

The State of Humoral Immunity in Women after Cesarean Section with Postplantar Intrauterine Contraception

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SUMMARY: The study of the role of factors of the immune system remains one of the important areas of modern medicine. Humoral immunity factors - interleukins - 1 and 8, as well as circulating immune complexes are the main participants in the immune mechanisms responsible for the compensatory response of immunity during surgical interventions and the introduction, in particular, of an intrauterine contraceptive. The protective and adaptive functions of the immune system are carried out thanks to the cytokines - IL-1 beta and IL-8. So, the intrauterine administration of a contraceptive to practically healthy women after surgical delivery did not affect the state of the local immune system, as well as the general condition, without causing inflammatory processes.

For the first time, studies of the humoral factors of immunity were carried out, which determine the development and formation of protective compensatory-adaptive reactions. It has been shown that the cytokines IL-1 β and IL-8, as well as the CIC, have important not only diagnostic, but also prognostic value in operative delivery and the introduction of an intrauterine contraceptive. The IL-1 β / IL-8 ratio turned out to be an important prognostic marker. Thanks to which it is possible to predict the level of compensatory, with a pronounced suppression of the index - the inflammatory process. Moreover, postplantar intrauterine contraception leads to certain changes in the balance of immunity mediators, which should be proportional to the degree of the inflammatory process.

Keywords. Caesarean section, postplantar intrauterine contraception, humoral immunity, circulating immune complexes, interleukins.

Topicality.

Today, thanks to modern advances in fundamental and applied immunology, molecular biology and biotechnology, new biologically significant markers of physiological and pathological processes have emerged that can help a practicing obstetrician-gynecologist work. We are talking about the possibility of early diagnosis, treatment and prediction of inflammatory processes in the reproductive organs. All these studies influence the further stages of observation and treatment of patients with inflammatory diseases of the pelvic organs [12, 14].

In this regard, according to the literature, we see that in recent years, much attention has been paid not only to the study of cellular and humoral factors of immunity, but to the study of the behavior of immunological markers depending on various human surgical interventions. This is a kind of indicators of the nature of the course of the disease, especially if there are any chronic recurrent processes [8,10].

It is known that the most important factor in preserving the reproductive health of women who have undergone a cesarean section is to solve the problem of unwanted pregnancy. It is

clear that the subsequent unplanned pregnancy, and the subsequent abortion, is a severe psychological and hormonal stress, leading to functional and organic disorders both in the reproductive system and in the immune system, thus forming a state of secondary immunodeficiency. An abortion performed in the first year after cesarean section during the formation of the scar, being a factor of trauma, contributes to the failure of the scar on the uterus and negatively affects the outcome of the subsequent desired pregnancy and childbirth [3,4,5,9].

In this regard, the use of contraception is considered as one of the most important directions in the rehabilitation of women after surgical delivery. Despite close attention to the problem of postpartum contraception, many issues related to the use of modern types of contraception after cesarean section remain controversial. Especially here in the first place comes the issue related to the state of the woman's immune system immediately after delivery, and the use of an intrauterine contraceptive. We pose questions about maintaining not just the state of physical health, but of course the state of the immune system, its usefulness and adequate implementation. Moreover, it is known that operative delivery is a surgical trauma to the usefulness of tissues, which will entail stress for the systemic immune system and local immunodeficiency. Also, it is known that the most acceptable method of contraception for socially unprotected women in a stable monogamous marriage is intrauterine contraception [1,6].

However, among clinicians there are many controversial opinions about the timing of the introduction of a contraceptive after surgery, which must also be calculated taking into account the work of the immune system. A number of authors recommend the introduction of a contraceptive into the uterine cavity directly during the operation [2,7,11,13]. As you can see, until now, these data are contradictory and uncertain, which requires further study of this issue in order to somehow resolve the issue of helping women to protect themselves. Of course, it is not just a matter of sparing after traumatization that is of great importance here, but the study of biological markers responsible for the activity of inflammatory processes in order to understand how pronounced the biological behavior of immune components is. Basically, non-specific mechanisms of immunity will be studied. Once again, it should be noted that the listed parameters of immunity are non-specific, i.e. universal factors, the study of which against the background of a specific nosology and comparison of the results obtained with the clinical manifestations of the disease are definitely important, specific value, because it is the above indicators of the immune system that accompany all processes of pathogenesis and outcome.

