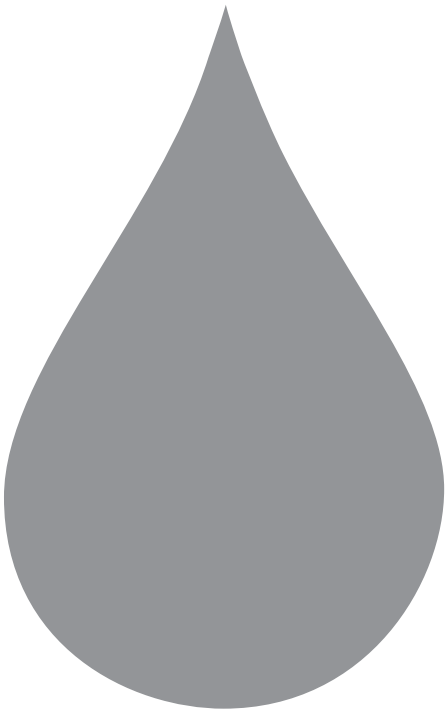
Neonatal transfusion practices

Lindern, J.S. von

Chapter 3

Potential use of autologous umbilical cord blood red blood cells for early transfusion needs of premature infants



Marijke Jansen, Anneke Brand, Jeannette S. von Lindern, Sicco Scherjon, and Frans J. Walther

Transfusion 2006; 46:1049-56

Abstract

Background This prospective study investigated whether the odds of receiving a red blood cell (RBC) transfusion in premature infants can be predicted at birth and for whom of these infants harvesting of umbilical cord blood (UCB) for autologous transfusion within 30 days after birth would be worthwhile.

Study design and methods Characteristics were evaluated from 288 premature infants with a gestational age between 24 and 36 weeks and who were admitted to our neonatal center. In 144 (63%) of these infants UCB collection was attempted and the early transfusion needs could be compared with the amount of UCB available for transfusion.

Results Sixty-nine of 114 (61%) inborn infants with a gestational age of less than 32 weeks received one or more RBC transfusions of 10 mL per kg within 30 days after birth. Apgar score at 1 minute of less than 6 and gestational age of less than 32 weeks were independently associated with the chance of receiving a transfusion in this group. In 31 of 69 (46%) infants, at least 15 mL of UCB per kg of birth weight was collected and in 28 of 69 (41%) this would have been sufficient to cover their early transfusion needs.

Conclusion The decision to collect UCB for postnatal transfusion can be made just after labor, based on Apgar score and gestational age. The collection of UCB is most effective and efficient for premature infants between 29 and 31 weeks of gestation. For infants less than 29 weeks of gestation, the technical aspects of UCB collection need improvement. This pilot study requires a prospective clinical study to evaluate the proportion of premature infants that can be fully or substantially supported with autologous UCB.

During the first weeks of life, premature infants often develop anemia and need allogeneic red blood cell (RBC) transfusions.[1;2] The number and amount of transfusions for premature infants and the donor exposure have decreased over the past decennia.[2-4] Nonetheless, these infants are exposed to risks inherent to allogeneic transfusions, such as transmission of infectious agents.[5;6] Use of autologous umbilical cord blood (UCB) may reduce these complications. Several investigators have demonstrated the feasibility of the collection, storage, and use of UCB RBCs for autologous transfusion in newborn infants. Approximately 20 mL of UCB per kg of body weight can be harvested,[1,6] and a linear association has been found between collected blood volume and birth weight with a greater relative blood volume from placentas of smaller newborns.[7;8] Few data are available on the question of which infants will need RBC transfusions.[1,9] We investigated whether the risk of receiving a RBC transfusion during the neonatal period can be predicted at birth, to estimate for which premature infants UCB should be harvested, tested, processed, and stored as a RBC product. We evaluated the characteristics and need for RBC transfusions of 288 infants born between 24 and 36 weeks of gestation. In addition, we report on the amount of UCB collected in relation to the transfusion needs.

