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RISK PREDICTION AND PREVENTION OF POSTPARTUM ENDOMETRITIS IN MATERNITY PATIENTS

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ABSTRACT

The article presents the results of a prospective cohort study, which included 26 pregnant women at high risk of infection, who in the postpartum period were divided into 2 groups: I – the main (n=14) and II – the comparison group (n=12). The groups were comparable in age, according to somatic and obstetric-gynecological anamnesis. The comprehensive examination included an assessment of anamnestic data and the results of clinical, microbiological, and instrumental research methods.

KEYWORDS

Intrauterine infection, postpartum endometritis, antibiotic prophylaxis.

INTRODUCTION

To date, numerous foreign and domestic studies have proven the role of infectious pathology of a woman's reproductive tract in the genesis of a large range of obstetric complications. Causing local and systemic inflammatory responses, infectious agents can cause

termination of pregnancy at any time, formation of placental insufficiency, pathology of the fetus and newborn. At the same time, if earlier, when studying this problem, issues related to the infectious pathology of the lower genitals were mainly discussed, today

there are more and more reports about the role of intrauterine infection (IUI) in the genesis of premature birth and unfavorable perinatal outcomes [2, 4, 5]. The implementation of IUI in pregnant women may be a consequence of ascending infection with the presence of infection of the lower reproductive tract, as well as the persistence of microorganisms in the endometrium in women with a history of chronic endometritis [1, 3]. Considering that accurate verification of IUI is possible only with a pathomorphological examination of the afterbirth, there is currently no consensus on the terminology, diagnostic criteria and management tactics of such patients. The search continues for non-invasive criteria for the diagnosis of IUI during pregnancy in order to timely prescribe therapeutic and preventive measures.

It is known that the dynamics of development, the severity and consequences of any infectious process caused by pathogenic or opportunistic microorganisms depend on many factors, the most important of which is the state of the immune system of the macroorganism. The same infectious agents, in some cases cause complications of pregnancy, and in others - practically do not affect its course. Thus, during pregnancy, the reactions of the maternal immune system become no less important than the direct influence of the pathogen. It is the immune mechanisms that play an exceptional role in the development and preservation of pregnancy [3, 5, 6].

The purpose of the study. Reducing the frequency of postpartum endometritis (PE) in women at risk of infection through the development of methods for forecasting and improving preventive measures.

Material and methods of research. A prospective cohort study was conducted, which included 26 pregnant women of high infectious risk, who in the postpartum period were divided into 2 groups: I - the main (n=14) and II - the comparison group (n=12). The groups were comparable in age, according to somatic and obstetric-gynecological anamnesis. The comprehensive examination included an assessment of anamnestic data and the results of clinical, microbiological, and instrumental research methods. The sampling of the material for microbiological examination was carried out at the period of 12-16 weeks of pregnancy. The inclusion criteria were the exacerbation of genital and extragenital diseases of an infectious nature during pregnancy.

In the postpartum period, molded sorbent was administered simultaneously with intravenous administration of an antibiotic to prevent infectious complications of intrauterine delivery. The size of the porous applicator: length 6 cm, width 1 cm, thickness 1 cm. In the comparison group, only traditional antibiotic prophylaxis of postpartum purulent-septic complications was carried out.

Evaluation of the microflora of the birth canal in patients was carried out by polymerase chain reaction (PCR), microbiological examination was carried out

according to the standard method. The material for the study was the vaginal discharge, cervical canal, aspirate from the uterine cavity. The material was collected under aseptic conditions. During the aspirate from the uterine cavity, sterile conductors in the form of a silicone tube were used, eliminating the possibility of contamination of the sample with vaginal and cervical microflora.

The determination of the subpopulation composition of lymphocytes was carried out on a flow cytofluorimeter with sample preparation, and the cytokine content was determined by enzyme immunoassay on test systems.

Statistical processing of the material was carried out using the STATISTICA-6 application software package, standard Microsoft Excel mathematical tables. To characterize the indicators devoted to the retrospective analysis of the birth histories of pregnant women. Fisher's exact criterion was used to select the most informative features.

Research results and discussion. The analysis of gynecological diseases in maternity patients of the infectious risk group showed that inflammatory diseases of the pelvic organs were most common – in 49.6% of those observed; acute vaginitis was noted in 38.5%; cervicitis – in 23.9%; surgical interventions on the fallopian tubes were registered in 8.5%; menstrual disorders – in 7.7%; fibroids uterus – in 3.4%; infertility in the anamnesis occurred in 3.4% of women.

