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REVIEW

Perfusionist strategies for blood conservation in pediatric cardiac surgery

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Abstract

There is increasing concern about the safety of homologous blood transfusion during cardiac surgery, and a restrictive transfusion practice is associated with improved outcome. Transfusion-free pediatric cardiac surgery is unrealistic for the vast majority of procedures in neonates or small infants; however, considerable progress has been made by using techniques that decrease the need for homologous blood products or even allow bloodless surgery in older infants and children. These techniques involve a decrease in prime volume by downsizing the bypass circuit with the help of vacuum-assisted venous drainage, microplegia, autologous blood predonation with or without infusion of recombinant (erythropoietin), cell salvaging, ultrafiltration and retrograde autologous priming. The three major techniques which are simple, safe, efficient, and cost-effective are: a prime volume as small as possible, cardioplegia with negligible hydric balance and circuit residual blood salvaged without any alteration. Furthermore, these three techniques can be used for all the patients, including emergencies and small babies. In every pediatric surgical unit, a strategy to decrease or avoid blood bank transfusion must be implemented. A strategy to minimize transfusion requirement requires a combined effort involving the entire surgical team with pre-, peri-, and postoperative planning and management.

Key words: Autologous blood predonation; Blood conservation; Cardiopulmonary bypass; Cell-salvage; Microplegia; Pediatric open-heart surgery; Prime volume reduction; Retrograde autologous priming; Ultrafiltration; Vacuum-assisted venous drainage

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INTRODUCTION

Blood transfusion is life-saving therapy but there is increasing concern regarding the drawbacks of homologous blood perfusion during pediatric heart surgery. Several studies suggested that a restrictive transfusion practice improved outcome by decreasing morbidity and mortality. Viral transmission is a historical risk, but stored blood bank transfusion generates inflammation, increases the risk of organ dysfunction and affects pulmonary and right ventricular function[1,2]. Immunomodulation with down-regulation of cellular immune function increases the risk of nosocomial infections[3,4]. Furthermore, transfusion of older blood raises the incidence of serious complications and increases time to ventilation[5-7]. Transfusion related acute lung injury, an uncommon but probably underestimated complication, is one of the leading causes of transfusion-related mor-

bidity and mortality[8,9]. Its incidence is estimated to be 1 out of 5000 units of packed red blood cells, 1 out of 2000 plasma-containing components and 1 out of 400 units of platelet concentrates[10]. Its immunological origin *via* an antibody-mediated reaction is strongly suspected. Graft *vs* host disease is a very rare but usually fatal complication that also demonstrates the conjunction of immunity and blood transfusion[11,12]. All these negative side effects of homologous blood transfusion are currently more obvious because of the dramatic decrease in postoperative mortality and morbidity. A reevaluation of our transfusion practice is needed to examine the risk/benefit ratio of blood transfusion during modern pediatric open-heart surgery.

There are several approaches to blood conservation among which reduction of prime volume *via* miniaturization of the bypass circuit and microplegia are the major factors[13-17].

Ultimately, blood conservation is a perfect example of team work; everyone must be motivated to optimize reduction in blood use[18].

The goal of this review is to analyze the different approaches to blood conservation and to describe their clinical advantages with regard to patient outcome.

BLOOD CONSERVATION STRATEGIES

Reduction in prime volume using a reduced bypass circuit

Reduction in prime volume is a major factor in blood conservation. If we assume a blood volume of about 80 mL/kg for neonates, the blood volume of a 3 kg baby is 240 mL. For this category of patients the prime volume is often equivalent or even higher than their blood volume. Therefore asanguineous priming is unrealistic except for rare cases with a high hematocrit level prior to surgery[18]. However, it is possible to downsize the bypass circuit and thus decrease the prime volume. The two smallest membrane oxygenators dedicated to neonatal perfusion are the Kids D 100 (Sorin-Group, Mirandola, Italy), the prime volume of which is 31 mL, and the Baby FX (Terumo, Tokyo, Japan) with a built-in arterial filter and a prime volume of 43 mL. In our experience, the maximal blood flow with the Kids D 100 is 1 L/min, and the maximal blood flow with the Baby FX is 1.5 L/min. Downsizing of the circuit not only includes a decrease in the length and internal diameter of the arterial, venous, and suction lines but also elimination of any non-essential components. A prime volume of 172 mL is obtained with a bypass circuit composed of a 1/8 inch arterial line and a 3/16 inch venous line, which are connected to either a Baby RX-5 Terumo oxygenator or to a Lilliput 1 Sorin oxygenator. This circuit, without an arterial filter, is used for patients up to 5.1 kg[15]. A bypass circuit with 3/16 inch tubing connected to a Kids D 100 oxygenator and a Sorin arterial filter D 130 allows reduction of the prime volume to 110 mL and its use is described for patients up to 4.1 kg[19]. An original circuit is composed of a distant roller pump and remote control unit (Tonokura Compo III; Tonokura Medical Inc., Tokyo, Japan). The roller pump is very near the patient so that the lengths of the venous and arterial lines are minimal. Tubing internal diameter is 3/16 inch for the pump boot and 5/32 inch for the lines. The prime volume of this circuit that includes an arterial filter is 140 mL[16]. With the same pump another circuit is composed of a Safe-micro oxygenator (Polystan, Vaerlose, Denmark) connected to 5/32 inch internal diameter tubing. This circuit has no arterial filter but includes a hemofilter. The minimal prime volume is 130 mL[20].

