

Obstetric management in Rh alloimmunized pregnancy

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Summary

Rh alloimmunization occurs when maternal immune system is sensitized to D(Rh) erythrocyte surface antigens.

The most common causes of maternal Rh alloimmunization are blood transfusion and antepartum or intrapartum fetomaternal hemorrhage (abdominal trauma, abortion, ectopic pregnancy, invasive obstetric procedures, placental abruption, external cephalic version). The risk of alloimmunization is affected by several factors, including the degree of fetomaternal hemorrhage and maternal immune responses.

Although the introduction of anti D prophylaxis reduced dramatically the rate of alloimmunization in susceptible women, his prevention is not universal and about 0.3% of susceptible women still become Rh D alloimmunized.

The aim of this article is to review the management of the Rh alloimmunized pregnant.

Evaluation of maternal ABO blood group, Rh type and anti D antibodies (indirect Coombs test) should be detected at every first prenatal visit.

Women who are Rh D negative with a positive anti D antibody screen test are considered Rh alloimmunized.

The following step should be the assessment of fetal Rh D status to determine if the pregnancy is at risk for the development of hemolytic disease of the fetus and newborn. In fact, if the fetus is Rh D-negative doesn't require any intervention irrespective of maternal antibodies titers.

When paternity is certain, if the father is Rh D negative the fetus is also Rh D negative. If the father is Rh D positive, he can be either homozygous or heterozygous for the D allele. If he is homozygous for the D allele, the fetus is Rh D positive.

However, if the paternal phenotype is D antigen positive and his genotype is heterozygous, fetal antigen status should be determined by amniocentesis at 15 weeks' gestation (by PCR of fetal cells).

Chorionic villus sampling is possible as well but it has the disadvantage of potentially worsening of maternal antibodies titers due to possible fetomaternal hemorrhage.

Anyway, because of the small risk of invasive prenatal diagnosis, many centres choose to perform amniocentesis only if the anti-Rh titer reaches the critical value of 1:16 or higher.

Management in first affected Rh alloimmunized pregnancy

In case of first affected pregnancy, Rh alloimmunized women should undergo determination of their anti-D antibody titers.

In general, women with titers higher than 1:4 should be considered Rh alloimmunized. Titers tend to correlate more reliably with the severity of fetal disease in the first sensitized pregnancy than in subsequent pregnancies. These are usually performed monthly until 24 weeks of gestation, after which time titers should be repeated every 2 weeks. If titers remain below the critical titer, delivery can occur at term.

A critical titer is defined as the titer associated with a significant risk for fetal hydrops.

Usually, pregnancies in which antibody titers are 1:8 or lower can be managed by serial monitoring of maternal antibody titers.

On the contrary, if the titer is 1:16 or higher, fetal wellness assessment is mandatory by ultrasonography to evaluate middle cerebral artery peak systolic velocity (MCA-PSV) or serial amniocentesis for delta OD₄₅₀ if the former is not available.

Management of women with a history of a previous anemic fetus or infant

When there is a history of a previous anemic fetus or newborn, the probability of subsequent affected Rh D-incompatible fetus is more than 80%.

In these cases, maternal antibody titers are not predictive for the severity of fetal anemia and fetal clinical surveillance, by assessment of middle cerebral artery peak systolic velocity (MCA-PSV) or serial amniocentesis for delta OD₄₅₀ should be started at 18 weeks anyway.

Fetal wellbeing assessment

Fetal detailed ultrasonography assessment has an essential role in diagnosis and management of fetal anemia.

The sonographic findings in case of hydrops include ascites, pleural and pericardial effusions and edema. Several other sonographic findings have been proposed as possible indicators of fetal hydrops (polyhydramnios, increased placental thickness, myocardial and bowel dilatation) but none of these has proven to be predictive of fetal hydrops.

In the past, spectrophotometric analysis of amniotic fluid, introduced by Liley in 1961, was routinely performed to detect the presence of fetal anemia. Because the wavelength at which bilirubin absorbs light is 420-460 nm, the amount of shift in optical density from linearity at 450 nm (delta OD₄₅₀) in amniotic fluid samples can be used to estimate the degree of fetal hemolysis.

The study of peak systolic velocity in the middle cerebral artery (MCA) has been introduced by Mari et al who demonstrated that it can be used to detect moderate and severe anemia in nonhydropic fetuses. Because of fetal anemia results in decreased blood viscosity, the peak systolic velocity (PSV) of blood flow results increased in case of anemia.

Study of MCA is preferred as it can be evaluated using a minimal angle of insonation. Generally, a value of 1.5 MoM is considered critical in establishment the timing of fetal blood sampling. Serial MCA Doppler studies are obtained every 1-2 weeks depending on the trend.

Evaluation of MCA-PSV can be obtained since 18 weeks of gestation, but care should be taken after 35 weeks because of the possible increase in false-positive rate.

Fetal blood sampling by cordocentesis, is the only definitive approach in diagnosing of fetal anemia and acidosis by direct measurement of the fetal hemoglobin and acid-base status.

When fetal hematocrits is less than 30%, the only therapeutic option is intrauterine fetal transfusion. The source of red cells for intrauterine transfusion is typically a blood type O, RhD-negative, cytomegalovirus-negative donor. Some centers prefer to use maternal blood as the source of red cells. Units are irradiated to prevent graft-versus-host reaction and processed through a leukocyte-poor filter. The purpose of intrauterine transfusion is to maintain the fetal hemoglobin value at more than 9 g/dL.

Serial intrauterine transfusions, if required, are usually performed until 34 weeks' gestation, because after this time the risk of the procedure is greater than benefits. In

determining the optimal delivery time, gestational age, severity of fetal anemia, and fetal lung maturity should all be considered. If fetal surveillance remains reassuring (MCA-PSV value < 1.5 MoMs or spectrophotometric analysis does not indicate severe fetal anemia), labour should be induced at 37-38 weeks of gestation. If fetal surveillance is not reassuring delivery should be planned after confirmation of fetal lung maturity. Immediate neonatal outcome is complicated by the need of repeated transfusions secondary to suppressed erythropoiesis. Long-term studies have revealed normal neurologic outcomes in more than 90% of cases.

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