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Bloodless Repair for a 3.6 Kilogram Transposition of the Great Arteries with Jehovah's Witness Faith

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Abstract: Achieving pediatric cardiac surgery using cardiopulmonary bypass (CPB) without allogeneic blood transfusion is challenging. There are many clinical and economic factors that point to the importance of avoiding blood transfusions. In some instances, honoring patients or parents beliefs may be the reason for avoiding blood transfusions. For example, patients or parents of the Jehovah's Witness faith refuse blood transfusion based on their religious beliefs. Over the last decade, our institution has seen a steady increase in our pediatric Jehovah's Witness patient population. Caring for these patients have allowed us to develop specific protocols that enable us to safely provide bloodless CPB in all of our patient populations. The success of such an approach to minimize the need for blood transfusions should not start in the operating room; it must include the preoperative period and the postoperative care by the critical care team in the cardiac intensive care unit (CICU). A multidisciplinary team approach has to be in place with clear communication between the cardiologist, anesthesiologist, cardiac surgeon, perfusionist, and the cardiac intensivist. We present a case of a 7 day old male (3.6 kg) with a preoperative diagnosis of Transposition of the Great Arteries and intact ventricular septum who underwent an arterial switch procedure without the transfusion of any blood products throughout his entire hospital stay. **Keywords:** Jehovah's Witness, bloodless, pediatric cardiopulmonary bypass. *J Extra Corpor Technol. 2017;49:307–311*

There are multiple obstacles in performing congenital cardiac procedures using cardiopulmonary bypass (CPB) in neonates and infants without the need for transfusion of allogeneic blood products. There are factors that are specific to infants and neonates because of their immature coagulation cascade resulting in prolongation of coagulation screening tests such as prothrombin time, activated partial prothrombin time, and thrombin clotting time. Also present are low levels of vitamin K-dependent factors (II, VII, IX, and X), contact factors (XI and XII), factor V, factor VIII, and fibrinogen. Low levels of antithrombin III, heparin cofactor II, protein C and protein S, and tissue factor pathway inhibitor were also found (1,2). Another vital aspect is the volume of the CPB circuit in relation to the patient's total circulating blood volume (CBV). The CPB prime of an adult circuit often represents no more than 30% of their total CBV (3). However, in the neonatal and infant population, a significant CPB prime incongruity exists that can result in hemodilution of two to three times their normal CBV, often necessitating the transfusion of allogeneic packed red blood cells (RBCs) (3). In an attempt to reduce such impact, our perfusion team has decreased the prime volume of our circuits and thus decreased hemodilution (4). Techniques such as acute normovolemic hemodilution (ANH), retrograde autologous prime (RAP), venous autologous prime (VAP), and zero balance ultrafiltration (ZBUF) have greatly decreased the use of allogeneic RBC transfusions at our institution in these patients (4,5). Our multidisciplinary team has implemented these techniques which in turn has decreased the necessity of allogeneic blood transfusions during these cases. The team including the surgeons, anesthesia, perfusion, and the cardiothoracic intensive care unit (CTICU) intensivists work hand in hand to increase the chances of a bloodless procedure (6). In addition to employment of ANH, RAP, VAP, and ZBUF as mentioned previously, modified ultrafiltration (MUF) is used after CPB on all of our infant and neonatal cases. What follows is the case report of a 7-day-old male (3.6 kg, 53 cm, .23 m^2) whose parents are of the Jehovah's

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Witness (JW) faith with transposition of the great arteries and an intact ventricular septum.

