Postponing early intrauterine transfusion with intravenous immunoglobulin treatment: the PETIT study on severe hemolytic disease of the fetus and newborn

TO THE EDITORS: Zwiers et al[1] report the first multicenter study of whether high-dose intravenous immunoglobulins (IVIg) defers the onset of severe anemia in pregnancies at risk for severe hemolytic disease of the fetus and newborn (HDFN). Using a retrospective case-control study, the authors compared the onset of severe fetal anemia in 24 pregnancies treated with IVIg vs 28 untreated pregnancies.

The main finding was that the onset of fetal anemia in index current pregnancies was postponed by 15 days in the IVIg group and occurred 9 days earlier in the untreated group. There was a 4 day between-group difference in favor of the IVIg group, which failed to reach significance because of the relatively small number of cases.

The main weakness of this study is represented by important differences in the protocol used among the centers, including gestational age at treatment initiation, the type of immunoglobulins used, different dose and frequency regimens of maternal administration, and a combination of IVIg and plasmapheresis in 8 cases. Interestingly, focusing on the 13 pregnancies in which immunoglobulins were started before 13 weeks, the effect was even more pronounced, with anemia developing 25 days later.

Using the same criteria to define a history of severe HDFN, we have treated 15 pregnancies since 2012 in our national referral center (13 anti-D, 2 anti-Kell). These cases were compared with previous pregnancies using the same study design as Zwiers et al.[1] The protocol was identical in all our cases: IVIg started from 11 weeks of gestation with a regimen of 1 g/kg weekly. The overall survival rate was similar: 13 of 15 (87%). The onset of fetal anemia occurred on average 4 weeks later in the IVIg group vs 1 week in the untreated group.

Unlike Zwiers et al, we monitored maternal antibodies quantitatively throughout the pregnancies and found a 43% decrease in the IVIg group vs 9% in the untreated group. In the 2 pregnancies in which no in utero transfusion was needed, this decrease was even more pronounced. We believe that these results provide additional arguments in favor of early IVIg treatment (<13 weeks) in cases with a history of severe HDFN. We agree that a randomized trial is needed and recommend inclusion in the trial design of quantitative monitoring of maternal antibodies. ■

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REFERENCE

1. Zwiers C, van der Bom JG, van Kamp IL, et al. Postponing early intrauterine transfusion with intravenous immunoglobulin treatment: the PETIT study on severe hemolytic disease of the fetus and newborn. Am J Obstet Gynecol 2018;219:291.e1–9.

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