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Comparative Analysis of Memory and Alertness in the Perioperative Period of Operative Delivery in Pregnant Women with Preeclampsia and Without it With Different Kinds of Anesthesia

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RELEVANCE The article investigates the choice of anesthesia technique during a caesarean section, which would minimally affect such components of cognitive functions as memory and alertness. The aim of the study is to increase the safety of anesthetic care in women of reproductive age by choosing the method of anesthesia.

MATERIAL AND METHODS Two groups of maternity patients were examined: with a normal pregnancy and preeclampsia. They were tested according to a specially designed examination, which included: MoCA test, Benton's test, Wechsler's test, self-assessment questionnaire, hospital scale of anxiety and depression before and after surgical delivery.

RESULTS According to the test results, it was found that memory and alertness in pregnant women were initially reduced (compared to the norm), especially with concomitant preeclampsia. When comparing the test results before and after abdominal delivery, it was found that the deterioration of memory and alertness parameters occurs less after the use of neuraxial methods (spinal and epidural anesthesia) compared to patients who underwent general combined anesthesia.

Keywords: pregnancy, preeclampsia, cognitive functions, memory, alertness, regional anesthesia, general combined anesthesia

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SAS – self-assessment scale
CNS – central nervous system
CS – cesarean section
DA – difficult airway
EA – epidural anesthesia
EEG – electroencephalography
GCA – general combined anesthesia
MoCA test – Montreal Cognitive Assessment Scale
MRI – magnetic resonance imaging
POCD – postoperative cognitive dysfunction
RA – regional anesthesia
SA – spinal anesthesia
TIVA – total intravenous anesthesia

INTRODUCTION

For a long time, it was believed that the problem of postoperative cognitive dysfunction (POCD) is relevant mainly for elderly patients, which, first of all, was associated with initial mental disorders, as well as the development of postoperative delirium [1]. The other risk group included patients mainly after cardiac surgery performed under cardiopulmonary bypass, as well as in cases of registration of intraoperative cerebral desaturation. It has been established that changes in nerve cells triggered by anesthesia can be detected in a young patients and children. Surgical interventions under general anesthesia provoke changes in the cognitive sphere, such as memory loss and distraction [2].

In obstetric practice, memory and attention disorders are observed already in the first trimester of pregnancy in every fourth woman. During the development of pregnancy, the incidence of cognitive impairment increases with the likelihood of occurrence for every second woman, and the manifestations increase and persist until the end of pregnancy. It was found that age and educational level do not have a significant effect on the development of cognitive impairment during pregnancy [3]. Cognitive dysfunctions during pregnancy are associated with high levels of estradiol and progesterone with normal blood levels of albumin, hemoglobin, and serum iron [4]. Pregnant women are prone to forgetfulness, disorientation, difficulty reading, and confusion. Systematic testing of cognitive functions and the level of hormones during pregnancy, revealed that cognitive deficits manifested not only in mood sluctuation, but also more complex phenomena such as the violation of the verbal learning difficulties in performing tasks that require high speed of thought [5].

Morphological changes in the brain with complicated forms of pregnancy are often found in the form of cerebral edema. With magnetic resonance imaging (MRI), such changes were found in 84.9% of cases with eclampsia, in 14.3% of cases - with severe preeclampsia [6]. Neurophysiological studies in women with preeclampsia and eclampsia are rare. In the studies of *M.A. Osmanagaoglu, the* pathology was revealed precisely by the method of electroencephalography (EEG). Changes were recorded in 20% of cases in patients with moderate preeclampsia, in 36% with severe preeclampsia, and in 83% with eclampsia. The relation between changes on the EEG and MRI was revealed, however, the EEG pattern of eclampsia is unreliable [7]. In patients with preeclampsia, according to the data of transcranial Doppler sonography, an increase in cerebral perfusion pressure and a decrease in the resistance of cerebral vessels were found in comparison with the data during a normal pregnancy [8].