DESCRIPTION

According to our institutional Jehovah's Witness (JW) protocol, preoperatively the patient received both erythropoietin® injections (Amgen, Inc., Thousand Oaks, CA) and ferrous sulfate supplements (Mead Johnson, Glenview, IL). EPO® (500 U/kg) was administered subcutaneously every other day for a total of two doses. Ferrous sulfate was given twice a day for a total of four doses. A Terumo FX05® oxygenator (Terumo Cardiovascular Systems Corporation, Ann Arbor, MI), 1/8 inch arterial line, 3/16 inch venous line, 3/16 inch arterial boot, and 3/16 inch suckers were used for the cardiopulmonary bypass (CPB) circuit. A slight modification to note from our typical neonatal circuit being that the rear facing roller head was changed out and replaced with a right angled roller head which faces the oxygenator allowing nearly 12 inches of our normal arterial boot to be removed. The reservoir was raised and placed at the patient level allowing removal of an additional 12 inches of arterial and 12 inches of venous tubing, thereby decreasing total prime volume by nearly 13 mL. In addition, a Minntech® Hemocor® HPH MINI hemofilter (Minntech, Minneapolis, MN) and a Sorin Cobe CSC-14 Custom 1:1 cardioplegia delivery system (Sorin Group USA Inc., Arvada, CO) were also used. A Maquet (Maquet, Hirrlingen, Germany) level sensor was placed at the manufacturer's suggested minimum operating level and a bubble detector (Maquet) was placed on the arterial line after oxygenator. The circuit was primed with Normosol-R™ (Hospira, Inc., Lake Forest, IL), 7 mEq sodium bicarbonate (Hospira, Inc.), 1,200 IU (1.2 mL) sodium heparin (Sagent Pharmaceuticals, Schaumburg, IL), 1,800 mg mannitol 25% (Hospira, Inc.), and 50 mL albumin 25% (CSL Behring AG, Bern, Switzerland). The total prime volume of the circuit, cardioplegia, and hemofilter constituents was 140 mL. During the consent process, the question of whether albumin usage is acceptable is asked of JW patient's and parents. In our experience most families accept the usage of albumin as it is acellular and therefore, not considered a foreign blood product. The parents of this patient did consent for its usage. Tranexamic acid 36 mg (Pfizer Inc., New York, NY) was also administered to the prime immediately after retrograde autologous prime (RAP)/venous autologous prime (VAP), just before the initiation of CPB. A three dose regimen of 10 mg/kg up to 1 g is our standard protocol. This patient received the first dose after the induction of anesthesia; a second dose was administered to the CPB pump by perfusion, and the final dose given following the administration of protamine after CPB. General anesthesia was induced and an arterial blood pressure monitoring line was placed. A preoperative blood gas analysis and activated clotting time (ACT) was performed (Table 1). Per protocol, JW patients do not receive preadmission blood analysis; therefore, this was used for baseline values. Our usual protocol employs the HMS Plus (Medtronic, Inc., Minneapolis, MN) for heparin management. To limit the amount of blood drawn from the patient for analysis, our protocol is to forego the heparin dose response cartridge and heparin concentration cartridges of the HMS Plus and opted to monitor only ACT values throughout the case. Therefore, an empirical dose of 400 u/kg was administered for the heparin load per protocol. The dilutional hematocrit on bypass was calculated to be >20%; therefore, per protocol 20 mL/kg of acute normovolemic hemodilution (ANH) was drawn in a continuous fluid filled loop with the patient (Figure 1) (4). A 60 mL syringe with 8 mL of anticoagulant citrate dextrose (ACD) was attached to the arterial blood pressure monitoring line. ANH blood was then drawn and pushed into a transfer bag that was also attached to the central venous line (CVL). After a subsequent 20 mL of ANH was taken in 3 mL ACD and transferred to the collection bag, it

Table 1. Blood analysis results.

	Hematocrit (%)	Hemoglobin (g/dL)	Sodium (mmol/L)	Potassium (mmol/L)	Calcium (mg/dL)	Glucose (mg/dL)	Lactate (mmol/L)	ACT (seconds)
Baseline 1321	44	15	140	3.8	1.27	113	1.24	142
S/p Heparin 1435	34	11.6	143	3.4	1.09	169	*	295
1st on CPB 1446	23	7.8	142	3.2	.97	165	2.88	>999
2nd on CPB 1614	20	6.8	137	3.9	1.04	348	2.70	>999
Last CPB 1740	19	6.5	134	4.9	1.26	373	4.30	>999
Off CPB 1809	21	7.1	140	3.7	1.02	252	5.19	237
CTICU	25	8.5	143	3.3	1.37	82	3.80	N/A
Discharge	21	7.1	136	2.7	.9	93	1.0	N/A

ACT, activated clotting time; CPB, cardiopulmonary bypass; CTICU, cardiothoracic intensive care unit.
*Lactate not ran to decrease blood volume used for analysis.

