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Title: Anemia of prematurity : time for a change in transfusion management?

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**Processing cord blood from premature infants into
autologous red blood cell products for transfusion**

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Abstract

Background & Objective: The use of umbilical cord blood (UCB) for transfusion purposes has gained interest the past years. UCB transfusion could serve premature infants, who often need red blood cell (RBC) transfusions early in life.

Material & Methods: We investigated the suitability of different storage media. UCB was collected after 25 0/7 – 35 6/7 gestational weeks and centrifuged to concentrate RBC subsequently stored in saline-adenine-glucose-mannitol (SAG-M) or in additive-solution-3 (AS-3), or stored as whole blood in citrate-phosphate-dextrose-adenine-1. Quality parameters were measured at 7 day intervals during 35 days, and compared to the standard RBC product.

Results: White blood cell- and platelet counts were higher in the UCB products. In the fractionated units, hemolysis remained below 1.0% in 64% after 14 days, and in 30% after 21 days. Storage in SAG-M or AS-3 showed similar quality. Whole blood UCB showed better pH and hemolysis rates after 21 days.

Conclusion: UCB can be processed into autologous products for premature infants. Shelf-life is limited to 14-21 days and compares unfavourably to stored whole blood. Considering the early transfusion needs in these infants, a short shelf-life would not be a practical objection.

Introduction

In the past years, the use of umbilical cord blood (UCB) for transfusion purposes has gained the interest of clinicians.¹⁻⁴ UCB could be used for either autologous or allogeneic transfusion purposes. For allogeneic use, whole blood UCB from term newborns has been used for paediatric and adult patients suffering from malaria.⁵ In the autologous setting, the use of UCB for transfusion has shown to be effective in avoiding allogeneic transfusions in neonates in need of surgery after birth.⁶⁻⁷ Next to these infants, autologous UCB could serve transfusion requirements in premature infants.^{1, 8-10} Despite the use of transfusion guidelines with restrictive triggers, premature infants are still frequently transfused.¹¹⁻¹⁴ Allogeneic red blood cell (RBC) transfusions have been incriminated to have adverse effects on the neonatal outcome, in particular on 'oxidative' diseases like bronchopulmonary dysplasia and retinopathy of prematurity.¹⁵⁻¹⁷ Whether the use of autologous RBC may overcome these possible side effects is still unknown. Several studies showed that it is feasible to collect UCB after premature birth for autologous RBC transfusion.^{2,9-10} In a randomized study we reported earlier on the logistics and the costs to incorporate autologous UCB transfusion for anemia of prematurity in standard blood bank practice.⁹ In this paper we present storage and quality parameters of UCB derived RBC, collected after premature birth, and stored in different extended storage media.

Material and Methods

UCB collection from premature infants

UCB was collected after deliveries between 25 0/7 - 35 6/7 gestational weeks. Exclusion criteria were active blood group incompatibility, hemoglobinopathies, maternal infections (HIV, HBV, HCV, HTLV, and syphilis), premature rupture of the membranes with fever treated with antibiotics, and congenital infections (CMV, Parvovirus B19, Toxoplasmosis). Informed consent for study participation was obtained from (one of) the parents before delivery. After a vaginal delivery, premature UCB (P-UCB) was collected from the undelivered placenta. In case of a caesarean section, collection was performed after the placenta had been delivered. The collection system consisted of a 150 mL bag (Fresenius, Bad Homburg, Germany) containing 5 mL of citrate-phosphate-dextrose-adenine-1 (CPDA-1) (Baxter, IL), a collection tubing system with 2 attached needles (Medisize, Hillegom, the Netherlands) and a syringe (Medisize, Hillegom, the Netherlands) containing (additional) 5 mL CPDA-1. The umbilical cord was sterilized with iodine, the cord vein was punctured and P-UCB was collected by gravity. After collection, the additional 5 mL CPDA-1 in the syringe was added to the collected P-UCB. The collection bag was then stored at 2-6 ° C, prior to transport to the blood bank for further processing.