Our group currently uses a bypass circuit with a prime volume of 100 mL including priming of the microplegia circuit. The membrane oxygenator is a Kids D 100 from Sorin-Group; the arterial and venous lines have an internal diameter of 4 mm, and there is no arterial filter or hemofilter. This circuit is, at the present time, used for blood flow up to 0.6 L/min but the maximal flow is still to be determined.

It is interesting to note the following observations: (1) the internal diameter of the arterial line may be decreased to 1/8 inch for patient weight up to 5 kg, or to 5/32 inch (which is about 4 mm) for patients up to 7 kg; (2) the arterial filter, usually known as a safety device, is no longer considered essential; and (3) the hemofilter is not a constant component of the bypass circuit (filling of the filter and its connective tubing increased prime volume, and thus hemodilution).

Another positive side effect of the miniaturized circuit is reduced blood contact with the surface of the cardiopulmonary bypass circuit; this contact is thought to activate the systemic inflammatory response.

Vacuum-assisted venous return

Vacuum-assisted venous return is helpful to further decrease prime volume. Such assisted venous drainage allows us to decrease declivity of the membrane oxygenator, and thus, to significantly decrease the length of the venous, arterial and suction lines. This technique was first developed in adult surgery and was considered a powerful system to decrease hemodilution during cardiopulmonary bypass[21]. Furthermore, vacuum-optimized venous return flow, and full support blood flow rates can be achieved through cannulae that demonstrate limited flow capacity under siphon drainage conditions. We currently use vacuum-assisted venous drainage, and we have lifted the oxygenator, so that the top of the cardiotomy reservoir is at the level of the patient's right atrium[22]. In this position gravity-siphon venous drainage is limited and, thus, insufficient to perform full-flow bypass. In cases of technical failure in the wall vacuum source, it is essential to find another way of generating negative pressure in the cardiotomy reservoir. A negative pressure, with values equivalent to those obtained by the use of vacuum wall source, can be achieved through a roller pump sucking air out of a closed cardiotomy reservoir[23].

An increase in gaseous microemboli is a complica-

tion related to vacuum-assisted venous drainage. However, this drawback is avoidable by adhering to specifc parameters[24,25]. If the maximal value of the vacuum remains under -40 mmHg, the level of embolic activity is equivalent to that seen during gravity-siphon venous drainage[26]. When using vacuum-assisted venous drainage, a pressure relief valve is an essential component of the circuit. This valve is built-in in the Kids D 100 oxygenator but must be added with the Baby FX membrane. The valve opens whenever the cardiotomy reservoir pressure increases above 5 mmHg or decreases below -80 mmHg. Before the use of this safety device, overpressurization of the cardiotomy reservoir was possible, with reverse flow in the venous line and left sided gas embolism through an atrial septal defect[27]. Continuous monitoring of the negative pressure in the cardiotomy reservoir is simple and important to increase the safety of the technique.

The hypothesis of an increase in hemolysis during use of the vacuum was ruled out by several investigators[28,29]. Vacuum-assisted venous return is a technique, without any obvious drawbacks, that is used by several pediatric centers with consistent ability to reduce homologous blood transfusion[19, 30-32].

Microplegia or miniplegia

The original composition of blood cardioplegia described by Buckberg was a mixture of 4 parts blood added to 1 part crystalloid; this has become the standard for cold blood cardioplegia[33]. Alteration of this composition was proposed by several authors when warm, or at least tepid, and blood cardioplegia was adopted[34,35] because the only rationale for dilution was to decrease high blood viscosity associated with hypothermia. Furthermore, at that time cardioplegia was retrograde and performed continuously through the coronary sinus. The risk of fluid overload and of clotting factor dilution was real with standard blood cardioplegia. Microplegia was then also used for intermittent warm blood cardioplegia[36-38]. The technique for continuous or discontinuous microplegia injection is identical. Blood is diverted from the arterial line or from a specific built-in port of the oxygenator through an occlusive roller pump. Downstream of the roller pump, the arresting agent is added *via* a syringe pump. In our experience, the result is a mixture of 60 parts of oxygenated blood to one part of crystalloid cardioplegia solution[39]. With this mixing ratio of 60, the rotor speed of the occlusive pump driving blood in mL per min is equivalent to the speed of the electrical syringe adding arresting agent in mL per hour.

