ORIGINAL ARTICLE

Blood Transfusion therapy in neonates admitted into the Special Care Baby Unit (SCBU) of University of Port Harcourt Teaching Hospital, Port Harcourt.

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ABSTRACT

Background: *Blood transfusion is associated with potential risks and adverse effects; it is therefore pertinent to ensure that it is given only when it is indicated.*

The objective of this study is to determine the rate and the indications of blood transfusion in neonates admitted into the Special Care Baby Unit (SCBU) of University of Port Harcourt Teaching Hospital (UPTH), Port Harcourt.

Method: *A prospective study of Neonates admitted into SCBU between January 1st 2003 and December 31st 2004 and who had blood transfusion during their hospitalization was carried out.*

Results: *Preterm babies are more likely to be transfused and are also more likely to receive multiple blood transfusions. Severe neonatal jaundice and severe anaemia are the commonest indication for blood transfusions in the neonates. Exchange blood transfusions (EBTs) were utilized more often than top up transfusions even among preterms. Adverse events were seen more in those that had EBT.*

Conclusion: *The rate of blood transfusion is still very high among neonates. Concerted efforts should be made to prevent severe neonatal jaundice and severe anaemia and thus reduce the rate of blood transfusion.*

KEYWORDS: Blood transfusion; Neonate; Port Harcourt.

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INTRODUCTION

Blood transfusion is a well known modality of therapy and although life-saving, is expensive and potentially dangerous. Sick neonate's especially preterm babies are among the most common of all patient groups to receive blood transfusion[1-4]. This is because many conditions and practices in neonates make blood transfusion an indispensable modality of management. They are also more commonly exposed to multiple blood transfusions from different donors[4,5]. Concerns about transfusion associated infections have not caused a major reduction in blood transfusion practices. In the developed countries, neonates are transfused with blood products for several reasons. Red Blood Cell transfusion is done for the replacement of blood drawn for investigation, maintenance of packed cell volume above 40% to ensure adequate tissue oxygenation during severe respiratory disease, symptomatic heart disease, severe anaemia, poor growth and feeding difficulty[1,2,6]. Platelets are transfused in cases of thrombocytopenia with bleeding, and granulocyte transfusion is mainly done for severe bacterial sepsis in conjunction with antibiotics[2,3,7].The objectives of this study were therefore to determine the rate of blood transfusion in the Special Care Baby Unit (SCBU) of University of Port Harcourt Teaching Hospital (UPTH), to determine the indications for blood transfusion and to compare the rate, frequency and type of blood transfusion in preterm and term neonates.

SUBJECTS AND METHOD

This was a prospective study. All neonates admitted into SCBU between Jan 1st 2003 and Dec 31st 2004 who received blood transfusion were included in the study. The sex, gestational age, the indication for the blood transfusion, the number of blood transfusion and the type of blood transfusion was noted. Double blood volume exchange transfusion (180mls/kg) was done for severe hyperbilirubinemia to remove the bilirubin already in circulation, as well as remove the antibody coated red blood cells (in order to reduce further haemolysis and bilirubin production). Single blood volume exchange transfusion (90mls) was done for severe anaemia complicated by heart failure or hypovolemic shock. Small volume transfusion of 15mls/kg (otherwise called Top-up transfusion) was utilised for investigational losses of blood and correction of moderate degrees of anaemia. Specific blood products like platelet concentrates or granulocytes are not available in our centre for transfusion and so, fresh whole blood was also used in cases of disseminated intravascular coagulopathy and overwhelming sepsis. Adverse events if any, following the blood transfusions were also noted. Statistical significance was placed at *p*-value =0.05.

RESULTS

A total number of 2035 (Males =1186; Females = 849; M:F =1.4:1) were admitted during the two-year

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period under study out of which 405(Male =247; Females=158; M:F =1.6:1) received 573 blood transfusions, giving the blood transfusion rate in neonates admitted into SCBU as 20%. The difference in the male: female ratio was not statistically significant (χ^2 =1.02, df=1; p >0.10). During the period also, there were 469(20.04%) deaths with 94 of them having been transfused (23.2% of all those transfused and 20% of all deaths in SCBU). Forty-six (48.9%) of these deaths were preterm babies and 48 (51.1%) were term babies. Table I shows the total number of neonates admitted and the number that were transfused as well as the difference in the rate of blood transfusion in term and preterm babies.