Fractionation of the P-UCB

A half mL whole blood was used to perform complete blood counts (Beckman Coulter Onyx, Brea, USA) and blood group typing (ABO-RhD, Diamed, Cressier, Switzerland). The remaining P-UCB was transferred to a closed centrifuge circuit (15 minutes at 1010x g, Biosafe Sepax, Eysins, Switzerland). This procedure was started if the collected total blood volume was at least 15 mL (excluding anticoagulant). RBCs were separated from buffy-coat and plasma and adjusted with either saline-adenine-glucose-mannitol (SAG-M) (Fresenius, Bad Homburg, Germany) or additive solution 3 (AS-3) (Braintree, MA) to a red blood cell concentrate (RBCC) with a hematocrit between 0.55 and 0.65 L/L. At least 10 mL of the removed CPDA-1-plasma was used for aerobic and anaerobic bacterial culture (BacTalert, Durham, USA).¹⁸ P-UCB was not tested on contamination of maternal cells. All processing was done within 24 hours after collection. Subsequently, P-UCB products were stored during 35 days at 2-6°C. At 7 day intervals 0.5 mL was removed for quality parameters.

Whole blood storage

UCB collections with a CPDA-1 : blood ratio of 1: < 4 were discarded. Twelve P-UCB collections with an anticoagulant : blood ratio of 1: ≥ 4, were stored as whole blood during 21 days at 2-6°C. Prior to storage, a volume of 10 mL whole blood UCB was used for aerobic and anaerobic bacterial culture (BacTalert, Durham). At 7 day intervals 0.5 mL was removed for quality parameters.

Storage stability

For the quality control we performed an automatic blood cell count (Beckman Coulter Onyx). Undiluted RBCC or whole blood P-UCB was used for sodium, potassium, free Hb and pH measurements. Hemolysis, lactate, glucose and osmotic resistance measurements were done using diluted RBCC or whole blood UCB (5 times diluted in NaCl 0.9%). Samples were centrifuged at 10.000 rpm (9615 x g) for 3 minutes. After centrifugation, the supernatant was kept at minus 80° C until analysis. Sodium and potassium supernatant levels were determined using a standard flame photometry method. The pH was measured on a blood gas analyzer (Bayer rapidlab, Siemens Healthcare Diagnostics, Deerfield, IL). Glucose, lactate, free Hb, hemolysis and osmotic resistance were measured by optical density on a Versamax® plate reader. (Molecular Devices, Silicon Valley, CA) For osmotic resistance measurement, a series of 0.2% - 0.8% NaCl was used to determine the NaCl concentration resulting in 50 % hemolysis.

Storage parameters were compared with pre-expiration values from 10 standard pedi-packs stored for 35 days under the same conditions. The standard pedi-pack consisted of 65 mL adult donor pre-storage leukocyte-depleted, RBC stored in SAG-M. Pedi-pack products have a hematocrit between 0.55 and 0.65 L/L and a white blood cell (WBC) count < 1x10e6/ unit (EC guideline 2004/33/EC).¹⁹

Statistical and data analysis

Data are presented as mean $\pm$ SD unless indicated otherwise. SPSS (version 16, Chicago, IL) for Windows was used for data analysis. Continuous variables were analyzed using independent t-tests. In view of the number of parameters included in our analysis, a p -value <0.01 was considered significant.

Results

P-UCB products

Fifty-nine collections were used for the validation study. Forty-seven of these were processed using a closed centrifuge circuit (Biosafe Sepax, Eysins, Switzerland), of which 34 were stored in SAG-M, with a mean volume of 34.4 ± 13.4 mL (including anticoagulant); and 13 in AS-3 with a mean total volume of 32.2 ± 20.5 mL (including anticoagulant), during 35 days at $2-6^\circ$ C. Twelve P-UCB collections were stored as whole blood during 21 days, mean volume 52.1 ± 20.9 mL (median anticoagulant : blood ratio 1:6, range 1:4 – 1:8). Seven percent of all products were microbially contaminated (4 of 59). The time interval in which we detected positive blood cultures was 13.2 hours – 74.4 hours after processing. The pathogens were identified as Coagulase negative staphylococcus species, Escherichia Coli species and Streptococcus agalactiae B species (2x).