Among the extragenital pathology in this group of patients, anemia prevailed (59.0%); chronic inflammatory diseases of the urinary tract (27.4%); obesity (17.1%); arterial hypertension (10.3%); thyroid pathology (5.1%); diabetes mellitus in 2.6% of cases.

During sonographic examination during pregnancy, the following markers of intrauterine infection were identified: lack of water was diagnosed in 42.9% of cases; violation of fetal-placental blood flow – in 39.5%; polyhydramnios – in 17.9%; thickening of the placenta exceeding the appropriate standards for this period of pregnancy was detected in 15.5%.

The most frequent complication of pregnancy in the observed patients was a recurrent threat of termination (46.7%), which was combined with inflammatory changes in the vagina. In second place in frequency was premature discharge of amniotic fluid (42.7%). Preeclampsia of varying severity occurred in 41.9% of the observed patients, including in combination with fetal growth retardation in 26.5% of cases. Exacerbation of infectious diseases of the urinary tract was noted in 17.9% of pregnant women.

The study of the vaginal biotope in the observed patients at the stage of pregnancy showed the predominance of the following microorganisms: Enterococcus (faecalis, faecium) – 33.9%; E. coli – 27.4%; Staphylococcus (epidermidis, haemolyticus, chromogenes) – 17.4%; yeast-like fungi of the genus Candida – 15.8%; Ureaplasma urealyticum - 12.7%; a combination of pathogens was observed in 83.2%.

Growth of the same pathogens was observed in the cervical canal: *Enterococcus* (*faecalis*, *faecium*) – 28,2%; *E. coli* – 22,5%; *Ureaplasma urealyticum* – 10,3%. Exacerbation of viral infection was noted in 33% of the observed. During the PCR examination of the cervical canal during pregnancy, the following pathogens were identified: Epstein–Barr virus – 17.2%; herpes simplex virus (HSV) type 6 - 8.0%; HSV type 1 – 4.6%; HSV type 2 - 2.3%; cytomegalovirus – 2.3%; rotavirus – 2.3%.

When assessing the immune status in pregnant women, data were obtained indicating the tension of the cellular link of immunity, which manifested itself in a change in the ratio of lymphocytes with a reduced immunoregulatory index ($p=0.0040$) against the background of increased activity of proinflammatory cytokines (interleukin (IL)-1 β). 33% of pregnant women with viral infection activation have a higher level of T-NK cells ($p=0.001$), which in our opinion indicates increased killer activity of lymphoid cells.

All patients underwent rehabilitation of the birth canal with local antiseptics before delivery. In the postpartum period, on the first day, sowing was carried out from the uterine cavity in order to assess the presence of pathogenic microflora. According to the results of primary sowing, the degree of contamination of the uterine cavity was assessed within 24 hours.

The results of the primary seeding of the patient of both groups were comparable: in the main group, massive growth of pathogenic microflora was

determined in 67.3% of cases, moderate – in 26.5%, meager – in 6.1%; in the comparison group, massive growth was determined in 55.9% of cases, moderate – in 27.9%, meager – in 16.2%. At the same time, *Ureaplasma urealyticum* was detected in 29.9% of cases; *Staphylococcus* (*haemolyticus*, *chromogenes*) was detected in 23.1% of cases; *Enterococcus faecalis* was detected in third place in frequency – 16.2%; *E.coli* was 7.7%; *Corynebacterium* – 6.8%; *Mycoplasma hominis* 6.8%; *Enterobacter cloacae* - 2.6%; *Klebsiella* and *Pseudomonas aeruginosa* – 1.7%.

In the main group, monoinfection occurred in 37.5% of cases; in the comparison group – in 36.8%. The most frequently observed associations were *Enterococcus* and *Ureaplasma urealiticum* (12.5%), *Enterococcus* and *Staphylococcus* (8.1%), *Enterococcus* and *Candida* (6.8%), *Enterococcus* and *E. coli* (2.7%).

