

NEW CRITERIA FOR THE DETECTION OF HEMOLYTIC DISEASE OF NEWBORNS

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Abstract

In our country, the number of pregnant women with rhesus sensibility every year remains unchanged and does not have a downward trend. This is due to insufficient prophylaxis after the termination of pregnancy (spontaneous abortion, ectopic pregnancy, the birth of a rhesus-positive fetus) with the use of immunoglobulin against antiretroviruses. Previously effective methods of treatment, such as desensitization of antigens, plasmapheresis, hemosorption and intravenous administration of immunoglobulins, have only historical significance.

Objective: to study and analyze the literature data of foreign and local authors on the diagnosis of hemolytic disease of the fetus, the use of non-invasive methods of Prevention of Rh-immunization.

Search strategy: the search for information contained information such as regulatory documents, diagnostic protocols, and the conduct of RH-controversial pregnancy. Also in the databases Google Scholar, the Cochrane Library, PubMed, Library full-text scientific articles were used.

Inclusion criteria: randomized, cohort study data, systematic reviews, diagnostic protocols, and Rh-conflict pregnancy.

Exception criteria: practice, report, newspaper publications, articles describing theses.

Results: studies have shown that the prophylactic purpose and administration of anti-D-immunoglobulin, which is used during 28-30 weeks of pregnancy, significantly reduces the development of immunization after childbirth. Conclusion: due to the wide application of anti-D-immunoglobulin in pregnant women and family planning, it will be possible to reduce the frequency of immunization, but the goal will be achieved only if a clear complex prevention of Rh-immunization is developed, in which the appearance of hemolytic disease of the fetus occurs. Nevertheless, the diagnosis and treatment of hemolytic disease remains an urgent problem and requires the use of new possibilities of modern medicine in the field of genetics, ultrasound diagnostics, invasive and non-invasive methods.

Keywords: Rh-is immunization, all immunization, hemolytic disease of the fetus, prevention, non-invasive diagnostic methods, dopplerometry, perinatal outcome.

Introduction

During pregnancy, a small amount of embryonic blood can enter the mother's bloodstream, as a result of which the immune reaction of the mother with Rh-negative bleeding occurs through the production of antibodies to the presence of Rh-positive erythrocytes in the fetus.

This condition is called sensitivity or all immunization. Sensibilization can occur at any time of pregnancy, in invasive processes, but most often in the third trimester and during childbirth, as





well as without potential factors. Fetal transfusion can be 3% of pregnant women in the first trimester, 12% in the second and 45% in the third, sensitivity in 90% of cases is diagnosed after 28 weeks of pregnancy. It is currently known that some women may be sensitive before the beginning of the first pregnancy. In this group, from 55% to 80% "silent sensitivity", that is, it can develop without any risk [7,34].

In repeated pregnancy, HDN is heavier than in the first pregnancy. The reason is that in the first pregnancy, the immune response to rhesus-sensibilization is formed faster and stronger [5,15]. In addition, other antigen systems cause hemolytic disease in newborns. Antigens such as Kell, Duffy, Kidd, MNSs, Lutheran, Diego, Xg, P, Ee and Cc are from entence.

In the pathogenesis of rhesus-sensibilization, antibodies IgG 1 and IgG 3 have a special effect, they complement system and pass through the placenta [26,29,33]. Risk factors for rhesus-immunization include: blood transfusion, invasive diagnostic and therapeutic interventions for women with Rhesus-Negative blood group (chorion biopsy, amniocentesis, cordocentesis), bleeding during pregnancy, antenatal death of the fetus, abdominal injury, fetal tumor sentence [32,33,35].

Prevention of rhesus-immunization.

One of the most important achievements in the history of modern obstetrics is the Prevention of rhesus sensibilization. In Great Britain, the mortality rate at HDN in the 50-ies of the 2180-th century was observed at 1 birth. Today, through the introduction of prophylactic measures of Neonatal care, this figure is the follow-up of mortality in 1 out of 20800 births [7,12].

In different countries, the prevalence of people with Rh-negative bleeding is sharply different, for example, in India this indicator reaches 5%, in North America it reaches 15%. However, in low-prevalence countries, due to the lack of profiling programs, HDN is still an important cause of disease and perinatal death. In such countries, perinatal death and damage to brain structures are observed in 14% of cases of dead births with Rh-conflict pregnancy, among and 50% of pregnancies born alive. In economically developed countries, the use of immunoglobulin D is a routine practice. However, despite the significant effectiveness of prevention, Rh-sensibilization cases have still been recorded due to non-compliance with the applicable protocols [9,36].

