

Original Article

Overview of the blood transfusion policy in preterms on the Neonatal Intensive Care Unit

Valerie Said Conti, Eugenio Azzopardi, Raymond Parascandalo, Paul Soler, Simon Attard Montalto

Abstract

Preterm infants on the Neonatal Intensive Care Unit receive a greater number of red cell transfusions than any other hospitalised group. Over the past twenty years research has focused on setting standards to determine when it is necessary to transfuse packed cells in this cohort, whilst exploring the use of red cell growth factors and other substrates judiciously in order to reduce and/or avoid red cell transfusions and limit donor exposure. One hundred and eighty-one blood transfusions were administered to 106 preterms less than 35 weeks gestation on the NICU during 2009 in Malta. The median (range) volume of blood used from each bag supplied by the Blood Transfusion Department was 25.8mls (10-50mls), the rest of which was discarded. Risk factors for transfusion included Extremely Low Birth Weight (less than 1kg) and a gestation of less than 30 weeks. The blood transfusion guidelines presently in use on the local NICU were reviewed and compared with more restrictive guidelines on other units and suggestions made to reduce transfusions in line with these guidelines.

A reduction in transfusion aliquots provided for neonates to just 50mls from the customary 250mls in a dedicated single-donor programme will safeguard limited health resources and minimise donor exposure.

Keywords

Infants, standards, blood transfusions, birth weight, health resources

Introduction

Preterm infants on the neonatal intensive care unit (NICU) receive a greater number of red cell transfusions (RCTs) than any other hospitalised group.¹ During the first weeks after birth when blood sampling is frequent, approximately 50% of extremely low birth weight (ELBW) infants receive their first transfusion.¹ By the time of discharge, approximately 85% of ELBW infants would have been transfused. A RCT aims to provide an immediate increase in oxygen delivery to tissues. Oxygen delivery can be increased by a RCT or by administering red cell growth factors (RCGF). Although the risk of transmission of known infectious agents (eg hepatitis B and C virus, human immunodeficiency virus) is relatively low, the risk of infectious agents newly identified in transfused blood (eg *Plasmodium* sp, Parvovirus B19) remains to be determined.²

Research to evaluate the efficacy of restrictive transfusion guidelines have lead to strategies to decrease RCTs in preterms.³ Controversy surrounds the haemoglobin value and clinical circumstances under which RCTs should be administered. If a preterm with a low haematocrit needs an immediate increase in oxygen to tissues then a RCT is required otherwise treatment with RCGF and appropriate substrates such as folic acid and oral iron should be considered. Limiting donor exposure is prudent for infants who are likely to receive multiple transfusions.⁴ Single-donor programmes limit donor exposure, cost less and lead to better preservation of limited blood resources without incurring additional risk. This programme involves dedicating an adult bag of red cells to a particular preterm by dividing the volume into aliquots for use by this preterm.

Valerie Said Conti MD, FRCPCH *

Department of Paediatrics,
Mater Dei Hospital, Malta
valerie.said@gov.mt

Eugenio Azzopardi MD, DPD

Department of Paediatrics,
Mater Dei Hospital, Malta

Raymond Parascandalo MRCP (UK), FRCPCH

Department of Paediatrics,
Mater Dei Hospital, Malta

Paul Soler MD, MRCP (UK)

Department of Paediatrics,
Mater Dei Hospital, Malta

Simon Attard Montalto MD (L'pool), FRCPCH

Department of Paediatrics,
Mater Dei Hospital, Malta

* corresponding author

Our study was designed to quantify the number of RCTs administered to preterms less than 35 weeks gestation, and to identify the cohort by birth weight and by gestation that was most likely to require repeated transfusions and would, therefore, benefit from a single-donor transfusion programme. The ideal volume of blood in each aliquot to make best use of resources was determined. Finally, the number of transfusions administered according to the local guidelines was compared with the number required if more restrictive guidelines were applied.

Methods

A prospective study on the NICU was carried out between 1st January and 31st December 2009.

Gestational age, birth weight, date of admission/discharge, any complications of prematurity including periventricular leucomalacia, intraventricular haemorrhage, chronic lung disease, necrotising enterocolitis, retinopathy of prematurity and any surgical intervention were recorded. The number of days on ventilatory support, nasal continuous positive airway pressure (nCPAP), nasal prong oxygen and with umbilical arterial/venous access or peripheral arterial access, were documented for each infant.