Cytokines are proteins that are produced predominantly by activated cells of the immune system, providing the functions of intercellular cooperation, positive and negative immunoregulation of the body's protective functions [13, 14]. It is known that cytokines regulate the amplitude and duration of inflammatory and immune responses [13, 16]. It is important to isolate, today, cytokines and nonspecific markers of immunity can be isolated into a new independent system of regulation of the basic functions of the body, existing along with the nervous and endocrine systems, and associated primarily with the maintenance of homeostasis [16]. It is known that at the tissue level, cytokines are responsible for the development of inflammation, and then the regeneration of tissues of homeostasis [2,8]. With the development of an inflammatory reaction, cytokines practically affect many organs and

systems of the body involved in the regulation of homeostasis [14]. It should be noted that in recent years, studies of cytokine levels in various conditions are based on the fact that they are key factors in the immunopathogenesis of a number of conditions and diseases, including infectious and non-infectious, while predetermining the outcome of the condition [1,8,12,15].

The purpose of this study was to study the features of the nonspecific link of immunity, i.e. markers of immunological inflammation in women after cesarean section using intrauterine contraception. For comparison, a group of women after a caesarean section without contraception was used. That is, we studied humoral protection factors, which are formed into inflammatory markers during surgery. Despite a significant deepening in the last decade of ideas in immunopathogenesis, many processes related to the mechanisms of the development of the inflammatory process and its progression remain open. In recent years, more and more data have been accumulating on the importance of immunological mechanisms in the development of one pathology or another. For the implementation of immunological studies, the material was the peripheral venous blood of women, which was taken 5-6 days after the operative delivery. We have described some cytokines of the immune system, which are not described in the literature for obstetric interventions, and are important in the development of inflammatory processes, especially in the processes of subclinical inflammation, which is observed with intrauterine contraception.

MATERIAL AND RESEARCH METHODS.

A total of 28 women with intrauterine contraception after childbirth and 38 women without contraception were examined. The age of the women ranged from 22 to 34 years. Peripheral blood for immunological studies was taken 5-6 days before discharge. Immunological examination included the study of the main immunity cytokines responsible for the development and outcome of inflammatory processes. Were investigated two cytokines with pro-inflammatory properties, the studies were carried out by enzyme immunoassay using commercial test systems "Vector-Best", Russia, Novosibirsk, 2017-2018. It is known that the test systems are based on the sandwich method of enzyme-linked immunosorbent assay using horseradish peroxidase as an indicator enzyme. The quantitative assessment of the results was carried out using an Excel 2014 program, reflecting the dependence of optical density on concentration for a standard antigen. The sensitivity of the method when using these test systems is 2-30 pg / ml. The determination of IL-1 Beta and IL-8 was carried out with kits, which are a set, the main reagents of which are MCABs to the studied cytokines, sorbed on the surface of the wells of a collapsible polystyrene plate. The kits are designed for the quantitative determination of human cytokines in peripheral blood serum and biological fluids. The measurement of optical density in each well was carried out using an automatic photometer for a microplate at a wavelength of 450 nm by enzyme immunoassay on a Stat-Fax analyzer (USA). Kits of reagents produced by "Vector-Best", Novosibirsk (RF).

