезиологического обеспечения и препаратами. В работе изучено влияние общей, нейроаксиальной и сочетанной анестезии на развитие ПОКД у женщин пожилого и старческого возраста при операциях в гинекологии. В исследование включили 43 пациентки (средний возраст — 65,0 ± 2,2 года). В группе с общей анестезией было 12 женщин, с нейроаксиальной — 23, с сочетанной — 8. Интраоперационный мониторинг включал снятие электрокардиограммы, неинвазивное измерение артериального давления, определение уровня насыщения крови кислородом (rSO_2), определение биспектрального индекса (BIS-мониторинг). За день до операции и на 5-й день после нее проводили нейропсихологическое тестирование с помощью теста слежения, краткой шкалы оценки психического статуса и батареи оценки лобной функции. Все интраоперационные показатели у всех пациенток были в норме. ПОКД была диагностирована у 3 женщин, находившихся под общей анестезией, у 7 — под нейроаксиальной и у 2 — под сочетанной (25, 30 и 25 % относительно общего числа пациенток в группах соответственно). Среднее значение показателя rSO_2 во всех группах было ниже исходного уровня: при общей анестезии — на 6 %, при нейроаксиальной — на 15 %, при сочетанной — на 10 %, однако различия были статистически незначимыми (p >0,05). Связь между типом анестезии и развитием ПОКД не была выявлена.

Ключевые слова: послеоперационная когнитивная дисфункция, когнитивное расстройство, общая анестезия, нейроаксиальная анестезия, сочетанная анестезия, пожилой возраст

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Postoperative cognitive dysfunction (POCD) is one of the pressing problems faced by modern anesthesiology. It is a disorder that develops in the early postoperative period, persisting for several days or weeks, and rarely for months. POCD is clinically manifested in the form of memory impairment, trouble concentrating, long holding of attention, and other disorders in higher cortical functions (thinking, speech, etc.). A patient with postoperative cognitive dysfunction develops learning problems, lower mental capacity and deteriorating mood (depression occurs) [1]. This can lead to reduced quality of life [2–4]. POCD is not included in the International Statistical Classification of Diseases and Related Health Problems (ICD-10) despite its high prevalence and the strong it attracts from the scientific community. Mild cognitive disorder (F06.7) — a diagnosis close to POCD — is the one included in the ICD.

The exact mechanism by which POCD develops still remains unknown. A number of studies associate the occurrence of this condition with the effect of anesthetics and depth of anesthesia [5–7]. Bianchi et al. [8] found that inhaled anesthetics affect amyloidogenesis in the brain, thereby promoting POCD. Monk et al. [7] suggested that inhalation anesthetics may be neurotoxic and cause brain aging, but that there are no human data evaluating this hypothesis to date. At the same time, the impact of surgical stress [9] and patients' preoperative status [7, 9] on POCD has been pointed out. For example, in patients who have suffered from cerebral infarction, the course of early POCD significantly worsens even in the absence of residual defects. Some researchers also consider POCD as a risk factor for Alzheimer's disease [10], while the etiology of both disorders remains unclear.

POCD and regional oxygen saturation index (rSO_2) have been found to be related: intraoperative decline in rSO_2 is a predictor of the disorder. Li et al. [11] showed this relationship in thoracic surgery in one-lung ventilation, while Papadopoulos et al. [12] did so through surgery for hip fractures in patients older than 75 years. It was advised that cerebral oximeter should be applied not only to identify the risk of POCD but also to determine the tactics for postoperative management [11, 13–16]. Some researchers have also reported on the relationship of cerebral oximetry and specific anesthetic agents [17, 18] with premorbid POCD background [19]. Salazar et al. [20] assumed that postoperative cognitive dysfunction develops with lower rSO_2 in patients undergoing surgery in a certain position. Although they were unable to identify significant association, the authors concluded that surgery protocols, which involve rSO_2 measurement, reduce the risk of POCD. Other researchers have noted a decline in rSO_2 in patients operated upon in a beach chair position [21].

Elderly age is considered an important risk factor for POCD. It is associated with natural decline of cognitive functions and with a variety of diseases, such as hypertension, atherosclerosis, coronary artery disease, thrombosis, stroke, etc. [1, 3, 6, 7, 12–15]. Moreover, the number of surgical procedures in elderly patients is growing as the number of articles published on POCD in elderly age increases [4]. Other risk factors include: organic brain syndrome and mental disorders [1, 3]; extent and duration of sugery, intra- and post-operative complications (hemorrhage, hemodynamic responses, etc.) [3–6]; chronic pain syndrome [8]; classes III-IV of the physical status classification by the American Society of Anesthesiologists]22].