Storage and quality characteristics - fractionated P-UCB products

The fractionated P-UCB products had a mean hematocrit of 0.605 ± 0.04 L/L. At the start, the RBCC products differed in lactate, sodium and potassium levels depending on the storage media ($p<0.01$). (Figure 1A-B) Remarkably, also the hemolysis rate at the start was higher in RBCC stored in AS-3 compared to SAGM ($p<0.001$). (Figure 1C)

During storage, we observed similar increases in lactate, potassium and hemolysis, as well as decreases in glucose, sodium and pH, when either stored in SAG-M or AS-3. (Figure 1A-C) After 14 days of storage, 47% (22 of 47) of the fractionated units had a hemolysis rate below 0.8%, and 64% (30 of 47) of the units below a rate of 1.0 %. After 21 days of storage, these hemolysis rates were respectively 21% (10 of 47) below 0.8% and 30 % (14 of 47) below 1.0% hemolysis. After 35 days of storage the mean corpuscular volume (MCV) of RBC stored in SAG-M was higher, compared to the RBC stored in AS-3 ($p=0.018$) (Table 1).

The P-UCB product storage data at 21 and 35 days were compared with data at pre-expiration day 35 from standard pedi-packs. WBC and platelet counts were higher in all P-UCB products. (Table 1). During storage the hematocrit of the P-UCB products gradually increased as did the MCV. (Table 1) Compared to the standard pedi-pack, the SAG-M products displayed significant differences in pH, hemolysis, and free Hb after 21 storage days ($p<0.01$). In addition, after 35 days lactate and potassium were also significantly higher in the P-UCB products stored in SAG-M

compared to the standard pedi-pack ($p<0.01$). Storage of the P-UCB products in AS-3 showed significantly higher free Hb and sodium levels after 21 days of storage ($p<0.01$) compared to the standard pedipack. At day 35, pH, hemolysis rate and potassium were also significantly different ($p<0.01$). (Table 2) Although the higher hemolysis rates indicated that the P-UCB derived RBC degraded significantly during storage, this was not seen in the osmotic resistance measurements. Storage in SAG-M or AS-3 showed no significant differences in osmotic resistance compared to the standard pedi-pack. Gestational age at the time of P-UCB collection had no influence on the storage parameters (data not shown).

Figure 1: Quality parameters of fractionated P-UCB products (stored in SAG-M or AS-3) and whole blood P-UCB products (stored in CPDA-1) during 35 days of storage