Determination of circulating immune complexes of various sizes (CIC) by ELISA analysis on a Stat-Fax analyzer (USA) was carried out in the laboratory of immunocytokines of the Institute of Immunology of the Academy of Sciences of the Republic of Uzbekistan. CIC sizes were determined using different PEG concentrations. Low concentrations of PEG precipitate large ones with a predominance of antigen, while high concentrations precipitate

small CICs with a predominant content of antibodies. Statistical analysis was carried out: anamnestic, clinical, laboratory and instrumental data were thoroughly analyzed. The obtained digital results were processed by the method of variation statistics. The arithmetic mean (M), error cf. (s) were counted on a computer using the statistical program Microsoft Excel, version 5.

THE RESULTS OBTAINED AND DISCUSSION.

We have analyzed serum concentrations of the main cytokines IL-1 beta and IL-8 in women, as well as circulating immune complexes of large and small values in women after cesarean section, which are markers of immune inflammation. For these purposes, we studied the state of nonspecific immunity in women after surgical delivery. Further, comparative studies were conducted to study nonspecific immunity in women, depending on the presence and without an intrauterine contraceptive.

Table 1.
The state of humoral immunity in women after surgical delivery, $M \pm m$, pg / ml, U

Groups of examined	IL-1 Beta	IL-8	CIC3%	CIC4%
Women after cesarean section	7,45±0,54*	12,6±1,71*	11,9±0,52*	16,5±1,24
Women with physiological delivery	4,35±0,14	8,22±0,62	7,4±0,40	14,4±0,91

Note: * - reliability of differences with control data.

Table 1 shows the differences in the state of the systemic humoral immune system in women with different deliveries. Thus, in the group of women after cesarean section, there is a significant increase in the peripheral blood serum of IL-1 beta, IL-8 and CIC3% of large values. Moreover, IL-1 Beta increased 1.7 times, IL-8 - 1.5 times, and CIC3% - 1.6 times compared with the data of women with physiological delivery ($p < 0.05$). It follows that the markers of the nonspecific immune system were significantly increased when compared with the data of the norm. Moreover, it should be noted that such an increase most likely indicates the activation of compensatory, and not pathological changes. This is evidenced by the lack of subjective and objective data of women about the presence of any inflammatory or purulent processes. Moreover, it is known that it is IL-1 and IL-8 that are the most key and immediate mediators of immunity, the immediate reaction of which activates the body's defenses.

A few words about cytokines and circulating immune complexes. Cytokines are considered as low molecular weight proteins that are produced by cells of various types and are mediators of intercellular interactions in the immune response. Being closely interconnected, they form a single and integral system - a cytokine network, these are pro- and anti-inflammatory cytokines that are actively involved in the formation and progression of compensatory and protective states [15]. We have studied the serum concentrations of pro-inflammatory cytokines (IL-1 β , IL-8). Of particular interest is the study of the ratio of cytokines, especially proinflammatory, which have various protective properties. So, for us,

the most diagnostic and prognostic ratio was the ratio between IL-1 β / IL-8. Therefore, the IL-1Beta / IL-8 ratio was 0.4 in the norm. Whereas, in the group of women after cesarean section 0.7. Such a difference is more indicative not of the development of the inflammatory process, but more of the activation of the compensatory abilities of the body.

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It should be noted that IL-1 β is a key proinflammatory cytokine produced by macrophages and phagocytes. IL-1 β initiates and regulates protective and inflammatory, immune processes, activates neutrophils, T - and B - lymphocytes, stimulates the synthesis of acute phase proteins, cytokines [13,14,16]. It is for IL-1 β that the triggering of the reaction of the inflammatory-regulatory cascade is characteristic, as well as the stimulation of macrophages and the synthesis of other cytokines that play an important role in the mechanisms of compensation and inflammation. Thus, an increase in IL-1 β during cesarean delivery plays a positive role. Moreover, we did not observe a pronounced overproduction of IL-1 β and symptoms of inflammation. Interleukin-8 (IL-8) is one of the smallest cytokines. The main producers of IL-8 are monocytes, macrophages, but other cells can also produce it: neutrophils, T-lymphocytes, natural killer cells, endothelial cells, fibroblasts [6,12,16]. IL-8 is one of the stimulators of angiogenesis [14,15]. As mentioned above, we did not reveal an excessively high level of IL-8, which basically indicates the possibility of the occurrence of undesirable immunopathological processes that contribute to the development of oxidative stress and inflammation.

