POSSIBILITIES OF CORRECTING CELLULAR-HUMORAL IMMUNE DISORDERS AND CYTOKINE STATUS IN HIGH-RISK PREGNANT WOMEN FOR THE DEVELOPMENT OF PREECLAMPSIA

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Summary

The development of pre-eclampsia is associated with immunological interactions between the foreign maternal and fetal tissues, which are characterized by a predominance of the influence of type 1 T-helper cells, leading to increased production of highly aggressive pro-inflammatory cytokines. However, the mechanism of cellular-humoral immune and cytokine changes leading to the manifestation of pre-eclampsia is not fully understood and no corrective measures have been developed.

Purpose. *To investigate the changes in the cellular-humoral immunity and cytokine profile in a cervical mucus of pregnant women at high risk for developing PE and to find out the effectiveness of the proposed secondary prevention of PE in the normalization of these indicators.*

Method and Materials. *The main group (MG) consisted of 91 pregnant women with risk factors for pre-eclampsia who had impaired blood flow in the uterine spiral arteries at 18-20 weeks of pregnancy. Among them, 59 patients (MG-II) received secondary prevention of pre-eclampsia from 18-20 weeks until delivery using metformin, vitamin D3, and corvitin, while the remaining 32 patients (MG-I) declined preventive measures. The control group (CG) consisted of 30 healthy pregnant women.*

The research was regulated by the rules of humane treatment of patients in accordance with the requirements of the Tokyo Declaration of the World Medical Association, the international recommendations of the Helsinki Declaration on Human Rights, the Convention of the Council of Europe on Human Rights and Biomedicine, and the laws of Ukraine.

TNF-α, INFγ and IL-10 levels were determined in cervical mucus by enzyme-linked immunosorbent assay (ELISA); peripheral blood lymphocyte CD3+, CD4+, CD8+, CD16+, CD22+ levels were assessed by indirect immunofluorescence. The CD4/CD8 ratio was calculated as an immunoregulatory index. Blood serum immunoglobulin (Ig) levels were determined by competitive enzyme-linked immunosorbent assay (A, M, and G). The concentration of circulating immune complexes (CIC) in blood serum was measured by the immunoturbidimetric assay.

The data were analyzed by mathematical-statistical methods, calculating the mean (M), variance (σ), and standard error (m), applying Student's t-test, and performing correlation analysis using the statistical program «STATISTICA» (StatSoft Inc., USA).

The paper is an excerpt from the initiative scientific research project of the Department of Obstetrics and Gynecology № 2 of the Poltava State Medical University entitled «Optimization of approaches to management of pregnancy in women at high risk of obstetric and perinatal pathology» (state registration number 0122U201228, duration: 10.2022-09.2027).

Results. *In women at high risk of developing pre-eclampsia (MG-I), a significant decrease in the concentration of T helper cells (CD4+), an increase in T suppressor/killer cells (CD8+), a decrease in the immunoregulatory index, a decrease in B cells (CD22+) and an increase in CIC were observed. In addition, CIC greater than 100 IU/ml strongly correlated with the development of pre-eclampsia. IgM levels were significantly elevated in women with pre-eclampsia, indicating possible trophoblastic stimulation of their immune system, while IgG levels were significantly reduced. Women with pre-eclampsia had a significant predominance of pro-inflammatory cytokines and a deficiency of anti-inflammatory cytokines. In women of the MG-II group who received the proposed complex of secondary prevention of pre-eclampsia, the content of T-helper cells (CD4+) and T-suppressor/killer cells (CD8+) was normalized. The immunoregulatory index increased significantly, and the number of CD22+ cells was about the level observed in healthy pregnant women. The concentrations of IgA and IgG increased to the levels observed in the control group, while the level of IgM decreased. The level of CIC decreased in pregnant women with MG-II, in contrast to the levels observed in women with MG-I. The levels of pro-inflammatory cytokines INF-γ and TNF-α decreased after preventive treatment. However, the levels of the anti-inflammatory cytokine IL-10 increased significantly in MG-II, leading to a significant reduction in the TNF-α/IL-10 ratio (p<0.001).*

