REDUCTION IN THE INCIDENCE OF POSTOPERATIVE COGNITIVE IMPAIRMENT AFTER CESAREAN SECTION DURING SPINAL ANESTHESIA WITH KVANADEX

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Abstract: *Postoperative cognitive dysfunction (POCD) is a common complication following surgical interventions and anesthesia, particularly in obstetric practice. This study aimed to reduce the incidence of POCD after cesarean section by optimizing anesthetic management during spinal anesthesia. A prospective clinical study was conducted from 2022 to 2023 at the multidisciplinary clinic of Samarkand State Medical University, involving 38 pregnant women at 37–40 weeks of gestation scheduled for elective cesarean section. All patients were classified as ASA II and were divided into two groups. In the first group, intravenous sedation was performed using sodium oxybutyrate (40 mg/kg), while in the second group dexmedetomidine (Kvanadex) was administered at a loading dose of 0.5–0.8 μg/kg followed by continuous infusion throughout the operation. Cognitive functions were assessed using the Mini-Mental State Examination (MMSE), and sedation depth was monitored with the Richmond Agitation-Sedation Scale (RASS).The results demonstrated that spinal anesthesia was effective in all patients, providing adequate sensory and motor blockade. The use of dexmedetomidine was associated with greater hemodynamic stability, absence of respiratory depression, lower stress hormone levels, and a significantly reduced incidence of early postoperative cognitive impairment compared to sodium oxybutyrate. MMSE scores in the dexmedetomidine group recovered more rapidly in the postoperative period.In conclusion, intraoperative sedation with dexmedetomidine during spinal anesthesia for cesarean section is a safe and effective strategy that improves hemodynamic stability and significantly reduces the risk of postoperative cognitive dysfunction, contributing to faster recovery and better postoperative outcomes.*

Keywords: *Postoperative cognitive dysfunction; cesarean section; spinal anesthesia; dexmedetomidine; sedation; cognitive function; obstetric anesthesia.*

Postoperative cognitive dysfunction syndrome (POCD) refers to disorders of higher mental functions that can develop in the postoperative period and are caused by surgery and anesthesia, as defined by L.S. Rasmussen is a cognitive disorder that develops in the early and persists in the late postoperative periods, clinically manifested by memory impairment, difficulty concentrating (concentrating) attention and disturbances of other higher cortical functions (thinking, speech, etc.), confirmed by neuropsychological testing[1]. In addition, anesthesia drugs are characterized by direct toxic effects. A number of authors describe the negative impact of anesthesia on cognitive functions [2,3]. Regional anesthesia methods make it possible to prevent the

cascade of reactions that initiate surgical stress. It has also been established that regional anesthesia provides more effective postoperative pain relief [4]. To date, the mechanisms of influence of individual anesthetics and related drugs on the vital activity of nerve cells and cognitive function have been formulated. Thus, propofol, barbiturates, benzodiazepines, isoflurane, halothane suppress neuronal activity, general anesthetics indirectly block glutamate and acetylcholine receptors in the limbic zone and thalamus. The concentration of these receptors is especially high in the structures responsible for behavior and emotions - the hippocampus, amygdala and thalamus opticus. In addition, barbiturates cause mitochondrial dysfunction, potentiating glutamate toxicity. Ketamine, nitrous oxide, and xenon also affect GABA receptors in the cortex, but indirectly through NMDA receptors [5].

The target is to reduce the risk of developing POCD after cesarean section by optimizing anesthetic management.