The aim of this study was to evaluate the effects of anesthesia (method, drugs) on the cognitive status of elderly patients undergoing gynecological surgery by comprehensive neuropsychological evaluation.

METHODS

The study conducted in 2015 featured female patients from the Kulakov Research Center for Obstetrics, Gynecology and Perinatology. The inclusion criteria were: 60–80 years of age and gynecological diseases requiring elective surgery. The exclusion criteria were: burdened neurological history and acute cerebrovascular diseases; organic lesions of the central nervous system, epilepsy and history of mental illness; severe concussion, stroke; severe somatic pathology; dementia (24 points or more in the Mini-Mental State Examination questionnaire); burdened alcohol, drug or poison history; expansion of surgical intervention; decompensation extragenital pathology. The study included 43 patients aged 65.0 ± 2.2 years.

Vaginal hysterectomy was carried out on 19 patients, laparoscopic hysterectomy on 8 patients, laparoscopic adnexectomy on 7 patients, laparotomy hysterectomy on 6 patients, laparoscopic cholecystectomy on 2 patients and stoma closure on 1 patient. Three types of anesthesia were used: general anesthesia (12 patients with an average age of 66.0 ± 5.6 years), neuraxial anesthesia (23 patients with an average age of 66.0 ± 4.9 years) and combined anesthesia (8 patients with an average age of 68.0 ± 6.4 years). Doses of preparations were selected individually according to the manufacturer's recommendations, age and sensitivity of the patients, as well as the required anesthetic effect. Then, the average doses of drugs were given for the patient groups (divided by type of anesthesia).

General anesthesia was performed according to the following procedure. Atropine sulfate premedication (Dalkhimpharm, Russia) and Dexamethasone premedication (Krka, Slovenia) were carried out. Propofol (AstraZeneca, UK) 1.3 ± 1.5 mg/kg and rocuronium (Hameln Pharmaceuticals, Germany) 0.9 mg/kg were used for induction. After induction, tracheal intubation was performed. Narcotic and respiratory mixture sevoflurane (Abbott Laboratories, UK) and oxygen with maintenance of minimum alveolar concentration at a 0.8–1.0 level were used to maintain anesthesia.

Spinal-epidural anesthesia was used for neuraxial anesthesia. Puncture of the spinal and epidural space was performed on the level of segments 2–3 of the lumbar vertebrae (L2–L3). Hyperbaric bupivacaine (AstraZeneca) was administered in the spinal space at a dose of 8.95 ± 3.05 mg. Ropivacaine (AstraZeneca) was administered in the epidural at a dose of 68.5 ± 12.0 mg. The punctures were preceded by atropine sulfate premedication and dexamethasone premedication.

Combined anesthesia consisted of general anesthesia and installation of an epidural catheter at the L1–L3 level after standard premedication (atropine sulphate and dexamethasone). Induction, tracheal intubation and general anesthesia were then performed. Ropivacaine (1 mg/kg) was administered in the epidural space.

Intraoperative monitoring was conducted according to the Oxford Standard (ECG, blood pressure, SpO_2) [23] with the Infinity Delta monitor (Draeger, Germany). BIS monitoring (measurement of bispectral index to assess the level of anesthesia and brain sedation) was performed using monitor console Infinity BISx SmartPod (Draeger). The INVOS 5100C monitor (Covidien AG, USA) was used for cerebral oximetry.

The cognitive status of the patients was assessed on a day before and 5th day after the surgery using three neuropsychological tests — Trail Making Test, Mini-Mental State Examination and frontal assessment battery.

Trail Making Test (TMT) [24] allows to evaluate the patient's attention, speed of thinking and coordination. It consists of two parts: In part A, the patient is instructed to connect a set of numbers from 1 to 25, while in part B, the patient is instructed to connect alternating letters and numbers in ascending order. The test is allocated 300 seconds. After that, the time taken by the patient to perform the task is estimated, and the degree of dysfunction is determined based on the scale of results (three degrees).

The Mini-Mental State Examination [25] includes 9 tests evaluating a patient's orientation in space and time, attention, memory and speech. The result is given in points.

Frontal assessment battery [26] consists of 6 tasks that allow to estimate the patient's ability to generalize, attentiveness, ability to concentrate, state of speech processes and motor activity. The results are also given in points.

The average values and standard deviations of test results before and after the operation were calculated for each group of patients and were compared for the purpose of identifying POCD — if after surgery, test result turned out to be by more than 10 % worse than the result prior to surgery, cognitive disorder was diagnosed. The average values and standard deviations of the rSO_2 index before and after surgery were also calculated for each group of patients. Statistical data analysis was performed using Student's t-test ($p < 0.05$).