Conclusions. *Pregnant women with a history of increased risk factors for PE and a decrease in the intensity of blood flow in the spiral arteries of the uterus at 18-20 weeks of gestation have a pronounced imbalance of the T-cell subpopulation, which is accompanied by a decrease in the production of T-helpers (CD4+) and an increase in the synthesis of T-suppressors/killers (CD8+), which causes a decrease in the immunoregulatory index. This is accompanied by the development of a cytokine imbalance with a predominance of pro-inflammatory cytokines and a deficiency of anti-inflammatory cytokines, and is also associated with a significant decrease in the concentration of IgG and a decrease in the number of B cells. Such changes are a consequence of the exhaustion of the reactivity of the humoral link of the general immunity, creating the conditions for the frequent manifestation of PE, which occurs in almost half of such women. The application of our proposed improved method of secondary prevention of pulmonary embolism in pregnant women with a high risk of developing this disease leads to significant positive changes in the work of the immune system and a corresponding improvement in clinical results. It makes it possible to reduce the frequency of PE development by 1.4 times and to prevent the occurrence of its severe forms by 2.6 times.*

Key words: *Preeclampsia; Cellular-humoral Immunity; Cytokines.*

Introduction

Despite the long-standing concern of researchers on the problem of pre-eclampsia (PE), this pathology continues to occupy a prominent position in the structure of perinatal and maternal morbidity and mortality, and its pathogenesis is not fully understood [1-4]. Therefore, obstetrics still

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lacks an effective treatment and prevention scheme for this disease [5-7].

Nowadays, one of the most accepted theories regarding the development of PE is the one that links the pathogenic processes of its development to the improper transformation of spiral vessels during the replacement of their endothelium by trophoblast cells [8-10]. In this case, the vascular endothelium remains sensitive to the action of numerous pressor factors, and a high-resistance blood flow prone to vasospasm is formed in the uteroplacental complex [11-15]. Immunological factors and changes in cytokine balance play an important role in this process [16-18].

During physiological pregnancy, trophoblast cells, which are foreign to the mother's body, initiate a series of immunological reactions, during which the level of production of proinflammatory cytokines of the Th1 type by monocytes decreases [19-21] and, on the contrary, the production of Th2 cytokines increases [16-22].

It is believed that the development of PE is associated with immunologic interactions between the foreign maternal and fetal tissues, with a predominant influence of type 1 T-helper cells, leading to increased production of highly aggressive pro-inflammatory cytokines [22]. However, the specific factors that initiate the switch in the immune response are still unknown. There is no formulated unified mechanism for the complex cellular-humoral immune and cytokine changes that lead to the manifestation of PE, nor are there reliable markers or predictors of these changes, nor have corrective measures been developed. Therefore, there is an urgent need for further investigation into the clinical and immunological mechanisms underlying the development of PE.

Purpose. To investigate the changes in the cellular-humoral immunity and cytokine profile in a cervical mucus of pregnant women at high risk for developing PE and to find out the effectiveness of the proposed secondary prevention of PE in the normalization of these indicators.

Method and Materials. We studied the cellular-humoral immunity and cytokine status in 121 pregnant women at 28-32 weeks of gestation. The main group (MG) consisted of 91 pregnant women with risk factors for the development of pulmonary embolism based on their medical history. The Doppler ultrasound performed at 18-20 weeks of pregnancy showed slow blood flow in the uterine spiral arteries. The MG patients were divided into two subgroups: 32 patients (MG-I) who declined our proposed secondary prevention of PE [7], and the other 59 patients (MG-II) who received enhanced secondary prevention of pre-eclampsia from 18-20 weeks of pregnancy until delivery, using metformin at a dose of 2000 mg/day, vitamin D3 at a dose of 4000 IU/day, and corvitin administered by 10-day monthly courses of intravenous infusions at a dose of 500 mg/day. The control group (CG) consisted of 30 healthy pregnant women with no risk factors for pulmonary embolism and no impairment of blood flow in the uterine spiral arteries.

The research was conducted in accordance with the rules of humanitarian treatment of patients, the provisions of the Tokyo Declaration of the World Medical Association, the requirements of the international recommendations of the Helsinki Declaration of Human Rights, the Convention of the Council of Europe on Human Rights and Biomedicine, the laws of Ukraine, and the requirements of the Ethical Code of Ukrainian Physicians.

