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Red cell and platelet transfusions in neonates: a population based study

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ABSTRACT

Objectives: Reports of neonatal transfusion practices have focused predominantly on premature neonates admitted to neonatal intensive care units (NICU), however little is known about transfusion among other neonates. This study aimed to describe the use of blood products among all neonates.

Design: Linked population-based birth and hospital discharge data from New South Wales (NSW), Australia was used to determine rates of blood product transfusion in the first 28 days of life. The study included all livebirths ≥23 weeks' gestation in NSW between 2001 and 2011.

Results: Between 2001-2011, 5326 of 989,491 live born neonates received a blood product transfusion (5.4 per 1000 births). Transfusion rates were 4.8 per 1000 for red cells, 1.3 per 1000 for platelets and 0.3 per 1000 for exchange transfusion. High transfusion rates were seen in neonates with prior in-utero transfusion (631/1000), congenital anomaly requiring surgery (440/1000) or haemolytic disorder (106/1000). Among transfused infants, 7% received transfusions in a hospital without a NICU. Of those transfused, 64% were born ≤32 weeks gestation (n=3384, 255/1000 births), with 96% of these receiving red cells. 36% were born >32 weeks gestation (n= 1942, 1.98/1000 births), with 76% receiving red cells and 38% receiving platelets.

Conclusions: In this population based study, high transfusion rates were seen in neonates with haemolytic disorders or requiring surgery, as well as in those born preterm. Thirty-six percent of neonates who received blood products were born >32 weeks gestation and 7% were transfused in hospitals without a NICU.

INTRODUCTION

Blood and blood product transfusions in neonates may be life-saving; however, blood products are a costly and limited resource and adverse effects are being increasingly recognized following neonatal transfusions.[1] Transfusion practices vary within and between countries, and over time, resulting in large variations in reported rates of transfusions in neonates.[2-5] Transfusion rates differ due to variation in clinician practice and transfusion thresholds, [6 7] but are also altered by case-mix variation within the population being reported.

Previous reports of transfusion practices in neonates have predominantly studied patients admitted to a neonatal intensive care unit (NICU), with most studies focusing on transfusions in premature or very low birth weight neonates.[2 4 5] Children born at term gestation may also require blood transfusions for a number of reasons including antenatal or post-natal blood loss, hereditary blood disorders, haemolysis or need for major surgery. The rates of transfusion for neonates with these problems have not been well documented, although neonates undergoing major surgery are known to have high transfusion requirements compared to older patients. [8]

Although the majority of neonates receiving blood and blood product transfusions for these conditions will be admitted to a NICU, some may be cared for in other settings. Population data provide a valuable source of data for all neonates, including those who are cared for outside the NICU environment in lower level nurseries, and can be used to identify trends over time. Population data have been used to explore the age distribution of transfusion recipients [9], the distribution of blood use in medical and surgical specialties[10] and transfusion rates in selected adult populations [11] but have not previously been used to identify rates and trends in transfusion among neonates.

This study aimed to determine rates of blood product transfusion among neonates in a population cohort and examine trends in transfusions over time. Secondary aims were to identify groups with pre-existing risk factors for transfusion and to provide information about blood product use in these groups.

METHODS

The study population included all livebirths of at least 23 weeks gestation in New South Wales (NSW), Australia between 2001 and 2011. New South Wales is the most populous state in Australia, with more than 7 million residents and approximately 90,000 births per year. Information on the pregnancy, birth and maternal characteristics ('birth data') was obtained from the Perinatal Data Collection (PDC), a statutory population based collection of all births in NSW of at least 20 weeks gestation or 400 grams birth weight. Information on procedures and diagnoses relating to hospital separations was obtained from the Admitted Patients Data Collection (APDC) ('hospital data'). The APDC is a census of public and private hospital separations in NSW. The hospital data was linked to the births data to provide information on the birth, transfers and subsequent admissions until 28 days after birth. Infants were followed from birth until 28 days or first discharge (whichever was longer). Information about maternal transfusions in the birth admission, and maternal conditions was obtained from maternal hospital data and linked with the corresponding infant data. NSW

Centre for Health Record Linkage performed probabilistic data linkage between the two data sets. Linkage proportions were over 98%.