was removed from the arterial line after ensuring it was still securely connected to the CVL (4). A total of 72 mL of the patient's blood, anticoagulated with 12 mL ACD USP (Fenwal, Inc., Lake Zurich, IL), was collected in the transfer bag. Anesthesia maintained hemodynamic stability with the administration of phenylephrine and 25% albumin, based on the cerebral saturation, blood pressure, and electrocardiographic (EKG) changes (4). During this process, the anesthetist administered phenylephrine 30 μg (PharMEDium, LLC, Memphis, TN) and 40 mL of 25% albumin to maintain hemodynamic stability. Per protocol, a decrease in MAP or cerebral saturation ≥20% of the patient's baseline is considered significant and ANH is ceased. During the collection, cerebral saturations of ANH

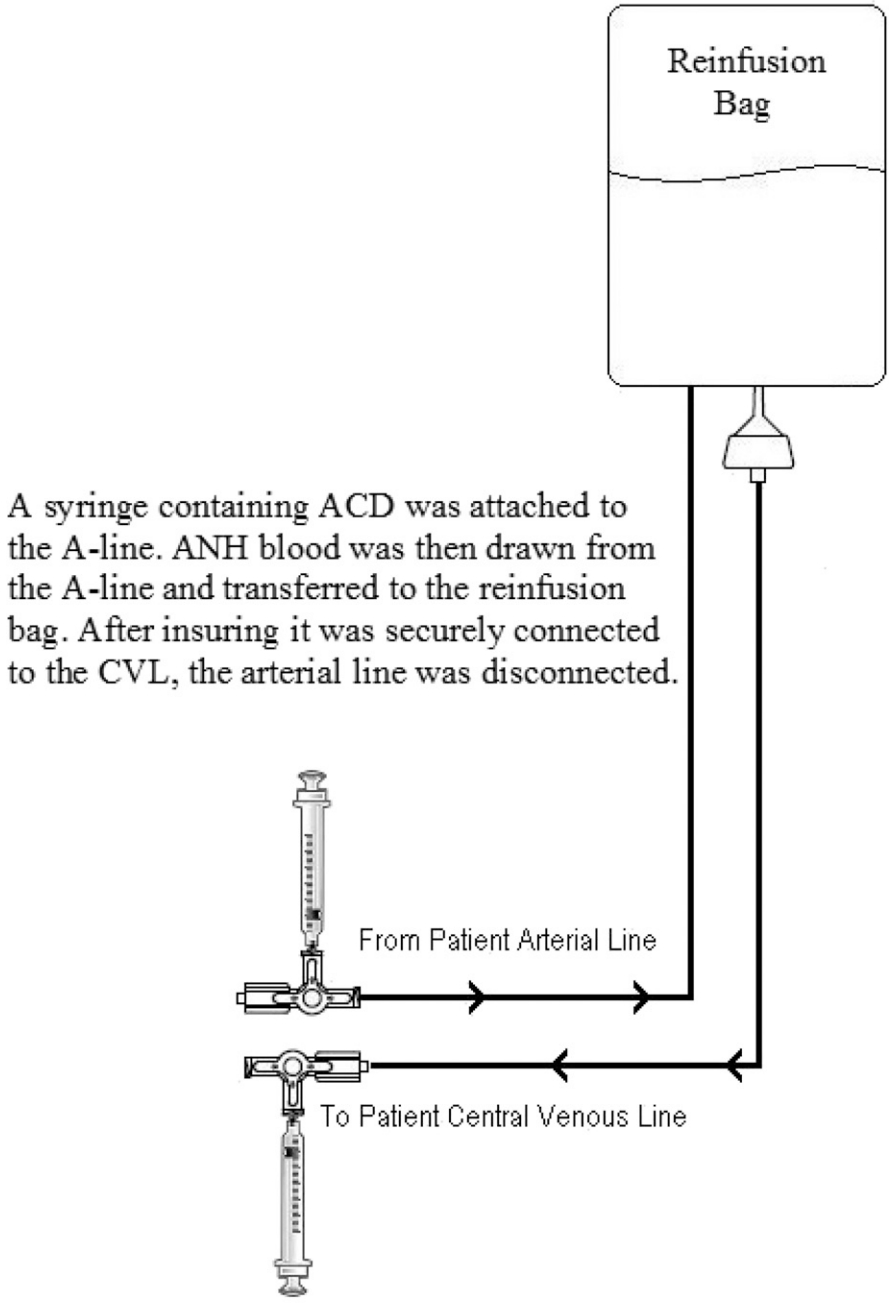

Figure 1. Acute normovolemic hemodilution (ANH) set up for Jehovah's Witness patients.