At 28-34 weeks of gestation, the levels of pro- and anti-inflammatory cytokines (TNF-α, INFγ, IL-10) in cervical mucus were determined by enzyme-linked immunosorbent assay (ELISA) using standard commercial kits from Vector BEST. Rates of cellular-humoral immunity were determined in blood samples. Lymphocyte phenotyping in peripheral blood was carried out by indirect immunofluorescence using commercial erythrocyte diagnostic kits for CD3+, CD4+, CD8+, CD16+, CD22+ antibody classes from Granum, RPL, LTD (Ukraine, Kharkiv). At present, monoclonal antibodies (MAb) of CD3+ class are considered to characterize the total population of T lymphocytes, CD4+ for T helper/inducer population, CD8+ for T suppressor/killer population, CD22+ for B cells. The immunoregulatory index CD4/CD8 was calculated, which indicates the ratio of lymphocytes with helper and suppressor activity. The functional activity of T lymphocytes was assessed using the lymphocyte blast transformation reaction (LBTR) with phytohemagglutinin (PHA) as a non-specific mitogen. [19]. Serum immunoglobulin (Ig) levels were determined using a test system based on the principle of competitive enzyme-linked immunosorbent assay (ELISA) with immobilized antigens (A, M and G) and [20]. The concentration of circulating immune complexes (CIC) in blood serum was determined by the method of immunoturbidimetric analysis (reagent kit of «CIC-HEMA» company).

The obtained data were processed using methods of mathematical statistics, calculating the mean (M), variance (σ), standard errors of the mean (m), applying the Student's t-test and correlation analysis using the statistical software «STATISTICA» (StatSoft Inc., USA).

The paper is an excerpt from the initiative scientific research project of the Department of Obstetrics and Gynecology #2 of the Poltava State Medical University entitled «Optimization of approaches to management of pregnancy in women at high risk of obstetric and perinatal pathology» (state registration number 0122U201228, duration: 10.2022-09.2027) [1].

Results and Discussion

The concentration of leukocytes in the blood of women with MG-I (total) was $6.3\pm0.3*10^9$/L and did not differ significantly from the values in women with MG-I with PE or from the values in CG. The absolute lymphocyte count in all patients in MG-I was $1.7 \pm 0.05*10^9$/L (p<0.05), which was almost similar to the values of this indicator in healthy pregnant women. The absolute number of T lymphocytes (CD3+) was $1.0 \pm 0.04*10^9$/L (p<0.05), with a tendency to decrease compared to control values.

Among T cells, a decrease in the number of T helper cells was observed in women with MG-I (overall) with $0.50 \pm 0.03*10^9$/L (p > 0.05) and in patients with MG-I with PE ($0.40 \pm 0.02*10^9$/L (p < 0.001). In healthy pregnant women this indicator was $0.58 \pm 0.03*10^9$/L. However,

the number of T-suppressor/killer cells increased in MG-I, especially in women with PE ($0.48 \pm 0.05 * 10^9$/L). At the same time, the values in healthy women were 0.37 ± 0.02 per 10^9/L (p <0.05).

The immunoregulatory index, i.e. the ratio of CD4+ to CD8+ cells, was significantly decreased in women with MG-I. In patients with PE from this group it was 0.83 ± 0.07 compared to 1.56 ± 0.10 in healthy pregnant women (p <0.001).

We also observed a decrease in the absolute number of CD22+ cells in patients with MG-I, which was $0.60 \pm 0.02 * 109$/L in the whole group (p <0.05) and $0.57 \pm 0.04 * 109$/L (p <0.050) in women with PE. In pregnant women in the control group, the value was $0.68 \pm 0.03 * 109$/L.

Apparently, patients with MG-I who did not receive the proposed treatment experienced a significant decrease in T-helper cells (CD4+) along with a significant increase in the concentration of T-suppressor/killer cells (CD8+). This led to a decrease in the immunoregulatory index, a decrease in the number of B cells (CD22+) and a tendency toward a decrease in the absolute number of T lymphocytes (CD3+). Pre-eclampsia occurred in 43.8 % of the cases in the women of this group.

The concentration of IgA tended to decrease in MG-I (1.89 ± 0.04 g/L vs. 2.08 ± 0.11 g/L in CG; p >0.1) compared to control values. IgM levels in women with PE of MG-I were significantly elevated (1.66 ± 0.03 g/L vs. 1.49 ± 0.06 g/L in CG; p <0.02), indicating trophoblastic stimulation of the immune system in these women [14]. IgG levels were significantly reduced both in the total MG-I (11.06 ± 0.3 g/L compared to the normal range of 13.97 ± 0.4 g/L; p <0.001) and in pregnant women with PE (9.28 ± 0.4 g/L; p <0.001). The decrease in IgG concentration correlated with a decrease in B lymphocytes (CD22+) both in the MG-I as a whole (r=0.47; p <0.05) and in patients in this group who developed PE (r=0.58; p <0.01).

