CASE REPORT

Red Cell Intrauterine Transfusion: A Blood Bank Experience

Suguna Somasundram[1,2], Nur Al-Kamaliah Harun[2], Nor Azhani Azmi[2], Eusni Rahayu Mohd Tohit[1]

[1] Department of Pathology, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400 Serdang, Selangor, Malaysia
[2] Department of Transfusion Medicine and Pathology, Hospital Sultanah Nur Zahirah, 20400 Kuala Terengganu, Terengganu, Malaysia.

ABSTRACT

Red cell intrauterine transfusion (IUT) is a procedure to correct the foetal anaemia most commonly due to haemolytic disease of foetus and newborn (HDFN) or uncommonly due to foetal parvovirus infection (1,2). Here we report a case of intrauterine transfusion for a Rhesus (Rh) isoimmunisation. Red cell IUT requires blood with specific criteria, thus a blood bank experience on requirements of blood for intrauterine transfusion is discussed here.

Keywords: IUT, Foetal anaemia, HDFN, Rh, Blood transfusion

Corresponding Author:
Eusni Rahayu Mohd Tohit, MPath
Email: eusni@upm.edu.my
Tel: +603-97692379

INTRODUCTION

Red cell intrauterine transfusion (IUT) is a procedure to correct the foetal anaemia most commonly due to haemolytic disease of foetus and newborn (HDFN) or uncommonly due to foetal parvovirus infection (1,2). The procedure involves the donor's blood transfused to the affected foetus through umbilical vein near the placental cord insertion. However, the red cell concentrate for intrauterine transfusion requires specific criteria to prevent unfavourable after-effects. Here we report a case of intrauterine transfusion for Rh D isoimmunisation and blood bank experience related to this uncommon case.

CASE REPORT

A 39-year-old Rh-negative mother was managed by Obstetrics and Gynaecology (O&G) team in Hospital Sultanah Nur Zahirah (HSNZ) Kuala Terengganu. The mother was at 17 weeks of gestation during her first visit. This was her 5th pregnancy. Her first pregnancy was uneventful, and subsequently she had a molar pregnancy where dilation and curettage were done. Her 3rd pregnancy was complicated where the child developed cerebral palsy and underwent multiple exchange transfusion (ET) post-delivery. It was unsure if the mother received any Rhogam in her earlier pregnancies. During her 4th pregnancy, IUT was performed twice as the foetus displayed signs of hydrops fetalis but unfortunately mother had a fresh stillbirth at 28 weeks.

Antenatally during this 5th pregnancy, the mother had gestational diabetes mellitus under diet control. Her anti-D titre was extremely high at 1:1024. The first IUT was performed at 27 weeks of gestation because foetus's middle cerebral artery peak systolic velocity (MCA PSV) value was 52-56 cm/s which indicated mild anaemia. A total of four IUTs were performed with mother's consent and all IUTs were uneventful (Table I). Decisions for IUTs were based on MCA PSV and ultrasound findings suggestive of foetal anaemia like cardiomegaly, pericardial effusion, ascites, and oedema (2).

Table I: IUT procedures

IUTs	MCA PSV (cm/s)	Pre transfusion Hb(g/dL)/HCT (%)	Post transfusion Hb(g/dL)/ HCT (%)	Volume transfused(ml)
First- 27w POA	52-56	4.8/15.7	12.1/37	50
Second - 28w3d POA	*	7.8/23	20/61.6	35
Third -30w POA	40	9.5/28.4	Sample clotted	50
Fourth – 32w5d POA	*	10/30	Catheter dislodged	46

* Not available

The blood supplied for all the procedures was fresh, leukoreduced and irradiated O negative red cell concentrate (RCC) with final haematocrit (Hct) level of 75-80 %. Cold chain was constantly maintained during storage and transportation of blood as well to ensure quality. The donor's blood was crossmatch compatible with mother's plasma to prevent further haemolysis. The blood requirement for IUT summarised in Table II.

