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N.A. Scherbina,

*National Medical University, Kharkov, Ukraine, Professor,
Doctor of Medical Sciences, Department of Obstetrics and Gynecology № 1,*

I.U. Kuzmina,

*National Medical University, Kharkov, Ukraine, Professor,
Doctor of Medical Sciences, Department of Obstetrics and Gynecology № 1,*

O.P. Lipko,

*National Medical University, Kharkov, Ukraine, Professor,
Doctor of Medical Sciences, Department of Obstetrics and Gynecology № 1,*

O.A. Kuzmina,

*National Medical University, Kharkov, Ukraine, Assistant Professor,
Candidate of Medical Sciences,
Department of Obstetrics and Gynecology № 1*

The state of circulating antiphospholipid antibodies and antibodies to co-factors in case of missed abortion in the first term of gestation

Abstract: The studies to determine the level of antiphospholipidic antibodies (APhA) and to co-factors APhA of APhA in case of missed abortion have been carried out. Prognostic markers allowing to determine missed abortion origin possibility in the first term of gestation have been determined.

Keywords: antiphospholipid antibodies, antibodies to beta.2-glycoprotein-1, to aneksin V, to prothrombin, missed abortion.

Missed abortion is a pathological state, when the in development stops and the fetal egg dies. Missed abortion or non-developing pregnancy can stop progressing and developing at any period of gestation, but, as a rule, it takes place in the first term of pregnancy [1].

The reason for missed abortion can be a whole complex of various factors, the most frequent of which are latent infectious and inflammatory diseases, hormonal

disorders, abnormalities of the body and neck of uterus structure, genetic and immune disorders [2].

When studying the missed abortion pathogenesis role the investigation of autoimmune reactions is of particular importance and specifically the formation of antibodies to some own phospholipids [3]. Circulating antiphospholipid antibodies (APhA) can influence the process of implantation, growth and the embryo development, the course and outcome of pregnancies [4]. They can also promote the development of thrombotic complications in the endometrial and chorionic tissues that lead to the blood flow disturbance and the pregnancy development cessation [5].

For the last few years it was determined that realize some immune process it is necessary to have in the organism not only antibodies to phospholipids, but also antibodies to the so-called co-factor whose binding form natural complex of antigen-antibody whereas cellular phospholipids act as "complete" autoantigens [6].

Among similar co-factors, the plasmatic component β 2-glycoprotein-1, which is present in patients serum with the antiphospholipid syndrome (APhS) is more widely studied nowadays [7]. Despite a great number of investigations concerning the study of the APhA influence on the implantation and the formation of the chorial-placental blood circulation, up till now there exists not a single common system of evaluation of APhA and antibodies to their co-factors, which could prognoses the probable embryo death in the early period of gestation.

Purpose of investigation – is the determination of the clinicodiagnostic value of APhA and co-factors APhA (annexin V, prothrombin, β 2-glycoprotein-1) and their prognostic role in the development of missed abortion in the first term of pregnancy.

Materials and methods of investigation

Complex clinical and laboratory examination of 80 women at the age of 21 to 36 years with missed abortion in the first term of gestation, who were in the main group has been conducted.

The control group included 30 patients of the same age, with the physiological course of pregnancy, unburdened of obstetric-gynecological and somatic anamnesis.

65 (80.9%) patients of the main group in anamnesis had 1 to 2 missed abortion. 15 (19.1%) women were primigravidas. None of the observed patients of the main group had delivery in anamnesis.

In the control group 20 (66.7%) women in anamnesis had 1 to 2 deliveries. 10 (33.3%) patients were primigravidas.

All the patients of the main group, who had of missed abortion in anamnesis, were conducted cytogenetic investigation of chorion, the investigations concerning on the presence Torch-infection, hormonal investigations and the homeostasis system evaluation that didn't detect any pathological abnormalities.

All the examined women were compared as to the peculiarities of anamnesis reproductive function and age.

The determination of APhA concentration and antibodies to annexin V, to β 2-glikoprotein-I, to prothrombin in the maternal blood were carried out using the method of immunoenzymatic analysis with the help of the set of tests (ELISA).

