Original Article

Use of Autologous Umbilical Cord Blood Transfusion in Neonates Undergoing Surgical Correction of Congenital Cardiac Defects: A Pilot Study

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Abstract

Background: Blood transfusion requirement during neonatal open heart surgeries is universal. Homologous blood transfusion (HBT) in pediatric cardiac surgery is used most commonly for priming of cardiopulmonary bypass (CPB) system and for postoperative transfusion. To avoid the risks associated with HBT in neonates undergoing cardiac surgery, use of autologous umbilical cord blood (AUCB) transfusion has been described. We present our experience with the use of AUCB for neonatal cardiac surgery. **Designs and Methods:** Consecutive neonates scheduled to undergo cardiac surgery for various cardiac diseases who had a prenatal diagnosis made on the basis of a fetal echocardiography were included in this prospective observational study. After a vaginal delivery or a cesarean section, UCB was collected from the placenta in a 150-mL bag containing 5 mL of citrate–phosphate–dextrose–adenine-1 solution. The collected bag with 70–75 mL cord blood was stored at 2°C–6°C and tested for blood grouping and infections after proper labeling. The neonate's autologous cord blood was used for postcardiac surgery blood transfusion to replace postoperative blood loss. **Results:** AUCB has been used so far at our institute in 10 neonates undergoing cardiac surgery. The donor exposure in age and type of cardiac surgery-matched controls showed that the neonates not receiving autologous cord blood had a donor exposure to 5 donors (2 packed red blood cells [PRBCs], including 1 for CPB prime and 1 for postoperative loss, 1 fresh frozen plasma, 1 cryoprecipitate, and 1 platelet concentrate) compared to 1 donor for the AUCB neonate (1 PRBC for the CPB prime). Postoperative blood loss was similar in both the groups of matched controls and study group. Values of hemoglobin, total leukocyte count, platelet counts, and blood gas parameters were also similar. **Conclusions:** Use of AUCB for replacement of postoperative blood loss after neonatal cardiac surgery is feasible and reduces donor exposure to the neonate. Its use, however, requires a prenatal diagnosis of a cardiac defect by fetal echo and adequate logistic and psychological support from involved clinicians and the blood bank.

Keywords: *Autologous umbilical cord blood transfusion, homologous blood transfusion, neonatal cardiac surgery*

Introduction

Neonatal open heart surgery requires homologous blood transfusion (HBT). Dangers of HBT leading to various complications have been described in several studies. These include immunologic reactions leading to organ dysfunction as well as transmission of infections and transfusion-related reactions.[1,2] Blood components are not only used to prime the extracorporeal circuit and oxygenator but also to correct anemia after cardiopulmonary bypass (CPB). This invariably leads to the use of a large quantity of HBT during the perioperative period. The small body weight (<4 kg) of neonates and the requirement of priming of the relatively large CPB circuit further compounds the total quantity of HBT up to 40%–50% of the total circulating blood volume.[3]

In spite of advances in terms of bloodless pediatric open heart surgeries, miniaturized bypass systems, modified ultrafiltration, retrograde autologous priming, cell salvage, etc. as of now, it is rarely possible to perform neonatal open heart surgeries without adding homologous blood in the extracorporeal circuit.

To decrease the complications associated with transfusion of the homologous blood, use of autologous blood in the form of umbilical cord blood (UCB) to be used

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perioperatively in the open heart surgeries on neonates has been advocated. The safety and effectiveness of predeposit autologous transfusion have been reported.[3-5] The placenta, which contains a reservoir of fetal blood, represents an ideal source of autologous blood for newborns.[6] With the advent of advanced diagnostic modalities such as fetal echocardiography for diagnosing congenital heart defects prenatally, as well as the development of the controlled environment for deliveries of such subset of babies near a pediatric cardiology center, collection and use of autologous UCB (AUCB) have been made feasible at various centers.

Several studies showed that it is feasible to collect AUCB after premature birth for autologous red blood cell (RBC) transfusion.[7-9] We hypothesized that the use of AUCB in open heart surgeries would lead to reduced use of homologous blood and reduced side effects of blood transfusion. It was proposed that our study would show the beneficial effects of AUCB in open heart surgeries in the Indian set up. Although the clinical usefulness and advantage of autologous AUCB transfusions (AUCBTs) over HBT has been described in earlier studies, in this pilot project, safety and feasibility of the same were looked into in our center. Once established, the practice of AUCBT has the potential to become a novel approach for improved neonate's surgical outcomes, thus ensuring advancement in patient safety.