The study was approved by the Biomedical Research Ethics Committee of the Kulakov Research Center for Obstetrics, Gynecology and Perinatology (Minutes No 1 of 29 January 2015). All the patients gave their written informed consent to participate in the study.

RESULTS

Electrocardiograms obtained in the course of surgery were characteristic of the age norm. Saturation was maintained at 97–99 %. Bispectral index remained normal (45–60 %), thereby allowing to exclude the influence of inadequate or excessive brain sedation on the patients' cognitive functions.

The average value of the rSO_2 index during surgery in all the three groups differed (decreased) from the baseline values as follows: 6 % decrease for general anesthesia, 15 % decrease for neuraxial anesthesia, and 10 % decrease for combined anesthesia. However, the differences were statistically not significant ($p > 0.05$).

Assessment of cognitive status of patients (by Trail Making Test and Frontal Assessment Battery) identified POCD in 12 patients: 3 women for general anesthesia, 7 for neuraxial anesthesia and 2 for combined anesthesia. However, ithe number of patients with POCD in each group turned out to be almost equal 25, 30 and 25 %, respectively. Cognitive deficits in the group of patients with general anesthesia averaged 23.8 and 25 % for the FAB and TMT respectively (see table). The average values of these same indicators in the group of patients with neuraxial anesthesia were equal to 18.6 and 27.9 % respectively, while in the group of patients with combined anesthesia — 25.0 and 23.7 % respectively. Postoperative test results obtained via MMSE differed from preoperative values by less than 10 %. Data were statistically significant only for the FAB and TMT tests ($p < 0.05$). It can be assumed that the MMSE test is less sensitive with respect to postoperative cognitive dysfunction.

DISCUSSION

Some researchers have noted that general anesthesia is related to more significant decline in rSO2 than neuraxial [27–29], while others believe that there are no differences [30, 31]. Indeed, the neuraxial block leads to changes in the central hemodynamics, which can affect the oxygenation level of the cerebral blood flow. However, in our work, significant reduction in rSO_2 during neuraxial anesthesia was unreliable. Perhaps this is due to the insufficient sample size.

Many authors attribute the occurrence of POCD to the type of anesthetic management [1, 2, 5, 7, 17, 28, 30]. But most researchers have formed a pilot group of elderly people who are predisposed to cognitive dysfunction due to age-related changes in the brain. In our study, we were not able to detect differences between the three types of anesthesia. Perhaps, extent of surgery, surgical stress and quality of patient management in the postoperative period are POCD risk factors to a greater degree [32, 33].

Children's surgery and cardiology could provide indirect evidence that type of anesthesia has no influence on POCD occurrence. In pediatric anesthesiology, the issue of cognitive dysfunction is as acute as in adults. But many researchers point out that despite individual POCD cases in school-age children, one cannot claim that a particular anaesthetic support has a higher effect on POCD development than the others [34]. Cardiac surgery procedures are associated with brain hypoxia, which should lead to cognitive dysfunction. However, some researchers studying the problem also reported that anesthesia type has no effect on POCD incidence [35].

CONCLUSIONS

Our study showed that the likelihood of developing postoperative cognitive dysfunction in elderly women undergoing gynecological surgeries does not depend on the type of anesthesia. Reduced cerebral oxygenation could be the cause of more frequent occurrence of POCD in neuraxial anesthesia. However, our findings on reduction of rSO_2 in neuraxial anesthesia are not statistically significant. The hypothesis should be further tested in a group consisting of large number of patients. We also noted that Trail Making Test and Frontal Assessment Battery are the most sensitive POCD detection tools.

Neuropsychological test results

Group (type of anesthesia)	Number of patients	Detected POCD, patients (percentage in the group, %)	FAB score			MMSE score			TMT score		
			before surgery, p	after surgery, p	change, %	before surgery, p	after surgery, p	change, %	before surgery, p	after surgery, p	change, %
General	12	3 (25.0)	14.5 ± 1.7	11.0 ± 1.3	24.0*	26.1 ± 4.0	24.3 ± 3.7	7.0	46.5 ± 6.6	62.0 ± 8.9	25.0*
Neuraxial	23	7 (30.0)	14.3 ± 2.9	11.6 ± 2.4	18.6*	26.5 ± 3.1	24.2 ± 2.2	8.7	48.4 ± 4.5	67.2 ± 6.2	28.0*
Combined	8	2 (25.0)	13.1 ± 3.6	9.8 ± 2.7	25.0*	25.1 ± 2.9	23.4 ± 2.7	6.9	50.2 ± 5.0	65.8 ± 6.5	23.8*

Note. FAB — Frontal Assessment Battery, MMSE — Mini-Mental State Examination, TMT — Trail Making Test. * — $p < 0.05$ (when comparing the average values of the attribute in the group before and after surgery).

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