Despite the improvement in the quality of medical care during delivery of patients with preeclampsia in general, the problem of prevention and treatment of POCD should be considered unsolved. Intraoperative awakening in 33–56% of patients during cesarean section (CS) leads to post-traumatic stress disorders, including cognitive impairments [9]. The obstetrician it is associated with superficial anesthesia to extract the fetus. The initial impairment of cognitive functions in pregnant women is the reason for the careful choice of anesthesia technique, since the risk of POCD increases several times. It was noted that under the influence of drugs for general anesthesia, the severity of pathology does not subsequently decrease and can progress, which most researchers associate with the initiation of delayed apoptosis of neurons [10]. The combination of the symptoms of POCD with depression also aggravates the situation, since a woman who underwent CS in the postoperative period has to deal with many psychological problems that relate to both the well-being of the child and the mother. The age and duration of anesthesia are less relevant in this group of subjects [3].

Thus, taking into account the initial cognitive deficit in pregnant women, especially in the course of complicated preeclapsia, it is important to continue the scientific search for types and methods of anesthesia that have a minimal negative effect on the cognitive status during operative delivery.

The aim of the study was to evaluate the effect of various types of anesthesia on memory and attention during operative delivery of a normal pregnancy and in the course of preeclampsia.

MATERIAL AND METHODS

We examined 68 pregnant patients. The average age of women in labor was 34 years. The work was carried out at the bases of the Clinic of Obstetrics and Gynecology of the S.M. Kirov Military Medical Academy and the D.O. Ott Research Institute of Obstetrics and Gynecology. The inclusion criteria were the consent of the patients for examination, planned surgical interventions (CS) under general combined anesthesia (GCA) or regional anesthesia (RA). Exclusion criteria were mental disorders, brain surgery, traumatic brain injury, and spinal surgery in history. The study was approved by the Independent Ethics Committee at the S.M. Kirov Military Medical Academy. CM. Kirov, an extract from the protocol No. 209 of the meeting of the Ethics Committee at the S.M. Kirov Military Medical Academy dated June 26, 2018.

The patients were divided into two groups. The first group included obstetric patients with normal pregnancies. Patients diagnosed with moderate preeclampsia made up the second group. The severity of preeclampsia was determined in accordance with the clinical classification of hypertensive disorders during pregnancy and clinically significant proteinuria according to ICD-10 (moderate - 013 and severe - 014). In the main groups, subgroups were identified: a - CS operation under GCA (the choice of anesthesia method was carried out with the voluntary consent of the patients), b - RA. To ensure the safety of patients in the case of GCA Department of Anesthesiology and Intensive Care provided laryngeal masks and tubes and a set of emergency conicotomy and video laryngoscope for difficult airway (DA). There were no situations DA, all intubations were uneventful. Comparative characteristics of the patients included in the study, according to individual indicators, are presented in Table 1.

Table 1

Comparative analysis of individual indicators in both groups

Indicators	Norm (*n*=34)		Moderate preeclampsia (*n*=34)	
	GCA (1a) (*n* = 17)	RA (1b) (*n* = 17)	GCA (2a) (*n* = 17)	RA (2b) (*n* = 17)
Age, years	34.26 ± 0.63	32.27 ± 0.7	35.5 ± 1.16	31.75 ± 1.14
Weight, kg	86.16 ± 1.72	78.36 ± 3.08	81.74 ± 3.02	82.3 ± 4.07
Height, cm	166 ± 0.78	165.3 ± 1.18	165.8 ± 1.63	166.1 ± 1.39
Pregnancy period, week	37.71 ± 0.25	38.2 ± 0.29	36.5 ± 0.53	37.05 ± 0.95