Designs and Methods

Study design and population

After institutional ethics committee approval and obtaining written informed consent from the parents of the neonates, consecutive neonates who had a prenatal diagnosis made on the basis of a fetal echocardiography and were scheduled to undergo correction surgery from September 2016 to September 2017 were included in this prospective observational study. Keeping in view of the rarity of in utero diagnosis of congenital heart disease (CHD), and pilot project nature of the study, 10 neonates, given AUCB have been studied. These were compared with 10 age- and surgery matched neonates who acted as the control group.

The study group (AUCBT) neonates had UCB collection done at the time of delivery. The control group (HBT) comprised age- and diagnosis-matched neonates who presented for open heart surgery and were planned to receive HBT perioperatively. Neonates with low birth weight (2500 g or less) or presence of any history of recent infections in the mother were excluded from the study.

Umbilical cord blood collection

After vaginal delivery, UCB was collected from the undelivered placenta. In case of a cesarean section, the collection was performed after the placenta had been delivered. The collection system comprised a 150-mL blood collection bag containing 5 mL of citrate–phosphate–dextrose–adenine-1 (CPDA-1). The umbilical cord was sterilized with iodine, the cord vein then punctured and UCB collected by gravity. The collection bag with 70–75 mL of UCB was then stored at 2°C–6°C, before transport to the blood bank for further processing. At the blood bank, the collected blood after proper labeling was tested for blood grouping and cross-matching besides testing for any infections, namely, venereal disease research laboratory, HIV, HBsAg, malarial parasite, and HCV. The cord blood was used for postoperative blood transfusion to replace blood loss in the postsurgical period. Cross-matching of the UCB and recipient blood was done in accordance with the standardized institutional protocols before surgeries to avoid any transfusion errors. Pall SQ40 Blood Transfusion Filter was used while transfusing blood to the neonate.

Anesthesia and cardiopulmonary bypass technique

Anesthesia in all the neonates included in the study was induced using inhalational anesthetic technique using sevoflurane. After the establishment of intravenous access ketamine, 1 mg/kg, fentanyl 1–2 μg/kg, midazolam 0.02 mg/kg, and rocuronium 1 mg/kg were given followed by the tracheal intubation. Monitoring at the time of induction included pulse oximetry, noninvasive blood pressure, and 5-lead electrocardiogram. After intubation of the trachea, the lungs were ventilated with 50% oxygen in air. Ventilation was controlled with tidal volume of 8–10 mL/kg and positive end-expiratory pressure of 0–5. Blood pressure monitoring and was done and near-infrared spectroscopy monitoring was applied. Anesthesia was maintained by intermittent dose of pancuronium, fentanyl, and midazolam as required.

All surgeries were performed on CPB using a neonatal membrane oxygenator (CAPIOX RX 05 Terumo) with mild hypothermia at 32°C–33°C, using CPB flows of 150–200 mL/kg. Prime solutions for both the groups were same and the hematocrit on CPB was maintained at 28%–30%, with packed RBCs (PRBC) as needed. Homologous blood was used in both the groups in the CPB circuits. AUCB was administered only in the postoperative period to the neonates. All neonates were warmed to 35° centigrade nasal temperature before weaning from CPB was attempted.

Postoperatively, the neonates were continuously monitored in the Intensive Care Unit (ICU) with the surface electrocardiography, transcutaneous pulse oximetry, and invasive arterial and central venous pressures. All neonates received continuous fentanyl infusion at 1 μg/kg/h for the 1st postoperative day. Inotropic support and vasopressors were started based on the hemodynamic parameters of the neonate. The neonates were gradually weaned off the mechanical ventilation support based on their clinical condition, hemodynamic stability, gas exchange status based on their arterial blood gas (ABG) analysis, spontaneous respiratory efforts, and chest X-ray findings.

Clinical data collection

Information on birth weight, sex, quantity of harvested UCB and transfused blood products, postoperative blood loss, and length of CPB were documented in both the groups and compared. Values of hemoglobin (Hb), total leukocyte count (TLC), platelet counts, and ABG parameters were also documented.

Statistical analysis

A total of 10 neonates in each group were compared in our pilot study. Data were compiled as mean ± standard deviation. Continuous variables were analyzed using Mann–Whitney U-test and Fisher's exact test for comparison of percentages. A $P \leq 0.05$ was considered statistically significant. All analyses were performed with IBM SPSS Statistics 23 (Armonk, NY, USA, IBM Corp).

