MATERNAL AND PRENATAL DETERMINANTS OF RED CELL TRANSFUSION AMONG SICK NEONATES

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ABSTRACT

BACKGROUND

In neonates, several maternal and prenatal factors can contribute to anaemia in preterm infants. Assessing those determinants can help in planning transfusion in an effective manner. We wanted to identify the maternal and prenatal determinants of red blood cell transfusion in sick neonates.

METHODS

This was a case control study done on 300 neonates (150 cases and 150 controls). Study sample included newborn babies with gestational age less than 37 weeks and/or birth weight less than 2500 grams admitted to the Neonatal Intensive Care Unit (NICU) of Sri Avittom Thirunal Hospital, Government Medical College Thiruvananthapuram. Study was done for a period of one and a half years, in the Department of Transfusion Medicine, Government Medical College, Thiruvananthapuram. Cases were sick neonates who were transfused with packed red cells. Controls were sick neonates who did not receive packed cells. Maternal demographic characteristics known to be associated with anaemia of prematurity were analysed. Statistical data was analysed using SPSS software version 16.

RESULTS

46.7 % of mothers were primi gravida. 39.7 % were second gravida and 13.7 % were third gravida. Mean age at delivery was 25.5 +/- 4.2. 43.3 % in the case group and 34.7 % in the control group delivered by caesarean section. On analysis, 88% in the case group had comorbid conditions compared to 81.3 % in the control group and was not statistically significant. 82 % of the case group had antenatal complications compared to 66 % in the control group and was statistically significant. 56.7 % of cases and 50 % of controls received steroids in the antenatal period and there was no statistically significant difference between the two groups.

CONCLUSIONS

Among the various ante-natal factors compared between case and control groups, ante-natal complications in general and PIH in specific was found to be a risk factor for RBC transfusion.

KEY WORDS

Red Cell, Low Birth Weight, Transfusion, Anaemia, Ante-Partum, Neonate, Prematurity, Haemorrhage

HOW TO CITE THIS ARTICLE: Viswanathan MC, Vilambil S, Usha KKC. Maternal and prenatal determinants of red cell transfusion among sick neonates. J. Evolution Med. Dent. Sci. 2019;8(28):2215-2218, DOI: 10.14260/jemds/2019/485

BACKGROUND

In neonates, blood loss, increased red cell destruction as in abnormalities of red cell membrane, decreased red cell production, obstetrical causes leading to blood loss, foetomaternal transfusion, twin-twin transfusion, internal haemorrhage, iatrogenic causes etc., are the factors leading to blood transfusions. Oxidative haemolysis secondary to sepsis, rapid growth with concomitant protein and iron deficiency, bleeding diathesis etc., can also contribute to anaemia in preterm infants.

Assessing the risk factors and clinical conditions before the first transfusion will improve the ability to estimate the need for RBC transfusions of low birth weight (LBW) infants. Such estimation can identify infants who require more number of red cell transfusions. This can further help in efficient inventory management.

'Financial or Other Competing Interest': None.
Submission 14-05-2019, Peer Review 27-06-2019,
Acceptance 03-07-2019, Published 15-07-2019.
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Aim of The Study

To identify the maternal and prenatal determinants of red blood cell transfusion in sick neonates.

METHODS

This was a case control study done on 300 neonates (150 cases and 150 controls). Sample population were newborn babies with gestational age less than 37 weeks and/or birth weight less than 2500 grams admitted to the Neonatal Intensive Care Unit (NICU) of Sri Avittom Thirunal Hospital, Government Medical College Thiruvananthapuram. Study was done for a period of one and a half years, in the Department of Transfusion Medicine, Government Medical College, Thiruvananthapuram. Cases were sick neonates admitted to the NICU who were transfused with packed red cells at least once during their hospital stay. Controls were sick neonates who did not receive packed cells. Infants with chromosomal abnormalities, congenital heart disease, other life-threatening congenital abnormalities, death within first 24 hours were excluded from the study.