The following describes one of the most important humoral markers of immunity, circulating immune complexes. They are diagnosed in two sizes, these are large and small. It has been established that one of the most important biological functions of immunoglobulins is antigen binding and the formation of circulating immune complexes (CIC) [12, 14]. An important characteristic of the CIC is their size, which indicates the different functions of the CIC. As you know, their main function is to attach antigens and form complexes, which should normally be decomposed by phagocytosis. So, the CIC of large values disintegrates rather quickly and does not form a pathological process. But the CIC of small values contributes to the formation of pathological processes, settling on tissues and organs, thereby forming pathological inflammatory foci.

Thus we found that the average value of large CICs in women after cesarean section was 1.6 times higher than the norm. In the CIC, small ones were not promoted and had practically no difference. Moreover, large CICs were also within the normative values. Consequently, we

also observed not pathological changes, but most likely compensatory changes in the state of humoral immunity factors in women after surgical delivery. The data obtained are presented in table 1.

Thus, the study of the state of humoral immunity in women after surgical delivery revealed a slight but significant increase in IL-1 beta by 1.7 times and IL-8 by 1.5 times and CIC3% of large values by 1.6 times. These markers, being humoral markers of immunity, indicate the activation of the compensatory protective capabilities of the body, in particular, the immune system. The diagnostic and prognostic criterion was the IL-1 β / IL-8 ratio, which was 0.4 in none, and 0.7 in women with operative delivery, which again indicates a slight increase in IL-1, which is a key mediator. inflammation, and helps to activate the organism's defenses.

We have analyzed the serum concentrations of the main cytokines IL-1 beta and IL-8 in women, as well as circulating immune complexes of large and small values in women after cesarean section who underwent intrauterine contraception. For these purposes, we also studied the state of humoral immunity in women after operative delivery with postplantar intrauterine contraception. Thus, Table 2 presents the differences in the state of the systemic humoral immune system in women with and without intrauterine contraception.

Table 2.

The state of humoral immunity in women after surgical delivery with intrauterine contraception, M \pm m, pg / ml, U

Groups of examined	IL-1 Beta	IL-8	CIC3%	CIC4%
Women after cesarean section (control)	7,45 \pm 0,54	12,7 \pm 1,5	11,9 \pm 0,55	14,5 \pm 1,25
Women after cesarean section with postplantation intrauterine contraception	6,42 \pm 0,11	15,68 \pm 0,92*	9,8 \pm 0,65	11,45 \pm 0,99

Note: * - reliability of differences with control data.

The analysis showed that women after cesarean section with postplantar intrauterine contraception did not reveal significant differences in the content of IL-1 beta in the peripheral blood serum. As for IL-8, we found a slight, but significant increase in serum in this group of women, which once again indicates the activation of local compensation against the background of the introduction of intrauterine contraception. Thus, the level of IL-8 was increased in this group of women by 1.2 times compared with those of women without contraception, which had a significant difference from the control data.

The values of circulating immune complexes of large and small values were within the normative values, which indicates the absence of any pronounced inflammatory purulent processes. Consequently, no pronounced changes on the part of humoral immunity factors were revealed, which indicates the absence of pronounced inflammatory processes that develop against the background of postplantar intrauterine contraception. As you can see, against the background of intrauterine contraception, no pathogenetically expressed

inflammatory changes were revealed. When compared with the clinical data of women, they do not make any complaints about the presence of inflammatory processes.

It is known that proinflammatory cytokines are actively involved in the immune response; their amounts are in a certain equilibrium. The literature indicates that the correct point of this balance is a condition for the successful suppression of pathogens and the subsequent "shutdown" of a specific immune response. Violation of this balance can lead to severe pathological consequences, since either the immune system is unable to suppress the pathogens, or after suppression the immune response continues. In particular, a significant excess of pro-inflammatory cytokines can also lead to chronic inflammation [6,7,9,10].