ACD: Anticoagulant citrate dextrose; A-line: arterial line; ANH: acute normovolemic hemodilution; CVL: central venous line.

ranged 78–82%, MAP 38–44 mmHg, and no EKG changes were noted. A medium sternotomy was performed, and a loading dose of 1,500 IU of heparin was administered by the surgeon directly into the right atrium. An 8 Fr DLP Medtronic arterial cannula (Medtronic, Inc.) was placed in the ascending aorta. RAP was initiated through the arterial cannula while the surgeon placed a 16 Fr Medtronic venous cannula (Medtronic, Inc.) in the right atrium. After the completion of RAP/VAP, tranexamic acid was added to the reservoir and bypass was initiated per surgeons' request. The anesthetist administered phenylephrine 130 μg during RAP and VAP to maintain acceptable MAP. CPB was initiated without the use of vacuum-assisted drainage to a full cardiac index flow of 2.2 L/min/m^2. Per surgeons' request, the patient was actively cooled to a core temperature of 24°C. Initial on bypass blood analysis was drawn. Cross-clamp was applied and the first dose of antegrade cardioplegia into the ascending aorta was administered using the Sorin CSC-14 Custom 1:1 delivery system (Sorin Group USA, Inc.) (Medtronic, Inc.) for a total of 15 mL/kg. Subsequent doses were given directly into the right and left coronary ostia using a 2 mm arteriotomy cannula (Medtronic, Inc.). Doses were repeated approximately every 30 minutes while the cross-clamp was applied. A final dose of cardioplegia was administered to the neoarota via the 2 mm arteriotomy cannula. ZBUF was initiated immediately after the administration of the first dose of cardioplegia and maintained throughout the case. Normosol-R™ was used as our zero balance ultrafiltration (ZBUF) solution and was buffered with 20 mEq/L sodium bicarbonate and 200 mg/L calcium chloride to prevent hypocalcemia. Blood gas analyses and ACTs were monitored approximately every 60 minutes. After 131 minutes, the aortic cross-clamp was removed and 1,800 mg mannitol 25% and 180 mg of magnesium sulfate were administered into the CPB pump. The patient was warmed to a core temperature of 37°C, blood analysis was drawn and out-of-range results were addressed (Table 1). Modified ultrafiltration (MUF) was initiated immediately after the cessation of CBP. The venous cannula was removed and the volume drained into the venous reservoir. MUF was discontinued after 10 minutes resulting in 100 mL of effluent removal. After MUF, 20 mg of protamine sulfate (APP Pharmaceuticals, LLC, Schaumburg, IL) was administered per anesthetist over 5 minutes via peripheral intravenous line to decrease adverse reactions. ANH was then readministered to the patient via the CVL through a filtered blood administration kit per American Association of Blood Banks Standards for Perioperative Autologous Blood Collection and Administration (Standard 5.4.5.1) (7). Immediately after ANH, Recombinant Factor VIIa (NovoSeven; Novo Nordisk Inc., Plainsboro, NJ) was administered per our institutional JW protocol for hemostasis. Table and sucker lines were flushed with Normosol-R™ and the remainder of the CPB circuit was then transferred to the Fresenius Continuous Auto Transfusion System (Terumo Cardiovascular Systems Corporation). CPB volume was then processed and 70 mL of cell saver blood was returned to the patient via pre-connected CVL line. Normosol-R™ is used for cell saver processing to decrease the amount of acid base, electrolyte, and hematologic changes that occur when using normal saline (8). After hemostasis was achieved, the patient was transferred to the CTICU intubated. Lowest hematocrit on CPB was noted immediately before the cessation of CPB and was 19% with a corresponding lactate value of 4.30 mmol/L (Table 1). The patient was extubated approximately 20 hours after operation and placed on a nasal cannula at 2 L/min. The anterior midline chest tube was removed on postoperative day (POD) 2 after a total of 114 mL of drainage from the time of placement in the OR. The patient continued to show improvement and was discharged to the cardiac stepdown unit on POD 3. He was discharged home on POD 7 without transfusion of allogeneic blood products.

