A Case for Comprehensive Antenatal Screening for Blood Group Antibodies

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Abstract

Objectives: To determine the frequency of various blood group antibodies responsible for haemolytic disease of the new born (HDN).
Design: A prospective study of all neonates and still born foetuses suspected to have haemolytic disease of the new born and their mothers.
Subjects: Neonates suspected to have HDN as per study criteria along with their mothers and mothers of still born foetuses with hydrops foetalis.
Methods: Pertinent serological tests, serum bilirubin estimation, haemoglobin estimation and reticulocyte count on neonate's blood samples and demonstration/titration of blood group specific antibodies in maternal bLood samples.
Results: Six cases of HDN due to blood group antibodies were detected so far. Four were due to anti-D and all were of mild severity as per study criteria. Two cases were of severe haernoLytic disease (hydrops foetalis). Both were due to anti Kell. Both women had history of previous blood transfusion and abortions.
Conclusion: Comprehensive antibody screening should be performed during antenatal period in women who have received blood transfusion and/or have history of un-explained abortions (JPMA 49:246, 1999).

Introduction

The incidence of severe haemo!ytic disease of the new-born (HDN) has been significantly reduced by the use of prophylactic anti-Rh D Immunoglobulin given to mother[1]. However it still occurs due to antibodies against other blood groups, most importantly anti-c anti-K[2]. In majority of these cases the antibody is a consequence of previous blood transfusion rather than pregnancy[3]. There are several reasons for this. Firstly these antigens are not as immunogenic as RhD antigen is, therefore a small foetomaternal haemorrhage may not elicit immune response but a large dose delivered by blood transfusion will do so. Secondly, in transfusion practice recipient and donor are only matched for ABO and Rh D blood groups and not for other antibodies[4]. Thirdly the frequency of antigen positive feotuses carried by antigen negative mother is very low[5,6].
Of all other blood group antigens causing HDN, Kell antigen is most important as it can cause severe HDN with hydrops foetalis early in pregnancy even in the absence of significant titres of antibody in maternal circulation[7]. Kell phenotype now has been demonstrated to comprise 21 antigens but it is only KI antigen which is highly immunogenic and is of clinical importance[8,9]. Unlike Rh blood group system, only 5% of Ki negative individuals produce anti-KI antibodies, therefore the incidence of Kell sensitisation is only 1.0-1.16/1000 pregnancies[7]. Because of this HDN due to anti-K antibodies is rare by may be very severe despite low antibody titre[7]. Since prophylactic administration of anti-Rh D immunoglobulin to RhD negative mothers has become a routine practice in all hospitals, there should have been negligible occurrence of at least severe HDN. On the contrary it appears that severe HDN,

particularly hydrops feotalis, does occur at a higher than expected frequency. This could be because of failure of receive Rh D prophylaxis or failed Rh D prophylaxis or the HDN is due to other blood group antibodies. To study the causes of HDN due to blood group antigen sensitisation a study has been organised by Armed Forces Institute of Pathology in collaboration with Armed Forces of Transfusion and other civil and military hospitals. This short communication deals with preliminary results of this study.

Patients, Methods and Results

All cases of suspected HDN were included in the study. The criteria for inclusion in the study is as under:

1. Still born/aborted foetuses with demonstrative antibody against a blood group antigen in maternal blood other than anti-a and Anti-B.
2. Neonates born with anaemia and/or hyperbilirubinaemia with positive direct antiglobulin test (DAT) and demonstrative antibody against a blood group antigen in maternal blood.

A detailed obstetric history was obtained from the mother. Neonatal blood samples were collected for estimation of Hb, reticulocyte count, serum bilirubin, direct antiglobulin test and other serological studies. Maternal blood samples were collected for indirect antiglobulin test (IAT) and antibody titre estimation. Where foetus was stillborn or aborted with hydrops, only maternal blood samples were collected for (tAT) and antibody titre determination.

Antiglobulin tests (direct and indirect) were performed by standard procedures using polyspecific antiglobulin serum made by Lorne Laboratories, Great Britain. Antibody detected in mothers serum was specified using Lorne Identicells made by Lorne Laboratories Great Britain which comprises of 11 phenotyped cells. Maternal antibody titre was perfbrmed using pooled cells positive for that blood group. Serum bilirubin was estimated on ACE Automated Chemistry Analyser (Biosystems, Netherlands).