The rate of blood transfusion in preterm babies was 27.2%, whereas that in term babies was 17.5%. This difference in the rate of blood transfusion in term and preterm babies was statistically significant (χ^2=14.66, df =1; p=0.000001).

Seventy- nine babies required two blood transfusions, twenty-two required 3 blood transfusions, eight had 4 blood transfusions, two had 5 blood transfusions and one each had 6 and 9 blood transfusions. All those requiring more than 3 blood transfusions were preterm babies (Table II).

Three hundred and fifty-six (62%) of the blood transfusions were exchange blood transfusion (double volume DV = 255, and single volume SV = 101) while 217(38%) were Top-up-transfusion only. There were a total of 573 blood transfusions: 236 were in the 139 preterm babies whilst 337 were done for 266 term babies (Table III). This difference in the total number of blood transfusion between term and preterm babies was statistically significant (χ^2 = 4.73, df=1; p < 0.05)

From Table IV, the commonest indications for blood transfusions were severe neonatal jaundice (NNJ) (44.5%) and severe anaemia (45.4%). Identified causes of the jaundice were sepsis (51%), prematurity (21.6%), and ABO incompatibility (10.6%). Glucose-6-phosphate dehydrogenase was assayed in 150 babies and was deficient in 31 babies (20.7%). Twenty-two of them received 25 blood transfusions for severe neonatal jaundice (9.8%). Three babies had Rhesus Isoimmunisation and they received a total of 10 (3.9%) blood transfusions for severe neonatal jaundice. In eight (3.1%) of the blood transfusions for severe NNJ, no cause was readily identified. Identified causes of the anaemia were repeated blood sampling, with removal of 10% of the infants total blood volume (49.6%), and acute haemorrhage (22.3%). Nine of those with concealed haemorrhage had cephalhaematoma, while four had subgaleal haemorrhage. Others (28.1%) were dilutional anaemia resulting from transfusion with poor quality blood especially following massive transfusions like exchange blood transfusion (34%) as well as anaemia from the disease process (36%) and poor intake leading to hypoalbuminemia with oedema (3%). The mean haemoglobin value of those with severe anaemia was 7.3g/dl (range 4.6-9.3g/dl).

Adverse Events

This was documented in 157 babies (38.8%). One hundred and one of them had EBT and 56 had top up transfusions. The commonest adverse event observed with both types of blood transfusion was development of malaria parasitemia and fever usually within 72 hours after the blood transfusion (Table V). Among those that had EBT, 30 neonates developed severe anaemia warranting another blood transfusion. Sixteen developed hypoglycemia and 6 developed hypocalcemia and both conditions manifested with seizures and were promptly corrected with the appropriate therapy. One child developed stage 2 Necrotizing Enterocolitis and one child who was in shock from acute blood loss from the umbilical stump and was transfused with group 0 Rhesus negative blood that was crossmatched on an emergency basis developed severe NNJ that required another EBT and phototherapy. Among those that had top-up transfusion (TUT), two developed cellulitis (from extravasation of blood) which required wound debridement and dressing and two had blood transfusion reactions (hyperpyrexia with urticarial rash). Twenty-two babies died within 6 hours after blood transfusion. Four of them were admitted with severe anemia secondary to bleeding from the umbilical stump (2), torn frenulum (1) and circumcision (1) and died during or soon after a single volume EBT whereas 15 were admitted with severe NNJ, acute bilirubin encephalopathy and gasping respiration and had double volume EBT. The remaining 3 also had severe anaemia following circumcision and had TUT due to failed umbilical vein cannulation for a single volume EBT.

Table I. Total number of neonates admitted and transfused and the rate of blood transfusion in relation to the gestational age

Gestational Age	Total No. Admitted	Total No. (%)Transfused	Rate of blood (%)Transfusion
PREM	511(25.1%)	139(34.3%)	27.2%
TERM	1524(74.9%)	266(65.7%)	17.5%
TOTAL	2035(100%)	405(100%)	

χ^2 = 14.66, df = 1; p= 0.000001

Table II Frequency of blood transfusion in term and preterm babies

No. of blood Transfusions(A)	No. of patients(B)	Term	Preterm	Total No. of blood transfusion(AxB)
1	292	205	87	292
2	79	49	30	158
3	22	12	10	66
4	8	0	8	32
5	2	0	2	10
6	1	0	1	6
9	1	0	1	9
Total	405	266	139	573