Statistical analysis of the received data was made with the help of the pack of applied statistic BMDP programs, oriented on the analysis of the biomedical results. The data are presented in the form of the arithmetical mean value (M) and standard deviations (m). For comparison of samplings Student's t-criterion was applied. Significant was considered to be trustworthy if $P < 0.05$.

Results and their discussion

As a result of research it was determined the APhA values and antibodies to co-factors APhA were different significantly between the main and control groups.

The circulating APhA in pregnant women of the control group are detected only in 3.6% of observations. Mean concentration of the circulating APhA made up $0,07 \pm 0,01$ U / ml.

In case of missed abortion the APhA concentration increased almost 8 times and their mean concentration in the main group made up $0,55 \pm 0,09$ U / ml ($P < 0.001$).

Thus, we have determined that the APhA concentration is equal or more than 0.5 U / mL is prognostically unfavorable for the further embryo development.

We have carried out the study of concentration in the blood of circulating antibodies to annexin V. In the control group the antibodies to annexin V were detected only in 2 (2.5%) patients, whose mean concentration of circulating antibodies to annexin V made up 0.013 ± 0.003 U / ml.

In the main group the circulating antibodies to annexin V were detected in 43 (53.8%) their mean concentration made up 0.22 ± 0.03 U / ml and was 17 times greater as compared to the control group of patients ($P < 0.001$).

So, it was determined that the concentration of antibodies to annexin V more or equal to 0.22 U / ml is also prognostically unfavorable as to the development of missed abortion in the first term of pregnancy.

In the control group of women the circulation of antibodies to β -2-glycoprotein 1 was detected in 11 (36.7%) patients. In the main group of women with missed abortion the given antibodies were determined in the overwhelming majority of pregnant women - 69 (86.2%).

The concentration of antibodies to β 2-glycoprotein-1 in women with missed abortion made up 1.76 ± 0.38 U / mL. At the same time in the control group the concentration of antibodies to β 2-glycoprotein was 10 times less and made up 0.17 ± 0.31 U / ml ($p < 0.001$).

While studying antibodies to prothrombin we determined that the frequency of circulating antibodies to prothrombin and their concentrations considerably different in the main and control groups. Circulating antibodies to prothrombin in the control group of pregnant women were detected only in 2 (6.7%) of the observed patients. The mean concentration of the circulating antibody to prothrombin in the control group made up 0.31 ± 0.046 .

In the main group of women with missed abortion, mean concentration in the blood of the circulating antibodies to protrombin was detected in 69 (86.2%) cases and made up $2,4 \pm 0,19$ U / ml ($p < 0.001$).

In connection with prognostically unfavorable development of missed abortion we determined the concentration of antibodies to prothrombin in pregnant women more or equal to 2.4 U / ml.

On the grounds of the conducted investigations one can come to the conclusion that in pathogenesis of missed abortion a special part is plaid the role autoimmune disorders that are evident in a considerable increase of the APhA production and antibodies to co-factors APhA, that can lean to the increased of blood coagulation properties and vascular disorders [9].

Against the background of changes in the natural anticoagulant activity, thrombosis in the endometrial and chorionic tissue are formed that promote the development and tropic disturbances of the fetal egg [10].

The danger of APhS complications is the course of pregnancy only increases. That is why to diagnosis the APhS and to treat accordingly is better in the early periods or before planning a pregnancy.

If APhS is diagnosed after pregnancy onset the patient needs in a regular case monitoring and adequate therapy. More over it is necessary to determine the level of APhA and antibodies to co-factors of APhA (annexin V, prothrombin, β 2-glycoprotein-1) in the pregnant woman in the first trimester of pregnancy.

Thus, the APhA and antibodies to co-factors of APhA are of important prognostic value in the development of missed abortion. Prognostically unfavorable markers concentration the development of missed abortion are: APhA > 0.55 U / ml, antibodies to annexin V > 0,22 U / ml; concentration to antibodies to β 2-glycoprotein-1 > 1.76 ± 0.38 U / ml and the antibodies to prothrombin > 2.4 U / ml.

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