It should be noted that in healthy pregnant women, the concentration of IgG in blood serum increases. This is associated with increased synthesis. In women with PE, we observed a significant decrease in Ig G. We hypothesize that this decrease is caused by exhaustion of the reactivity of the humoral part of the general immune system in PE [17].

We also observed an increase in CIC in MG-I (95.5 ± 4.6 IU/ml compared to the normal range of 84.1 ± 3.5 IU/ml; p <0.05), especially in pregnant women with PE (103.7 ± 5.1 IU/ml). An increase in CIC above 100 IU/ml was associated with the development of PE (r=0.76, p<0.05).

Significant increases in pro-inflammatory cytokine levels, particularly INF-γ and TNF-α, were also observed in patients in the above group. At this time point, the level of INF-γ in cervical mucus in women with MG-I was 13.06 ± 0.70 pg/mL compared to 10.42 ± 0.51 pg/mL in the control group (p <0.01), and the concentration of TNF-α in MG-I was 7.05 ± 0.54 pg/mL compared to 3.40 ± 0.24 pg/mL in the control group (p < 0.001). In women with PE of MG-I, the level of pro-inflammatory cytokines was significantly increased not only compared to women in the control group but also compared to the total group of pregnant women of MG-I (INF-γ was 15.80 ± 0.85 pg/ml; TNF-α was 8.79 ± 0.48 pg/ml).

In contrast to the increased levels of pro-inflammatory cytokines, the concentration of the anti-inflammatory cytokine IL-10 was significantly decreased in the studied pregnant women. It was 4.90 ± 0.25 pg/ml in women with PE compared to 9.56 ± 0.63 pg/ml in the control group and 6.14 ± 0.19 pg/ml overall in the MG-I (p<0.001). This indicates immunosuppression in pregnant women with PE, which likely contributes to the inability of trophoblast cells to fully invade the uterine spiral arteries, leading to the development of endothelial dysfunction.

The changes in the levels of pro- and anti-inflammatory cytokines caused the increase in the TNF-α/IL-10 ratio. It was 3.2 times higher in total MG-I (1.15 ± 0.06 vs. 0.36 ± 0.02 in the control group; p <0.001) and 5 times higher in pregnant women with MG-I who developed PE (1.80 ± 0.09; p <0.001 in the same comparison).

We hypothesize that the excessive release of pro-inflammatory cytokines in the presence of deficient anti-inflammatory cytokines, along with increased levels of T-suppressor/killer cells and increased production of IgM, indicates an exaggerated inflammatory response in the maternal organism, likely directed against foreign fetal antigens [16-18]. This response leads to incomplete invasion of trophoblast cells into the spiral arteries of the uterus, resulting in systemic endothelial dysfunction and the development of pre-eclampsia [18-20].

Application of the proposed treatment in women with MG-II contributed to significant improvement in rates of cellular-humoral immunity and cytokine profile. The levels of CD4+ T-helper cells and CD8+ T-suppressor/killer cells in women with MG-II were almost similar to the levels observed in the control group. Despite a slight increase in CD4+ cells in MG-II compared to MG-I, the immunoregulatory index, which was significantly decreased in MG-I women (1.22 ± 0.06 compared to 1.56 ± 0.10 in CG; p <0.02), increased slightly in MG-II and reached 1.35 ± 0.11 (compared to 1.56 ± 0.10 in healthy pregnant women; p >0.1). The increased absolute level of CD22+ in women with MG-I, MG-II was not significantly different from that observed in healthy pregnant women (0.65 ± 0.07).

In MG-II women, the concentration of IgA, which showed a tendency to decrease in MG-I (1.89 ± 0.04 g/L compared to 2.08 ± 0.11 g/L in CG; p >0.1), was 1.97 ± 0.09 g/L, which was not significantly different from the values in healthy pregnant women. The level of IgM in the MG-II women was 1.38 ± 0.07 g/L, which was also not significantly different from the control values (p>0.1). The level of IgG, which was significantly lower in untreated women (11.06 ± 0.3 g/L compared to the normal range of 13.97 ± 0.4 g/L; p <0.001), increased to 12.8 ± 0.6 g/L in treated pregnant women of MG-II, which was significantly higher than the level of this immunoglobulin in MG-I, but did not reach the level observed in CG (p <0.01). The concentration of CIC in pregnant women with MG-II was decreasing, in contrast to the levels in women with MG-I (90.4 ± 5.6 IU/ml vs. 95.5 ± 4.6 IU/ml, respectively; p >0.02).