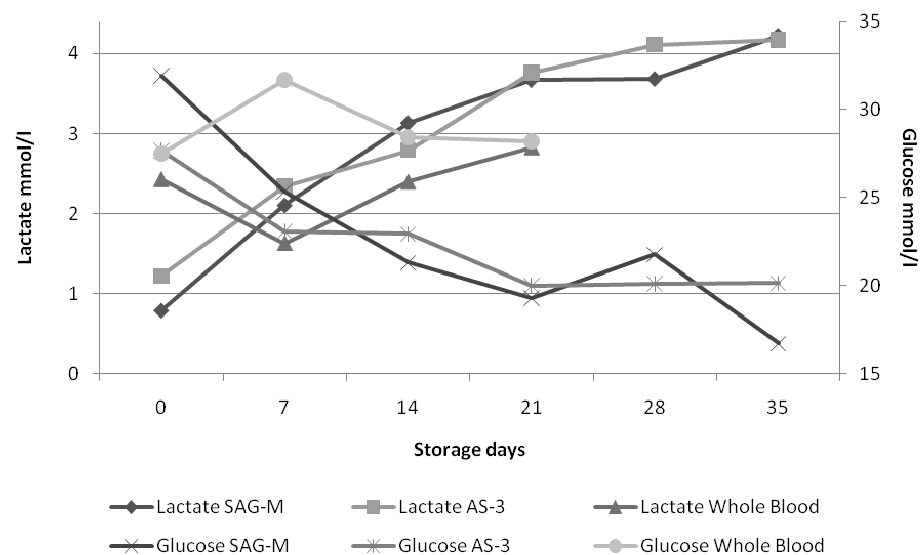


Figure 1A: Lactate and glucose levels during storage
 Whole blood lactate at day 21 was significantly lower than SAG-M and AS-3 ($p<0.001$)
 Whole blood glucose at day 21 was significantly higher than AS-3 ($p<0.001$)
 Abbreviations:P-UCB: premature umbilical cord blood; SAG-M: Saline Adenin Glucose Mannitol; AS-3: additive solution 3; CPDA-1: citrate phosphate dextrose adenine 1

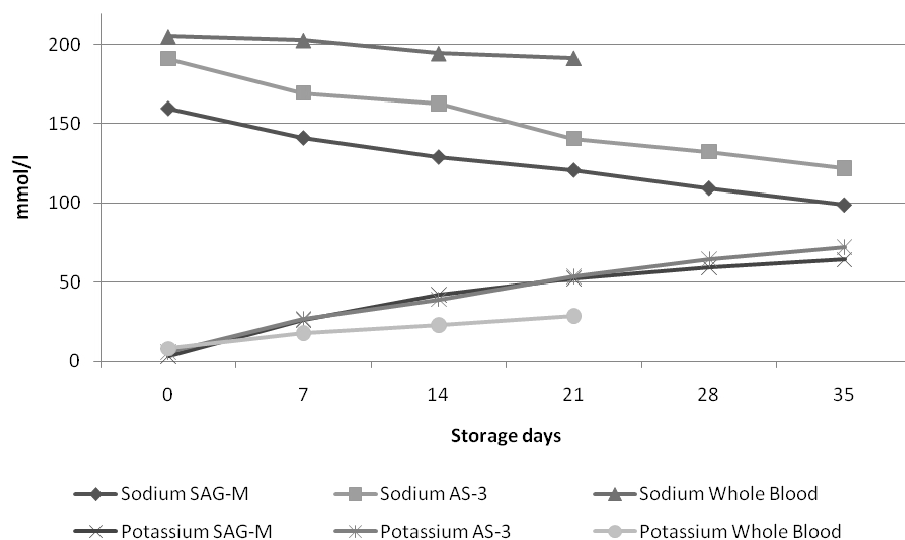


Figure 1B: Sodium and potassium levels during storage

Sodium levels in SAG-M was significantly lower compared to AS-3 and whole blood ($p < 0.01$)

Potassium levels in whole blood was significantly lower compared to SAG-M and AS-3 ($p < 0.01$)

Abbreviations: P-UCB: premature umbilical cord blood; SAG-M: Saline Adenin Glucose Mannitol; AS-3: additive solution 3; CPDA-1: citrate phosphate dextrose adenine 1