Materials and methods

Patients

Informed consent to collect UCB was obtained from the parents before delivery if the delivery took place in the Leiden University Medical Center. The Medical Ethical Committee of the Leiden University Medical Center approved the study protocol. Neonates included in this study were all premature infants born in 2002 at a gestational age between 24 and 36 weeks and admitted immediately or within 1 day (without any phlebotomy losses) to the neonatal center. Infants were included irrespective of disease severity, duration of hospitalization, and the level of care provided. As a cutoff point in following the course of premature infants, we used a period of 30 days, corresponding to the expected shelf life of the cord RBCs.
Exclusion criteria for participation in this study were diseases for which autologous blood transfusion was contraindicated, such as active blood group antagonism (hydrops fetalis) and HPA antagonism. Nonviable premature infants were excluded. The existence of twin-to-twin transfusion syndrome was not considered as an exclusion criterion.
During a 3-month period, 22 consecutively (in)born infants at a gestational age of less than 32 weeks, who were admitted to the neonatal center, were closely monitored for a period of 14 days to estimate the amount of blood loss for diagnostic purposes and to correlate the amount of phlebotomy losses and RBC transfusions.

Collection of UCB

In vaginal deliveries, the placenta was still in utero when blood was harvested. No drugs were given to increase uterine muscle tone. In cesarean section deliveries, the placenta was removed from the uterus before blood was harvested. The umbilical cord was double clamped, transacted, and cleansed. UCB was collected with an adapted collection system including a 150-mL collection bag (Compoflex, Fresenius, Emmer Compascuum, the Netherlands) to which a collection system (Medisize 1992.002D, Macopharma, Langen Germany) was attached. The collection bag contained 5 mL of CPD-A. The collection system included two cannulas with needles to permit two punctures of the umbilical vein. To increase the volume of blood collected after the ceasing of spontaneous blood flow, a syringe (volume of 20 mL) containing 5 mL of CPD-A could be attached to a three-way tap. A buffy coat-depleted packed RBC suspension was prepared from the UCB by centrifugation in a Sepax device (Biosafe, Switzerland) and adjusted with SAG-mannitol to a hematocrit (Hct) of 55 to 65%. The supernatant plasma was used for bacterial culture (BacT/ALERT, bioMérieux, Hazlewood, MO) and the buffy coat was used for research purposes. The RBC products were stored for 30 days at 2 to 6°C. The quality control variables during storage will be reported separately. Because some UCB collections could not be processed due to technical and logistic reasons, the analysis is based on preliminary approved products (defined as a collection of at least 15 mL of UCB exclusive CPD-A, without visual clots) instead of finally approved blood products in all instances. None of the collected cord blood RBC products were transfused in this pilot study.

Patient data

Clinical data of infants and their mothers were obtained from the hospital chart and hospital and laboratory information systems. Information was recorded on gestational age, sex, Apgar scores, umbilical arterial pH, birth weight, placental weight, method of delivery, singleton or multiple birth, length of hospitalization, RBC transfusions, and death. Data collection specified the number and volume of RBC transfusions during the 30-day observation period. The indication for RBC transfusions was based on local transfusion guidelines, which consider age of the infant after birth, ventilatory status, and hemoglobin concentration. At each transfusion 10 mL of RBCs per kg was infused over 3 h.

Statistical analysis

The infants' clinical characteristics are presented as medians and their ranges, numbers, and percentages. The differences between the subgroups of infants are presented as p values and were calculated with the two-tailed t-test for continuous variables and the chi-square test for the categorical variables. The differences between the four groups in Table 3 were analyzed

with the independent samples t-test. To investigate the correlations between different variables, Spearman's correlation coefficient rho was calculated (except birth weight, none of the variables followed a Gaussian distribution).
The chance of an infant receiving at least one RBC transfusion within the first 30 days of life and the variables influencing this chance were calculated by backward stepwise logistic regression analysis with the dependent variable "transfused within 30 days" (no=1, yes=2) and several variables (gestational age, birth weight, sex, Apgar scores, placental weight, and hospitalization unit). The selection of the variables was based on the significant differences of these variables between transfused and nontransfused infants ($p<0.05$). Logistic regression analysis was used to correct for mutually connected confounders.