The hospital data contain diagnoses and procedures for each separation coded according to the 10th revision of the International Classification of Diseases, Australian Modification (ICD-10-AM) [12] and the Australian Classification of Health Interventions. [13] The first 20 of these procedure codes were used to identify admissions involving transfusion of blood products, including red cells, platelets, and exchange transfusion. These procedure codes have been shown to have good ascertainment (sensitivity/specificity red blood cell transfusion: 83.1%/99.9%, platelets and coagulation factors 73.1%/100.0%). [14] Transfusion may have occurred in one or more hospital admissions, however each infant was only counted once. A hospital was considered to have a NICU if it had a neonatal or paediatric intensive care unit providing intensive care for neonates, including mechanical ventilation. If any of the infant transfusions occurred in a hospital without a NICU these were counted as non-NICU transfusions (irrespective of whether the infant had also been transfused in a NICU hospital).

In order to identify conditions associated with high rates of neonatal blood product transfusions, a hierarchy of congenital or early neonatal conditions associated with anaemia or risk of haemorrhage was developed. The hospital diagnoses codes were checked progressively for these conditions, including (in order): severe fetal anaemia requiring in-utero transfusion, fetal blood loss, birth trauma with haemorrhage, hereditary red blood cell disorders (sickle cell disorders, thalasaemia, other hereditary anaemia); hereditary coagulation disorders (Factor VIII and Factor XI deficiency, other coagulation defects); major congenital cardiac and non-cardiac abnormalities requiring surgery in the neonatal period; haemolytic disorders (immune haemolytic disease of fetus and newborn, Rh incompatibility, kernicterus, G6PD deficiency, jaundice due to excessive haemolysis) and preterm birth. Infants with multiple diagnoses were only counted in one of these groups based on the hierarchy above. The proportion of children receiving transfusions in each of these high risk groups was then determined.

Rates are calculated per 1000 births and proportions are proportion of births, unless otherwise specified. Trends were assessed using the Cochran Armitage test for trend. All analyses were performed in SAS 9.3. Ethical approval was obtained from the NSW Population and Health Services Research Ethics Committee.

RESULTS

There were 989491 infants born in NSW between January 2001 and December 2011. Of these, 5326 were given a blood product transfusion on at least one occasion, giving a transfusion rate of 5.4 per 1000 livebirths. Amongst all infants, transfusion rates were 4.8 per 1000 for red cells, 1.3 per 1000 for platelets, and 0.3 per 1000 for exchange transfusions. Of the 5326 infants who received a blood product, 3956 (74.3%) received red cells only. Most infants received a transfusion of blood products during only one admission (99.2%), with the majority of transfusions being during the birth admission (93.2% of transfusions). Transfusions were predominantly given to neonates who were admitted to a hospital with a neonatal intensive care unit, however, 7% (n=385) of neonates received at least one transfusion in a hospital without an NICU, and 12.5% of exchange transfusions were given in non- intensive care environments.

The overall rate of transfusions of blood products in neonates stayed constant between 2001 and 2011 (2001: 5.0 per 1000, 2011: 5.4 per 1000, p for trend 0.27). A significant increase was seen in transfusion of platelets (p=0.03) and this primarily occurred among babies born >32 weeks (2001: 0.6 per 1000, 2011: 0.7 per 1000, p for trend 0.01). There was no overall change in red cell transfusions (p=0.07) over the period, although use increased among babies born at 32 weeks or earlier (2001:213.4 per 1000, 2011:263.7 per 1000, p for trend 0.02). Altogether 264 neonates received an exchange transfusion, with the rate of exchange transfusion decreasing from 0.42/1000 births in 2001 to 0.11/1000 births in 2011 (P<0.001) (Figure 1).

Blood transfusion was more common among earlier gestations, with a transfusion rate in infants born at 23-28 weeks gestation of 551.6 per 1000 livebirths, compared with 1.4 per 1000 at term (Table 1). Among infants with an APGAR score below 7 at 5 minutes the transfusion rate was 77.2 per 1000. Singletons had lower transfusion rates than multiple births (4.5 per 1000 vs 34.3 per 1000). Higher transfusion rates were also seen in infants whose mother had a blood or blood product transfusion during the birth admission (18.0 per 1000), infants who were small for gestational age (9.9 per 1000), and whose mother had hypertension (9.3 per 1000).