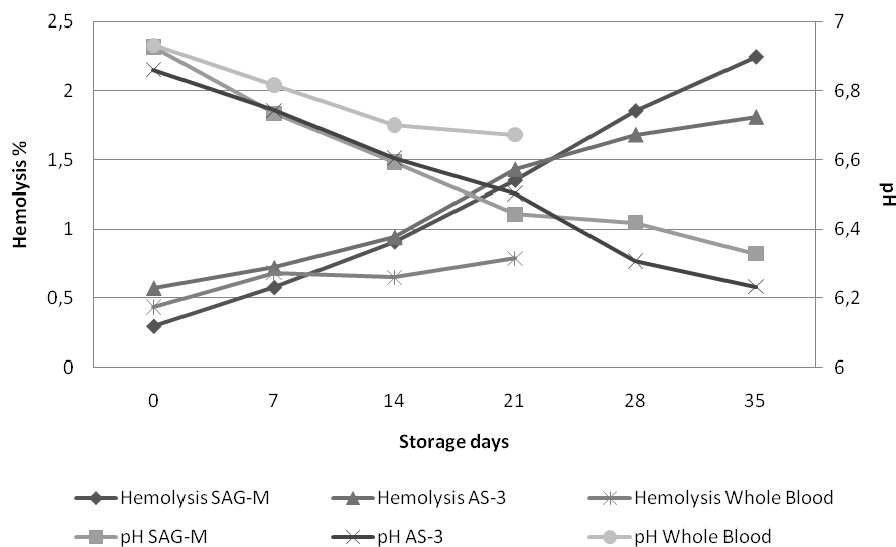


Figure 1C: Hemolysis rate and pH during storage

AS-3 hemolysis rate at day 0 was significantly lower than SAG-M ($p < 0.001$)

Whole blood hemolysis rate at day 21 was significantly lower than SAG-M and AS-3 ($p < 0.001$)

Whole blood pH at day 21 was significantly higher than SAG-M and AS-3 ($p < 0.001$)

Abbreviations: P-UCB: premature umbilical cord blood; SAG-M: Saline Adenin Glucose Mannitol; AS-3: additive solution 3; CPDA-1: citrate phosphate dextrose adenine 1

Table 1: Product cell content after storage 21-35 days at 2-6° C

	SAG-M (n=34)^	AS-3 (n=13)^	Whole blood (n=12)^	Standard Pedi-pack (n=10)*
<u>After 21 days of storage</u>				
RBC concentration, x10e12/l	5.4 ± 0.48	5.6 ± 0.49	3.7 ± 0.88#	
MCV, fl	117.9 ± 6.67	113.8 ± 6.39	110.8 ± 5.98	
Hematocrit, l/l	0.64 ± 0.05	0.64 ± 0.06	0.41 ± 0.08 #	
WBC concentration, x10e9/l	4.5 ± 2.27	4.5 ± 1.74	7.1 ± 4.48	
Thrombocyte concentration, x10e9/l	94 ± 40.7	96 ± 44.6	175 ± 102.4	
<u>After 35 days of storage</u>				
RBC concentration, x10e12/l	5.5 ± 0.50	5.6 ± 0.45	Na	6.5 ± 0.51
MCV, fl	122.1 ± 7.6	116.1 ± 6.9	Na	90.5 ± 3.87
Hematocrit, l/l	0.67 ± 0.05	0.65 ± 0.06	Na	0.58 ± 0.03
WBC concentration, x10e9/l	3.9 ± 2.16	3.7 ± 1.51	Na	<0.001
Thrombocyte concentration, x10e9/l	83.3 ± 37.7	96 ± 43.9	Na	<0.015

Data are indicated as mean ± standard deviation, or as indicated otherwise

RBC: red blood cells; MCV: mean corpuscular volume; WBC: white blood cell; SAG-M: saline adenine glucose mannitol; AS-3: additive solution 3; Na: not applicable

*: only pre-expiration measurement at day 35; ^: p<0.01 compared to Standard pedipack; #: p<0.0001 compared to SAG-M/AS-3/ standard pedi-pack

P-UCB whole blood storage

After 21 days of storage, the increase in hemolysis and MCV and the decrease in pH, were less pronounced in P-UCB stored as unprocessed whole blood, compared to the P-UCB RBCC in storage solutions. (Figure 1-C) In addition, the whole blood P-UCB products had significant lower lactate-, maintained higher glucose- and had lower potassium levels (Figure 1 A-B). The pH and hemolysis rate in the whole blood products after 21 days were not statistically different when compared to the pre-expiration data of the standard product. The osmotic resistance of the whole blood UCB derived RBC was also similar. (Table 2)