When conducting tests for antibiotic sensitivity, a high frequency of resistance of pathogenic flora was revealed: *Enterococcus faecalis* in 66.7% of cases showed resistance to azithromycin, in 47.6% – to benzylpenicillin and co-trimoxazole, in 42.8% – to doxycycline. *Staphylococcus haemolyticus* showed resistance to benzylpenicillin in 72.2% of cases, erythromycin in 66.7%, ofloxacin in 55.6% and cefotaxime in 33.3%. *Ureaplasma urealyticum* showed resistance to josamycin in 74.5%, clarithromycin in 29.5%, erythromycin in 22.9% and clindamycin resistance in 14.8%.

Based on the data obtained, a scale for predicting infection risk was developed, based on the calculation of the individual number of points, taking into account the data of anamnesis, sonographic examination, immunoreactivity indicators, both during pregnancy and childbirth, bacteriological examination.

In the postpartum period, the mothers of the main group underwent complex preventive therapy: traditional antibiotic prophylaxis and intrauterine applications of molded sorbent. The sorbent is injected three times into the uterine cavity. The duration of a single application was 24 hours, after which the used sorbent was extracted and a new one was introduced. At the same time, only traditional antibiotic prophylaxis was carried out in the comparison group. Antibiotic prophylaxis in both groups was carried out with cephalosporins of the second generation according to the scheme: 1.0 g of antibiotic intravenously drip once 30 minutes before delivery.

In the maternity patients of the main group, three control seeding was carried out from the uterine cavity after each sorbent was extracted. After the extraction of the first sorbent after 24 hours, 21.7% of patients maintained a massive growth of pathogenic microflora, 43.5% showed moderate and 34.8% showed scant growth of microorganisms. After extraction of the second sorbent, no microflora growth was detected in 52.2% of patients, moderate microflora growth remained in 39.1% and scant microflora growth in 8.7%. In the control of crops after the extraction of

the third sorbent, the growth of microorganisms was not detected in 100% of cases. In the comparison group of maternity patients in the control gravidar endometrial culture, three days after antibiotic prophylaxis, pathogenic microflora continued to be determined in 66.2% of maternity women.

The problem of prevention and treatment of purulent-inflammatory postpartum diseases is complicated by the fact that proinflammatory cytokines accumulating during the inflammatory process in the uterine cavity, as well as toxins secreted by pathogens, lead to disruption of local hemostasis processes, reduced tissue perfusion and to the additional development of tissue hypoxia, complicating the regeneration and epithelialization of the endometrium. In this regard, the level of proinflammatory cytokines and lactoferrin in the aspirate from the uterine cavity was determined. The sampling of the material was carried out before and after the completion of preventive therapy. The volume of the uterine cavity was also assessed, ultrasound examination was performed on the 1st and 3rd days of the postpartum period.

When analyzing the data obtained, there was a significant ($p=0.01172$) decrease in the activity of the acute-phase protein lactoferrin by 1.3 times and the proinflammatory cytokine IL-1 β by 2.3 times ($p=0.01252$) in the aspirate from the uterine cavity in patients of the main group in comparison with similar indicators of the comparison group. Indicators of the number of leukocytes and the leukocyte index of

peripheral blood intoxication after preventive treatment decreased equally in both groups. In the main group, after using the molded sorbent, there was a decrease in the volume of the uterine cavity by 1.2 times, while with the use of traditional antibiotic prophylaxis, there was a decrease in the volume of the uterine cavity by 1.05 times.

CONCLUSIONS

1. In the development of purulent-inflammatory diseases in pregnant women of the infectious risk group, mixed infection is of the greatest importance, in which the leading role in the formation of pathology belongs to the bacterial gram-positive microflora with a high level of antibiotic resistance, as a result of which traditional antibiotic prophylaxis is ineffective.
2. For pregnant women of the infectious risk group, the presence of tension of the immune system due to inflammatory diseases of the genital tract suffered during pregnancy or exacerbation of somatic chronic infectious diseases has been proven.
3. After traditional antibiotic prophylaxis, despite a decrease in leukocytes and leukocyte intoxication index in peripheral blood, pathogenic microflora continues to be detected in crops from the uterine cavity in more than 50% of cases, and at the same time, high activity of local proinflammatory cytokines remains, which indicates the risk of delayed, sluggish endometritis.

4. The proposed method for the prevention of postpartum endometritis in women at risk of infection by intrauterine injection of a molded porous carbon sorbent is more effective than the traditional approach and reduces the frequency of PE.

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