High rates of blood product transfusion were evident in neonates with congenital or early neonatal conditions known to be associated with anaemia or risk of haemorrhage, with 63.1% of neonates who had received an in-utero transfusion prior to birth, 44.0% of those with a major congenital anomaly requiring surgery and 10.6% of those with a haemolytic disorder receiving a transfusion in the neonatal period (Table 2). Transfusion rates were higher for neonates undergoing cardiac surgery (55.0%) than for those requiring surgery for other major congenital abnormalities (17.3%).

Among very preterm neonates (<=32 weeks) who received a transfusion, 28% had a specific condition associated with anaemia or haemorrhage. The majority of very preterm neonates who required a transfusion received red blood cells (n=3259, 96%), with a smaller proportion receiving platelets (25%) or exchange transfusion (2%).

Of neonates born at term or late preterm (>32 weeks) who required a transfusion, 66% had an identified condition associated with anaemia or risk of haemorrhage. Of the 34% (n=663) who received a transfusion without an underlying risk factor for anaemia or haemorrhage, 404(61%) required mechanical ventilation for severe respiratory illness. Three-quarters (76%) of term or late

preterm neonates who required a transfusion received red cells and 38% required platelets. The most common conditions associated with transfusion in term or late preterm neonates were haemolytic disorders (31%) and surgery for major congenital abnormality (26%).

DISCUSSION

This study provides the first reported population level data on the use of blood and blood products in the neonatal period. Transfusion of blood products occurred in 1 in every 185 neonates born in NSW between 2001 and 2011; with an overall transfusion rate of 5.4/1000 live births. This rate is higher than at any other time during childhood [9] and similar to some of the reported rates of transfusion seen in women during an obstetric delivery admission. [11 15] Among the infants transfused, 88.9% received a red cell transfusion and almost a quarter (23.9%) received platelets, either alone or in combination with a red cell transfusion.

The majority (64%) of neonates who received a transfusion were born before 33 weeks gestation with a transfusion rate of 552/1000 in neonates <29 weeks gestation. This high transfusion rate in very preterm neonates is consistent with other studies reporting red blood cell transfusions in 50-61% of neonates <32 weeks gestation [4 16] with higher rates (>85%) reported among neonates of birth weight <1000g, even with restrictive transfusion thresholds. [5-7]

A substantial proportion (36%) of infants receiving transfusions were born at term or late preterm gestation. Haemolytic disorders and major congenital anomalies requiring surgery accounted for more than half of transfusions in term and late preterm neonates, with many of these children receiving both red cells and platelets.

Haemolytic disorders may present before birth with fetal anaemia or after birth with hyperbilirubinaemia and anaemia. In the past, exchange transfusion was common in neonates with haemolysis due to Rh incompatibility, however, the incidence of haemolytic disease has fallen significantly with the widespread use of anti-D immunoglobulin [17 18] and the need for exchange transfusion has decreased further in those with haemolysis with the introduction of in-utero transfusions for severe fetal anaemia, more effective phototherapy devices and the use of IVIG in neonates approaching exchange transfusion levels. This was reflected in the decrease in exchange transfusions seen in our study.

Despite a significant reduction in the need for exchange transfusions, haemolytic disorders remain a frequent indication for transfusion. Among neonates who received an in-utero transfusion, 63% required a post-natal transfusion within 28 days of birth and 10.6% of neonates with an identified haemolytic disorder received blood products in the neonatal period (n=1227). Although the risks of a blood product transfusion are less than those associated with an exchange transfusion, these children remain at risk of adverse transfusion outcomes.