Age	Case		Control		Total	
	Number	Percent	Number	Percent	Number	Percent
< = 20	13	8.7	18	12.0	31	10.3
21 - 25	69	46.0	55	36.7	124	41.3
26 - 30	52	34.7	50	33.3	102	34.0
➢ 30	16	10.7	27	18.0	43	14.3
Mean ± SD	25.3 ± 4		25.7 ± 4.5		25.5 ± 4.2	
Table 1. Comparison of Age Based on Groups						
t = 0.75, p = 0.452						

Gravida	Case		Control		Total	
	Number	Percent	Number	Percent	Number	Percent
1	73	48.7	67	44.7	140	46.7
2	50	33.3	69	46.0	119	39.7
➢ = 3	27	18.0	14	9.3	41	13.7
Mean ± SD	1.7 ± 0.9		1.6 ± 0.6		1.7 ± 0.8	
Table 2. Comparison of Parity						
t = 0.91, p = 0.363						

Mode of Delivery	Case		Control		Total		χ^2	p
	Nos.	Percent	Nos.	Percent	Nos.	Percent		
Normal	65	43.3	72	48.0	137	45.7	2.58	0.275
CS	65	43.3	52	34.7	117	39.0		
Assisted	20	13.3	26	17.3	46	15.3		
Table 3. Comparison of Mode of Delivery								

Co Morbid Conditions	Case		Control		χ^2	p
	Number	Percent	Number	Percent		
No	18	12.0	28	18.7	2.57	0.109
Yes	132	88.0	122	81.3		
Table 4. Comparison of Co Morbid Conditions Based on Groups						

Comorbid Conditions		Case		Control		χ^2	p
		Number	Percent	Number	Percent		
Anaemia	No	115	76.7	112	74.7	0.16	0.686
	Yes	35	23.3	38	25.3		
Antepartum Haemorrhage	No	120	80.0	125	83.3	0.56	0.456
	Yes	30	20.0	25	16.7		
Hypertension	No	121	80.7	132	88.0	3.05	0.081
	Yes	29	19.3	18	12.0		
Cardiac diseases	No	142	94.7	138	92.0	0.86	0.355
	Yes	8	5.3	12	8.0		
Diabetes Mellitus	No	141	94.0	133	88.7	2.7	0.101
	Yes	9	6.0	17	11.3		
Eclampsia	No	141	94.0	142	94.7	0.06	0.803
	Yes	9	6.0	8	5.3		
Renal Diseases	No	149	99.3	146	97.3	1.83	0.176
	Yes	1	0.7	4	2.7		
Table 5. Comparison of Co Morbid Conditions Based on Groups							
**: - Significant at 0.01 level							

Antenatal Complication	Case		Control		χ^2	P
	Number	Percent	Number	Percent		
Normal	27	18.0	51	34.0	9.98**	0.002
Abnormal	123	82.0	99	66.0		
Table 6. Comparison of Antenatal Complications Based on Groups						
**: - Significant at 0.01 level						

Antenatal Complications		Case		Control		χ^2	p
		Number	Percent	Number	Percent		
PROM	No	116	77.3	127	84.7	2.62	0.105
	Yes	34	22.7	23	15.3		
APH	No	138	92.0	139	92.7	0.05	0.828
	Yes	12	8.0	11	7.3		
Anaemia	No	124	82.7	126	84.0	0.1	0.757
	Yes	26	17.3	24	16.0		
GDM	No	138	92.0	130	86.7	2.24	0.135
	Yes	12	8.0	20	13.3		
PIH	No	130	86.7	142	94.7	5.67*	0.017
	Yes	20	13.3	8	5.3		
Eclampsia	No	139	92.7	139	92.7	0	1.000
	Yes	11	7.3	11	7.3		
Abruptio placenta	No	142	94.7	148	98.7	3.72	0.054
	Yes	8	5.3	2	1.3		
Table 7. Comparison of Antenatal Complications							
*: - Significant at 0.05 level							

Antenatal Steroids	Case		Control		Total		χ^2	p
	Nos.	Percent	Nos.	Percent	Nos.	Percent		
Given	85	56.7	75	50.0	160	53.3	1.34	0.247
Not given	65	43.3	75	50.0	140	46.7		
Table 8. Comparison of Antenatal Steroids Based on Group								

The maternal demographic characteristics known to be associated with anaemia of prematurity were recorded. The details of the mother included age, parity, mode of delivery, co-morbid conditions, ABO blood group and Rh type, untoward events like premature rupture of membranes (PROM), ante-partum haemorrhage, abruptio placentae, anaemia, gestational diabetes mellitus, hypertension, cardiac diseases, eclampsia or any other relevant illness. Use of ante-partum steroid injection was also assessed.