Special antenatal prophylaxis involves the use of anti-Rh (D) – immunoglobulin in pregnant women without Rh immunization [3,17].

Crowther, Caroline A. and his co-authors conducted a randomized study in 6 pregnant women who received anti-D-immunoglobulin, belonging to the Rh-Negative blood group, but without sensibilization. The results showed that high doses of profilactics (up to 200-mcg) were more effective in preventing Rh - conflict in subsequent pregnancies than low doses (up to 50-mcg) [11]. The ways of using Anti-D-immunoglobulin are equally effective, whether intramuscularly or intravenously, it depends on the selected amount, the presence of the drug and the desire of the woman [23]. However, the optimal dose results are contradictory. Rebecca M. Turner, Myfanwy Lloyd - Jones, Dilly A. C. Anumba and others compared the effectiveness of the use of different amounts of anti-D-immunoglobulin through metargression analysis. Thus, at 1250XB 28 and 34% in 83 Weeks, the amount at 500xb 28 and 34% in 15 weeks gave effect. According to NICE, a one-time amount of 28-30 XB given in 1500 weeks gave 76% effect. The use of a single dose of



immunoglobulin was based on large studies conducted in the UK, which, unlike other projects, were assessed by the absence of sensitivity during subsequent pregnancies, which also gave its effect on the economic side [8,25].

Many indications that have a prophylactic purpose, also recommend the use of immunoglobulin to all sensibilizational women after childbirth, it is also possible to do during 72 hours, when the Rh-positive factor in the fetus is detected. If anti-D-immunoglobulin is not taken during these periods, it can be taken up to an additional 28 days [14,37].

The use of Anti-D-immunoglobulin has a small risk of local and systemic allergic reactions of the body. In addition, given the use of donor blood for its production, the parenteral way of transmission of infections can be observed, despite strict control.

In the period from 1972 to 1983 year, Croatian scientists conducted research that analyzed the meeting of Rh-isoimmunization. In women who did not receive anti-D immunoglobulin after the birth of a Rh-positive child in pregnancy, the incidence rate was 11,76%. In women taking Anti-D immunoglobulin, this indicator was determined at 0,77% ($p < 0,05$). Perinatal mortality rate in HDN was 20%, and in six years it decreased by 60%, and the incidence rate decreased by 50% [21].

KaeSheenWong, ConnanK. etal. They conducted a study to assess the effect and safety of the use of anti-D-immunoglobulin in pregnant women with Rh-sensibilization. In this case, immunoglobulin has been proposed as a less invasive, alternative treatment option. There is no randomized evidence in this direction, but according to some data, it can lead to the knowledge of the appearance of evening anemia in the fetus [30].

Modern obstetrics have great success in the prevention and treatment of RHD sensitization. Determination of free DNA of the fetus from the mother's plasma allows to determine the state of the Rh of the fetus by conducting directed immunoprophylaxis [6,40].

Diagnose

In recent decades, there have been major changes in helping a prenatal fetus with RhD. Usually, when antibodies appear in the blood of pregnant women with a Rh-negative group, titration is required. Cell, serological and quantitative analysis of antibodies in the mother's blood was developed to estimate the severity of the hemolytic disease of the fetus and the newborn. When accurately measuring the level of antibodies, it is more expedient to use a quantitative method than serological methods. In some cases, in mild forms of the disease, the development of a large number of antibodies can be deepened, and in severe cases, a small amount of cleavage of antibodies is also observed. In addition to the severity of this disease is influenced by the lower class of antibodies, the speed of IgG transmission to the fetus, the functional maturity of the fetus, the presence of inhibitory antibodies and other factors. In these cases, the use of cellular methods is required [16,31].

Earlier, when the titration of antibodies reached a high level, the optical density of bilirubin in the amniocentesis obtained amniotic fluid was determined. Bilirubin accumulates in the amniotic fluid as a result of hemolysis, the idea that the heavy course of hemolysis is directly related to its amount was established. Currently, amniocentesis has little data and is not used to determine the optical





density of bilirubin [4,13,21,22]. Unlike cordocentesis, amniocentesis is a less invasive method, which may indicate incorrect results of bilirubin measurements in amniotic fluid.