Table III. Type of blood transfusion given to preterm and term babies

GA	SV	DV	TUT	SV/TUT	DV/TUT	TOTAL
Preterm	8	37	85	19	87	236
Term	20	40	132	54	91	337
Total	28	77	217	73	178	573

(GA = gestational age; SV= single volume; DV= double volume; TUT= top up transfusion)

Table IV. Indications for the blood transfusion in 405 neonates admitted into the SCBU

Indications	Number	Percentage
1.Severe unconjugated NNJ*	255	44.5
a. sepsis – 130 (51%)		
b. prematurity – 55(21.6%)		
c. ABO incompatibility – 27(10.6%)		
d. G-6-P-D deficiency 25 (9.8%)		
e. Rhesus incompatibility – 10 (3.9%)		
f. others – 8 (3.1%)		
2. Severe Anaemia	260	45.4
a. Cumulative blood loss from repeated blood sampling - 129(49.6%)		
b. Haemorrhage- 58(22.3%)		
i.bleeding from circumcision site-9		
ii.bleeding from the cord - 8		
iii.bleeding from torn frenulum - 7		
iv.blood loss post operatively – 21		
v.concealed haemorrhage-13		
c. Others – 73(28.1%)		
3. DIC*	47	8.2
4. Severe Neonatal sepsis	8	1.4
5. PPHN*	3	0.5
TOTAL	573	100.0

*(NNJ = neonatal jaundice; DIC = Disseminated Intravascular Coagulopathy; PPHN = Persistent Pulmonary Hypertension of the Newborn).

Table V. Adverse events observed in 157 neonates transfused in SCBU

Adverse events	EBT	TUT
Malaria	56	51
Severe Anaemia	30	0
Cellulitis	0	2
Hypoglycemia	16	0
Transfusion reaction	0	2
Hypocalcemia	6	0
Acidosis	2	0
Necrotizing enterocolitis	1	0
Severe NNJ	1	0
Death	19	3

DISCUSSION

As much as 20% of neonates admitted into SCBU of UPTH are transfused. This agrees with the rate from a preliminary report in the same centre thus showing that the rate is yet to drop[8]. Preterm babies are not only likely to be transfused, but they are also more likely to receive multiple blood transfusions. This is as a result of a combination of factors which include a higher predisposition to developing neonatal jaundice and anaemia, a smaller total blood volume coupled with repeated blood sampling for the various investigations they may have to undergo. Practices like repeated blood sampling for investigations predispose the neonate to severe anaemia and thus increase the likelihood of blood transfusion[4,6]. In this study, repeated blood sampling (with cumulative blood loss of at least 10% of the infants total blood volume) accounted for 49.6% of the cases of anaemia. Lenes and Sacher[9] and Radhakrishnan[1] in their studies reported that replacement of blood drawn for laboratory studies accounted for as high as 90% of neonatal blood transfusions. A lot of workers have advocated for a more restrictive approach towards blood transfusions especially in preterm infants in order to reduce the number of exposure to blood products in them[2,10-12]. Bell and co-workers[13] in their study to determine if restrictive guidelines for red blood cell (RBC) transfusions for preterm infants can reduce the number of transfusions without adverse consequences concluded that although the restrictive approach reduced the number of blood transfusions, however, major adverse neurologic effects occurred more in the restrictive than liberal transfusion group.

Neonatal jaundice (NNJ) is quite common in our environment and was the indication in 44.5% of the total blood transfusion in the neonates. In developed countries, intensive and effective phototherapy has drastically reduced the need for exchange transfusion for hyperbilirubinemia[14]. The causes of severe NNJ were severe sepsis, prematurity and ABO blood group incompatibility. This agrees with other studies done in some parts of the country where septicaemia was identified as the predominant aetiologic factor in neonatal jaundice[15-17]. It however differs from findings from other parts of the country where glucose -6-phosphate dehydogenase (G6PD) deficiency was reported to be the single most important cause of neonatal jaundice[18-21]. Assay for G-6-P-D level is not routinely done in our centre. In this study, the assay could only be done in 150 babies and hence, it is difficult to accurately determine the contribution of the deficient status to the aetiology of NNJ. It should be noted also that in the presence of hemolysis, G6PD levels can be elevated, which may obscure the diagnosis in the

newborn period so that a normal level in a hemolyzing neonate does not rule out G6PD deficiency. Uko *et al*[22] in their study reported a prevalence rate of 38% of G6PD deficiency among jaundiced babies. Preterm babies are especially prone to developing NNJ because of a higher rate of haemolysis, inadequate caloric intake with increased entero-hepatic circulation and immature conjugating system. Only three babies developed severe NNJ from Rhesus iso-immunisation. This agrees with other studies which showed that Rhesus incompatiblity plays an insignificant role in the causation of neonatal jaundice in our environment[15-21]. This is because only 3-6% of West African population are Rhesus D negative.

