

Influence of spinal anesthesia of caesarean section on maternal levels of proinflammatory and antiinflammatory cytokines

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Introduction

Cytokines are significant mediators of the immune response to surgery and also play a role in parturition. Stress factor of abdominal delivery and anesthetic techniques can have an influence with unfavorable effect on the mother's organism. Acute stressor exposure and immunogenic challenges can synergistically increase behavioral, endocrine and neuroinflammatory responses [2].

The cytokines are a group of polypeptide mediators of intercellular cooperation, participating mainly in forming and adjusting of protective reactions of organism at introduction of pathogens and violation of integrity of tissues, and also in adjusting of the normal physiological functions.

Jin et al., 2013 [5] had proven that asters considerably have an influence with cognitive functions. Asters activating, induced by chronic cerebral hypoperfusion, results to cognitive dysfunctions. Hyppocampal proinflammatory cytokines (IL-1 β , IL-6, TNF α) have active negative influence with spatial memory for mice.

The great number of works confirms a working hypothesis, that neuroinflammation has impact on development of the postoperative cognitive dysfunctions. The surgery duration and anaesthesia duration influence the postoperative cognitive dysfunctions was proven on animal models. This effect correlates with the changes of proinflammatory cytokines [4].

Hypotheses of the causes of the postoperative cognitive dysfunctions are based on experimental evidence that anesthetics can impair mechanisms of learning and memory on a neuronal level and might lead to neurodegeneration. Additionally, surgery can result in neuroinflammation which could also underlie the postoperative cognitive dysfunctions. The most important strategy to avoid the postoperative cognitive dysfunctions is to maintain the patient's physiological homeostasis perioperatively. According to the presently available clinical studies recommendations in favor or against certain anesthesiological procedures cannot be given [6].

The interaction of the Class 2 alpha-helical cytokines consist of IL-10 with their specific receptor molecules initiates a broad and varied array of signals that induce cellular antiviral states, modulate inflammatory responses, inhibit or stimulate cell growth, produce or inhibit apoptosis, and affect many immune mechanisms. The information derived from crystal structures and molecular evolution has led to progress in the analysis of the molecular mechanisms initiating their biological activities. These cytokines have significant roles in a variety of pathophysiological processes as well as in regulation of the immune system. Further investigation of these critical intercellular signaling molecules will provide important information to enable these proteins to be used more extensively in therapy for a variety of diseases [7].

Maternal separation also increases cortical expression of the NR2A NMDA receptor subunit in adolescence, which is prevented by IL-10 treatment. These data suggest that inflammatory damage to parvalbumin interneurons may occur via aberrant glutamatergic activity in the prefrontal cortex. These findings provide a novel interactive mechanism between inflammation and neural dysfunction that helps explain deleterious effects of early life adversity on prefrontal cortex interneurons [8].

A stress factor of abdominal delivery and anesthetic techniques can have an influence with an adverse effect on a motherorganism [1].

The Goal: to study influence of spinal anesthesia on plasma proinflammatory and antiinflammatory cytokines levels of parturients after a caesarean section.

Materials and methods

Having agreed with local ethics committee and obtained informed consent, 15 pregnant (at 37-42 weeks gestation, who delivered by the caesarian section under the neuraxial anesthesia) were examined. Criteria of exception were: age to 18 and 45 more than, term of pregnancy to 36 weeks, severe preeclamsia or eclampsia, decompensated extragenital pathology, diabetes mellitus, psychical diseases, signs of bacterial or viral infection, mycoses, abandonment of woman from participating in the research at any of it stages, use ketamine in an anaesthetic manual. The women received intrathecal 0.5% hyperbaric bupivacaine 1.8-2.2 mL.

Duration of the caesarian section was $27,1 \pm 2,3$ min. The operation and the anaesthesia had no any complications. For all the patients postoperative pain was less than 30-40 mm on VAS.