This treatment allows you to increase the level of hemoglobin, reduce the risk of developing a tumor form of the disease and continue pregnancy. However, this method is included in invasive prenatal diagnostic procedures and has contraindications in infectious processes, cervical insufficiency, large myomatous nodes, as well as in violation of blood clotting in pregnant women [1,38]. Cordocentesis is also not carried out at the risk of miscarriage of the fetus. In addition, this treatment is associated with certain complications, bleeding from injection points, violation of the heart rhythm of the fetus, chorioamnionitis, hematoma, termination of pregnancy, etc. [24,25,27]. In addition, all invasive methods can provoke Rh-isoimmunization of a pregnant woman. Dopplerometry this is a noninvasive prenatal diagnostic method, which is used for 20 years in determining the peak rate of blood flow in the middle-brain artery of the fetus when detecting anemia syndrome. Its effectiveness is favorable for the non-use of invasive methods (amniocentesis, cordocentesis) in Rh-conflict pregnancy [2,4,19].

The effect is based increasing blood flow rate in the middle brain artery, increasing blood flow out of the heart and reducing blood clotting, Ven saturation of venous blood, reduction of heart pressure and cause peripheral vasodelytasia. And such a process does not allow the heart to be saturated with oxygen and there will be pressure [36,37]. Thus, it is expedient to use noninvasive diagnostics of fetal anemia by increasing the rate of blood flow in the middle cerebral artery, aorta, lower hollow vein, venous canal and spleen artery in the current period [20,39].

The method of measuring blood flow in the spleen artery, in particular, thalassemia and Bart's disease, was studied by foreign scientists in hereditary blood diseases of the fetus [22,27]. Both these diseases are accompanied by blood hemolysis of the fetus. Relying on this information, Bahado-SinghR., Azo.Doppler and co-authors with the help of doppler determined the maximum systolic speed of the spleen artery in severe anemia of the fetus. The researchers found that the highest rate of systolic blood flow in the spleen artery pre-determined severe anemia of the fetus and also recommended dopplerometry of the spleen artery of the fetus to reduce the use of cordocentesis [4].

Correa M.D., CastroM.J. and the co-authors conducted an examination to determine the relationship between dopplerometry of the spleen artery and the level of hemoglobin in the fetus in rhesus-sensibilizia. The project involved 20 pregnant women with gestation from 35 to 35 weeks, who had antibodies in the blood. Dopplerometry of the spleen artery in the fetus (the highest systolic velocity and pulsation index), up to 80 treatments were carried out directly under certain conditions, that is, during the absence of apnea and movements in the fetus. The anemia of the fetus was determined on the basis of hemoglobin deficiency in it, which was checked by subtracting from the expected average hemoglobin level for the gestational age, the amount of hemoglobin measured. Given the hemoglobin deficiency, the fetus was diagnosed with mild ($>2\text{G/dl}$), moderate weight ($>5\text{G/dl}$) and severe ($>7\text{ g/dl}$) anemia. When measuring Hb, there was no Hb deficiency above the expected level and it was equal to 0. Indications for blood transfusion into the fetus were considered moderate-weight ($>5\text{G/dl}$) and severe ($>7\text{ g/dl}$) anemia. As a result, when conducting cordocentesis, anemia was detected in 51 pregnancies (64%). Mild anemia was found in 20 (25%) cases, moderately severe 14 (18%) and severe 17 (21%) cases. The highest





systolic speed of the spleen artery gave the following results, moderate severe anemia ($p = 0,001$), severe ($p = 0,000$) and mild ($p = 0,189$).

A statistically significant difference in the measurement of the pulsating index was recorded in data from the group of severe anemia ($p = 0,001$). The result of this study showed that high indicators of the spleen artery (PI and high systolic speed) are directly correlated with the degree of fetal anemia [10].

Conclusion

For the purpose of prophylaxis, anti-D-immunoglobulin is recommended for 28-30 weeks, in the postpartum period, as well as in case of danger, when conducting invasive processes during pregnancy, for all women belonging to Rh-Negative blood. Conducting prophylactic measures at 28 and 34 weeks of pregnancy, minimally reducing sensibilization allows, protecting against hidden fetal transfusions. In order to timely diagnose the hemolytic disease of the fetus and achieve 100% survival of babies born with hemolytic disease, it is possible only to observe the basic principles of diagnostics, careful dynamic observation and self-treatment.

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