Results

AUCB has been used in 10 neonates undergoing surgery using CPB, included in the study group. Out of 13 neonates with a prenatal diagnoses of a cardiac defect on a fetal echo, 9 neonates had transposition of the great arteries (dTGA) and underwent an arterial switch operation (ASO), 2 neonates had a congenital diaphragmatic hernia (CDH) repaired with extracorporeal membrane oxygenation support, one neonate had a congenital complete heart block requiring a permanent pacemaker implantation, and 1 had tetralogy of Fallot (TOF) requiring a neonatal shunt. In the neonate with TOF, only 15 mL of blood could be withdrawn because of a small-sized placenta, and this blood was not transfused. The neonate undergoing pacemaker implantation did not require any transfusion. Neonates who did not require any blood transfusion during the surgery were not included in the study. One of the neonates in the study group who had undergone ASO required additional HBT perioperatively due to increased intraoperative bleeding. The HBT group had 9 neonates with dTGA who underwent ASO. One neonate had CDH repair surgery.

Mean volume of harvested UCB (excluding anticoagulant) was 70 + 15 mL. The demographic profiles of the neonates in both the groups are compared in Table 1. On comparing mean average age (20.2 days in AUCBT group and 22.5 days in HBT group) and birth weight (2.69 kg in AUCBT group and 2.88 kg in HBT group) of neonates in each group, no differences in gender between the two groups. The average CPB times (90.3 min in AUCBT group and 93.1 min in the HBT group), average time to extubation (60.2 h in AUCBT group and 63.6 h in HBT group), and average ICU stay (5.4 days in AUCBT group and 5.8 days in HBT group) in both groups were comparable.

Perioperative clinical characteristics are compared in Table 2. Postoperative blood loss (in 24 h) was similar in both the groups of matched controls and study group.

Table 1: Demographic characteristics

Characteristics	AUCBT group (*n*=10)	HBT group (*n*=10)	*P*
Age at time of surgery (days)†	20.2 (1.93)	22.5 (3.21)	0.07
Males (%)	4 (40)	6 (60)	0.4
Birth weight (kg)†	2.69 (0.25)	2.88 (0.35)	0.17
Surgery performed#			
ASO	8 (80)	9 (90)	0.56
CDH repair	2 (20)	1 (10)	0.56
CPB time (min)†	90.3 (4.22)	93.1 (3.7)	0.13
Time to extubation (h)†	60.2 (5.25)	63.6 (5.17)	0.16
ICU stay (days)†	5.4 (0.7)	5.8 (0.63)	0.2

†Values are mean (SD), #Values are total *n* (%). ASO: Arterial switch operation, CDH: Congenital diaphragmatic hernia, SD: Standard deviation, AUCBT: Autologous umbilical cord blood transfusions, HBT: Homologous blood transfusion, CPB: Cardiopulmonary bypass, ICU: Intensive Care Unit

Table 2: Perioperative clinical characteristics

Characteristics	AUCBT group (*n*=10)	HBT group (*n*=10)	*P*
Hematocrit level at induction†	44.6 (5.56)	45.9 (6.42)	0.63
Mean postoperative blood loss (mL)†	80 (6.46)	84.6 (4.74)	0.09
Hematocrit level on POD 1†	45.4 (5.44)	45.9 (3.67)	0.81
Postoperative TLC (×1000)†	8.8 (1.25)	8.7 (1.64)	0.9
Postoperative platelet counts (×1000)†	96.5 (12.75)	102.2 (16.51)	0.4
POD PaO_2†	113.6 (8.33)	116.1 (9.52)	0.54
POD lactate levels†	1.76 (0.46)	1.73 (0.4)	0.8

†Values are mean (SD). POD: Postoperative day, TLC: Total leukocyte count, AUCBT: Autologous umbilical cord blood transfusions, HBT: Homologous blood transfusion, SD: Standard deviation

Values of Hb, TLC, platelet counts, and blood gas parameters postoperatively were also similar. No adverse reactions to blood were seen in either of the two groups. When the total exposure to blood products including autologous blood transfusions in each group was evaluated, AUCBT group had mean exposure of 2 units (one HBT in CPB prime fluid and one AUCBT in postoperative period) while the HBT group had mean exposure of 5 units (one PRBC in CPB prime fluid and one each of homologous PRBC, fresh frozen plasma (FFP), platelet concentrate, and cryoprecipitate in postoperative period.