Notes: GCA - general combined anesthesia; RA - regional anesthesia

GCA was carried out according to the following procedure. Prior to the operation, the patients were prescribed orally phenobarbital at a dose of 0.1 g, ketoprofen - 100 mg, and sibazon - 5 mg. After catheterization of the peripheral vein on the operating table, a 0.1% solution of atropine sulfate was injected intravenously at a dose of 0.01 mg/kg. Prior to induction of anesthesia, preoxygenation was performed for 3 minutes with 100% oxygen, then 1% propofol solution was injected intravenously at a dose of 2.5 mg/kg and 0.05% fentanyl solution - 3-5 μg/kg. Tracheal intubation was performed after infusion of 1–1.5 mg/kg succinylcholine solution. Artificial ventilation of the lungs with the *"Dräger"* device was carried out in the normal ventilation mode with FiO_2 equal to 50%. After intubation, 0.05% fentanyl solution was injected - 3-5 μg/kg and 1% propofol solution - 2 mg/kg/h. In order to maintain myoplegia, pipcuronium bromide was administered intravenously in a bolus at a dose of 10–15 μg/kg.

In the case of surgical intervention under spinal anesthesia, a similar premedication was used. After insertion of a peripheral venous catheter, infusion therapy was started with 0.9% sodium chloride solution at a rate of 4 ml/kg/h. The subarachnoid space was punctured with 27 *G Pencan* needles at the L_2 –L_3 and L_3 –L_4 levels. 2.8-3.0 ml of 0.5% solution of "Markain® Spinal Heavy" was injected fractionally. The patient was placed first on her side, then on her back. The infusion rate was increased to 15 ml/kg/h, the volume of infusion therapy during anesthesia was 1100 ml. The level of anesthesia was assessed by a pin test with a sterile needle for loss of pain sensitivity, and the degree of motor block was assessed using the *Bromage* scale. The operation began with the development of a complete motor block.

When choosing epidural anesthesia (EA), puncture and catheterization of the epidural space at the level of L_2–L_3 and L_3–L_4 in the supine position were performed, *B. Braun* catheters were used. The epidural catheter was inserted 4 cm in the cranial direction and fixed, then a test dose of 3 ml of 2% lidocaine solution was injected. To create anesthesia, a 0.75% solution of ropivacaine hydrochloride at a dosage of 100–130 mg was administered epidurally in fractional bolus, focusing on the level of the sensory and motor block. On the eve of the operation, the patients were prescribed 100 mg of ketoprofen. Hemodynamic parameters were monitored perioperatively.

To assess memory and attention, prior to the surgical intervention, testing was performed according to a formalized survey card, which included five tests for assessing cognitive functions (*MoCA* test, Benton's test, Wechsler's test, self-assessment questionnaire, hospital scale of anxiety and depression). Subsequently, a similar examination was carried out on the 3rd day after anesthesia and surgery.

Using the *MoCA* test, various aspects of cognitive activity were assessed: memory, "frontal" functions, speech function (naming animals), visual-spatial praxis (cube, clock). The sensitivity of the *MoCA* test was high enough to detect mild cognitive impairment. For patients, this testing methodology was presented on a separate sheet of paper in the form of a table, which had to be filled out with the doctor during testing.

The *Hospital Anxieti and Depression Scale (HADS)* was used to screen and assess the severity of depression and anxiety. For the patient's response, a clear framework for answering questions and filling out the scale was established (about 20-30 minutes). When interpreting the data, the total indicator for each subscale (anxiety and depression) was taken into account, while there are 3 ranges of values: score 0-7 - normal, score 8-10 - subclinically expressed anxiety/depression, score 11 and higher - clinically expressed anxiety/depression.

The self-assessment questionnaire (SAS) was used to study subjective well-being and to identify the presence of somatic complaints. The survey was carried out using special forms, when the patient was offered 7 pairs of polar statements characterizing a certain condition with an assessment of the severity of each.

