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ORIGINAL ARTICLE

Prediction of fetal anemia by middle cerebral artery Doppler

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Abstract *Objectives:* To assess the value of peak systolic velocity in the middle cerebral artery (MCA) in prediction of fetal anemia as a non invasive method in non hydropic fetuses.

Methods: The study included 30 pregnant women with non hydropic fetuses and with known red cell antibodies. Full ultrasound examination was done and peak velocity of systolic cerebral blood flow in MCA was measured. If severe anemia was suspected, fetal blood sampling by cordocentesis was performed.

Results: Thirty fetuses were examined, 22 were anemic and eight had a hemoglobin value within a normal range. The mean MCA peak systolic velocity for fetus with the normal hemoglobin (Hb) was 48.98 ± 13.94 while that for the anemic fetus was 64.79 ± 11.97 and $P = 0.004$.

Sensitivity of increased peak velocity of systolic blood flow in MCA for prediction of fetal anemia was 90.5% and specificity was 78.6%.

Conclusion: Doppler of peak velocity of systolic blood flow in MCA can be reliable in predicting anemia so delaying invasive methods until treatment (blood transfusion) is expected to be necessary.

1. Introduction

Maternal alloimmunization occurs when a pregnant woman has an immunologic response to a paternally derived red-cell antigen that is foreign to the mother and inherited by the fetus. The antibodies may cross the placenta, bind to antigens present on the fetal erythrocytes, and cause hemolysis, hydrops fetalis, and fetal death (1). Women with rising red cell antibody levels, with or without a history of a previously affected pregnancy, are usually referred to fetal medicine units for specialized managements (2). Survival rates can exceed 90 percent if anemia is diagnosed and treated with intrauterine blood transfusions (3).

The most accurate test to assess the degree of fetal anemia, and thus the need for transfusion, is the fetal hemoglobin (Hb) measurement by fetal blood sampling (4). However, the standard test to evaluate the need for fetal transfusion is serial amniocentesis for the determination of bilirubin levels in amniotic fluid. Hemolysis leads to the accumulation of bilirubin in amniotic fluid, so its level correlates with the severity of hemolysis. The bilirubin level is quantified by spectrophotometry and expressed as the change in optical density at a wavelength

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of 450 nm (ΔOD_{450}); the ΔOD_{450} values are then plotted on a Liley chart to estimate the severity of anemia (5). Both procedures have a significant rise of causing miscarriage, premature rupture of membrane, preterm delivery and increase antibody concentration (6).

Several non-invasive methods for the prediction of fetal anemia have been assessed, aiming to defer the use of invasive testing until transfusion is necessary (2,7,10). The association of increased blood flow velocity in the fetal middle cerebral artery (MCA) with fetal anemia is the most promising of these non-invasive tests as has subsequently been reported (9,8). Fetuses with anemia have a high cardiac output and decreased blood viscosity, resulting in high blood-flow velocities that could be used in prediction of fetal anemia (11,12). Brennad showed that in anemic fetus changes in cardiac output & blood-flow velocities are reflected by an increase in peak systolic velocity in the middle cerebral artery (13).

The objective of the current study is to assess the value of measuring peak systolic velocity in the middle cerebral artery (MCA) as a non invasive method in non hydropic fetuses for prediction of fetal anemia due to maternal red-cell alloimmunization.

2. Methods

2.1. Subjects' studies

The study included 30 pregnant women with red cell antibodies referred for assessment and management. Patients were mainly referred if there was an increase in antibody levels in the maternal serum, or if there was a previous obstetric history of an anemic fetus or neonate. Assessment consisted of ultrasound examination for fetal biometry, exclusion of any structural abnormalities, liquor volume assessment, umbilical artery Doppler blood flow studies and Doppler blood flow velocity studies of the MCA. Hydrops was defined as fluid collection in body cavities or skin edema, and hydropic fetuses were excluded from the study. Cordocentesis was performed on 18 patients at their first visit and for the remaining, follow- up was arranged and those whose assessment was suggestive of worsening anemia underwent cordocentesis on the second visit.

2.2. Doppler studies

Doppler examination of the MCA was performed before cordocentesis in all cases. An axial section of the brain, including the thalami and the cavitas septi pellucidi, was obtained. The circle of Willis was visualized and the middle cerebral artery of one side was examined close to its origin in the internal carotid artery. We have found that the systolic velocity decreases with distance from the point of origin of this vessel, so the angle between the ultrasound beam and the direction of blood flow was kept as close as possible to 0 and in all cases not to exceed 30°. The highest point of the wave from peak systolic velocity (PSV) was measured. Doppler images were recorded at a time when there was an absence of marked fetal body and respiratory movements, to avoid false elevation in PSV with fetal heart rate acceleration. At least three measurements were taken and the highest one is accepted as the final value. The reference test for the diagnosis of fetal anemia was measurement of peak systolic velocity of the MCA more than 1.5 multiple of median

(MOM) using reference produced by Mari and his colleagues (9). Practical approach is to convert actual values into MOM to account for changes in gestational age, internet based calculator is available at www.perinatology.com.

2.3. Cordocentesis

Fetal blood sampling was performed by cordocentesis from the umbilical vein at the placental cord insertion with blood ready for fetal transfusion if necessary. Fetal blood was immediately examined for the determination of the full blood count and, if anemia was confirmed, intravascular transfusion was performed.

The reference test for the diagnosis of fetal anemia was measurement of the hemoglobin level in umbilical-cord blood. Fetal anemia is defined as Hb less than 0.65 times the median for gestational age, with the use of the published reference range (9).

2.4. Statistics

Statistical presentation and analysis of the present study was conducted, using the mean by SPSS V.16.

Mean value $\bar{X}$: the sum of all observations divided by the number of observations:

$$\bar{X} = \frac{\sum x}{n}$$

Where Σ = sum & n = number of observations.

ROC-curve: Receiver Operating Characteristic curve analysis

Sensitivity: Probability that the test results will be positive when the disease is present (true positive rate, expressed as a percentage).

Specificity: Probability that the test results will be negative when the disease is present (true negative rate, expressed as a percentage).

3. Results

This study included 30 pregnant women with alloimmunization and non-hydropic fetuses. Twenty three cases had RhD antibodies. Other 5 cases were with Rh C antibodies and last 2 cases were with anti E antibodies.

Medium gestational age was 29.27 ± 3.54 (range 24–35 weeks). Medium maternal age was 31.1 ± 5.67 (range 22–44 years). All patients were multi gravid. Among the 30 fetuses at risk of anemia, 22 were anemic (Hb 8.07 ± 0.93) and 8 had normal Hb (Hb 10.08 ± 0.96).

Fetal blood was taken by cordocentesis for hemoglobin analysis in 22 cases, 18 at first visit and four at second visit. In the other 8 cases the MCA Doppler was within normal range (48.98 ± 13.94) and follow up antibodies titer remains stable and hemoglobin was determined in fetal cord blood obtained at birth and show normal Hb or mild anemia.

The mean MCA peak systolic velocity for fetuses with normal Hb was 48.98 ± 13.94 while that for anemic fetuses was 64.79 ± 11.97 ($P \leqslant 0.004$). The MOM of MCA for fetuses with normal Hb was 1.22 ± 0.21 while that for anemic fetuses was 1.62 ± 0.08 ($P \leqslant 0.001$).

There were non significant correlations between fetal Hb and maternal age with $P = 0.19$ (Fig. 1), while there were