Because of the presence of fetal Hb in the AUCB, with its leftward shifted Hb dissociation curve, there was a theoretical concern of lower oxygen delivery to tissues when the same was transfused in neonates in AUCBT group as compared to the HbA2 present in the homologous blood used in the other group, resulting in significant differences in postoperative values of PaO_2 and lactate

levels. However, on comparing PaO_2 and lactate values on postoperative day 1 after the blood products had been transfused, no statistically significant differences were found.

Discussion

Extreme hemodilution during neonatal cardiac surgeries leading to severe anemia is caused by an underbalanced ratio between circulating blood volume and volume of extracorporeal circuit of the heart–lung machine.[10] There is a requirement of large amount of homologous blood during neonatal cardiac surgeries. On the one hand, it prevents extreme hemodilution, but nevertheless it is associated with various immunological and nonimmunological complications leading to significant neonate morbidity and mortality.[1,2] Various blood management strategies such as miniaturized bypass systems, modified ultrafiltration, retrograde autologous priming, cell salvage, and autologous blood donation have been tried with the main aim of avoiding risks of HBT, especially in congenital cardiac surgeries.[11-14]

UCB, collected at the time of delivery for autologous transfusions in neonatal open-heart surgeries has proven to be an effective and safe practice.[15] Khodabux *et al*. in their study investigated the suitability of different storage media for collection and storage of UCB to be used later for autologous transfusion. They measured quality parameters at 7-day intervals during 35 days and compared it to the standard RBC product. Depending on the results, they concluded that UCB can be processed into autologous products for premature infants. However, the shelf-life is limited to 14–21 days and compared unfavorably to stored whole blood.[16] In our study, we have used the UCB as whole blood conserved by CPDA till 3 weeks after harvesting for autologous transfusions during neonatal cardiac surgeries.

Prenatal diagnosis of complex CHD is critical for timely collection of UCB for the future use. The same is helpful in proper planning of treatment strategies for the newborns with complex congenital heart defects. Delay in diagnosis and treatment can result in preoperative cerebral ischemia and injury.[17] and prenatal diagnosis of complex CHD reduces risks of profound hypoxemia.[18] With these prognostic principles in mind, Fedevych *et al*. described their first clinical experience of complete repair of complex CHD in the 1st h of life using AUCB. After analyzing the postoperative outcomes of the surgeries, they concluded that use of AUCB is very much feasible in neonatal open heart surgery.[15] In our experience, to have an effective and feasible treatment program, it not only requires a prenatal diagnosis of a cardiac defect by fetal echocardiography but also an equally important adequate logistic and psychological support from involved clinicians and the blood bank.

Use of AUCBT in the perioperative period reduces the overall exposure of the neonates to risk of transfusion reactions as has been brought out by our study. In the AUCBT group, the neonates were exposed to only one homologous donor when one PRBC was added for priming of the CPB circuit. AUCBT was used in the postoperative period. On the other hand, in the HBT group, the neonates were exposed to a minimum of five homologous donors. Besides adding homologous blood in the CPB circuit, neonates were transfused with PRBC, platelets, FFP, and cryoprecipitate derived from homologous donors in the postoperative period in this group. Hence, the risk for transfusion reactions also increased five-fold in this subset of neonates.

Chasovskyi *et al*. used AUCB for priming of the CPB circuit for neonates undergoing arteial switch operations in their study at Ukrainian Children's Cardiac Center, Keiv, Ukraine between September 2009 and February 2011. After comparing various variables such as hematocrit, lactate levels, postoperatively, they concluded AUCBT is a safe and an efficient alternative to homologous blood in neonatal open-heart surgery.[10] Although we have used the homologous blood for priming of CPB circuits in both the groups, AUCBT transfusion postoperatively effectively reduced the exposure of neonates to HBT adverse reactions. Postoperatively, blood products were transfused based on clinical judgments guided by platelet counts, Hb values, ABG values, and other hemodynamic parameters. No fixed point of care testing was employed, which can be seen as a limitation of the study.

Our study, despite having few participants in each group is the first on the topic in the Indian setup. It provides a preliminary report to assess safety and feasibility of the new blood management strategy in neonatal cardiac surgeries. The relatively small number of neonates in this study is a reflection of the requirement for close coordination and planning required between the obstetrician, fetal echocardiographer, pediatric cardiologist, transfusion medical specialist, cardiac surgeon, cardiac anesthesiologist, and perfusionist, who must work together to reduce exposure of the neonate to autologous donor blood. Our study lays the foundation for a larger multicenter randomized clinical trial which would give more valuable information about the potential safety and efficiency of AUCBT and evaluate the limitations and overall benefits of this novel new approach.