Material and methods. To fulfill the assigned tasks on the basis of the multidisciplinary clinic of Samarkand State Medical University in the period 2022 to 2023, 38 women with a gestation period of 37-40 weeks were examined and delivered by planned cesarean section, which included: full-term pregnancy, uterine scar after cesarean section, congenital or acquired pathology of the pelvic bones, preeclampsia, and high myopia. Exclusion criteria were: massive blood loss (more than 30% of blood volume), eclampsia, chronic nonspecific and acute lung diseases, cardiovascular diseases, morbid obesity, the patient's refusal to undergo SA, as well as patients with fluctuations in blood pressure (intraoperative decrease in blood pressure by 30% from the initial value or more), hemodynamic instability, as well as those who required vasopressor support were excluded from the study. All patients were examined by an anesthesiologist on the eve of surgery and corresponded to ASA class II. All pregnant women gave written informed consent to anesthesia and research. All pregnant women underwent standard preoperative preparation: compression bandaging of the lower extremities, preliminary infusion of 0.9% sodium chloride solution - 500 ml.

All women were divided into 2 groups. In group I (n = 15), sedation was performed with sodium Oxybutyrate 40 mg/kg. Puncture of the subarachnoid space was performed at the level LII–LIV using Pencil-Point G 25–26 needles in a lateral position. A hyperbaric solution of 0.5% bupivacaine solution with a solution density of 1.026 was slowly (over 2 min) injected. The dose of anesthetic was calculated in accordance with the proposed dosage [3]. In group II (n = 15), starting from the moment of premedication, 0.5 mcg/kg Kvanadex (Yuria Pharm) was administered intravenously for 15 minutes, the maintenance dose was 0.5–0.8 mcg/kg/h per throughout the operation until its completion. Cognitive functions were assessed using the following scales: MMSE (Mini Mental State Examination), the depth of sedation was controlled using the RASS scale and maintained at a level of -2, -3. There were no cases of death or development of life-threatening complications. Two women were excluded from the study due to refusal of neuropsychological testing in the postoperative period according to the study protocol.

Statistical processing was performed in the “Data Analysis”, “Descriptive Statistics” sections using the Microsoft Excel 2013 software package with a statistical processing application package. The significance criterion was the value of the error probability indicator, or the probability of accepting an erroneous hypothesis (p) - no more than 5% ($p \leq 0.05$).

Research results and discussion.

As our studies showed, SA was highly effective in all 38 women. The level of distribution of complete sensory-motor block corresponded to Th4-S5 dermatomes. During the entire operation, including during its most traumatic stages, the patients did not react and did not complain. Signs of respiratory depression were observed in group I in 5 women in labor. SpO2 was 90-94%. In the main group, no signs of respiratory depression were observed. Hemodynamic stability was maintained (see Table 1). However, when assessing changes in hemodynamics in the 1st group, in contrast to the 2nd group of women, an increase in heart rate (HR) was found from 88.2±2.3 beats/min to 94.8±2.5 beats/min, an increase in SBP at all stages of observation, a slight decrease in cardiac index (CI) and an increase in peripheral vascular resistance. Activation of the sympathetic link of regulation was also greatest in the 2nd group of women when using Kvanadex, while the tension index (TI) was 398.2±9.1 c. at the most traumatic stage of the operation, however, a low level of total cortisol (TC) of 120.8±3.1 nmol/l was noted in women. (See table 1). After fractional administration of sodium hydroxybutyrate (40 mg/kg) (I group) and a 15-minute intravenous loading dose of Kvanadex (0.8 mcg/kg) (II group), the degree of sedation was observed in patients of group I - 2.8 ± 0 .42, while in II – 2.6±0.36 points. At the height of anesthesia before the skin incision, RASS in group I increased by 7.4% to a moderate degree, and in group II it decreased by 4.2% (P>0.05) to a mild degree. After extraction of the fetus RASS I gr. increased by 10.4% (P0.05) by the end of the operation and 4 hours after its completion decreased, respectively, by 8.7 (P>0.05) and 70.8% (P 0.05) relative to the initial stage. In group II, the degree of sedation at all stages of the study according to RASS remained stable within the range of –2.1 and –1.8 points (P>0.05) (see Table 1).

Table 1. Some indicators of the main life support systems during intravenous sedation with sodium hydroxybutyrate and kvanadex for cesarean section.