Ethics

The study was approved by the human ethical committee and research committee, Government Medical College, Thiruvananthapuram. The parents of the study subjects were counselled about the nature of the study. A written consent was obtained from the parents of the new borns included in the study.

Statistical Analysis

All statistical data were analysed using SPSS software version 16. Continuous variables were expressed as mean +/- standard deviation. Qualitative data was expressed as percentage. Independent t test was used for comparing quantitative data between two groups. Categorical variables were compared using χ^2 test. The predictive variables were calculated by univariate analysis.

RESULTS

This was a case control study done in 300 neonates admitted in the NICU of Sri Avittom Thirunal Hospital, Government Medical College, Thiruvananthapuram. Study subjects were divided into cases (n = 150) and controls (n = 150). Maternal and prenatal characteristics were studied and compared.

Age distribution of the study groups showed that the mean age at delivery was 25.5 +/- 4.2. Maximum number of mothers was in the age group of 21 - 25 years in both groups. Mean age of cases and controls was compared with independent t test. No significant difference was observed. (t = 0.75, p = 0.452).

Regarding parity of the total study groups, 46.7 % of mothers were primi gravida. 39.7 % were second gravida and 13.7 % of third gravida. Parity of mothers of cases and controls were compared with independent t test. Statistically, significant difference was not observed. (t = 0.91 p = 0.363).

When mode of delivery was analysed, it was found out that 43.3 % in the case group delivered by caesarean section as compared to 34.7 % in the control group. Of the total number of cases, 45.7 had normal deliveries, 15.3 % had assisted delivery.

On analysis, 88% in the case group had co morbid conditions compared to 81.3 % in the control group. Study on case group revealed anaemia in 23.3 %, ante-partum haemorrhage in 20 %, hypertension in 19.3 %, cardiac diseases in 5.3 %, diabetes mellitus in 6 %, eclampsia in 6 % and renal diseases in 0.7 %. Study on control groups revealed anaemia in 25.3 %, ante-partum haemorrhage in 16.7 %, hypertension in 12 %, cardiac diseases in 8 %, diabetes mellitus in 11.3 %, eclampsia in 5.3 % and renal diseases in 2.7 %. The results did not show any statistical significance.

On analysis, 82 % of the case group had antenatal complications compared to 66 % in the control group. p value 0.002 was statistically significant. Assessment of the

antenatal complications in the case group revealed premature rupture of membranes (PROM) in 22.7 %, anaemia in 17.3 %, ante partum haemorrhage (APH) in 8%, gestational diabetes mellitus (GDM) in 8 %, pregnancy induced hypertension (PIH) in 13.3 %, eclampsia in 7.3 % and abruptio placenta in 5.3 %. Study on control group showed PROM in 15.3 %, anaemia in 16 %, APH in 7.3 %, GDM in 13.3 %, PIH in 5.3 %, eclampsia in 7.3 % and abruptio placenta in 1.3 %. PIH was significantly more in the case group compared to the control group.

56.7 % of cases and 50 % of controls received steroids in the antenatal period. There was no statistically significant difference between the two groups.

DISCUSSION

Majority of the neonates with low birth weight and gestational age require transfusions of red blood cells during their neonatal period. Most of these transfusions will be administered in the first postnatal month. Preterm infants are often anaemic and typically experience heavy blood losses from frequent laboratory sampling in the first few weeks of life. Although their anaemia is multifactorial, repeated blood sampling and reduced erythropoiesis with extremely low serum levels of erythropoietin are major determining factors. Therefore, preterm neonates comprise the most heavily transfused group of patients. About 85 % of extremely low birth weight newborns receive a transfusion by the end of their hospital stay. Approximately one half of all RBC transfusions administered to extremely low birth weight (ELBW) infants before discharge are given in the first 2 weeks of life, when neonatal cardiorespiratory illness is most severe and laboratory blood sampling is greatest. RBC transfusion can reduce the morbidity associated with anaemia especially anaemia of prematurity and maybe lifesaving in neonates with severe blood loss.