Cultural practices like circumcision and frenulectomy by traditional birth attendants pose risks of uncontrolled haemorrhage. This has not been reported in other studies. Of great concern is the large number of transfusions that were given as a result of anemia which developed following a double volume EBT (for severe NNJ) with poor quality donor blood, with the effect that the newborn's blood with a higher haematocrit is continuously removed and replaced with the donor blood with a lower haematocrit.

In this study, the commonest type of blood transfusion was exchange blood transfusion (62%) which contrasts with findings from other studies [1,9] where top-up transfusion accounted for over 90% of all neonatal blood transfusion. The reason might not be unconnected with the indication for the blood transfusion since in our centre, phototherapy units are inadequate and hence most of the babies with severe hyperbilirubinemia end up having exchange transfusion to prevent the development of bilirubin toxicity. Owa and Ogunlesi[23] reported an exchange blood transfusion (EBT) rate of 5.8% for only babies with severe NNJ, however this rate was calculated based on the number of babies that had EBT and not the total number of EBT received by these babies.

Adverse events like thrombocytopenia, hypocalcemia, sepsis, hypoglycemia, necrotizing enterocolitis and even cardiac arrest and death are known to occur more with massive blood transfusion like EBT than with small volume transfusion[3,24-26]. In this study, adverse events were documented in 38.8% of the newborns. This is much lower than the 74% reported by Patra *et al*.[24] This may be due to the fact that majority of the adverse events associated with exchange transfusion are laboratory abnormalities and are asymptomatic and may not be detected easily if not actively sought for. The commonest adverse event was malarial parasitemia. This is not surprising as malaria is endemic in our area and blood is not routinely screened for malarial parasitemia before blood donation. The death of nineteen babies during and a few hours after EBT is much higher than the 3 deaths/1000 procedures previously reported by Jackson [25] and Keenan *et al*[26]. These deaths occurring during and a few hours after the exchange transfusions might suggest a probable relation to the procedure. It is however difficult to determine whether these deaths were possibly related to the EBT procedure or to their poor clinical condition since these babies were already critically ill before the procedure.

CONCLUSION

The rate of blood transfusion in SCBU of 20% is quite high. The commonest indications are severe anaemia (from repeated blood sampling, haemorrhage and the disease process) and severe NNJ (from severe sepsis, prematurity and ABO blood group incompatibility). Preterm babies are not only more likely to be transfused, but are also more likely to have multiple blood transfusion. Exchange blood transfusion is the commonest type of blood transfusion in neonates and this large volume transfusion pose great risks to the neonate. The risks of blood transfusion are significant and blood components should be given only when necessary. Consequently we recommend that blood sampling should be limited to necessary investigations and can be further limited via the use of indwelling catheters with specific transducers, transcutaneous electrodes and monitors. Our Laboratories can also help by providing modern micro-analyzers which utilizes minimal blood for investigations. Aliquots from a single donation can be dedicated to a single neonate to allow for sequential transfusions from the same donor especially for preterm babies who are likely to require multiple small volume transfusions. Since severe neonatal jaundice is a very common indication for blood transfusion and the commonest aetiological factor is sepsis, its prevention through hygienic delivery, proper care of the cord, and effective phototherapy will go a long way in reducing the rate of blood transfusion. Erythropoetin for neonatal anaemia especially for preterm babies will also limit the rate of blood transfusion. Traditional birth attendants and the general populace should be discouraged from performing minor surgical procedures which in untrained hands can result in uncontrollable bleeding.