Table 2: Red cell biochemical parameters after storage 21–35 days at 2–6° C

	SAG-M (n=34)	AS-3 (n=13)	Whole blood (n=12)	Standard Pedipack (n=10)*
<u>After 21 days of storage</u>				
pH	6.44 ± 0.13 [^] (6.09-6.72)	6.5 ± 0.96 ⁻ (6.34-6.63)	6.67 ± 0.19 (6.36-7.02)	
Hemolysis rate, %	1.35 ± 0.64 [±] (0.42-3.47)	1.43 ± 0.91 (0.56-3.36)	0.79 ± 0.42 (0.30-1.59)	
Free Hemoglobin, g/dL	0.63 ± 0.31 [±] (0.18-1.16)	0.82 ± 0.69 [±] (0.23-2.38)	0.13 ± 0.06 (0.05-0.23)	
Osmotic resistance (% NaCl), median (IQR) [†]	0.51 (0.49-0.54)	0.49 (0.46-0.51)	0.48 (0.47-0.51)	
Sodium, mmol/l	120.7 ± 12.9 [^] (94-143)	140.6 ± 11.9 [^] (115-155)	191.5 ± 29.8 [†] (163-262)	
Potassium, mmol/l	52.4 ± 10.1 [^] (36.0-77.0)	53.7 ± 10.8 [†] (35.9-77.5)	28.8 ± 7.9 [†] (16.9-45.3)	
Glucose, mmol/l	19.3 ± 6.3 (10.6-25.1)	19.9 ± 10.5 (7.31-44.5)	28.2 ± 14.9 (10.4-57.3)	
Lactate, mmol/l	3.67 ± 0.71 [^] (2.36-5.1)	3.76 ± 0.77 ⁻ (2.79-5.3)	2.8 ± 0.62 [†] (1.39-3.51)	
<u>After 35 days of storage</u>				
pH	6.23 ± 0.16 [†] (6.00-6.78)	6.32 ± 0.06 [†] (6.25-6.74)	Na	6.56 ± 0.14 (6.38-6.74)
Hemolysis rate, %	2.2 ± 0.67 [±] (1.1-3.5)	1.8 ± 1 [†] (0.76-3.67)	Na	0.7 ± 0.14 (0.32-0.84)
Free Hemoglobin, g/dL	1.05 ± 0.4 [†] (0.48-1.88)	1.32 ± 1.2 [†] (0.29-3.38)	Na	0.13 ± 0.03 (0.05-0.18)
Osmotic resistance (% NaCl), median (IQR) [†]	0.53 (0.50-0.61)	0.49 (0.47-0.59)	Na	0.52 (0.51-0.57)
Sodium, mmol/l	106.6 ± 12.8 [†] (82-129)	122.1 ± 12.1 [†] (98-140)	Na	113.8 ± 1.8 (111-117)
Potassium, mmol/l	69.3 ± 11.3 [†] (50-91)	72.2 ± 12.4 [†] (51-95)	Na	45.2 ± 3.0 (41-50)
Glucose, mmol/l	16.7 ± 10.7 (2-28)	20.1 ± 10.9 (7-40)	Na	22.1 ± 6.3 (9.7-29.7)
Lactate, mmol/l	4.2 ± 0.8 [†] (2.6-5.9)	4.2 ± 1.1 (1.1-5.3)	Na	3.45 ± 0.31 (1.1-5.25)

Data are indicated as mean ± standard deviation (min-max range), or as indicated otherwise

SAG-M: saline adenine glucose mannitol; AS-3: additive solution 3; Na: not applicable

[†]: % NaCl causing 50% lysis of RBC

*: only pre-expiration measurement at day 35

[†]: Compared to day 35 standard pedi-pack p <0.01; [‡]: Compared to day 35 standard pedi-pack p<0.001

