

## Intrauterine Transfusions in FHD: When and How?

Mirosław Wielgos, Robert Brawura-Biskupski-Samaha

### ABSTRACT

Intrauterine fetal blood transfusions still remain the gold standard of prenatal therapy in severe cases of fetal hemolytic disease due to mother-fetus immunization. Middle cerebral artery-peak systolic velocity (MCA-PSV) measurements plays the most important role in diagnosing the disease. A value of MCA-PSV  $\geq 1.5$  allows us to diagnose severe or moderate anemia and prompts us to treat the patient. The time of subsequent transfusions is estimated by the hemoglobin level directly after the transfusion and the fact that the concentration of fetal hemoglobin in blood decreases at a rate of 0.3 g% per day. Even though effective, these procedures carry with them major risks and that is why prophylaxis is essential.

**Keywords:** Fetomaternal immunization, Anemia, Cordocentesis, Middle cerebral artery-peak systolic velocity.

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### INTRODUCTION

Intrauterine fetal blood transfusions still remain the gold standard of prenatal therapy in severe cases of fetal hemolytic disease due to mother-fetus immunization.<sup>1-4</sup> However, there is no doubt that a notable achievement of recent years is the improvement of diagnostic methods used in this pathology of pregnancy.<sup>5-7</sup> The most important role is played by the Doppler examination. The introduction of this method in general clinical practice allows now to avoid performing invasive diagnostic procedures, such as amniocentesis or cordocentesis.<sup>8-10</sup> These treatments—like any invasive procedure—are related to a specific risk of serious complications, including loss of pregnancy.<sup>11,12</sup>

The use of Doppler imaging for the diagnosis of hemolytic disease of the fetus is based on the observed strong correlation between the degree of fetal anemia and the parameter values of blood flow in the fetal circulation. The most commonly used vessel for this purpose is the middle cerebral artery (MCA), and the blood flow parameter, preferably correlated with anemia, is the maximum peak systolic velocity (PSV) (Fig. 1). This correlation is due to the fact that the greater the anemia the more diluted is the blood, leading to lower viscosity and as a result hyperkinetic circulation.<sup>8-10</sup> Since PSV measurements change with gestational age, it is essential to eliminate the effect of this parameter on the results obtained.

Therefore, to assess the severity of the disease we use multiples of the median (MoM) instead of the absolute value of the PSV.<sup>8-10</sup> Archiving-descriptive programs, applied to ultrasound, have the appropriate calculators to permit the calculation of MoM after introducing the gestational age and empirically determined values of PSV. There are also free internet-based calculators, e.g. on the [www.perinatology.com](http://www.perinatology.com). Doppler of MCA-PSV should be performed in women with evidence of maternal-fetal immunization, from the 18th week of pregnancy onwards. Interpretation of the results is as follows:

- MCA-PSV  $< 1.5$ —no severe anemia
  - Observation, serial Doppler ultrasound
- MCA-PSV  $\geq 1.5$ —current severe or moderate anemia
  - Needs immediate treatment

The presence of immune hydrops fetalis allows us to skip the diagnostic process because, in this case it is quite clear that we have severe hemolytic anemia of the fetus. Therefore, besides hydrops fetalis, the only indicator for intrauterine treatment is an abnormal result of Doppler measurement of MCA-PSV. Intrauterine treatment should be implemented only in cases when the fetus is not mature enough for extrauterine life. Otherwise, it is recommended to deliver the fetus and treat the neonate.

For fetal transfusion, packed red blood cells with 'O' Rh (-) group are used and it is obviously bereft of any target antigens for antibodies in a non-RhD conflict. It is recommended that before transfusion the blood is irradiated and filtered.<sup>4-7</sup>

Typical intrauterine transfusion is not an exchange transfusion, but only a complementary one (Fig. 2). Attempts undertaken in some centers to perform exchange transfusions are associated with a high risk of serious complications, so it is not currently the recommended form of therapy. After introducing the needle into the vessel, before transfusing the blood, hemoglobin concentration should be examined; the deficit is both, a confirmation of hemolytic disease of the fetus, as well as the basis for determining the volume of blood needed to be transfused.<sup>6</sup> Therefore, a necessary condition to perform the transfusion safely is having a portable hemoglobin level analyzer in the procedure room. The volume of transfused blood is determined by special calculation programs that take into account the gestational age, current fetal hematological parameters and the hematological parameters of the packed red blood cells.<sup>10</sup>

