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CLINICAL AND LABORATORY PARAMETERS IN PREGNANT WOMEN WITH A HISTORY OF RECCURENT MISCARRIAGES

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Abstract
The analysis of clinical, anamnestic and laboratory examination of 80 women with hyperandrogenism syndrome in the first trimester of pregnancy was carried out in order to identify risk factors for reccurent miscarriages. Our data are consistent with the results of other studies that obesity and insulin resistance are risk factors for habitual miscarriage [6, 7]. In this case, possible pathogenetic links are insulin resistance, hyperinsulinemia, hyperandrogenism.

Keywords: Reccurent miscarriages, hyperandrogenemia syndrome, pre-pregnancy preparation.

Introduction

In recent years, numerous factors have been identified that are involved in the pathogenesis of various pregnancy complications and adverse perinatal outcomes [1,3]. With the exclusion of genetic, endocrine, anatomical, hemostatic disorders and/or their correction, it is not always possible to determine the cause of habitual miscarriage [8]. The identification of new links in the pathogenesis of reproductive losses and the use of the obtained criteria as screening criteria make it possible to preserve the reproductive health of a woman and the health of her unborn child [2,4].

The purpose of the study was to identify risk factors for reccurent miscarriages, clinical and anamnestic, immunological features in women with hyperandrogenemia syndrome.

Materials and methods

The analysis of clinical, anamnestic and laboratory examination of 80 women in the first trimester of pregnancy was carried out.

Criteria for inclusion in the study: signs of the threat of early termination of pregnancy in women with a history of habitual miscarriage; single pregnancy.

Exclusion criteria: pregnancy resulting from the use of assisted reproductive technologies; the presence of extragenital pathology in the decompensation stage, multiple pregnancies, acute infectious and inflammatory diseases and exacerbation of chronic ones.

The main group consisted of 60 women with threatening miscarriage in the first trimester and habitual miscarriage of early pregnancy. The control group consisted of 20 pregnant women with no signs of threatened termination of pregnancy at the time of examination and a history of habitual miscarriage.

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Clinical research methods included the study of general somatic, obstetric and gynecological anamnesis, features of reproductive function, anthropometric characteristics, the course of this pregnancy, childbirth. In newborns, weight and weight indicators, an Apgar score, the duration of stay in the maternity hospital, and the need for rehabilitation in other medical institutions were analyzed. Standard laboratory methods were used, immunological examination (determination of lupus anticoagulant, anticardiolipin antibodies, antibodies to chorionic gonadotropin), assessment of the infectious status was carried out (determination of the level of immunoglobulins of the IgM classes to Herpes simplex virus, Cytomegalovirus, Toxoplasma gondii, Chlamydia trachomatis, IgA to Mycoplasma hominis, Ureaplasma urealyticum by enzyme immunoassay), ultrasound examination of the fetus and placenta.

Intracellular cytokine synthesis by monocytes was determined using monoclonal antibodies by two-color flow cytofluorometry on a FACSCanto device.

Results and Discussion

We determined that the average age of women in the main group was significantly higher than in the control group, and amounted to 30.62±0.51 and 26.52±0.75 years, respectively ($p<0.001$). Patients with reccurent miscarriages were significantly more likely than patients in the control group to be unmarried (respectively 15% and 0; OR 1.47; 95% CI 1.29—1.67; $p<0.05$) or remarried (20% and 0; OR 1.56; 95% CI 1.35—1.81; $p<0.001$), which may indicate the role of social factors in the genesis of habitual miscarriage. Pregnant women of the main group were significantly more likely than those of the control group to be exposed to low temperature (6.25% and 0; OR 1.48; 95% CI 1.3—1.6; $p<0.02$), psychological stress (41.25 and 22.22%; OR 1.28; 95% CI 1.02-1.6; $p<0.05$) in the course of performing professional activities. At the same time, the duration of exposure to adverse occupational factors in women of the main group was significantly longer (5.93±0.6 years in the main group and 3.63±0.63 years in the control group; $p<0.02$). When studying the lifestyle, it was found that patients with reccurent miscarriages, compared with patients of the control group, observed the daily routine less often (42.5 and 77.78%; OR 1.55; 95% CI 1.2—1.99; $p<0.001$). When studying the family history of mothers of patients with reccurent miscarriages, stillbirths were significantly more common (6.25 and 0%; OR 1.48; 95% CI 1.3—1.68; $p<0.02$). When analyzing the obstetric and gynecological history, the onset of the first pregnancy in women of the main group was noted at an earlier age than in patients of the control group (21.84±0.38 and 23.42±0.57; $p<0.05$), while it was less likely to end in timely delivery (28.75 and 88.89%; OR 1.64; 95% CI 1.26—2.14; $p<0.001$) compared to women in the control group. Upon the onset of this pregnancy, pregnant women of the main group went to a women's consultation at an earlier date than patients of the control group (7.05±0.23 and 9.5±0.25 weeks; $p<0.001$). When analyzing the structure of gynecological diseases in pregnant women with habitual miscarriage, markers of acute mycoplasma (17.07% and 0; OR 1.38; 95% CI 1.16—1.65; $p<0.02$), acute herpetic (21.95% and 0; OR 1.44; 95% CI 1.19—1.74) were detected significantly more often than in the control group; $p<0.01$), acute cytomegalovirus infection (12.2% and 0; OR 1.39; 95% CI 1.17—1.65; $p<0.05$), salpingoophoritis (25 and 8.33%; OR 1.35; 95% CI 1.08—1.67; $p<0.05$), endometritis (35 and 2.78%; OR 1.62; 95% CI 1.34—1.95; $p<0.001$), uterine fibroids (17.5% and 0, OR 1.55; 95% CI 1.34—1.78; $p<0.001$), ectopic pregnancy (7.5% and 0; OR 1.49; 95% CI 1.3—1.69; $p<0.01$).