Results

During the 12-month observation period, 288 premature infants with a gestational age of less than 36 weeks were admitted to the neonatal center, of whom 16 met the exclusion criteria. A total of 140 of the 272 infants included were inborn with a gestational age of less than 32 weeks. Clinical characteristics of the study population are shown in Table 1.

RBC transfusions

The number of RBC transfusions administered during hospitalization was recorded up to 30 days after birth. Ninety-six of the 272 (35%) premature infants received one or more RBC transfusions. Premature infants with a gestational age of less than 32 weeks received more transfusions than infants with a gestational age between 32 and 36 weeks, respectively, 82 of 140 (59%) and 14 of 132 (11%). There was only a weak correlation, however, between the number of transfusions and gestational age within the group of less than 32 weeks of gestation ($n=140$, $r=-0.553$, $p=0.000$).
The median birth weight of all infants less than 32 weeks ($n=140$) was 1244 g (range, 538–2155 g) and of the 82 infants who received transfusions, 1082 g (range, 538–1895 g). Among the infants with a birth weight of less than 1500 g ($n=104$), 69% ($n=72$) received at least one transfusion; the median number of transfusions was 2 (range, 1–9). The large majority (89%) of infants with a birth weight of less than 1000 g received at least one transfusion with a median number of 3 (range, 1–9).

Likelihood of transfusion

In premature infants of less than 32 weeks of gestational age, Apgar scores at 1 and 5 minutes, birth weight, placental weight, duration of hospitalization, and death influenced the chance of receiving a RBC transfusion (all $p<0.05$ in univariate analyses). In the logistic regression analyses,

Table 1. Characteristics of included infants (n=272)

	Gestational age (weeks)				
	24-28	28-30	30-32	32-34	34-36
Number	34	46	60	40	92
Birth weight (g)					
<1000	25	10	2	1	0
1000-1449	9	30	28	7	4
1500-1999	0	6	29	20	23
2000-2499	0	0	1	12	40
>2500	0	0	0	0	25
1-min Apgar score					
<6	22	19	22	17	14
≥6	11	26	38	23	78
Unknown	1	1	0	0	0
Neonatal unit					
Intensive care	34	46	57	32	34
Special care	0	0	3	8	58
Umbilical cord pH					
≤7.0	20	2	3	2	4
>7.0	3	33	43	25	66
Not available	11	11	14	13	22
Delivery					
Vaginal	28	26	31	19	61
Cesarean section	6	20	29	21	31
Placental weight (g)					
<200	2	2	0	0	0
200-499	22	29	44	19	51
500-749	2	5	3	5	21
≥750	0	0	0	0	1
Unknown	8	10	13	16	19
Hospitalization (days)					
<4	3	5	12	9	37
4-7	4	6	10	16	28
8-14	8	12	23	10	19
15-30	8	18	10	4	7
>30	11	5	5	1	1
Deceased					
Yes	16	10	3	0	1
No	18	36	57	40	91

duration of hospitalization and death were not considered suitable as variables because these data are not available at birth. The Apgar score at 1 minute after birth was selected because of the strong correlation between these scores at 1 and 5 minutes.

The sensitivity and specificity of the Apgar score were 63.8%(95% CI 0.532–0.743) and 79.3%, respectively. In the three gestational age subgroups (24–28, 28–30, and 30–32 weeks), respectively, 93.9%, 62.2%, and 35.0% of the infants received transfusions. In the three birth weight subgroups (<1000, 1000–1499, and 1500–1999 g), respectively, 88.9%, 57.6%, and 27.8% received transfusions. Logistic regression analyses showed that birth weight and Apgar score at 1 minute were independently associated with the odds of receiving a RBC transfusion (p=0.033 and p=0.000, respectively).

Infants born at a gestational age between 24 and 28 weeks had 8.88 times the odds of receiving a transfusion as infants born at 30 to 32 weeks of gestation (p=0.016), but the risk of receiving a transfusion at a gestational age between 28 and 30 weeks was not significantly greater than for those born between 30 and 32 weeks of gestation (p=0.138). Infants of less than 1000 g had 7.71 times the odds of receiving a transfusion compared to infants of 1500 to 1999 g (p=0.014). Likewise, the odds for infants with a birth weight between 1000 and 1499 g and those with a birth weight between 1500 and 1999 g were similar (p=0.078). Premature infants with an Apgar score of less than 6 had 7.25 times the odds of receiving a transfusion as those with an Apgar score of at least 6 (p=0.000).