[#]: SAG-M compared to AS-3 p <0.001; [~]: Compared to Whole blood p<0.01

[^]: Compared to Whole blood p<0.001

Discussion

In this study we collected P-UCB which was either fractionated using a closed centrifugation circuit and stored in extended storage medium SAG-M or AS-3 or stored as whole blood in CPDA-1. Quality parameters were compared to the standard pedi-pack, consisting of leukocyte-depleted filtered adult donor RBC after 35 days of storage, which are validated for neonatal transfusions.

Comparison of the P-UCB products stored in either SAG-M or AS-3 showed no differences in biochemical parameters. Fractionated P-UCB stored in SAG-M or AS-3 showed a higher hemolysis rate and increase in MCV compared to the standard pedi-pack. The mean hematocrit of the fractionated P-UCB products fulfilled product release requirements of standard pedi-packs. However, residual WBC and platelet counts in the P-UCB products were significantly higher as compared to pre-storage filtered pedi-packs¹⁹ (Tables 1 and 2), indicating that the centrifugation method aiming to remove the buffy-coat with a low loss of RBC, in fact removed few WBCs and platelets. Hemolysis rates after 14 days of storage maintained below the European limit of 0.8% in 47% of the fractionated P-UCB units and below the American limit of 1.0% in 64% of the fractionated P-UCB units. After 21 storage days, 21% of the fractionated P-UCB product remained below 0.8% hemolysis and 30 % below 1.0% hemolysis. This indicates that these P-UCB products have a significant shorter shelf life, and frequent quality control is necessary if these products are used in clinical practice. The osmotic resistance, also an indicator of RBC fragility, did however not differ compared to the standard pedi-pack. This could suggest that mechanical stress, due to collection and/or processing, contributes more to the vulnerability of the cord blood red cells, rather than the fragility caused by swelling of the cells during storage.

The storage parameters from the whole blood P-UCB stored in CPDA-1 showed a better pH, lower hemolysis rate and lower lactate and potassium levels up to 21 days, when compared to the fractionated P-UCB. This may be the result of a lower RBC concentration, resulting in a more diluted cell product including nutrients, or that fetal RBC are less resistant to the mechanical stress of centrifugation. An advantage of whole blood storage is furthermore that it is a less laborious product and there is no RBC loss due to processing, while immature hematopoietic precursor cells, probably of benefit for the infant are not removed along with the leukocytes. The drawback is that stored whole blood showed variability in cell count and in the ratio CPDA-1: collected blood. Despite higher as well as lower ratio's (median 1:6; range 1:4 to 1:8) compared to standard RBCC products (anticoagulant: blood ratio - 1:7), the biochemical parameters maintained rather well up to 14-21 days of storage. However, in view of the lower and variable hematocrit and the high WBC content, it is more complicated to formulate quality parameters under blood bank conditions to use whole blood as an alternative for allogeneic RBC transfusion in premature infants. In comparison to leuko-reduced UCB products, the higher platelet and WBC count could increase the risk on the formation of platelet-leukocyte aggregates upon cold storage

and exert immunomodulation.²⁰ The WBC in cord blood are more naïve and immature. As such it might be that these cells would have less potential to induce an immunosuppressive effect in a recipient as compared to allogeneic adult WBC. However, studies in adults showed that the clinical immunomodulatory effects on post transfusion infections and mortality of allogeneic and autologous leukocyte-(aggregate)-containing RBC products are controversial.²¹

Another drawback of using whole blood is the volume needed for appropriate microbial testing, in contrast to the waste plasma that was used after P-UCB fractionation. Although a volume of 10 mL (even 20 mL) is optimal for bacterial culture¹⁸; the use of a smaller volume for microbial testing, for instance 1-2 mL blood, as is used in neonatal practice²²; is acceptable in cord blood banking. In this study we observed a contamination rate of 7%, which is not at variance with collections for cord blood bank purposes.²³ The pathogens that were identified are known to cause neonatal sepsis. In clinical practice an incubation period of 72 hours is kept before a blood culture is released, as this interval is sufficient to detect all clinically important pathogens.²² To prevent transfusion of a contaminated autologous product, a similar quarantine period could be held for product release, as most pathogens were found within this time interval.