DISCUSSION

The balance between honoring the wishes of the parents and patients of JW faith and the risks of allogeneic blood transfusions can be a daunting task to a cardiac surgical team. The purpose of this case study is to present a safe and reproducible process to facilitate a cardiac surgical procedure using CPB without the need for allogeneic blood transfusions. Ultimately the multidisciplinary team must maintain end organ perfusion as noted by NIRS, urine output, and lactate. Therefore, we do recognize that there is a need for allogeneic blood products in certain situations, but the multidisciplinary team must determine this need based on the patient's condition, not a preconceived transfusion parameter (6). It also has been shown that complications from blood transfusions include higher mortality rates and longer ventilator times after operation and increased lengths of stay in the intensive care unit (9,10). These factors have driven our multidisciplinary team to identify and modify areas that will result in a higher probability of achieving this goal. These areas have included using patient-specific CPB circuits, performing ANH per patient's preoperative parameters and administration of tranexamic acid to promote after CPB hemostasis. Using patient-specific CPB circuits has helped to greatly decrease prime volumes and hemodilution (Table 2). Minimizing the circuit prime volume during complex congenital defects reduces the need for blood transfusion without jeopardizing tissue oxygenation or patient safety (11). Using ZBUF throughout the case enables removal of tumor necrosis factor, interleukin, myeloperoxidase, C3a, and a significant postoperative blood loss, time to extubation, and postoperative alveolar–arterial

Table 2. Patient-specific circuit sizes and volumes.

	Blood Flow (mL/min)	Arterial Line (inches)	Venous Line (inches)	Raceway (inches)	Hemofilter	Cardioplegia 1:1 Ratio	Prime Volume (mL)
≤6 kg	≤.7	1/8	3/16	3/16	Minntech HPH Jr	Sorin CSC-14	176
≤15 kg	≤1.5	3/16	1/4	1/4	Minntech HPH Jr	Sorin CSC-14	230
15–32 kg	1.5–2.5	1/4	5/16	3/8	Sorin DHF0.2	Sorin CSC-14	450
≤45 kg	2.5–3.0	1/4	3/8	3/8	Sorin DHF0.2	Sorin CSC-14	487
≤90 kg	3–4.5	3/8	3/8	1/2	Terumo CX*HC05S	Sorin CSC-14	642
≥91 kg	>4.5	3/8	1/2	1/2	Terumo CX*HC05S	Sorin CSC-14	825

oxygen gradients (12). In addition, ZBUF allows removal of excessive crystalloid administration because of multiple 1:1 cardioplegia dosing. ANH allows us to sequester fresh whole blood before CPB with the benefit of increased hemostasis after re-administration post CPB. A protocol was established to determine the appropriate ANH volume, taking into account the patient's preoperative blood analysis and parameters. Our current protocol is to draw approximately 10–20 mL/kg for patients' ≤5 kg and 10–20% of CBV for patients' ≥6 kg with the goal of a hemodilutional hematocrit ≥20% on CPB. During ANH, a decrease in MAP or cerebral saturation ≥20% of the patient's baseline is considered significant and this procedure is ceased immediately if observed. Finally, the three dose regimen of tranexamic acid provides additional post CPB hemostasis. These improved techniques have benefitted all of our patient populations as we are able to perform more and more complex bloodless pediatric CPB cases on smaller and smaller patients. However, even with implementing these techniques, often the success of accomplishing a bloodless procedure comes down to the patient's preoperative preparation. This patient's congenital defect necessitated that a surgical procedure be performed within the first week of life. Although erythropoietin and ferrous sulfate were administered, full benefit from these therapies takes several weeks to achieve their effect. Patients that are able to receive a full course of erythropoietin and ferrous sulfate will present to the operating room with much higher hematocrits (>50%). Erythropoietin and ferrous sulfate can result in decreasing allogeneic blood transfusions, a shorter hospital stay, and an increase in patient survival (13). Only two full doses of each were given preoperatively and the hematocrit actually decreased from 49% on admission to 43% on the day of the procedure (Table 1).

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