The cytokines concentration was determined by the method of IFA analysis. We used the kits of reagents JSC "Vector-Best" A- 8756 for TNF α with the range of measureable concentrations: 0-250 pg/ml. For IL - 6 was used the kit of reagents Human IL-6 ELISA kit Diaclone (France) with the range of measureable concentrations: 0-200 pg/ml, and Human IL-10 ELISA kit Diaclone (France) with the range of measureable concentrations: 0-400 pg/ml was used for determination of IL-10.

Levels of IL-6, TNF α , IL-10 were determined: upon admission to the obstetrical department (P1), 24hours after the surgery (P2), on the 5-7th day after the surgery (P3). The parameters of regional norm for IL-6, TNF α , IL-10 levels were determined for non-pregnant healthy women aged 25-40

before the study. The blood samples for analyses were taken on an empty stomach at 9-11 a.m. The Normal values were 1.40 ± 0.15 pg/mL for IL-6, 9.37 ± 1.07 pg/mL for TNF α , 4.50 ± 0.28 pg/mL for IL-10.

Results and Discussion.

Initially in the latest 3d trimester of pregnancy (before delivery) (P1) levels of IL-6 and IL-10 were increased and its values were 3.51 ± 0.21 pg/mL ($p<0.0001$) and 7.55 ± 0.55 pg/mL ($p=0.0002$). However the analysis of TNF α level showed that its level in P1 was 1.43 ± 0.11 pg/mL ($p<0.0001$) that was significantly decreased in relation with regional norm (Fig.1).

[Fig.1] Cytokines levels ratio in the latest 3d trimester of pregnancy.

Level of IL-6 was increased to 36.32 ± 5.84 pg/mL in P2 ($p=0.001$) and did not change ($p=0.44$) in P3 (33.67 ± 3.88 pg/mL). The analysis of TNF α level changes showed that its level in P1 was 1.43 ± 0.11 pg/mL ($p<0.0001$) and kept its level on in P2 (1.39 ± 0.12 pg/mL ($p=0.051$)) and in P3 (1.75 ± 0.22 pg/mL ($p=0.18$)). The analysis of IL-10 level showed that its level in P1 was increased up and kept its value on in P2 (7.75 ± 0.59 pg/mL ($p=0.81$)) and in P3 (7.20 ± 0.41 pg/mL ($p=0.45$)) too (Fig.2).

[Fig.2] Cytokines levels after cesarean section under spinal anesthesia.

It has been shown that the features of cytokine profile of pregnant at 37-42 weeks gestation are conditioned by the reliable increasing of levels both IL-6 and IL-10, but IL-6 level significantly dominates. However level of proinflammatory TNF α is reliable decreased. The cytokine profile after a caesarian section for pregnant at 37-42 weeks gestation is reliable correlated to the days after surgery. IL-6 level is remains significantly increased from 1st till 5-7 day after surgery under neuraxial anesthesia. The surgery leads to pike increasing of IL-6 level and its level kept on by 5-

7 day after a surgery under the spinal anesthesia. I agree with ideas of Dotsenko, 2012 [3] whose results showed anti-inflammatory features of bupivacaine. But Dermitzaki et al.,2009 [2] presented study design anesthetic technique did not affect IL-6 or TNF-alpha concentrations in parturients undergoing elective cesarean section. Serum IL-6 levels increased 24 h postoperatively independently of anesthetic technique. Our study is going on with estimation both total intravenous anesthesia and spinal anesthesia influence proinflammatory and antiinflammatory cytokines after cesarean section.

Conclusions. At the end of the 3rd trimester of pregnancy TNF α level goes down, and the increase of IL-6 level dominates over the increase of IL-10 level.

The neuraxial anesthesia of caesarean sections does not influence the levels of TNF α and IL-10, and IL-6 level significantly increases 24h after a surgery and remains increased by day 5-7.

It needs to continue study for investigation of anesthetic technique effects on maternal cytokines levels in postpartum period.

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