The predicted odds of receiving at least one RBC transfusion during the first 30 days of life are shown in Fig. 1. In all three gestational age subgroups, with a corresponding Apgar score, the odds of receiving a transfusion diminished with increasing birth weight. This association

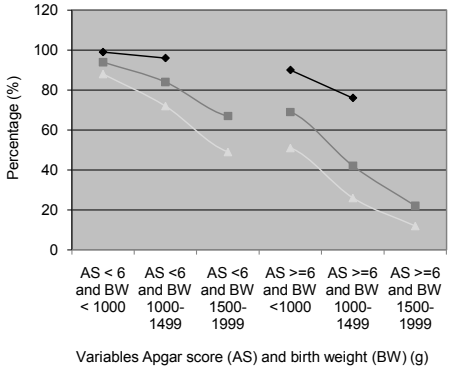


Fig 1. Percentage chance of receiving at least one RBC transfusion within 30 days after birth in infants with a gestational age of less than 32 weeks

(◆)Gestational age 24 to 28 weeks, n=33; (■) gestational age 28 to 30 weeks, n=45; (▲) gestational age 30 to 32 weeks, n=60

is most obvious in infants with a gestational age of greater than 28 weeks. Irrespective of gestational age, almost all infants with an Apgar score of less than 6 and a birth weight of less than 1000 g received transfusions, whereas only a few infants with an Apgar score of at least 6 and a birth weight of 1500 to 1999 g needed any transfusion.
Logistic regression analyses were also performed on all 272 infants born at less than 37 weeks. Only gestational age (p=0.007) and Apgar score at 1 minute (p=0.000) were independently associated with the chance of receiving a RBC transfusion. Infants with an Apgar score of less than 6 had 4 times the odds of receiving a transfusion compared to infants with an Apgar score of at least 6.

UCB collections

As shown in Fig, 2, 227 of the 288 premature infants admitted to the neonatal center were born in our hospital, of whom 96 (48 deliveries) were twins. An attempt to harvest UCB was performed in 111 deliveries and resulted in 144 UCB collections, of which 91 (63%) were greater than 15 mL (excluding CPD-A). After processing and bacterial culture of these 144 UCB collections, 88 (61%) resulted in a product suitable for potential transfusion. In 114 infants with a gestational age of less than 32 weeks, 69 attempts to collect cord blood resulted in 32 (46%) in a collected volume of greater than 15 mL, of which 30 (43%) were approved for transfusion. UCB was tested for aerobic and anaerobic bacterial contamination (BacT/ALERT). From all processed collections, 6 of 91 were contaminated (7%).
After all processing was completed (i.e., with RBCs at a Hct level of 60 ± 5% in storage medium), the volume of the units available for transfusion was approximately 70% of the harvested blood volume. The mean volume of the 88 approved blood products was 22 mL/kg of birth weight (range, 7–68 mL/kg) and of the 30 collections from infants less than 32 weeks of gestation 23 mL/kg of birth weight (range, 10–55 mL/kg).
In premature infants of less than 32 weeks, no correlation was found between the amount of UCB per kg of birth weight harvested and gestational age (n=69, r=0.219, p=0.071), birth weight (r=0.150, p=0.218), placental weight (r=0.077, p=0.531), or method of delivery (r=0.244, p=0.064).

Missed UCB collections

The reasons why no attempts were done to collect UCB at 68 deliveries are summarized in Table 2. Only in a few cases a clear explanation for the failure could be identified. In most cases there were no complicating circumstances (19 deliveries), and failures were often secondary to an urgent spontaneous delivery or cesarean section (n=16); only three times was no consent given for collection of UCB.