For each transfusion administered we noted the date, gestation and weight at transfusion; whether the baby was symptomatic with poor feeding, tachycardia, bradycardia, apnoeas/desaturations; the need for inotropes; the mode of ventilation and any improvement post-transfusion, as well as the amount in millilitres of blood transfused/discarded, and haemoglobin pre- and post- transfusion.

Results

RCT by birth weight and gestation (Table 1).

Table 1: RCT by birth weight

Birth weight category	Number of preterms	% of all preterms admitted	Number of preterms transfused	% of category preterms transfused
<1000g ELBW	13	12	12	92
1001-1500g VLBW	22	21	12	55
1501-2500g LBW	59	56	15	25
>2501g	12	11	1	8
Total	106	100	40	37.7

106 preterms less than 35 weeks gestation were admitted during the study period. 12 (92%) ELBW babies were transfused; 12 (55%) VLBW babies required a transfusion; 15 (25%) LBW preterms were transfused and 1 (8%) preterm less than 2.5kg was transfused. The most heavily transfused were the ELBW babies, followed by those of VLBW. 8% of preterms were between 24-26 weeks gestation and, of these, 75% required a RCT. 12% were between 27-29 weeks and all required a RCT. In comparison, 28% were between 30-32 weeks gestation and 50% required a RCT, whereas 52% were between 33-35 weeks and only 7% of these required a RCT (Table 2). These data show that babies less than 30 weeks gestation are the most heavily transfused.

Table 2: RCT by gestational age

Birth weight category	Number of preterms	% of all preterms admitted	Number of preterms transfused	% of category preterms transfused
<1000g ELBW	13	12	12	92
1001-1500g VLBW	22	21	12	55
1501-2500g LBW	59	56	15	25
>2501g	12	11	1	8
Total	106	100	40	37.7

RCTs in individual preterms by birth weight (Figure 1)

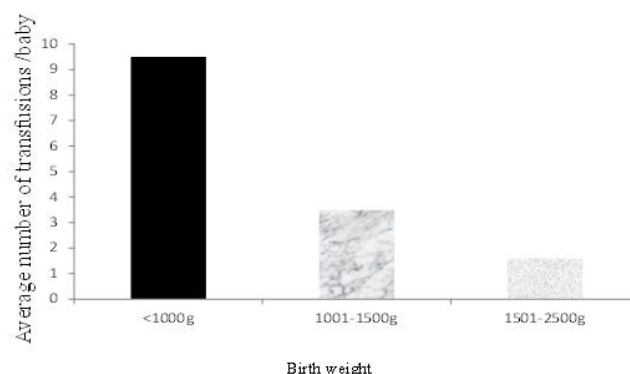


Figure 1: number of RCT by birth weight

All infants less than 1000g required 4 or more RCTs (with the exception of two babies, one of whom was recruited in the last days of the study and data from 2010 was omitted, and another who died within a few hours from birth). 80% of babies less than 1500g had 2 or more transfusions. Most preterms greater than 1501g required only one blood transfusion. The cohort most highly transfused and most likely to benefit from

a single-donor transfusion programme included preterms weighing less than 1500g.

RCTs in individual preterms by gestational age (Figure 2)

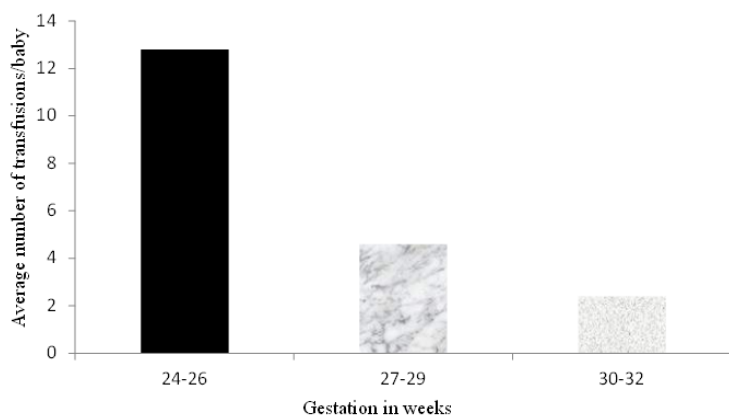


Figure 2: Number of RCT by gestation

All infants between 24-26 weeks had 4 or more RCTs, whilst 77% of those between 27-29 weeks received more than 4 RCTs. 56% of 30-32 week gestation babies received more than 2 RCTs, and all preterms greater than 33 weeks gestation had one 1 RCT. Thus preterms less than 32 weeks gestation are most highly transfused and would benefit from having a single-donor programme.