After the preventive treatment, the levels of the pro-inflammatory cytokines INF-γ and TNF-α, which were elevated in patients with MG-I, decreased. The level of INF-γ in cervical mucus was 11.30 ± 0.70 pg/mL in MG-II

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compared to 13.06 ± 0.70 pg/mL in MG-I (p <0.02), and the amount of TNF-α was 4.04 ± 0.82 pg/mL in MG-II compared to 7.05 ± 0.54 pg/mL in MG-I (p <0.001). On the contrary, the concentration of the anti-inflammatory cytokine IL-10 increased significantly in MG-II, reaching 8.93 ± 0.54 pg/ml, compared to 6.14 ± 0.19 pg/ml in pregnant women of MG-I (p<0.001). The TNF-α/IL-10 ratio was significantly decreased in MG-II compared to MG-I (0.45 ± 0.10 vs. 1.15 ± 0.06; p <0.001).

Thus, in contrast to the suppression of cellular-humoral immunity and the imbalance of pro- and anti-inflammatory cytokines observed in women who did not receive the improved prevention of the development of PE proposed by us, in the group of pregnant women who received it, we noted an improvement in indicators of immunity and their normalization to levels typical of healthy pregnant women. This was associated with a more favorable course of pregnancy. Thus, the improved approach to the prevention of the occurrence of PE made it possible to reduce the frequency of the development of PE by 1.4 times. The frequency of severe pulmonary embolism in women who received the proposed complex of preventive measures decreased by 2.6 times compared to the frequency of severe forms of this complication in patients who did not receive the indicated treatment.

Conclusions:

1. Pregnant women with a history of increased risk factors for PE and a decrease in the intensity of blood flow in the spiral arteries of the uterus at 18-20 weeks of gestation have a pronounced imbalance of the T-cell subpopulation, which is accompanied by a decrease in the production of T-helpers (CD4+) and an increase in the synthesis of T-suppressors/killers (CD8+), which causes a decrease in the immunoregulatory index. This is accompanied by the development of a cytokine imbalance with a predominance of pro-inflammatory cytokines and a deficiency of anti-inflammatory cytokines, and is also associated with a significant decrease in the concentration of IgG and a decrease in the number of B cells. Such changes are a consequence of the exhaustion of the reactivity of the humoral link of the general immunity, creating the conditions for the frequent manifestation of PE, which occurs in almost half of such women.

2. The application of our proposed improved method of secondary prevention of pulmonary embolism in pregnant women with a high risk of developing this disease leads to significant positive changes in the work of the immune system and a corresponding improvement in clinical results. It makes it possible to reduce the frequency of PE development by 1.4 times and to prevent the occurrence of its severe forms by 2.6 times.

Prospects for further research. The identified features of immunosuppressive mechanisms in pregnant women with PE call for further research to investigate alterations in nitric oxide metabolism in this patient population.

Conflict of Interests. The authors have no conflicts of interest to declare.

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МОЖЛИВОСТІ КОРЕКЦІЇ ПОРУШЕНЬ КЛІТИННО-ГУМОРАЛЬНОГО ІМУНІТЕТУ ТА ЦИТОКІНОВОГО СТАТУСУ У ВАГІТНИХ ГРУПИ ВИСОКОГО РИЗИКУ ПО ВИНИКНЕННЮ ПРЕЕКЛАМПСІЇ

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Резюме.

Розвиток прееклампсії пов'язаній з імунологічними відносинами між чужорідними тканинами матері та плоду, які перебігають з превалюванням впливу Т-хелперів 1 типу, внаслідок чого зростає вироблення високоагресивних прозапальних цитокінів. Однак досі не вивчений механізм клітинно-гуморальних імунних та цитокінових змін, що приводять до маніфестації прееклампсії, не розроблені засоби її корекції.

Мета дослідження. Дослідити зміни клітинно-гуморального імунітету та цитокінового профілю у цервікальному слизі вагітних з високим ризиком розвитку ПЕ та з'ясувати ефективність запропонованої вторинної профілактики ПЕ у нормалізації цих показників.

Матеріал та методи дослідження. Основну групу (ОГ) склали 91 вагітна з наявністю факторів ризику прееклампсії, які в 18-20 тижнів вагітності мали сповільнений кровотоку в басейні спіральних артерій матки. 59 пацієнток (ОГ-ІІ) з 18-20 тижнів до розродження отримували вторинну профілактику прееклампсії з використанням метформіну, вітаміну D3 та корвітину; інші 32 пацієнтки (ОГ-І) відмовились від профілактики. Контрольну групу (КГ) склали 30 здорових вагітних.