Baby was delivered via Caesarean section at 33 weeks because the ultrasound at 32 weeks showed oligohydramnios. Baby was born not vigorous with poor

Table II: Blood for IUT

Process		Remarks
1. Blood donation	-Blood group O Rhesus negative (rr phenotype) blood from regular donor (≥5 donations, last donation ≤6 months) in our setting. -Fresh blood (≤ 5 days old)	-Reduce risk of hyperkalaemia
2. Nucleic acid testing	-Sample sent to PDN -Takes 24 hours for the result to be available	
3. The whole blood processed into red cell concentrate (RCC)	-Target haematocrit 70 to 85 %	-High Hct to minimise the frequency of IUT
4. Red cell leukoreduction	-Residual leucocyte count of less than 1 X 10^6 per unit	-Reducing the risk of cytomegalovirus (CMV) transmission.
5. Crossmatch	-Crossmatch donor cell and mother's plasma -Need to be compatible	
6. Irradiation	-Sent to Hospital Universiti Sains Malaysia -Maintain cold-chain (2 to 10 degree Celcius) during transport -2 hourly temperature monitoring during transportation -Insulated box with coolant pack. Avoid direct contact with coolant.	-To prevent transfusion-associated graft versus host disease (TA-GVHD) -RCC recommended to be transfused within 24 hours post irradiation to reduce risk of hyperkalaemia. -Irradiated blood product is recommended for infants up to 6 months post-IUT.

muscle tone and poor breathing effort. Hence baby was intubated and ventilated for a day. Baby's haemoglobin level at birth was 17.4 g/dL and physically not hydropic. The baby underwent exchange transfusion (ET) the next day as the bilirubin level was 107 umol/L exceeding the ET level (100 umol/L). The pathological jaundice was attributed to haemolysis due to maternal anti-D antibody. Intravenous immunoglobulin 0.5 g/kg over 2 hours was administered 2 days after delivery to alleviate further haemolysis.

The infant subsequently required 2 blood transfusions; the last transfusion was at day 47 of life. These transfusions were likely due to persistent maternal anti-D antibody causing haemolysis, anaemia of prematurity and bone marrow suppression secondary to multiple intrauterine transfusions.

DISCUSSION

HDFN is a condition where the maternal IgG specifically IgG1 and IgG3 act against the red blood cell (RBC) antigens of foetus/neonate leading to premature removal of foetal/neonatal RBC by reticuloendothelial system. This occurs when the foetus inherits paternal RBC antigen which the mother lacks and leads to sensitization and production of maternal alloantibody. Most common blood systems involved in HDFN are ABO and Rh blood system.

The probability of Rh-D negative mother of developing alloantibody is variable. Some mothers are not sensitized even after multiple exposure to Rhesus D positive red blood cells. In certain circumstances Rh D positive foetal red cells as low as 0.1 ml are sufficient to sensitise Rh D negative mothers (3). On the other hand, some mothers require Rh D positive foetal red cells as high as 200 ml for sensitisation to occur (3). In this case the isoimmunisation most probably happened during the first pregnancy as there was no documentation of Rhogam given in subsequent pregnancies. It was unsure if the mother received the anti-D immunoglobulin during first pregnancy as she was followed up elsewhere.

Rh isoimmunisation especially anti-D alloantibodies inevitably leads to foetal / neonatal morbidity and mortality if not detected and managed in timely manner. Shortened life span of foetal / neonatal RBC brings about severe anaemia and subsequently hydrops fetalis, a condition incompatible with life which can occur in this case if IUTs were not performed. The administration of anti-D immunoglobulin had significantly reduced the morbidity and mortality of Rh D isoimmunisation but in this case as isoimmunisation had occur, administration of anti-D immunoglobulin was futile.

Measurement of MCV PSV is crucial for decision of IUT. If the MCA PSV is > 1.5 multiples of median (MoM), IUT may be indicated (2). All the IUTs in this case were performed due to the MCA PSV value > 1.5 MoM. IUT are performed every 2 to 3 weeks and the main aim is to increase the haematocrit level to 0.45 L/L (1) as seen in this case (Table I), however no post transfusion Hb were obtained in 3rd and 4th IUT procedure due to sample clotting and catheter dislodgement.

IUT procedure requires specialised foetal maternal unit with requisite interventional skills and expertise (1). It is an invasive ultrasound guided procedure where donor's red cell concentrate is transfused to foetus via umbilical vein at placental cord insertion. In certain situations, where IUT is indicated, the blood bank team need to expedite the supply of blood for this specialised procedure.