Determination of best aliquot size (Figure 3)

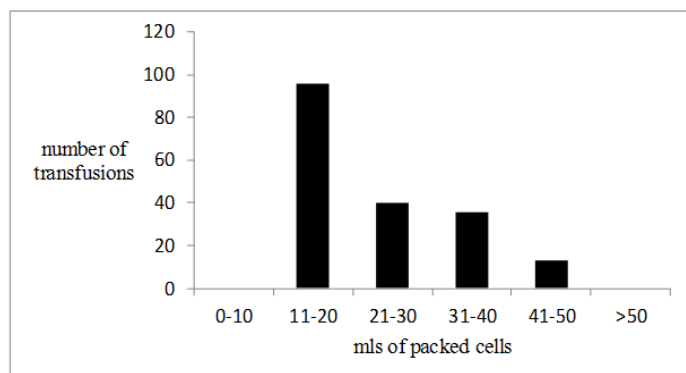


Figure 3: Volume of red cells required for each transfusion

The total number of RCTs administered during the study period was 181. Each volume transfused was 20mls/kg body weight. The mean (mode, range) volume of packed cells transfused was 25.8mls (20mls, 10-50mls). During the study period, at least 150-200mls of blood per bag was discarded.

In this study 'high-risk' preterms less than 32 weeks gestation received 162 bags of red cells. However, if a single-donor transfusion programme was in operation, only 56 bags (assuming 5 aliquots of 50ml per 250ml

bag) would have been required. This would translate in a net reduction of 106 bags (65% less).

Comparison of transfusion guidelines

Each neonatal unit has its own transfusion guidelines. Using local criteria (Table 3) 156 (86%) transfusions were required in oxygen-dependent preterms (70 in ventilated preterms, 61 in preterms on nCPAP, 25 in preterms on nasal prong oxygen), whilst 25 (14%) were required in preterms in room air (23 babies were asymptomatic, 1 was feeding poorly, 1 had apnoeas/oxygen desaturations).

Table 3: Recommendations for the administration of RCT in preterm infants in Malta

Criteria for administering packed RCT	Hb Level
Neonates who are in oxygen, whether ventilated, on nasal CPAP or using nasal prongs	< 12g/dL
Neonates who are not in oxygen and who have a reticulocyte count of < 100 000/uL	< 10g/dL

Comparison with British transfusion guidelines⁵ for neonates receiving intensive care showed that the same number of transfusions would have been required. We equated chronic oxygen dependency in the British guidelines to nCPAP/nasal prong oxygen in the local guideline. Using British criteria (Table 4), 34 less transfusions would have been required (86 transfusions given locally to babies on nCPAP/nasal prongs vs. 52 if British criteria were used).

Table 4: Recommendations for RCT in preterm infants proposed by the British Standards in Haematology Transfusion Task Force 2009

Criteria for administering packed RCT	Level
Anaemia in the first 24h	Hb < 12 g/dL
Cumulative blood loss in 1 week, receiving intensive care	10% blood volume
Neonate receiving intensive care	Hb < 12 g/dL
Acute blood loss	10% blood volume
Chronic oxygen dependency	Hb < 11 g/dL
Late anaemia, stable patient	Hb < 7 g/dL

Late anaemia in the stable patient by British standards was equated to asymptomatic babies in room air: 9 less transfusions would have been given (23 vs. 14) in this subgroup. Using a single-donor system *and* restrictive guidelines in clinically stable preterms would translate

in an overall further total reduction of 4 bags. An attempt was made to correlate the presence of indwelling arterial/central venous lines with increased risk for RCT due to increased phlebotomy losses but the number was too small and there were too many confounding factors to draw any conclusions.