A high proportion (44.0%) of neonates undergoing surgery also received transfusions. In all neonates undergoing surgery, even a relatively small loss of blood may have a major impact on tissue perfusion and a need for blood transfusion due to their low circulating blood volume. For children undergoing surgery for congenital cardiac disorders, additional blood is needed to “prime” the

extracorporeal circuits required for cardio-pulmonary bypass and treatment with plasma and platelets may be required to treat coagulation disorders that can be induced by the bypass procedures. [19] Processes that aim to reduce the use of blood products have been instituted in many centres; however, these children remain a group with high transfusion requirements. [20]

For many neonates, blood transfusions may be life-saving, however, benefits of transfusions must outweigh risks. Studies assessing risks and benefits of transfusions in neonates have predominantly assessed red blood cell transfusion in premature neonates, [6 7] with few studies assessing transfusions in term or late preterm neonates. Although the risk of haemolytic transfusion reactions and transfusion associated infections in neonates is low with modern transfusion practices, recent studies have identified other potential risks associated with neonatal transfusion including activation of the immune system, generation of inflammatory cytokines, priming of neutrophils and activation of platelets, [1 21] transfusion related lung and gut injury [22] and a possible increased risk of intraventricular haemorrhage. [23] These effects have been reported following transfusions of red blood cells, platelets [24 25] and other blood products.

As transfusions in neonates may have long term consequences, and blood products are a limited resource, it is important that we understand which neonates are receiving blood products. Strengths of this study include the use of population-based rather than NICU-based data to identify all neonatal transfusions and the ascertainment of use of both red blood cells and platelet transfusions. Administration of blood and blood products are accurately reported in adults and therefore likely to be accurately reported in these data, however there is potential for some under-ascertainment. A limitation of this study is the lack of detail on amount of blood product transfused and the timing of transfusion during the birth admission. A further limitation is that we were unable to ascertain the use of immunoglobulin and coagulation factors in this cohort, because of changes in coding definitions for these blood products over the course of the study.

The data in this study provide reassurance that the number of neonates receiving red blood cell transfusions is not increasing over time. However, other studies have reported a decrease in red blood cell transfusion rates over a similar time period following the implementation of standard guidelines for transfusion. [26] While we were able to identify neonates with specific conditions associated with anaemia or risk of haemorrhage, the available health record data did not record the reason for transfusion, so we were unable to determine whether neonates were receiving transfusions based on generally accepted guidelines. Our finding that just under 40% of neonates receiving blood products were born at term or late term, with an increase in platelet transfusions in these more mature infants over the course of the study, suggests that further investigation of the indication for blood transfusions in these neonates may be warranted.

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What's known on this subject

Blood and blood product transfusions are commonly used interventions in neonatal intensive care units, particularly among very low birth weight and preterm infants.

Little is known about neonatal transfusion in term neonates or infants outside neonatal intensive care units.

What this study adds

In this population based study, 36% of neonates who received blood products were born >32 weeks gestation.

High transfusion rates were seen in neonates with haemolytic disorders (132/1000) and congenital abnormalities requiring surgery (508/1000), as well as in those born preterm.

Table 1: Characteristics of infants receiving blood products, 2001-2011

		Any blood Product	No blood Product	Transfusion rate (per 1000)
Total		5326 (100.0)	984165 (100.0)	5.4
Maternal Age	Under 20	264 (5.0)	36586 (3.7)	7.2
	20-34	3780 (71.0)	733868 (74.6)	5.1
	35 or over	1282 (24.1)	213711 (21.7)	6
Maternal pregnancy hypertension	Yes	848 (15.9)	90328 (9.2)	9.3
Maternal transfusion	Yes	223 (4.2)	12193 (1.2)	18
Place of birth	NICU hospital	4426 (83.1)	406188 (41.3)	10.8
	Other Public hospital	543 (10.2)	321609 (32.7)	1.7
	Private hospital	357 (6.7)	256368 (26.0)	1.4
Baby gender	Male	2952 (55.4)	505841 (51.4)	5.8
	Female	2374 (44.6)	478324 (48.6)	4.9
Multiple Birth	Yes	1027 (19.3)	28875 (2.9)	34.3
		4299 (80.7)	955290 (97.1)	4.5
Gestational Age	23-28	2359 (44.3)	1918 (0.2)	551.6
	29-32	1025 (19.2)	7934 (0.8)	114.4
	33-36	638 (12.0)	53157 (5.4)	11.9
	37-38	587 (11.0)	223673 (22.7)	2.6
	39-41	703 (13.2)	682622 (69.4)	1
	42+	14 (0.3)	14861 (1.5)	0.9
Low Apgar	1 min <4	1305 (24.5)	20295 (2.1)	60.4
	5 min <7	1263 (23.7)	15089 (1.5)	77.2
Birthweight	SGA - <10th centile	912 (17.1)	91628 (9.3)	9.9
	AGA	4011 (75.3)	787136 (80.0)	5.1
	LGA - >90th centile	403 (7.6)	105401 (10.7)	3.8