REFERENCES

1. Radhakrishnan KM, Chakravarthi S, Pushkala S, Javaraju J. Component therapy. Indian J Peadiatr. 2003; 70(8) 661-6.

2. Murray NA, Roberts IAG. Neonatal transfusion practice. Arch Dis Child Fetal Neonatal Edition 2004; 89: F101.
3. Strauss RG. Transfusion Therapy in Neonates. AJDC. 1991; 145: 904-911.
4. Ringer SA, Richardson DK, Sacher RA, Keszler M, Churchill WH. Variations in transfusion practice in neonatal intensive care. Paediatrics 1998;101(2):194-200.
5. Levy GJ, Strauss RG, Hume H, National survey of neonatal transfusion practices I: Red blood cell therapy. *Pediatrics.* 1993; 91:523-529.
6. Fetus and Newborn Committee. Red blood cell Transfusions in Newborn Infants: Revised Guidelines. Paediatrics and Child Health 2002;7(8):553-558.
7. Strauss RG, Levy GJ, Sotello-Avila C, *et al*. National survey of neonatal transfusion practices II. Blood component therapy. Paediatrics 1993; 91: 530-6.
8. Eneh AU, Oruamabo RS. Blood Transfusion Practices in Neonates at the University of Port Harcourt Teaching Hospital: A Preliminary Report. TNHJ 2004;3(12): 189-192.
9. Lenes BA, Sacher RA. Blood component therapy in neonatal medicine. Clin Lab Med 1981; 1:285-309.
10. Maier RF, Sonntag JS, Walka MM, Liu G, Metze BC, Obladen M. Changing practices of red blood cell transfusions in infants with birth weights less than 1000 g. J Pediatr 2000;136:220-4.
11. Widness JA, Seward VJ, Kromer IJ, Burmeister LF, Bell EF, Strauss RG. Changing patterns of red blood cell transfusion in very low birth weight infants. J Pediatrics 1996; 129:680-7.
12. Donovan EF. Practice variation: Implications for neonatal red blood cell transfusions. J Pediatr 1998; 133:589-90.
13. Bell EF, Straus RG, Widness JA, Mahoney LT, Mock DM, Seward VJ, Cress GA *et al*. Randomized Trial of Liberal versus Restrictive Guidelines for Red Blood Cell Transfusion in Preterm Infants. Paediatrics 2005;115(6):1685-1691.
14. Maisels MJ, Watchko JF. Treatment of jaundice in low birthweight infants. Arch Dis Child Fetal Neonatal Edition .2003;88:F459.
15. Coulter JIBS, Akpabio MA, Jikemi SON, Kay T. Neonatal jaundice in Northern Nigeria. Nig J Paediatr 1978; 5:12-15.
16. Werblinska B, Stankiewics H, Oduloju MO, Atuchukwu CMA. Neonatal jaundice in Zaria, Northern Nigeria. Nig J Paediatr 1981; 8:3-10.
17. Ahmed H. Yakubu AM, Hendrickse RG. Neonatal jaundice in Zaria, Nigeria: A second prospective study. West Afr J Med 1995;14:15-23.
18. Effiong CE, Aimaku VE, Bienzle U, Oyedeji GA, Ikpe DE. Neonatal jaundice in Ibadan. J Nat Med Ass 1975; 67:208-213.
19. Ransome-Kuti O. Problems of Paediatic emergencies in Nigeria. Nig Med J 1972; 2:62-70.
20. Owa JA, Taiwo O, Adebiyi JAO, Dogunro SA. Neonatal jaundice at Wesley Guild Hospital, Ilesa and Ife State Hospital, Ile-Ife. Nig J Paediatr 1989;16:23-30.
21. Owa JA, Dawodu HA. Familusi JB. Kernicterus in Nigerian infants. West Afr Med J. 1987;6:11-20.
22. Uko EK, Agwunobi SN, Udoh JJ. Glucose-6-Phosphate Dehydrogenase (G6PD) levels in jaundiced neonates in Calabar. Nig Med J 2003;12(2):98-102.
23. Owa JA, Ogunlesi TA. Why we are still doing so many exchange blood transfusions for neonatal jaundice in Nigeria. Nig J Paed 2004;31(3):112 (Abstracts of proceedings of the 35th Annual Conference of the Paediatric Association of Nigeria, Zaria, January 21-24, 2004).
24. Patra K, Storfer- Isser A, Siner B, Moore J, Hack M. Adverse events associated with neonatal exchange transfusion in the 1990s. J Paediatrics 2004; 144(5):626-631.
25. Jackson JC. Adverse events associated with exchange blood transfusion in healthy and ill newborns. Paediatrics 1997; 99(5):e7. Available at www.pediatrics.org/cgi/content/full/99/5/e7.
26. Keenan WJ, Novak KK, Sutherland JM, Bryla DA, Fetterly KL. Morbidity and mortality associated with exchange transfusion. *Pediatrics* 1985;75 (suppl) :41721.