Conclusions

Use of AUCB for replacement of postoperative blood loss after neonatal cardiac surgery is feasible and reduces donor exposure to the neonate. Its use, however, requires a prenatal diagnosis of a cardiac defect by fetal echo and adequate logistic support from involved clinicians and the blood bank.

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Conflicts of interest

There are no conflicts of interest.

References

1. Society of Thoracic Surgeons Blood Conservation Guideline Task Force, Ferraris VA, Ferraris SP, Saha SP, Hessel EA 2nd, Haan CK, *et al.* Perioperative blood transfusion and blood conservation in cardiac surgery: The society of thoracic surgeons and the society of cardiovascular anesthesiologists clinical practice guideline. Ann Thorac Surg 2007;83:S27-86.
2. Spiess BD. Blood transfusion: The silent epidemic. Ann Thorac Surg 2001;72:S1832-7.
3. Silvergleid AJ. Safety and effectiveness of predeposit autologous transfusions in preteen and adolescent children. JAMA 1987;257:3403-4.
4. The use of autologous blood. The national blood resource education program expert panel. JAMA 1990;263:414-7.
5. Kemmotsu H, Joe K, Nakamura H, Yamashita M. Predeposited autologous blood transfusion for surgery in infants and children. J Pediatr Surg 1995;30:659-61.
6. Linderkamp O. Placental transfusion: Determinants and effects. Clin Perinatol 1982;9:559-92.
7. 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;159:790-1.
8. Khodabux CM, von Lindern JS, van Hilten JA, Scherjon S, Walther FJ, Brand A, *et al.* A clinical study on the feasibility of autologous cord blood transfusion for anemia of prematurity. Transfusion 2008;48:1634-43.
9. Jansen M, Brand A, von Lindern JS, Scherjon S, Walther FJ. Potential use of autologous umbilical cord blood red blood cells for early transfusion needs of premature infants. Transfusion 2006;46:1049-56.
10. Chasovskyi K, Fedevych O, Vorobiova G, Zhovnir V, Maksimenko A, Boychenko O, *et al.* Arterial switch operation in the first hours of life using autologous umbilical cord blood. Ann Thorac Surg 2012;93:1571-6.
11. Miyaji K, Kohira S, Miyamoto T, Nakashima K, Sato H, Ohara K, *et al.* Pediatric cardiac surgery without homologous blood transfusion, using a miniaturized bypass system in infants with lower body weight. J Thorac Cardiovasc Surg 2007;134:284-9.
12. van Son JA, Hovaguimian H, Rao IM, He GW, Meiling GA, King DH, *et al.* Strategies for repair of congenital heart defects in infants without the use of blood. Ann Thorac Surg 1995;59:384-8.
13. Ando M, Takahashi Y, Suzuki N. Open heart surgery for small children without homologous blood transfusion by using remote pump head system. Ann Thorac Surg 2004;78:1717-22.
14. Huebler M, Boettcher W, Koster A, Emeis M, Lange P, Hetzer R, *et al.* Transfusion-free complex cardiac surgery with cardiopulmonary bypass in a 3.55-kg Jehovah's witness neonate. Ann Thorac Surg 2005;80:1504-6.
15. Fedevych O, Chasovskyi K, Vorobiova G, Zhovnir V, Makarenko M, Kurkevych A, *et al.* Open cardiac surgery in the first hours of life using autologous umbilical cord blood. Eur J Cardiothorac Surg 2011;40:985-9.
16. Khodabux CM, van Beckhoven JM, Scharenberg JG, El Barjiji F, Slot MC, Brand A, *et al.* Processing cord blood from premature infants into autologous red-blood-cell products for transfusion. Vox Sang 2011;100:367-73.
17. Bartlett JM, Wypij D, Bellinger DC, Rappaport LA, Heffner LJ, Jonas RA, *et al.* Effect of prenatal diagnosis on outcomes in D-transposition of the great arteries. Pediatrics 2004;113:e335-40.
18. Kumar RK, Newburger JW, Gauvreau K, Kamenir SA, Hornberger LK. Comparison of outcome when hypoplastic left heart syndrome and transposition of the great arteries are diagnosed prenatally versus when diagnosis of these two conditions is made only postnatally. Am J Cardiol 1999;83:1649-53.