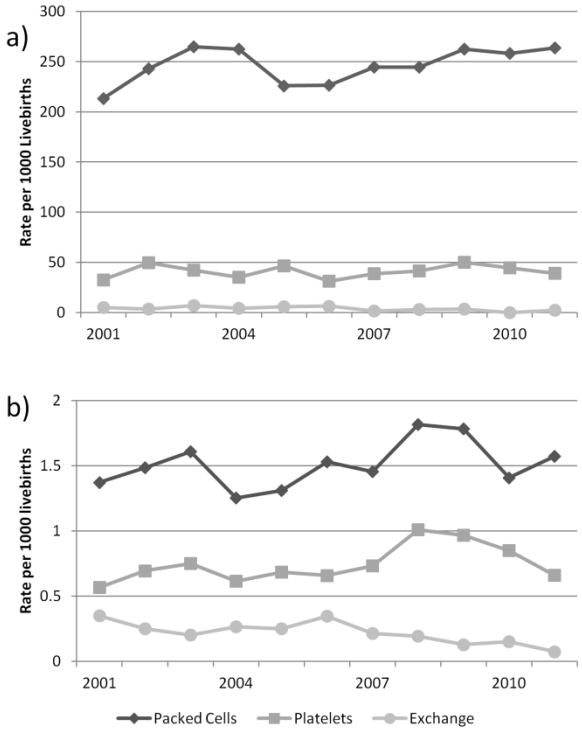
Table 2: Blood product use amongst infants with conditions associated with anaemia or haemorrhage*, 2001-2011

	Births	Red cells	Platelets	Exchange	Blood products	No Blood products
Total Infants	989491	4737 (0.5)	1272 (0.1)	264 (0.0)	5326 (0.5)	984165 (99.5)
Severe fetal anaemia requiring In-utero transfusion	65	36 (55.4)	** (8)	10 (15.4)	41 (63.1)	24 (36.9)
Fetal blood loss	195	139 (71.3)	25 (12.8)	** (3)	140 (71.8)	55 (28.2)
Birth trauma with haemorrhage	184	15 (8.2)	10 (5.4)		18 (9.8)	166 (90.2)
Hereditary blood cell disorder	130	38 (29.2)	6 (4.6)	7 (5.4)	43 (33.1)	87 (66.9)
Hereditary coagulation disorder	45	** (11)	** (9)	** (2)	7 (15.6)	38 (84.4)
Major congenital abnormality requiring surgery	1670	697 (41.7)	375 (22.5)		735 (44.0)	935 (56.0)
Haemolytic disorders	11594	992 (8.6)	230 (2.0)	210 (1.8)	1227 (10.6)	10367 (89.4)
Preterm <=32 weeks	11779	2361 (20.0)	339 (2.9)	8 (0.1)	2452 (20.8)	9327 (79.2)
33-36 weeks ventilated infants	1910	137 (7.2)	43 (2.3)	** (0)	154 (8.1)	1756 (91.9)
Other preterm infants, 33-36 weeks	50221	70 (0.1)	44 (0.1)	** (0)	111 (0.2)	50110 (99.8)
Term ventilated infants	3428	184 (5.4)	102 (3.0)	** (0)	250 (7.3)	3178 (92.7)
Other term infants	908270	63 (0.0)	89 (0.0)	13 (0.0)	148 (0.0)	908122 (100.0)

* Infants can only appear in one cell; infants with 2 or more conditions were assigned to the first diagnosis appearing in the above list

** Numbers ≤5 are not shown and corresponding percentages have been rounded

Figure 1 Trend in blood and blood product usage in a) infants ≤32 weeks' gestation and b)>32 weeks' gestation, NSW, 2001-2011.



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