A few studies on storage of cord blood RBC have been reported. Our P-UCB products stored in SAG-M had significant higher hemolysis rates after 35 days of storage compared to the studies by Garritsen et al, Brune et al and Widing et al, who also stored fractionated cord blood RBC in SAG-M. We found after 35 storage days, a mean hemolysis rate of $2.2 \pm 0.67\%$, compared to their observations, respectively $1.1 \pm 0.8\%$, $1.0 \pm 0.7\%$ and 0.9% (range 0.6-1.1).^{3, 20, 24} The pH in our SAG-M stored P-UCB was comparable to the centrifuged UCB products in the study by Garritsen et al and the filtrated UCB products in the study by Brune et al; 6.23 ± 0.16 versus respectively 6.1 ± 0.1 and 6.4 ± 0.1 .^{3, 24} It may be that the premature RBC we collected may be more fragile after processing compared to RBC derived from full term cord blood, which generally contains a mean proportion of 30% HbA.²⁵ Also the more fragile vessels in the preterm placenta may enhance RBC damage during UCB collection.

Similarly, in whole blood P-UCB, hemolysis rate after 21 days of storage ($0.79 \pm 0.42\%$) exceeded the rate reported by Bifano et al after 28 days of storage of whole blood UCB collected at term ($0.39 \pm 0.05\%$), despite similar mean hematocrit and pH of our whole blood products compared to Bifano et al (Ht, 0.41 ± 0.08 L/L versus 0.41 ± 0.02 L/L and pH 6.67 ± 0.19 versus 6.51 ± 0.12 , respectively).²⁶

Brune et al have shown that filtration of UCB is also feasible, but RBC loss was only acceptable when at least 60 mL UCB was available.³ Premature placentas are smaller and several studies showed that the volume of UCB that can be collected is either related to gestational age or birth weight.^{1-2, 10, 27-28} Subsequently, the collected volumes are often less than 60 mL and would need adjusted filters to prevent significant RBC loss.

P-UCB products stored in either SAG-M or AS-3 showed a significant increase in hemolysis and decrease in pH compared to the standard pedi-pack. This underscores that macrocytic fetal RBC

may be more vulnerable during storage. In particular, in SAG-M, this swelling was evident. (Table 1) Osmotic fragility was, however, not different when compared to the standard pedi-pack. This vulnerability was not related to the degree of prematurity of the cord blood RBC.

In our clinical study we used the autologous P-UCB products stored in SAG-M for transfusion needs in the first 21 days after birth, under the condition that in case of product release between 14 and 21 days of storage, hemolysis rate was < 0.8%. We showed that premature infants, in particular born before 30 weeks, could be treated with autologous UCB. The first transfusion needs in these infants were at median day 6 after birth (interquartile range 2-13, total range 0-33).⁹ Considering the early transfusion needs of these premature infants, the shorter shelf life of autologous P-UCB would not be a major obstacle.

In conclusion, P-UCB can be collected and RBC can be stored for approximately 14 – 21 days for autologous transfusion to premature infants. SAG-M or AS-3 as extended storage media for packed P-UCB cells had no advantage over whole blood storage on the quality of the RBC. P-UCB derived RBC seem more vulnerable for mechanical stress and/or storage at higher hematocrit in extended storage media. Although we showed that the use of autologous P-UCB red cells under blood bank qualifications, including viral testing, is cost-increasing⁹, the use of an autologous UCB product for premature infants could potentially be further developed as an alternative for allogeneic transfusion.

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