Parameters studied	Research stages					
	I		II	III	IV	V
Heart rate, per 1 minute	1 гр.	90,7±3,1	91,9±2,1*	90,2±2,6*	96,6±2,3	92,2±1,1*
	2 гр.	89,7±2,1	84,9±1,1*	84,2±1,6*	85,6±1,3	82,2±2,1*
Sys.BP.mm.Hg	1 гр.	97,2±1,4	89,6±1,2*	83,2±2,1*	92,4±1,6	91,1±1,2*
	2 гр.	96,4±1,9	84,6±1,8*	85,2±1,6*	90,4±2,6	94,1±1,3*
CI, l/m2/min	1 гр.	2,65±0,1	2,58±0,09	2,70±0,07	2,62±0,09	2,65±0,09
	2 гр.	2,75±0,09	2,77±0,13	2,81±0,09	2,69±0,1	2,81±0,07

-total peripheral vascular resistance, dyn×s/cm5	1 гр.	1412,1±42,2	1314,3±46,3*	1311,4±44,2	1412,3±43,1*	1511,3±46,2*
	2 гр.	1414,3±46,1	1288,3±42,3*	1293,4±48,4	1372,4±46,3	1304,2±42,3*
-TI, in conventional units	1 гр.	358,8±9,3	352,1±7,2*	354,2±10,1 Δ	398,2±9,1	354,4±9,4 Δ
	2 гр.	356,4±10,2	278,4±8,4*	337,6±11,4 Δ	381,3±10,8	334,5±8,0 Δ
TC, nmol/l	1 гр.	400,8±44,2	467,7±53,3	–	680,8±53,2* Δ	406,2±67,8* Δ
	2 гр.	398,4±36,3	304,2±50,3	–	319,4±46,6* Δ	240,4±42,2* Δ
Norepinephrine in urine, nmol/l	1 гр.	9,2±1,2	-	-	-	18,1±2,1
	2 гр.	8,9±0,8	-	-	-	11,4±1,4
RASS scale (points)	1 гр.		-2,7±0,1	-2,4±0,7	-1,8±0,4	0,5±0,12
	2 гр.		-2,5±0,14	-2,4±0,2	-2,1±0,8	0±0,0

Note: * - significance of differences (P <0.05) relative to the initial values; Δ - significance of differences (P <0.05) relative to the previous stage of the study. Stages: I – before the start of the operation; II – on the operating table; III – after a skin incision; IV – traumatic stage of the operation; V – end of operation.

Table 2. Indicators of cognitive functions in the pre- and postoperative period

Cognitive status	1st group (n = 18)	2nd group (n = 17)	p
Mini mental state examination scale, preoperative period, points	29 [27; 29]	29 [28; 29]	0,001
Mini mental state examination scale on the 1st day, points	24 [26; 27]	27 [27; 28]	0,05
Mini mental state examination scale on the 5th day, points	28 [27; 29]	30 [28; 29]	0,001

As can be seen from table. 2, the initial cognitive status the day before surgery did not have statistically significant differences between the groups. According to the Mini mental state examination scale, the median in group 1 was 29 points, in group 2 – 29 points, cognitive status on all scales used in the study was lower on the 1st day after surgery, it should be noted that the effect of the drugs for anesthesia, by the time

neuropsychological testing had ended and all women were clearly conscious. The incidence of POCD in the early postoperative period of both groups was 14.3% (5 patients), of which 11.4% (4 women) belonged to group 1 and 2.9% (1 woman) to group 2. The dynamics of cognitive status indicators in the postoperative period are shown in Table. 2

Conclusions: The use of 0.8 mcg/kg Kvanadex as a sedative against the background of SA ensures hemodynamic stability throughout the operation and is quite acceptable for anesthesiologic management of abdominal delivery. The use of Kvanadex leads to a decrease in the incidence of cognitive impairment in the early postoperative period, a decrease in the intensity of pain, and a beneficial effect on recovery and activation after surgery.

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