The theoretical advantages of non-diluted cardioplegia are as follows: (1) a higher myocardial oxygen supply because of a higher hemoglobin level and a rightward shift of the oxyhemoglobin dissociation curve; (2) a negligible fluid balance of the cardioplegia (the volume of blood diverted from the circuit is sucked from the coronary sinus to the cardiotomy reservoir so that the balance is limited to a few milliliters of crystalloid-arresting agent); (3) a decreased tendency for tissue edema with non-diluted *vs* diluted cardioplegia demonstrated in experimental data[40]; and (4) cost-effectiveness when compared to the standard cardioplegia technique.

In clinical studies there are either similar results for microplegia and standard blood cardioplegia with regards to in-hospital morbidity and mortality, or better results for microplegia *vs* standard cardioplegia with regard to myocardial protection[36-38]. However, in all these studies the benefit to hydric balance of microplegia *vs* standard cardioplegia is observed. When using standard cardioplegia with a blood to crystalloid ratio of 4/1, cardioplegia is sucked into the cardiotomy reservoir, dilution of the circulating blood increases during each cardioplegia injection. The dilution is significant during complex procedures that require prolonged cross-clamp times. When standard cardioplegia is wasted, blood is also wasted; and crystalloid or colloid must be added to restore the level in the cardiotomy reservoir.

Autologous blood predonation

Preoperative blood donation in pediatric cardiac surgery is not common practice except in some countries such as Japan for children between 3 and 10 years old and with a minimum weight of 12 to 13 kg[41-44]. The technique is said to be safe and efficient in decreasing homologous blood transfusion. A study was performed in 37 patients ranging from 3 to 9 years old and weighing from 13 to 20 kg; multiple donations were performed over a 2 mo period. The result was a blood storage volume of 48 ± 17 mL/kg such that no homologous blood transfusion were used in the preoperative donation group *vs* 80% in the control group[44]. More recently, 23 children with simple cardiopathies were included in a preoperative blood donation program and compared to a control group of 27 age- and weight-matched children. Their age varied from 6 mo to 5 years, and their body weight ranged from 6.1 to 14 kg. In the donation group, two donations of 10 mL/kg were performed *via* the femoral vein under mild general anesthesia about 3 wk and 2 wk before surgery. The two groups had similar hemoglobin levels before, during and after surgery, however, the incidence of homologous blood transfusion was 44.4% in the control group compared with 4.3% in the donation group[45]. One important factor is the preoperative level of hemoglobin as there is a risk of proceeding to surgery with a lower hemoglobin level. To overcome this risk, concomitant treatment with erythropoietin has been proposed. The best results were obtained when a higher dosage of erythropoietin (300 units/kg) was injected 1 wk before the first donation and 300 units/kg at each of the two subsequent donations. With this protocol the decrease in hematocrit was minimal, from 39.0% ±0.6% before donation to 37.5% ± 0.5% before surgery[46]. Another study was performed on 39 patients with well-tolerated simple cardiopathies (atrial or ventricular septal defect), pretreatment hemoglobin levels of between 10 to 14 g/dL. The group treated

with erythropoietin received 100 units/kg three times a week for 3 wk and 100 units/kg the day of surgery to a total dose of 1000 units/kg. Despite a moderate decrease in hemoglobin during the autologous blood donation period in the treated group, there were less blood bank transfusions from 61.5% in the control group to 7.7% in the treated group[47]. To avoid the delay necessary for preoperative blood donation and the constraints of the technique, a single subcutaneous dose of erythropoietin given one has been studied. However, this therapeutic approach failed to exhibit any significant reduction in homologous blood transfusion[48]. There are many limitations to preoperative autologous blood donation. The technique is not suitable for neonatal surgery or emergencies. A weight less than 5 kg, complex cardiopathies and low hemoglobin levels are contraindications. Furthermore, the technique is inconvenient for children and families. It is also time consuming for medical staff and expensive for hospitals, especially erythropoietin is used. The benefits of preoperative autologous blood donation are real but further work is needed: (1) to compare donation to other ways of decreasing homologous blood transfusion and (2) to find the correct indication for preoperative blood donation and/or preoperative erythropoietin therapy.

