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Commentary

Management of haemolytic disease of the foetus & newborn: Steps to improve the outcomes

Before the 1970s, haemolytic disease of the foetus and newborn (HDFN) was a major obstetric problem, with a large impact on foetal and neonatal morbidity and mortality. However, with the long-standing established use of anti-D in Rhesus (Rh) negative women for post-natal prophylaxis, together with its increasing routine use for antenatal prophylaxis, the incidence of Rh-(D) sensitization has dramatically fallen[1]. Nevertheless, Rh-D alloimmunization together with sensitization against other red cell antigens still affects a large number of pregnancies every year, with significant health and financial implications[2]. Without an appropriate antenatal detection and treatment programme, up to 50 per cent of untreated HDFN cases will result in neonatal death or damage. In developing countries, especially those lacking an efficient prophylaxis progamme, this will cause a big public health problem and costs. It has been estimated that more than 50,000 foetuses could be affected by this condition every year in India[3]. On the other hand, if anaemia is diagnosed and treated with intrauterine blood transfusions in a timely manner, survival rates can exceed 90 per cent[4]. Women with rising red cell antibody levels are usually referred to tertiary foetal medicine units for specialized management. The main challenge facing foetal medicine specialists today is not the skill required for invasive therapy, but rather the non-invasive monitoring of the disease so that its progress can be detected to guide the need and timing of intrauterine transfusions and especially to avoid or minimize unnecessary invasive testing[2].

The study by Varghese & colleagues in this issue[5] evaluates the presence of alloimmunization to red cell blood group antibodies and the proportion of minor blood group antibodies in the antenatal population of a tertiary care center located in south India. They raise the issue of the policy in some developing countries of antenatal screening solely for detection of anti-D, claiming that routine screening in positive Rh women is not beneficial in view of the low prevalence of alloimmunization in these patients. They showed presence of alloimmunization in 1.48 per cent of the antenatal women included in the study, and taken together with the expected presence of other clinically significant antibodies, their results were similar to reports in other publications from India[6,7]. However, being a hospital based cohort, the results do not necessarily reflect the exact prevalence of sensitization in population. The authors have also calculated that one out of approximately 1250 Rh (D) positive women would have clinically significant antibodies[5]. With a birth rate of over 27 million per year[8] and assuming that up to 50 per cent of untreated HDFN will result in death or severe brain damage means that up to 10,000 foetuses could be in danger of developing serious disease if routine screening for RH+ women is not established. It can be argued that the percentage could be a little lower if we consider that the risk of HDFN is smaller in non D patients, but will still involve a large number of foetuses and newborn.

Assuming the universal administration of prophylactic anti-D to all D negative women who deliver an Rh (D) positive newborn as the basis of the prevention of HDFN, the identification of patients at risk of developing the disease by screening during pregnancy is the next and fundamental step in the pyramid of the detection and management of this disease. Without this step, there is no possibility of monitoring patients at risk with Doppler ultrasound of the foetal middle cerebral artery for intrauterine diagnosis of anaemia, and, therefore, the possibility of intrauterine transfusion when necessary is excluded. The current management of HDFN represents one of the genuine successes of foetal therapy and clinical management has moved from a previous invasive approach to a non-invasive one. An example includes the detection of foetuses at risk of HDFN with the use of cell-free foetal DNA in the plasma of pregnant women for the determination of

foetal antigen genotype, because if the foetus is antigen negative, then it is not at risk and no further monitoring or invasive procedures are required[9]. If the foetus is antigen positive, the appropriate management of the pregnancy can be arranged. In some countries maternal plasma testing for foetal Rh(D) genotype has enabled the screening of all D negative pregnant women, thereby confining the administration of prophylactic anti-D only to those women who need it. In addition, when a foetus is antigen positive, the follow up is for the detection of moderate or severe anaemia non-invasively by Doppler ultrasonography on the basis of an increase in the peak velocity of systolic blood in the middle cerebral artery (MCA). Several studies have used the MCA Doppler's in a clinical basis for the prediction of foetal anaemia with at-risk cases, without ultrasound evidence of foetal hydrops, showing a good correlation with foetal haemoglobin[10]. This non-invasive investigation can be reliable in predicting anaemia in cases in whom the need to sample foetal blood is not certain, therefore, delaying invasive testing until treatment is likely to be required. The neonatal outcome where invasive testing was avoided (based on reassuring MCA Doppler velocity results) did not result in life-threatening foetal or neonatal morbidities[11]. Therefore, the routine use of MCA Doppler's can avoid unnecessary invasive procedures on at-risk foetuses. When anaemia is suspected, an invasive approach is required in order to perform an intrauterine blood transfusion which should only be attempted when the foetus needs transfusion[12]. Neonatal outcomes for pregnancies managed for HDFN with intrauterine transfusion are positive in the short-term, and results from different studies can be viewed as reassuring by parents of affected pregnancies[13-15].

In summary, this paper[5] addresses an important issue of the identification of women at risk of developing HDFN, by determining alloimmunization to blood group antibodies in a tertiary care centre in India. Without red cell antibody screening, a significant number of foetuses and newborn babies will be exposed to a high risk of morbidity and mortality. However, if this first step is taken, prenatal management with correct monitoring to identify foetal anaemia and timely planned intrauterine transfusion, can avoid as much as 90 per cent of this pathology of foetuses and newborn.

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