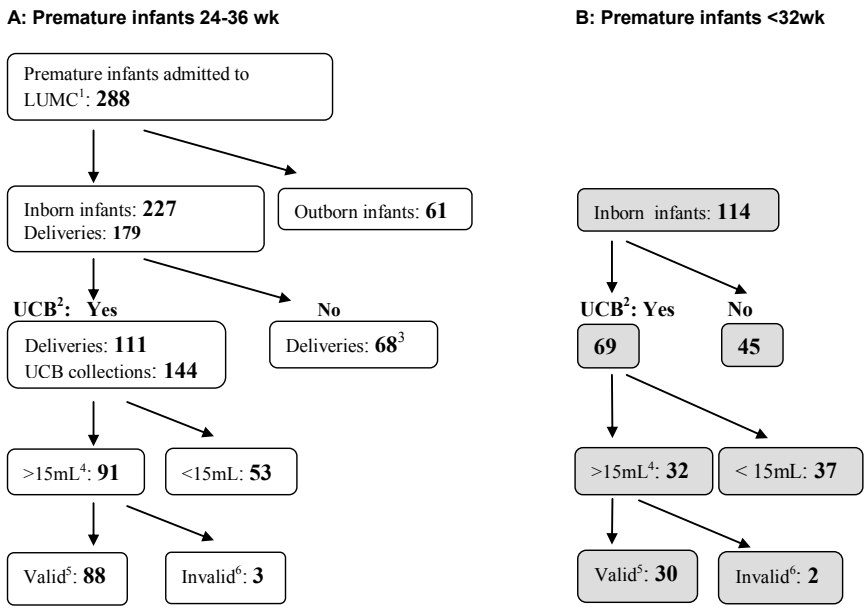


Fig 2. UCB collections

[1]: All premature infants (24–36wk) admitted during the study period

[2]: (Delivery at which) UCB collection was performed

[3]: No UCB collection was or could be performed by complicating circumstances

[4]: Volume excluded CPD-A

[5]: Suitable for transfusion

[6]: UCB contained clots, cell counting problems, separation problems, positive bacterial culture

Potential coverage of transfusion needs with autologous cord blood

In, respectively, 63% and 54% of the 144 infants for whom UCB collection was attempted, at least 15 mL and more than 15 mL/kg of birth weight was available. For the 69 premature infants of less than 32 weeks of gestation for which collection was attempted, these percentages were 46% and 45%. This would have covered the total need for early transfusions in 28 of 69 (41%) premature infants of less than 32 weeks of gestation with an available UCB product (≥15 mL).

Dividing the infants of less than 32 weeks into four different groups according to “transfused” or “not transfused” and “cord blood product available” or “no cord blood product available” shows that for 24 of 39 (62%) of the premature infants who needed transfusions no UCB product was available (Table 3). For 11 of 39 (28%) premature infants who received transfusions who could receive autologous RBCs, the collected UCB would have covered their transfusion needs during the first 30 days after birth.

Table 2. Circumstances of deliveries (n=68) at which no attempt at cord blood collection was done

Circumstance	Singletons	Twins	Triplets
Forgotten	3		
Urgent delivery or cesarean section[1]	13	1	2
Primary cesarean section	4	1	
Allo-immunisation[2]	3	2	
Respiratory problems[3]	2		
GBS/PROM[4]	2	2	
Corticosteroid study	1		
Placenta praevia	1		
Lasered TTTS		1	
Complications twins[5]	2		
Not possible by broken placenta	1		
Delivery in emergency room via other hospital	2		
GBS	1		
Unknown	19	1	
PPROM		1	
No consent	3		

[1] Because of solutio placentae/maternal condition (preeclampsia, HELLP)/fetal condition

[2] Anti D/intracranial hemorrhage(ICH)/hydrops fetalis/twin-to-twin transfusion syndrome (TTTS) and severe ICH/intrauterine growth retardation and idiopathic thrombocytopenic purpura

[3] Respiratory distress syndrome (RDS) III/hydrothorax/postdelivery pneumothorax

[4] Group B streptococcus (GBS)/(premature) prolonged rupture of membranes (P)PROM/lasered TTTS and PROM and GBS/PROM and cord prolapse and sepsis (twins)