Haemoglobin estimation and reticulocyte count were performed by standard procedures. HDN was classified into mild, moderate and severe on the basis of following criteri[10].

1. Mild HDN mmol/1.

a. Indirect bilirubin Jeve1 does not exceed 340
b. Hb level does not drop below 110 g/l.
c. No treatment is required.

2. Moderate HDN

a. Hydrops feotalis does not develop.
b. Serum indirect bilirubin exceeds 340 mmo l/L
c. Hb level drops below 70 g/l.
d. Treatment is required.

3. Severe HDN

Hydrops foetalis develops in utero.

So far six cases ofHDN have been detected. Clinical and laboratory details of these cases are shown in the table.

Table. Clinical and Laboratory data of all cases of HDN.

S. No.	Gravida	Mother Previous Transfusion	Abortions	IAT	Ab Specificity	Ab Titre	Hb (g/dl)
1.	3	-	Nil	++	Anti-D	1/128	120
2.	3	-	Nil	++	Anti-D	1/64	100
3.	2	-	Nil	++	Anti-D	1/32	142
4.	2	-	Nil	++	Anti-D	1/64	147
5.	5	4	4	++++	Anti-K	1/256	-
6.	4	3	3	++++	Anti-K	1/256	-

Out of six cases, two were of severe HDN (hydrops foetalis) and in both antibody detected in maternal btood was anti-K. Remaining 4 cases were of mild HDN and in all of them anti-D was detected in maternal blood. All these mothers gave history of prolonged jaundice in children born previously. Thus anti-K was responsible for one third of the cases of HDN and for all cases of severe HDN. Only in these cases there was a history of previous blood transfusion and abortions.

Comments

Before the introduction of Rh D immunoprophylaxis, anti-D accounted for over 90% of all cases of HDN of which 10-20% used to die in utero or in early neonatal period[6]. After the introduction of Rh D immunoprophylaxis both the incidence and severity of HDN due to anti-D has substantially decreased but it still occurs due to failed immunoprophylaxis". In developing countries, where majority of pregnant women do not receive antenatal care, Rh D immunisation still remains the most common cause of HDN. When there is a history of prolonged and moderate to severe neonatal jaundice in previous pregnancies only then these women seek antenatal care. This is evident from preliminary results of this study. In all the four cases of HDN due to anti-D there was a similar history in previous pregnancies. Two of these mothers sought antenatal care in 3rd pregnancy while two attended antenatal clinic in 2nd pregnancy. The cause of prolonged and moderately severe neonatal jaundice in first pregnancy could not be fou d. However HDN in all the cases was not severe (Table) and required no treatment.

Most interesting aspect of these results is that there were two cases of hydrops feotalis. In both cases responsible antibody was anti-K, although the titre in maternal circulation was not very high to cause hydrops foetalis. Both the ladies gave birth to one normal child in first pregnancy. Later both of them had early abortions, one had two and the other had three. Both of them had received blood transfusions during previous obstetric accidents. Since antibody screening is not practiced in most of blood banks as a routine, it is quite possible that anti-Kell antibodies were missed earlier. These were detected as a result of deliberate search this time.

Although anti-Kell antibody is the third most common antibody involved in HDN but it is responsible for a higher percentage of severe HDN, particularly hydrops foetalis[7]. The frequency of detectable antibody in pregnant women in much lower (1/100 pregnant women) because around 80% foetuses are Kell negative[2,11]. Previous blood transfusions rather than pregnancy appear to be the cause of sensitisation as 88% of these women have a history of previous blood transfusions[3,7].

The antibody is however notorious, in several aspects. There is poor correlation between antibody titre

and severity of HDN[11]. Amniotic fluid bilirubin is disproportionately low and so is the cord blood reticulocyte count. This is because this antibody has disproportionate effect on red blood cell precursos than mature red blood cells thus causing anaemia more rapidly.

The preliminary results of this study are in line with the above discussion. Hence there appears to be a very good case for including a comprehensive antibody screening in antenatal care rather than anti-D screening alone. To make it cost effective this may be confined to cases where there is history of blood transfusion and/or repeated abortions without obvious cause.

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