Дослідження регламентувалися Правилами гуманного ставлення до пацієнта згідно з вимогами Токійської декларації Всесвітньої медичної асоціації, Міжнародними рекомендаціями Гельсінської декларації з прав людини, Конвенцією Ради Європи щодо прав людини і біомедицини, Законами України.

Визначали: TNF-α, INFγ, ІЛ-10 у цервікальному слизі за допомогою імуноферментного аналізу; рівень лімфоцитів периферичної крові класів CD3+, CD4+, CD8+, CD16+, CD22+ методом непрямої імунофлуоресценції з розрахнком імунорегуляторного індекск CD4/CD8; рівень сироваткових імуноглобулінів (Ig) методом імуноферментного аналізу; сироватковий рівень циркулюючих імунних комплексів (ЦІК) методом імунного турбометричного аналізу.

Дані обробляли шляхом розрахунку середніх вибіркових значень (М), дисперсії (σ) та помилок середніх значень (m), з оцінкою критерію Ст'юдента та проведенням кореляційного аналізу за допомогою статистичної програми «STATISTICA» («StatSoft Inc.», США).

Стаття виконана як фрагмент ініціативної науково-дослідної роботи, яка проводиться співробітниками кафедри акушерства та гінекології № 2 Полтавського державного медичного університету «Оптимізація підходів до ведення вагітності у жінок груп високого ризику по виникненню акушерської та перинатальної патології» (№ держреєстрації 0122U201228, термін виконання 10.2022-09.2027).

Результати дослідження. У жінок з високим ризиком розвитку прееклампсії (ОГ-І) виявлене зменшення рівнів Т-хелперів (CD4+), підвищення кількості Т-супресорів/кілерів (CD8+), зниження імунорегуляторного індексу, зменшення кількості В-клітин (CD22+) та зростання ЦІК. При цьому сироватковий рівень ЦІК, що перевищував 100 од/мл, був тісно пов'язаний з розвитком прееклампсії. У пацієнток з прееклампсією достовірно зростала концентрація IgM зменшувалася кількість IgG, що може бути пов'язаним з трофобластичною стимуляцією імунної системи цих пацієнток. Окрім цього, знайдені зрушення балансу цитокінів цервікального слизу, що проявляються значним домінуванням прозапальних цитокінів при недостатку протизапальних. У жінок ОГ-ІІ після застосування запропонованого комплексу вторинної профілактики прееклампсії нормалізовувався вміст Т-хелперів

(CD4+) та Т-супресорів/кілерів (CD8+); достовірно збільшився імунорегуляторний індекс, кількість CD22+ наближалася до значень у здорових вагітних. Концентрація IgA та IgG підвищувалася до рівня, притаманних контрольній групі. Зменшувався рівень Ig M. Кількість ЦІК у вагітних ОГ-II знижувалася, на відміну від показників у жінок ОГ-I. Рівні цитокінів INF-γ та TNF-α після проведеного профілактичного лікування, знижувалися. Натомість концентрація протизапального цитокіну IL-10 в ОГ-II достовірно зростала, що призвело до достовірного зниження коефіцієнту TNF-α/IL-10 (p<0,001).

Висновки. Вагітні з факторами підвищеного ризику ПЕ в анамнезі і зниженням інтенсивності кровоплину в спіральних артеріях матки в 18-20 тижневому терміні гестації мають виражений дисбаланс субпопуляції Т-клітин, що супроводжується зниженням вироблення Т-хелперів (CD4+) і підвищенням синтезу Т-супресорів/кілерів (CD8+), що викликає зменшення імунорегуляторного індексу. Це супроводжуються розвитком цитокінового дисбалансу з превалюванням прозапальних і дефіцитом протизапальнихцитокінів, а також поєднується з суттєвим падінням концентрації IgG і зниженням кількості В-клітин. Такі зміни є наслідком виснаження реактивності гуморальної ланки загального імунітету і створюють передумови для частої маніфестації ПЕ, притаманної таким жінкам майже в половині випадків. Застосування запропонованого нами удосконаленого методу вторинної профілактики виникнення ПЕ у вагітних з високим ризиком розвитку цього захворювання призводить до позитивних змін у роботі системи імунітету і відповідного покращення клінічних наслідків. Воно дає змогу в 1,4 рази знизити частоту розвитку ПЕ і в 2,6 рази профілактує виникнення тяжких її форм.

Ключові слова: пре еклампсія; клітинно-гуморальний імунітет; цитокіни.

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