[5] First infant born 2 days before second infant/first infant died: intrauterine fetal death

Phlebotomy losses

Twenty-two infants were divided in two groups according to gestational age: Group A (25 to <30 weeks) and Group B (≥30 to 32 weeks). The median gestational age of Group A was 27^{+5} weeks (range, 25^{+9}–29^{+6} weeks), the median birth weight was 1125 g (range, 809–1699 g) and the median 1-minute Apgar score was 3 (range, 1–9). For Group B, these values were 31^{+0} weeks (range, 30^{+0}–31^{+5} weeks), 1277 g (range, 558–1735 g) for birth weight and 8 (range, 2–10) for Apgar score.

After 14 days the infants of Groups A and B had median total phlebotomy losses of, respectively, 6.4 (5.2–10.7) and 5.7 (5.3–9.9) mL/ kg. During this period the infants of Groups A and B received, respectively, 15.0 (0–54.1) and 8.2 (0–19.6) mL/kg RBCs (Fig. 3). The volume of phlebotomy loss came close to the volume of transfused RBCs in infants of Group B. In infants of Group A, however, after 2 weeks of hospitalization, the volume of RBCs transfused exceeded the volume drawn for diagnostic purposes with approximately 10 mL/kg of birth weight.

Table 3. Transfusion volume during the first 30 days after birth and available UCB volume (excluding CPD-A) in infants <32 weeks gestation (n=69)

Group (n)	Tx	Product*	Median volume (mL) Tx†	Median volume (mL) UCB‡	Median product volume (mL/kg)	Median gestational age (weeks^{+days})	Median birth weight (g)	Median Apgar score
A (17)	No	Yes		39 (17-81)	23 (11-55)	31^{+0} (29^{+3}-31^{+6})	1500 (1198-1933)	8 (5-10)
B (24)	Yes	No	22 (8-73)			28^{+5} (25^{+0}-31^{+1})	998 (536-1711)	5 (1-10)
C (15)#	Yes	Yes	17 (13-76)	26 (16-63)	22 (10-42)	30^{+2} (25^{+4}-31^{+2})	1400 (812-1895)	4 (2-10)
D (13)	No	No				30^{+4} (28^{+0}-31^{+2})	1386 (1115-1840)	7 (1-9)

* At least 15 mL of UCB collected

† Allogenous transfusions (mL) calculated as 10 mL per kg birth weight; Hct level of 0.60

‡ Collected UCB (minus CPD-A)

In 4 of 11 infants the cord blood was sufficient to support all of their transfusion needs

Tx=transfusion

Discussion

This observational study among 272 premature infants born at a gestational age between 24 and 36 weeks focused on the question whether the odds of receiving a RBC transfusion can be predicted at birth. The aim of the study was to estimate whether appropriate collection, testing, processing, and storage of autologous cord blood with the aim of transfusion and avoidance of waste of resources is feasible.

Various studies of premature infants investigated the possibilities for collection, storage, and use of UCB RBCs for autologous transfusion[1,8,9], but few epidemiologic data are available on

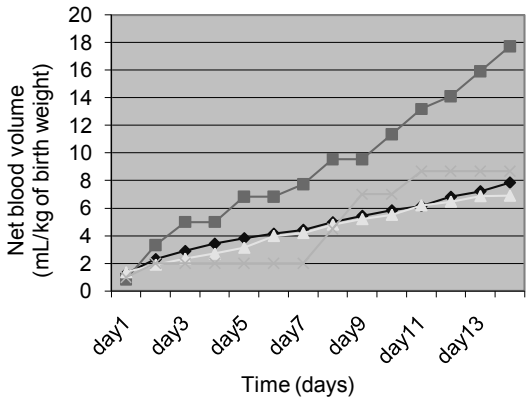


Fig 3. Drawn (mL/kg/day) versus transfused (mL/kg/day), cumulatively
(♦) Cumulative drawn, Group A; (■) cumulative transfused, Group A; (▲) cumulative drawn, Group B; (X) cumulative transfused, Group B.

the contribution of autologous cord blood to circumvent allogeneic transfusions. This is the largest study regarding this subject in an unselected population of premature infants. Gestational age and Apgar score were significant predictors for the odds of receiving an RBC transfusion. In particular for infants born at more than 32 weeks of gestation, which as a group have a low risk for transfusion (11%), a 1-minute Apgar score of less than 6 increased the risk to receive a transfusion by 20%. Within the group of infants with a gestational age of less than 32 weeks, also birth weight significantly determined the odds of receiving a transfusion.