Discussion

181 RCTs were administered to preterms during the study period. The most heavily transfused were preterms between 24-29 weeks gestation closely followed by those between 30-32 weeks gestation and those less than 1000g closely followed by those weighing 1001-1500g. Thus, a gestation of less than 32 weeks and weight of less than 1.5kg are the major risk factors for transfusion.

This study shows that aliquots of 50mls of blood would be adequate. With this practice the number of donor units required can be reduced by 65% leading to more cost-effective use of this limited resource.

With a single-donor programme high-risk preterms are identified, and the Blood Transfusion Department will dedicate a set of aliquots, reducing the risks of donor exposure.

Adopting restrictive guidelines on our NICU, as is the trend in Europe, Canada and the US⁶ would translate into a smaller number of transfusions without any additional risks to babies. Indeed, comparison with these guidelines shows that for intensive care babies the present protocol of transfusing when the haemoglobin is below 12g/dL is recommended by both. However, it would appear to be safe practice to adopt more restrictive transfusion guidelines in the more stable, chronic cohort. Two randomized clinical trials have addressed the controversy of whether restrictive or liberal RCT criteria should be applied in infants^{7,8}. Bell et al showed that although neonates transfused using restrictive criteria required fewer RCTs they did have significantly more apnoea, intraparenchymal brain haemorrhage and periventricular leukomalacia.⁹ Thus, it is postulated that the higher haemoglobin values confer protection against apnoea and brain injury. On the other hand, in the PINT study, Kirpalani et al showed that maintaining a higher haemoglobin level in ELBW babies results in more infants receiving transfusions without any additional benefit.⁷ These same authors followed up the neurodevelopmental outcome of this cohort of preterms at 18 and 21 months and concluded that there was no statistically significant difference in the combined death or severe adverse neurodevelopmental outcome between the restrictive and the liberal transfusion groups.

A number of non-transfusion approaches have been suggested, including cord blood collection as a

form of 'autologous' donation⁸ and delayed cord clamping (30s delay transfers 10-15mL/kg body weight of blood). Studies found lower rates of intraventricular hemorrhage and late-onset sepsis in the infants who underwent delayed cord clamping. In other studies, a delay in cord clamping of 30s resulted in improved iron status, fewer transfusions, and an association with improved neurodevelopmental outcomes.¹⁰

Controversy still surrounds the use of erythropoietin (EPO) and erythropoiesis-stimulating agents.¹¹ A Cochrane meta-analysis concluded that late administration of rhEPO (after the first postnatal week) reduced the number and volume of RCTs, but the clinical importance of this was considered marginal.¹² In a second Cochrane meta-analysis comparing late with early (first postnatal week) administration of EPO, the authors reached similar conclusions and observed an increase in the risk of retinopathy of prematurity. They could not recommend early or late administration of EPO and suggested that future studies focus on methods for reducing donor exposure and phlebotomy losses.¹³

Materno-fetal transfer of minerals, vitamins and iron mainly occurs in the last trimester of pregnancy therefore preterms become deficient rather easily. This fact, together with their higher requirements for growth and need to combat serious illness, makes adequate supplementation of vitamin B12, folate and iron important in preventing anaemia.

Conclusion

The introduction of a single donor programme for high-risk preterms would significantly reduce the number of donor units required by up to 65%. Furthermore, this study has shown that the provision of red cell aliquots of 50mls of blood would suffice and significantly reduce wastage in this limited resource.

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Corinthia Group Prize in Paediatrics, 2013



The Corinthia Group Prize in Paediatrics for 2013 was awarded to Dr Jessica Pace, who obtained the highest aggregate mark over the combined examinations in Paediatrics in the fourth and final year of the undergraduate course. Whilst offering our congratulations to Dr Pace, we would also like to congratulate all those who performed admirably during the undergraduate course in Paediatrics, some of whom were only marginally 'pipped to the post' by Dr Pace. In the accompanying photograph, Dr Pace is seen receiving a cheque for €233 from Professor Simon Attard Montalto, Head of Paediatrics, in the Medical School Museum. Finally, the Academic Department of Paediatrics and Medical School remain indebted and are extremely grateful to the Corinthia Group for their ongoing support.

Professor Simon Attard Montalto