Many aspects of haematopoiesis are either incompletely developed in preterm infants or are adapted to serve the foetus. This lack of development and/ or adaptation to extra uterine life diminishes the capacity of the neonate to produce red cells, platelets and neutrophils particularly during the stress of life-threatening illnesses encountered after pre term birth such as sepsis, severe pulmonary dysfunction, necrotising enterocolitis, and immune cytopenias. The serious medical and surgical problems of preterm birth can be further complicated by phlebotomy losses, bleeding, haemolysis and consumptive coagulopathy. Preterm infants begin life with quantities of blood cells and clotting proteins that are barely adequate. These infants have a diminished ability to increase production adequately to compensate for the haematologic problems they experience. Preterm infants especially those with birth weight less than 1.5 kg and with respiratory distress are given numerous red cell transfusions early in life because of several interacting factors. Neonates delivered before 28 weeks of gestation are born before the bulk of iron transport has occurred from the mother to foetus before the onset of marked erythropoietic activity of foetal marrow. Several diseases during neonatal period require repeated blood sampling leading to iatrogenic anaemia. Preterm infants are unable to mount an effective erythropoietin response.

Blood loss increased red cell destruction and decreased production as in abnormalities of red cell membrane, obstetrical causes leading to blood loss, foetomaternal transfusion, twin-twin transfusion and internal haemorrhage, iatrogenic blood loss etc are the factors leading to blood transfusions. Oxidative haemolysis secondary to sepsis, rapid growth with concomitant protein and iron deficiency, bleeding diathesis also contribute to anaemia in preterm infants.

An important reason for the lower haemoglobin values of preterm infant than those of term infants is that preterm infants have a relatively diminished erythropoietin plasma level in response to anaemia. The major physiological impact of anaemia of prematurity is decreased oxygen delivery to the tissues which result in compensatory responses like increase in heart rate, cardiac output and cerebral blood flow, poor growth, decrease in activity etc. Low RBC mass contributes to tachypnoea, dyspnoea, apnoea, tachycardia, bradycardia, feeding difficulties and lethargy and these problems can be alleviated by PRC transfusions.

In our study, neonates who had received transfusions were included in the case group and those who had not received transfusions were included in the control group. Our study compared the ante-natal characteristics and variables which are known to be associated with transfusion of packed red cells in neonates.

Transfusion of Whole blood creates hazards to the patients was noted in last few decades. So transfusion of blood components has been considered as a better and safe procedure.[1] An increasing need for stricter guidelines for transfusing blood products has been recognized by many a countries and they have started implementing the same. Sticking to the guidelines can minimize side effects of blood transfusion.[2] In almost all western countries, whole blood is not used for transfusion for the patients.[3] Routinely it is processed into various blood components and only that specific components are used for the patient.

Preterm neonates are the most frequently transfused group of patients. In that 85 % of extremely low birth weight newborns receive a transfusion by the end of their stay in hospital.[4]

On analysing the maternal data, the mean age at delivery was 25.5 ± 4.2. Both the case and control groups had similar age distribution. The highest number of mothers was in the age group 21-25 years. The case and control groups had similar distribution of parity. Of the total number of mothers, 46.7 % were primi gravida. On analysing the mode of delivery, 43.3 % of the case group and 34.7 % of the control group had caesarean section. In our study, the frequency of transfusions was found to be higher in the neonates born by caesarean section, which is statistically significant. In the case group, 22.7 % of mothers had Premature Rupture of Membranes (PROM) while only 15.3 % of mothers had PROM in the control group, which shows a significant association.

On assessing the co morbid conditions of the mothers in both the groups, we found that the incidence of pregnancy induced hypertension was 13.3 % in the case group and only 5.3% in the control group. So pregnancy induced hypertension was a high risk factor in our study. This is in contrast to the observation by Dos Santos et al who found that frequency of pregnancy induced hypertension was more in the non-transfused group.[5] Their study compared maternal

characteristics like diabetes, age at delivery and mode of delivery etc. They could not find any significant association between the two groups.

Use of antenatal steroids for maturation of lung of the foetus was compared in our study. Of the total number of 300 cases, 53.3 % received antenatal steroids. There was no significant difference between the two groups.

CONCLUSIONS

Among the various ante-natal factors compared between case and control groups, ante-natal complications in general and PIH in specific was found to be a risk factor for RBC transfusion.

ACKNOWLEDGEMENT

We thank Dr K C Usha, Professor and HOD, Department of Transfusion Medicine, Sree Mookambika Institute of Medical Sciences, Kulasekharam, Kanyakumari, Tamilnadu, Dr Lalitha Kailas Professor and HOD in Dept. of Paediatrics, Gokulam Medical College, Trivandrum, and Dr. Shobha Kumar, Professor in Dept. of Paediatrics, Govt. Medical College Trivandrum, for their scholarly guidance in the course of this work.

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