Only two previous studies addressed a similar question. Kling and coworkers investigated the occurrence of RBC transfusions in 47 premature infants of <1500 g, who were compared for demographic characteristics, phlebotomy blood loss, diagnosis, medications, and score for neonatal acute physiology (SNAP). They found phlebotomy loss and SNAP score at 7 days of life to be significant predictors of the number of transfusions.[9] Brune and colleagues reported that almost 65% of premature infants with a birth weight of less than 1500 g receive at least one RBC transfusion during the first week of life.[1]

The overall incidence of transfusions in our population is in agreement with previous reports showing that 45 to 60% of very low-birth-weight infants (<1500 g) received transfusions, although the number of units administered showed wide variation among studies.[1,3,8,9] In our cohort, only 15% of the transfused infants needed more than three transfusions. Variations of clinical condition, transfusion policy, and phlebotomy loss in the nursery may explain the differences between the results of the different studies.

Several studies reported on the collection of UCB RBCs.[1,5-8,10-13] Anderson and colleagues[7] and Eichler and colleagues[8] found a linear association between collected blood volume and birth weight with a greater relative blood volume from placentas of smaller newborns. Brune and colleagues collected approximately 20 mL of placental blood per kg of body weight irrespective of birth weight.[1] Surbek and colleagues collected a mean volume of 23.1 ± 1.1 mL cord blood per kg for infants with a mean gestational age of 32 ± 4 weeks and showed a correlation between collected cord blood volume and birth weight.[6] Correspondingly, we collected a median volume of 23 mL per kg for infants of less than 32 weeks without a linear correlation between collected cord blood volume and gestational age, placental weight, or birth weight. Many collection attempts, however, were not successful because of difficulties to obtain vascular access and blood flow. Both Eichler and coworkers[8] and Brune and coworkers[1] reported a poor correlation between the volume of cord blood collected and the transfusion requirements and thus often too little or too much RBC products were prepared. Therefore, Brune and coworkers[1] concluded that autologous blood seems not effective for treatment of anemia of prematurity because the collected amount is generally too small to cover transfu-

sion requirements, although for certain categories of newborn infants cord blood can replace or at least reduce allogeneic transfusions.[10] To investigate whether UCB could cover the early transfusion needs, we compared the amount of UCB collected and the amount of allogeneic transfusions received during the first 30 days after birth. We could have provided 45% of the infants with a gestational age between 24 and 32 weeks with at least 15 mL of cord blood per kg of birth weight. Sufficient cord blood RBCs to supply all needs for transfusions during the first 30 days after birth were available for 41% of these infants. This implies that not enough cord blood was available to meet the (complete) early demand for blood in 59% of premature infants with a gestational age below 32 weeks. In contrast, it seems not useful to collect UCB for all premature infants with a gestational age over 32 weeks because only a minority will need RBC transfusions. If gestational age, birth weight, and Apgar score are taken into account, it can be decided to collect cord blood if the likelihood of transfusion is higher than 30 to 50%. This approach (and associated costs) should be prospectively tested in a study with sufficient patients to draw conclusions on the feasibility of autologous cord blood RBC transfusions.

Moreover, attempts to reduce allogeneic transfusions can be undertaken by strict indications for laboratory tests.[3,9,14,15] Hume performed a retrospective review in premature infants and reported a diminishing number of transfusions if phlebotomy losses for diagnostic purposes were diminished and a more conservative transfusion policy was applied.[3] We calculated phlebotomy losses in a subgroup and found that in premature infants of greater than 30 weeks of gestation, phlebotomy losses almost equal transfusion requirements.