Thus, the study of the state of humoral immunity in women after surgical delivery revealed a slight increase in IL-8 by 1.2 times. At the same time, the values of circulating immune complexes remained within the normal range. As you can see, the insignificant changes that we identified indicate the activation of the compensatory protective capabilities of the organism, which in this situation are manifested by an increase in IL-8, which is a pronounced chemokine of the immune system. The values identified by us can be of a diagnostic and prognostic nature of changes in the immune system. That is, according to the above criteria, it is possible to carry out early diagnosis of pathogenetic immunological changes in women with postpartum intrauterine contraception.

We have studied the serum concentrations of proinflammatory cytokines (IL-1 β , IL-8) and circulating immune complexes that take an active part in the state of acute intervention in the constancy of the organism, and have a pronounced potential of the immune response in the body. As mentioned and described above, IL-1 β is a key proinflammatory cytokine that is produced by macrophages and phagocytes. IL-1 β actively initiates and regulates protective and inflammatory, immune processes, activates neutrophils, T - and B - lymphocytes, stimulates the synthesis of acute phase proteins, cytokines [2,8]. It is for IL-1 β that the triggering of the reaction of the inflammatory-regulatory cascade is characteristic, as well as the stimulation of macrophages and the synthesis of other cytokines that play an important role in the mechanisms of compensation and inflammation. Thus, we found an increase in IL-1 β during cesarean delivery, which most likely played a positive role in the course of women's recovery. In turn, IL-8, being also a pro-inflammatory cytokine produced by macrophages, epithelial and endothelial cells, plays an important role in the innate immune system, while acting as a chemoattractant for innate immune cells. The local action of IL-8 is important, which leads to an increase in the penetration of activated macrophages, which contributes to the compensation and adaptation of the organism, thereby playing a protective function [11].

Of particular interest is the study of the ratio of cytokines, especially proinflammatory, which have various protective properties. So, for us, the most diagnostic and prognostic ratio was the ratio between IL-1 β / IL-8. Therefore, the IL-1 β / IL-8 ratio was 0.4 in the norm. Whereas, in the group of women after cesarean section 0.7. Such a difference is more indicative not of the development of the inflammatory process, but more of the activation of the compensatory abilities of the body.

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Consequently, postplantar intrauterine contraception leads to certain changes in the balance of immunity mediators, which, of course, should be proportional to its severity. The complex of changes in cytokines and complexes identified by us is associated with a slight imbalance in the production of pro-inflammatory cytokines, and can be considered as a compensatory-adaptive reaction of the body.

It is known that cytokines are pleiotropic mediators with a wide range of biological activity, which is produced by both lymphoid and non-lymphoid cells of the body. The data we have obtained only contribute to the understanding that with insignificant values of cytokines, activation of the humoral link of immunity is observed, which in turn spurs on the cellular factors of immunity, thereby contributing to the activation of all the body's defenses. Consequently, our data have not only diagnostic, but also prognostic value in determining the studied cytokines. And of course, it should be noted that the cytokine spectrum is an integral indicator, the determination and analysis of which is necessary for understanding clinical and laboratory markers.

CONCLUSIONS

1. The state of the humoral link of the immune system of women with cesarean section was characterized by a slight increase in the key cytokine IL-1 beta by 1.7 times, IL-8 by 1.5 times, CIC3% of large values by 1.6 times, which indicates activation of compensatory and adaptive mechanisms of immunity. The IL-1 / IL-8 ratio was 0.7, which is also due to the compensatory activation of humoral immunity factors.
2. In women with postplantar administration of intrauterine contraceptive, a slight increase in IL-8 is observed, indicating an immune response against the background of the introduction of contraception. The values of IL-1 beta and circulating immune complexes remain within normal limits.

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