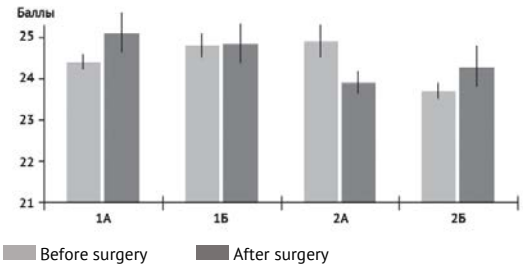
Benton's test was used to identify and assess attention deficit disorder, mainly visual short-term memory, by reproducing (sketching) shapes that are presented as references for a certain at a strictly fixed time. The set of geometrically relatively abstract shapes contains 10 series.

Memory and attention were examined using the Wechsler test (a subtest of repetition of digital series). Its implementation required a lot of concentration, since the results are subject to both external and internal interference associated with the emotions of the patients. Failure to pass the test is considered by many authors as a sign of internal anxiety, anxiety, preventing the patient from concentrating on the task.

The collection of information was carried out using a survey card, which results were calculated and entered into the *ARSTAT* program. Calculation of statistical parameters - *M* - arithmetic mean, *t* - Student's test for independent samples, *p* - statistical significance indicator, determined by Student's method, was calculated in the *ARSTAT* program. The test results were displayed on histograms in the *Excel* program.

RESULTS

The results of the *MoCA* test (Fig. 1) demonstrated initially low test rates in the entire sample (normal value - 26 points) with an insignificant but statistically significant difference between the main groups. Such results could support baseline cognitive impairments associated with encephalopathy in pregnancy. After surgery and anesthesia, the test indices did not reach normal values, however, the indices in RA were comparatively better than after GCA.

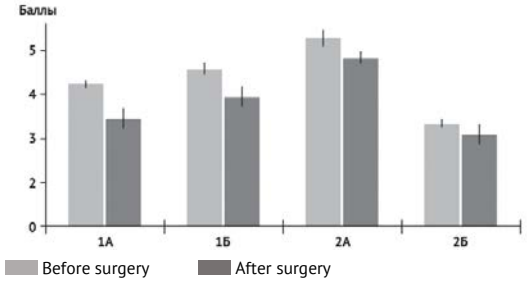


1А – pregnant women after general anesthesia
1Б – pregnant women after regional anesthesia
2А – women with moderate preeclampsia after general anesthesia
2Б – women with moderate preeclampsia after regional anesthesia

Fig. 1. Results of MoCA test in pregnant women of groups before and after cesarean section

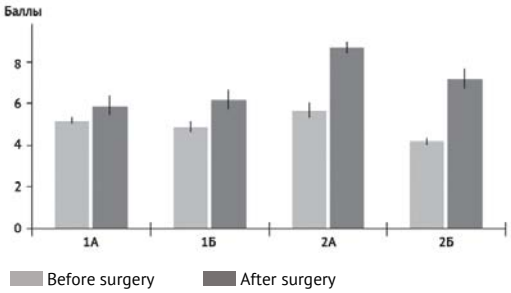
Testing of patients by GCA revealed a satisfactory subjective state in both groups of patients in the range of 5–6 walls at all stages of the examination. However, the repetition of numbers in reverse order revealed that the amount of short-term memory and alertness declines after anesthesia - from 4.5 ± 0.15 to 3.0 ± 0.3 and 3.6 ± 0.24 to 3.2 ± 0.27 - after general combined anesthesia and from 5.0 ± 0.24 to 3.5 ± 0.21 and from 4 ± 0.27 to 4.4 ± 0.23 after regional anesthesia, where an increase in the indicator in the group of pregnant women with moderate preeclampsia.

The survey results using the Hospital Anxiety and Depression Scale before CS the demonstrated subclinical expressed concern before the upcoming of GCA, apparently, it is associated with the fear of loss of control over the process of delivery and RA features allow patients to be awake during the childbirth, even if the deliveries do not go through the natural birth canal. After CS, this indicator decreased to 4–7, which should be regarded as normalization of the psychoemotional state of the patients. The test results on histogram evidenced initially normal state of health of the patients, however, after surgery and anesthesia some growth of depression was observed, remaining within the permissible range (Figure 2, 3.).