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When evaluating anthropometric indicators, we found that the body mass index in women of the main group was 24.21±0.46 kg/m2 and was significantly higher than in women of the control group — 21.7±0.55 kg/m2 (p<0.001). The ratio of waist circumference to hip circumference in women with a history of habitual miscarriage was 0.85±0.007, in women of the control group — 0.80±0.01 (p<0.001).

Hyperandrogenemia was diagnosed in 33.7% of the patients in the main group, uterine abnormalities in 7.5%, antiphospholipid syndrome in 8.9%. When assessing the infectious status, we found that in women of the main group, compared with control patients, markers of acute infection were significantly more often determined (64.8 and 44.4%; OR 1.29; 95% CI 1.0—1.65; p<0.05), in particular, IgA to Mycoplasma hominis (17.5 and 2.63%; OR 1.46; 95% CI 1.2—1.78; p<0.01). At the same time, markers of acute bacterial mixed infection were significantly more common in women with threatened miscarriage and reccurent miscarriages compared with those of the control group (6.8% and 0; OR 1.44; CI 1.28-1.62; p<0.01).

We revealed significantly lower indicators of the relative number of IL-10 monocytes in women of the main group compared with the parameters of the control group. When assessing the relative number of TNF-α monocytes, we established significantly higher values of this indicator in the main group of women compared with the indicator in the control group.

During the analysis of the course of the present pregnancy, it was revealed that among the gestational complications in patients of the main group, threatening early miscarriage (100 and 22.58%; p<0.001), threatening late miscarriage (42.68 and 3.22%; p<0.001) were significantly more common than in the control group. At the same time, threatening miscarriage was diagnosed in 63.75% of patients in the main group, and miscarriage began in 36.25%. The detachment of the fetal egg during ultrasound examination was determined in 12.5% of women with habitual miscarriage. Threatening premature birth was observed in 33.33% of cases in the main group and in 6.45% in the control group (p<0.01). Placenta previa was significantly more common in pregnant women with habitual miscarriage (8.93% and 0; p<0.01). Premature births in women of the main group were significantly more frequent than in the control group (25.5% and 0; p<0.001). When analyzing the method of delivery, it was found that 60.7% of women in the main group had a cesarean section, whereas in the control group — 36.67% (p<0.05). At the same time, indications for surgery were a scar on the uterus after surgery, extragenital pathology, burdened obstetric and gynecological history, acute fetal hypoxia, clinically narrow pelvis, ineffectiveness of drug treatment of preeclampsia, labor abnormalities, extragenital pathology.

When assessing the weight parameters of newborns, it was revealed that in the main group of women, compared with the control group, body weight (3137.2±86.7 and 3443±87.72 g; p<0.02) and length (50.37±0.53 and 52.13±0.42 cm; p<0.02) were significantly lower. When analyzing the Apgar score, it was found that the newborns of the main group had a significantly lower score both on the 1st (7.04±0.22 and 7.69±0.1 points; p<0.02) and on the 5th minute (8±0.22 and 8.69±0.1 points; p<0.01) after births compared to newborns of the control group. We revealed significantly longer stay times for children (6.83±0.49 and 5.2±0.22 days; p<0.02) and women (6.25±0.2 and 5.2±0.22 days; p<0.001) of the main group compared with the control group in the maternity hospital. At the same time, newborns of women in the main group were significantly more likely to need treatment in pediatric intensive care (9.26% and 0; p<0.01).

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Conclusion

Thus, the results of our study are consistent with the data of a number of authors that unfavorable social and professional factors, psycho-emotional stress, and the presence of bad habits significantly affect the course of pregnancy, increasing the frequency of spontaneous miscarriages. It is possible that psychosocial stress, observed in various situations, affects the processes of maternal adaptation to pregnancy, prevents the formation of immunological tolerance [2], leads to inhibition of progesterone production and to the appearance of a defect in immune tolerance in the mother, which subsequently leads to rejection of the fetus [5].

Our data are consistent with the results of other studies that obesity and insulin resistance are risk factors for habitual miscarriage [6, 7]. In this case, possible pathogenetic links are insulin resistance, hyperinsulinemia, hyperandrogenism. Although these laboratory changes may not be accompanied by pronounced clinical symptoms, hormonal disorders may contribute to miscarriage. TNF-α synthesis by visceral adipose tissue is also known.

In recent years, evidence has emerged linking adverse pregnancy outcomes with the state of the urogenital tract microbiota, in particular, mycoplasma infection plays a dominant role in miscarriage [1, 4]. It has been established that the presence of urogenital infection leads to the development of autoimmune disorders, antiphospholipid syndrome, increased synthesis of pro-inflammatory TNF-α and decreased production of anti-inflammatory IL-10 cytokines [10], which is an unfavorable factor for the progression of pregnancy.

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