Cell-salvage techniques

Cell salvage techniques scavenge blood loss. There are two main techniques of cell-salvage: the blood is either collected and reinjected without any treatment (non-wash technique), or the blood is treated and anticoagulated, washed and centrifuged in a cell-saver machine to obtain a concentrate of red blood cells. The washing technique is said to remove debris from shed blood thus reducing the risk of cerebral thromboembolism and improving neurological outcome. Washing also removes platelets, coagulation factors and other plasma proteins leading to coagulopathy, and an increased risk of organ failure and of systemic inflammatory response[49-53]. However, the safety of the cell salvage technique has been shown in multiple studies[54-56]. The benefits of cell salvage in reducing allogeneic blood transfusion is controversial. A meta-analysis failed to find any significant benefit from cell salvage in cardiac surgery[57], while other studies demonstrated a significant reduction in blood transfusion with washed salvaged blood[55-58]. One of the major limitations of washing blood in pediatric surgery is that it is time-consuming during which the blood is unavailable to the patient. Recent progress has been made with the introduction of a small-volume centrifugal bowl dedicated to pediatric patients. The HaemoLite 2 plus device with a 100 mL centrifugal bowl (Haemonetics, Bothwell, UK) was tested in a pediatric center on a group of 59 patients and compared to a control group of 63 patients. All the patients had undergone first-time cardiac surgery. The control group had cell-salvage limited to residual volume of the circuit while the studied group also underwent intraoperative cell salvage. Transfusion of allogeneic red blood cells in the ICU was used in 59% of patients in the control group and only 27% of patients in the studied group. However, for 83% of the children with a body weight less than 10 kg, blood collected during surgery was not sufficient to fill the 100 mL bowl. Consequently, salvage blood was not treated with the cell-saver device and not available for transfusion. The difference in cell saving volume product was only 31 mL, from 152 ± 57 mL in the control group to 183 ± 56 mL in the studied group. Furthermore, the cost of shed blood collection was higher than the savings from reductions in the number of banked blood transfusions[59].

Obviously, the results of the cell-saver technique are widely influenced by surgical hemostasis by the motivation for blood preservation. Another component influencing the results of cell salvage is the use of residual volume in the circuit after coming off cardiopulmonary bypass. Some centers add this residual blood to the cell-saver for washing while transfuse it directly into the patient. We advocate collection of residual blood from the circuit without any further treatment. The quality of this blood is exactly the same as the quality of the patient' s blood at the time of discontinuation of cardiopulmonary bypass. We pool the residual blood with the remaining blood bank products, if any, in a bag. This blood is used during the post-bypass period when necessary. This blood contains coagulation factors that are otherwise removed during cell-saver treatment. It also contains heparin which can be removed by adding additional protamine as needed. This policy has proven to be safe, efficient, simple and less expensive than cell salvage[13].

Ultrafiltration

Reductions in blood transfusion is described following ultrafiltration. However, it is unclear whether this benefit is due to the volume of fluid removed from the circulating bypass blood *vs* the modified ultrafiltration[60-63]. There are conflicting results about the different ultrafiltration techniques, because in neonatal surgery, removal of fluid from a miniaturized circuit during cardiopulmonary bypass, corresponding to conventional ultrafiltration, is difficult and inconsistent when fluid replacement is needed to maintain adequate reservoir level[64]. Modified ultrafiltration is performed after discontinuation of cardiopulmonary bypass to reduce hemodilution and decrease tissue edema. In most studies, modified ultrafiltration has improved dilutional coagulopathy and reduced blood transfusion requirements[65]. However, the technique also has drawbacks, and 82% of the centers using modified ultrafiltration experienced complications related to the technique[66]. Modified ultrafiltration may be obsolete as there are strategies to avoid or at least minimize hemodilution[15]. In several centers where miniaturized bypass circuits have been implemented, ultrafiltration is no longer used[13-15,18,19].

Maneuver of retrograde autologous priming

Retrograde autologous priming consists of total or partial

replacement of the crystalloid prime by using the patient's blood being drained from the arterial and venous lines. During this drainage, the bloodless prime is redirected to a separate reservoir. This is a well established way to decrease autologous blood transfusion in adult cardiac surgery[67,68]. This strategy is very uncommon in pediatric cardiac surgery, but it could be part of a bloodless surgical program[69]. The technique is dependent on the size of the patient and the individual hemodynamic tolerance of blood withdrawal.

CONCLUSION

There are several ways to decrease the number of blood bank transfusions or even perform donor blood-free pediatric cardiac surgery. The effects of the different techniques are not always cumulative. The major techniques are as follows: (1) downsizing of the bypass circuit which decreases dilution and dilutional coagulopathy; (2) vacuum-assisted venous drainage when its use is associated with further reduction of the bypass circuit prime; (3) microplegia; and (4) cell salvage of the residual blood from the circuit without treatment. These four techniques are simple, inexpensive, safe and efficient in all patients regardless of age or weight. The other techniques (autologous blood predonation, cell-salvage, ultrafiltration, retrograde autologous priming) could be used in combination with the major techniques, with some benefit, in selective cases.

However, the success of any program of blood conservation is not only linked to the perfusionist's experience but also depends on the motivation of all the actors involved in the patient's care before, during and after surgery.

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