1А – pregnant women after general anesthesia
1Б – pregnant women after regional anesthesia
2А – women with moderate preeclampsia after general anesthesia
2Б – women with moderate preeclampsia after regional anesthesia

Fig. 2. Results of indicators of anxiety in pregnant women and women with moderate preeclampsia



1А – pregnant women after general anesthesia
1Б – pregnant women after regional anesthesia
2А – women with moderate preeclampsia after general anesthesia
2Б – women with moderate preeclampsia after regional anesthesia

Fig. 3. The results of indicators of depression of pregnant women and women with moderate preeclampsia

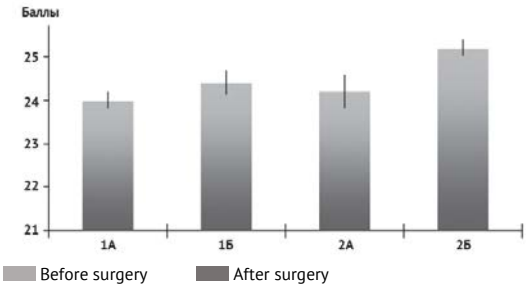
According to the results of the Benton test, initially low indicators were found, after GCA there was a decrease in testing indicators from 6.12 ± 0.25 to 4.0 ± 0.37, after RA there was no decrease. After CS and anesthesia, the indices in the GCA group decreased, while in the RA group they remained unchanged (Table 2, Fig. 4).

Table 2

Comparative analysis of the results of testing memory and alertness in pregnant women before and after surgery

Indicators	1A		1B		2A		2B	
	Before surgery	After surgery	Before surgery	After surgery	Before surgery	After surgery	Before surgery	After surgery
MoSA test	24.54 ± 0.32	25.15 ± 0.57	24.85 ± 0.54	24.85 ± 0.51	25 ± 0.39	23.9 ± 0.51	23.4 ± 0.87	24.4 ± 0.7
SAS	5.92 ± 0.23	5.68 ± 0.44	5.32 ± 0.37	5.36 ± 0.34	5.65 ± 0.25	4.9 ± 0.42	5.2 ± 0.37	5.45 ± 0.37
Anxiety	6.63 ± 0.4	5 ± 0.51	7.35 ± 0.78	5.8 ± 0.68	9.42 ± 0.44	7.79 ± 0.82	4.8 ± 0.6	4.65 ± 0.55
Depression	5.13 ± 0.32	5.8 ± 0.76	4.95 ± 0.63	6.45 ± 1.13	5.85 ± 0.79	8.8 ± 0.99	4.47 ± 0.48	7.26 ± 0.88
Count numbers in direct order	5.61 ± 0.18	5.4 ± 0.31	6.35 ± 0.33	5.9 ± 0.34	5.35 ± 0.39	5.7 ± 0.36	5.6 ± 0.33	5.65 ± 0.23
Count numbers in reverse order	4.5 ± 0.15	3.0 ± 0.3	5.0 ± 0.24	3.5 ± 0.21	3.6 ± 0.24	3.2 ± 0.27	4 ± 0.27	4.4 ± 0.23
Benton test	6.12 ± 0.25	4.0 ± 0.37	6.2 ± 0.37	4.5 ± 0.41	6 ± 0.32	6.25 ± 0.4	6 ± 0.57	6.75 ± 0.4

Notes: SAS - self-assessment questionnaire; MoCA test - Montreal Cognitive Assessment Scale



1А – pregnant women after general anesthesia
1Б – pregnant women after regional anesthesia
2А – women with moderate preeclampsia after general anesthesia
2Б – women with moderate preeclampsia after regional anesthesia

Fig. 4. The results of Benton test in pregnant women and women with mild preeclampsia after Cesarean section

DISCUSSION

Various methods of anesthesia can be one of the causes of disorders of higher nervous activity in the postoperative period, among which POCD occupies a special place. The initial cognitive deficit in pregnant women is proved by the results of the *MoCA* test. After surgery and anesthesia, the situation was aggravated in the group of patients with moderate preeclampsia, who underwent CS under GCA. Patients with moderate preeclampsia deserve the most careful attention, since the choice of anesthesia method in this case should be the safest. RA met the necessary criteria as shown by the results of testing the *MoCA* test and the Benton test.