The approach in choosing IUT blood products is discussed as per guidelines. The red cell concentrate intended for IUT needs to meet special criteria to ensure safety for the patient. Regular donors with no previous history of transfusions and donated more than 5 times with the last donation being less than 6 months, were recruited for donation for this foetus in our setting to

reduce the possibilities of transfusion-transmitted infection. The blood products were subjected to nucleic acid testing (NAT) against HIV, HBV, HCV, and syphilis infection in reference centre (National Blood Centre). Group O negative blood with low haemolysin titre (isohaemagglutinin titres ≤1:50) is preferred, if the isohaemagglutinin titres is > 1:50 the blood need to be reconstituted with AB plasma (4) but this was not performed in this case due to unavailability of the test. Fresh blood less than 5 days old is important to prevent risk of hyperkalaemia. The blood was collected in double bag containing citrate phosphate dextrose anticoagulant. The additive solutions must be avoided due to theoretical risk of toxicity (1). The whole blood was processed to red cell concentrate (RCC) with target haematocrit level of 75 to 80 %. High haematocrit is crucial to minimise the frequency of IUT as higher haematocrit can increase foetus's haemoglobin to an acceptable level. The red cell concentrate was subsequently leuko-filtered so that the residual leucocyte count of less than 1 X 10^6 per unit. This reduces the risk of cytomegalovirus (CMV) transmission. The donor red blood cells need to be crossmatch-compatible with mother's plasma. Then the RCC is sent for irradiation to prevent transfusion associated-graft versus host disease (TA-GVHD). Due to unavailability of blood irradiator, the blood bank in HSNZ sends its blood products to another nearby hospital for irradiation. Cold chain shall be maintained at 2 to 10 °C during transportation of blood product. Temperature shall be monitored every 2 hours during transportation to ensure cold chain. Irradiated blood products recommended to be used in 24 hours to reduce risk of hyperkalaemia (1). Irradiated blood product is recommended for infants up to 6 months post-IUT (1).

For exchange transfusion and subsequent blood transfusions, fresh O negative leukoreduced and irradiated red cell concentrates were supplied. Criteria of blood for IUT summarised in Table III.

Table III Criteria of blood for IUT

1. Blood from regular male donor with no history of transfusion (4)
2. Fresh (<5 days old) (1)
3. Blood collected in Citrate phosphate dextrose (CPD) anticoagulant (4)
4. Leukoreduced (4)
5. Group O with low haemolysin titre (4)
6. Blood processed into red cell concentrate with haematocrit level of 0.75 to 0.85 L/L (1)
7. Irradiated blood for IUT. Irradiated blood recommended up to 6 months of age post-IUT (1)
8. Donor's RCC need to be crossmatch-compatible with mother's plasma. (4)

IUT is not only lifesaving in HDFN cases due to anti-D, anti-c or anti-K antibodies but also important in management of foetal parvovirus infection. HDFN due to anti-K is rare in Malaysia as most of the population have kk phenotype. The neonates affected by HFDN need to be followed up closely as persistent maternal antibodies in neonates can continue haemolysing neonate's RBC for weeks to months. The bone marrow also tends to be hypo-regenerative especially after multiple intrauterine transfusions. Weekly monitoring of reticulocyte and haematocrit can guide clinicians regarding the need of transfusion and assess marrow recovery (5).

CONCLUSION

This case illustrates how early recognition and management of foetal anaemia due to Rh isoimmunisation is successfully managed with close multidisciplinary approach.

ACKNOWLEDGEMENTS

We would like to thank the Obstetrics and Gynaecology team, Dr Mohd Muhaimin Kambali, paediatric team, haematopathologists, medical officers and all the laboratory and blood bank staffs in Hospital Sultanah Nur Zahirah for their expertise.

REFERENCES

1. New HV, Berryman J, Bolton-Maggs PH, Cantwell C, Chalmers EA, Davies T, Gottstein R, Kelleher A, Kumar S, Morley SL, Stanworth SJ. Guidelines on transfusion for fetuses, neonates and older children. British journal of haematology. 2016 Dec;175(5):784-828.
2. Prefumo F, Fichera A, Fratelli N, Sartori E. Fetal anemia: Diagnosis and management. Best Practice & Research Clinical Obstetrics & Gynaecology. 2019 Jul 1;58:2-14.
3. Hensley JG, Coughlin KP, Klein LL. A curious case of anti-D antibody titer. Journal of midwifery & women's health. 2009 Nov 1;54(6):497-502.
4. Clarke G, Bodnar M, Lozano M, Nadarajan VS, Lee C, Baud D, Canellini G, Gleich-Nagel T, Torres OW, Rey PL, Bub CB. Vox Sanguinis International forum on the selection and preparation of blood components for intrauterine transfusion. Vox sanguinis. 2020 Nov;115(8):e18-38.
5. Delaney M, Matthews DC. Hemolytic disease of the fetus and newborn: managing the mother, fetus, and newborn. Hematology. 2015 Dec 5;2015(1):146-51.