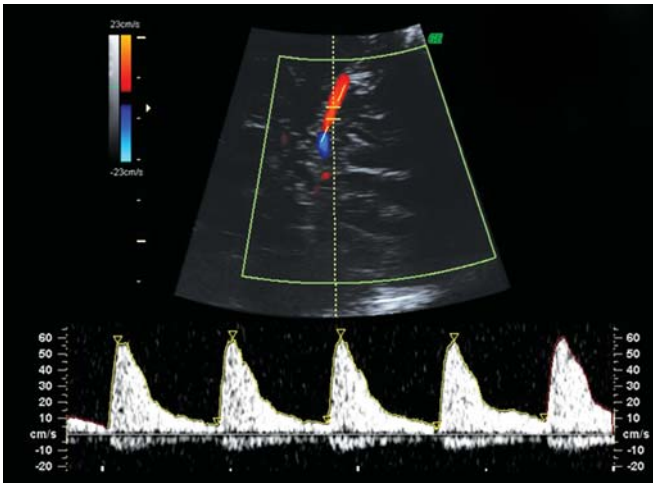


Fig. 1: Middle cerebral artery Doppler measurement



Fig. 2: Cordocentesis

Another important problem is determining the date of the next blood transfusion. In this case, Doppler measurements are not as useful as in the untreated patients.<sup>10</sup> As a result of changes in the circulatory hemodynamics due to the transfusion and differences in the physicochemical properties of red blood cells as compared to fetal blood, the correlation between the values of the MCA-PSV and fetal anemia is greatly reduced.<sup>9</sup> Therefore, a factor useful for determining the subsequent transfusion is the hemoglobin level directly after the transfusion and the fact that the concentration of fetal hemoglobin in blood decreases at a rate of 0.3 gm% per day.<sup>9,10</sup>

It is now realized that the intrauterine treatment of hemolytic disease of the fetus should be continued until the end of 34 weeks of pregnancy. After 35 weeks the risk of complications of invasive therapy is so large that it is safer to complete a pregnancy within a period not exceeding 2 weeks from the last transfusion and treat newborn, which at the current level of neonatal care is most reasonable.

It is now considered that the intrauterine treatment of hemolytic disease of the fetus should be continued until the end of 34 weeks of pregnancy. After 35 weeks the risk of complications of invasive therapy is so high that it is safer to deliver within a period not exceeding 2 weeks from the last transfusion and treat the newborn, which at the current level of neonatal care is most reasonable.

An exception is the presence of hydrops, for which the performance of intrauterine transfusion, even after 35 weeks of pregnancy is a common practice, improving prognosis and chances of the fetus/newborn survival.

Finally, we should mention the most common complications of fetal blood transfusion. Besides complications that are characteristic for each cordocentesis (bleeding, reflex bradycardia, intrauterine infection, hyperimmunization, uterine activity), in the case of therapeutic

cordocentesis there is a risk of volume overload of the fetal circulatory system.<sup>11,12</sup> This is why during the transfusion fetal heart activity is constantly monitored—either using CTG/UPD or Doppler, unless on the USG monitor a cross-section of the heart or aorta is visible. It is important to remember that the first symptom of the blood circulation overload is bradycardia. In the case of bradycardia, it is recommended to stop the transfusion and to accurately assess the situation. Another serious complication can be the umbilical vessel occlusion that may occur as a result of the protrusion of the needle from the vessel into Wharton's jelly.<sup>12</sup> In such a situation, the injection of even 2 to 3 ml of blood around the vessel may lead to occlusion of umbilical vein that may lead to grave hemodynamic complications. The risk of the most severe complications, including fetal demise, related to fetal blood transfusion, is estimated to be around 0.5 to 1.0%.

So far, no effective, noninvasive method that could be widely used in prenatal treatment of hemolytic disease has been developed. Plasmapheresis that raised high hopes years ago has been proved not to be an effective enough procedure. On the other hand, using high doses of blocking human gamma globulins—irrespective of how effective the method is in experimental studies—is extremely expensive, hindering its widespread use. Research on the use in pregnant women with maternal-fetal immunization selective immunomodulatory therapy is conducted, but so far only in animal models.

Irrespective of the possibilities of prenatal therapy, there is a very important issue that remains, namely immunization prophylaxis—whether nonspecific, or and most importantly specific, using immunoglobulins anti-D in all cases where a risk of immunization exists. Solely, the proper use of prophylaxis—during the pregnancy as well—renders it possible to effectively decrease the frequency of serological conflicts and fetal hemolytic disease.

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