GCA, on the contrary, should be used only according to indications and in exceptional cases, since it can aggravate cognitive dysfunction and provoke various complications. A meta-analysis of 600 literature sources for 1980–2010 was published in *CNS Drugs* journal in 2010 based on a *MEDLINE* search. To date, there is no unequivocal answer to the question: which of the anesthetics initiates POCD least of all. However, the work of recent years increasingly testifies against total intravenous anesthesia (TIA) in favor of modern inhalation anesthetics - sevoflurane and desflurane. Early POCD with TIA (propofol) was observed in 67.5% of patients, and with inhalation anesthesia with desflurane - in 49.4% of cases [11].

Cognitive impairment with sevoflurane anesthesia is of a shorter duration than with propofol-based TIA [12].

To date, the question of the neuroprotection or neurotoxicity of inhaled anesthetics is the hottest topic of scientific research. These are two completely opposite effects, and each is supported by laboratory and experimental data. The available clinical data confirm the presence of neuroprotection. Clinical results have not yet been obtained in favor of the neurotoxicity of inhalation anesthesia [13].

A number of authors indicate that there is no difference in the depression of cognitive functions when using general and epidural anesthesia. Thus, *S. Newman* in 2007 described cognitive dysfunctions of an equal degree a few weeks after noncardiac surgery under conditions of both epidural and general anesthesia [14].

M.V. Korolev (2017) and colleagues conducted a study and believe that maternal memory deteriorates after pregnancy complicated preeclampsia/eclampsia [15]. In a study by *A.M. Aukes et al.* women who underwent such complications of pregnancy also subsequently showed a higher level of cognitive impairment [16]. The work revealed a hypothesis that the negative consequences of eclampsia in terms of the cognitive component may be associated with damage to the white matter of the brain. *I.R. Postma et al.* confirmed that the characteristic features of neuroimaging in eclampsia are consistent with cerebral edema, located mainly in the parietal and occipital lobes [17, 18]. *M. Baeckeet et al.* the results of neurocognitive tests concluded that the objective and subjective cognitive functions, anxiety and depressive symptoms were not associated with damage to the white matter of the brain. [19]

The study of cognitive function in pregnant women before and after surgery makes it possible to assess the effect of various anesthetics on the most vulnerable types of cognitive activity - memory and alertness. The study of this problem is very important for the preservation of the cognitive and psychological health of mothers and children.

CONCLUSIONS

1. Indicators of memory and alertness in pregnant women according to the test results were initially deviated from the norm, especially in moderate preeclampsia. The results of the *MoCA* test are below score 26. The volume of short-term memory and alertness decreases after anesthesia, 4.5 ± 0.15 to 3.0 ± 0.3; 3.6 ± 0.24 to 3.2 ± 0.27 after general combined anesthesia and 4 ± 0.27 to 4.4 ± 0.23 after regional anesthesia. According to the results of the Benton test, initially low indicators were found; after general combined anesthesia, a decrease in testing indicators was observed from 6.12 ± 0.25 to 4.0 ± 0.37.

2. During regional anesthesia (spinal and epidural), the best results were revealed when testing individual indicators of memory and alertness compared to the results of testing after general combined anesthesia. *The MoCA* test ranges from 23.4 ± 0.87 to 24.4 ± 0.7. According to the results of the Benton test after regional anesthesia, the indicators improve in pregnant women with preeclampsia 6 ± 0.57 and 6.75 ± 0.4.

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