In this study we used a period of 30 days as a cutoff point in following the course of premature infants. The cutoff point corresponds to the expected shelf life of the umbilical cord RBCs of 30 days. This limits the scope of our study because we only considered the early transfusion needs of these premature infants, but not the need for “late” transfusions, which many very premature infants receive and cannot be met by placental blood.

In summary, the decision to collect cord blood with the intention for early transfusion can be made just after labor. The collection of UCB may be effective and efficient for premature infants between 29 and 31 weeks of gestation and a birth weight between 1000 and 1500 g. For infants born at less than 29 weeks of gestation, the organizational and technical aspects of the UCB collection need improvement to optimize the collected volume and reduce the proportion of premature infants that need allogeneic transfusions. As our study was a theoretical exercise, because collected and processed cord blood RBCs were not transfused, a clinical feasibility study is needed to test these assumptions.

Acknowledgements

The authors thank the staff and nurses of the delivery room and the neonatal center of the Leiden University Medical Center for their support, Saskia le Cessie and Leo van de Watering for statistical advice, Marjan Venekamp for collection of the data on phlebotomy losses, Manon Slot for providing data on collected umbilical cord blood, Frans Klumper for the data from obstetrical patients, and Jacqueline van Beckhoven and Godelieve van Roosmalen for coaching of the medical students collecting cord blood.

Reference list

1. Brune T, Garritsen H, Witteler R, Schlake A, Wullenweber J, Louwen F et al. Autologous placental blood transfusion for the therapy of anaemic neonates. Biol Neonate 2002; 81(4):236-243.
2. 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 Pediatr 1996; 129(5):680-687.
3. Hume H. Red blood cell transfusions for preterm infants: the role of evidence-based medicine. Semin Perinatol 1997; 21(1):8-19.
4. Maier RF, Sonntag J, 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(2):220-224.
5. Ballin A, Arbel E, Kenet G, Berar M, Kohelet D, Tanay A et al. Autologous umbilical cord blood transfusion. Arch Dis Child Fetal Neonatal Ed 1995; 73(3):F181-F183.
6. Surbek DV, Glanzmann R, Senn HP, Hoesli I, Holzgreve W. Can cord blood be used for autologous transfusion in preterm neonates? Eur J Pediatr 2000; 159(10):790-791.
7. Anderson S, Fangman J, Wager G, Uden D. Retrieval of placental blood from the umbilical vein to determine volume, sterility, and presence of clot formation. Am J Dis Child 1992; 146(1):36-39.
8. Eichler H, Schaible T, Richter E, Zieger W, Voller K, Leveringhaus A et al. Cord blood as a source of autologous RBCs for transfusion to preterm infants. Transfusion 2000; 40(9):1111-1117.
9. Kling PJ, Sullivan TM, Leftwich ME, Roe DJ. Score for neonatal acute physiology and phlebotomy blood loss predict erythrocyte transfusions in premature infants. Arch Pediatr Adolesc Med 1997; 151(1):27-31.
10. Ballin A, Kenet G, Gutman R, Samra Z, Zakut H, Meytes D. Autologous cord blood transfusion. Acta Paediatr 1994; 83(7):700-703.
11. Berzuini A, Pozzobon T, Terramoci R. Autologous cord blood transfusion in extremely low birth weight (ELBW) newborns. Blood 1998; 92(Suppl 1):130b.
12. Bifano EM, Dracker RA, Lorah K, Palit A. Collection and 28-day storage of human placental blood. Pediatr Res 1994; 36(1 Pt 1):90-94.
13. Brune T, Garritsen H, Hentschel R, Louwen F, Harms E, Jorch G. Efficacy, recovery, and safety of RBCs from autologous placental blood: clinical experience in 52 newborns. Transfusion 2003; 43(9):1210-1216.
14. Ohls RK. Erythropoietin treatment in extremely low birth weight infants: blood in versus blood out. J Pediatr 2002; 141(1):3-6.
15. Shannon KM, Mentzer WC, Abels RI, Freeman P, Newton N, Thompson D et al. Recombinant human erythropoietin in the anemia of prematurity: results of a placebo-controlled pilot study. J Pediatr 1991; 118(6):949-955.