Editorial

Cardiopulmonary bypass - Are pediatric patients safer now?

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Undoubtedly, the answer is an emphatic yes. In May, 1953, Dr. John H. Gibbon, Jr. reported the first successful use of cardiopulmonary bypass (CPB) using the Gibbon-IBM heart-lung machine at Jefferson Hospital, Philadelphia, Pennsylvania, USA, when he operated on an 18-year-old woman with an atrial septal defect.[1] Since then the practice of extracorporeal circulation and the extracorporeal circuit (ECC) itself has undergone many changes.

The past years have witnessed extraordinary growth in the understanding of pathophysiology of adverse effects, complications associated with CPB and means to overcome or attenuate them. The technological advances in ECC have also contributed to enhanced safety of CPB in pediatric patients. The oxygenators underwent a sea change; from reusable discs to disposable hard shell bubble oxygenators with integrated heat exchangers and, since 1967, the integrated membrane oxygenators.[2] The pumps also underwent developmental changes from roller pumps during the inception to centrifugal pumps and now the third generation pumps. The membrane oxygenator together with roller pump and/or centrifugal pump is considered a standard of care now. The practice of hypothermia has been integral to CPB since its inception. Cardioplegia was introduced later to enhance the prevailing myocardial protective techniques provided by topical and whole body hypothermia. Regular use of the membrane oxygenator, cardioplegic myocardial protection, hypothermia, nonhemic prime, minimizing prime volume, arterial line filter, hemofiltration, among others, improved the outcome.

Online monitoring of hematocrit, arterial and venous oxygen saturation, arterial and cardioplegia line pressure, and venous reservoir level allow immediate application of corrective measures such as adjustments of O_2 and CPB flow and addition of blood or fluid to perfusate to adjust hematocrit and/or perfusate level in the venous reservoir; the measures increase the safety of CPB. Additionally, placement of air bubble detector on the arterial line automatically alarm and shut off the systemic roller pump if a a bolus of air inadvertently enters the arterial line proximal to the sensor.

In the 1950s, the technological challenge was to create a practical and safe device which could oxygenate the blood and remove the carbon dioxide. The technological challenges of the past have been overcome and presently the mortality associated with repair of congenital heart defects in bigger children has fallen dramatically, and in many conditions approaches zero.[3] Today, in newborns and infants adverse neurologic outcome after CPB is the major issue. The post-CPB neurologic injury is estimated to range from 2 to 30%.[4,5] Keeping in mind the lifetime burden of neurologic injury, measures that prevent neurologic disability are socially and individually worthwhile.[6]

A combination of factors including - the patient, disparity between CPB circuit size and the patient, extreme hemodilution, necessity of adding blood and blood products to the prime, use of deep hypothermic circulatory arrest (DHCA) and/or low flows

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during bypass for enhancing accuracy of surgical correction. The overwhelming inflammatory response to extreme physiological stress makes neonates and infants susceptible to short and long term adverse outcomes. Pre existing neurologic disability is common among patients presenting with congenital heart diseases. Magnetic resonance imaging (MRI)-detected abnormalities are present preoperatively in 33% of cardiac neonates and postoperatively in as many as 93%[7] Early in life, the brain undergoes an intensive period of neuronal development and axonal growth. A number of predispositions such as, fragile vasculature, high metabolic activity, and immature cerebral autoregulation render the immature brain particularly susceptible to increased permeability, edema formation and ischemia-reperfusion injury. MRI-detected periventricular leukomalacia, the necrosis of the deep white matter adjacent to the lateral ventricles owing to injury to immature oligodendroglial cells, occurs in greater than 50% of neonates after cardiac surgery.[8] Clearly, the immature brain of neonates and infants, is susceptible to injury, and poorly placed to tolerate inflammatory responses of CPB. The immaturity of various organs such as lungs and kidney can indirectly further aggravate neuronal injury. The relative pulmonary immaturity predisposes neonates to the development of pulmonary edema, pulmonary hypertension and inefficient ventilation and oxygenation. The renal autoregulatory functions are also reduced in neonates than adults. This leads to limited sodium reabsorption, and excretion, concentration and dilution mechanisms, and decreased ability to regulate acid–base homeostasis.[9] Clearly the neonates and infants have limited ability to deal with increased body water that invariably occurs during conventional hemodilutional CPB. Evidently, to improve results, in addition to surgical innovations, the mechanizms of "CPB-related inflammatory responses, tissue edema, and multiple organ dysfunctions" need to be thoroughly understood and suitably modified.

Apparently, two mechanisms are at the core of causation of capillary leak. The first, physical changes produced by the effects of hemodilution. Secondly the changes due to hypothermia and systemic inflammatory response due to CPB.[10] These mechanisms lead to two different CPB management strategies:[1] moderate hypothermia and crystalloid-based hemodilution (hematocrit ~20%) at full or reduced flow[11] with selective use of DHCA or low flow in selected cases; the strategy aims to avoid or minimize addition of blood and blood products to prime.[2] higher-hematocrit (greater than or equal to 30%) and maintained colloid oncotic pressure with moderate hypothermia or warm CPB; the aim of maintaining higher hematocrit levels and colloid oncotic pressure is to maintain the physical characteristics of prime close to normal by adding blood and colloids or fresh frozen plasma to the prime. The two CPB techniques have important surgical and CPB management implications. A relatively high hematocrit implies need for donor blood, higher flow during CPB, an aggressive approach to cannulate systemic veins to allow exposure of the inside of the heart,[10] and to augment venous return by kinetic assist devices. The lowest temperature at which higher hematocrit can be tolerated is not clear precluding widespread use of this technique.

An experimental study using crystalloid-based hemodilution technique reported inadequate oxygen delivery during cooling and low flow bypass or DHCA.[12] There is disagreement about the precise relationship between duration of DHCA and cognitive performance, but generally, more than 40 to 45 minutes of DHCA increases the risk of late cognitive impairment.[13] Some interventions which may limit brain injury from DHCA include a low gradient during cooling (a minimum 20 minutes of cooling to ensure adequate cerebral protection), pH stat - blood gas management during cooling, hyperoxygenation before DHCA, packing the head in ice, limiting DHCA, intermittent cerebral perfusion between 15-20-minute periods of DHCA, controlled re warming, and optimizing hematocrit by using hemofiltration during re warming and after CPB.[14,15] The episodes of low cardiac output should be prevented by good correction of the cardiac defects, appropriate inotropic support, and delayed sternal closure if necessary.[10] When hemodilution is used during CPB, hemofiltration during and after CPB [Conventional ultrafiltration (CUF) or modified ultrafiltration (MUF)] may be required with an aim to achieve hematocrit values of 40-45% at the end of CPB. Users of both the techniques claim excellent results.[3] However, there is considerable controversy over the most appropriate strategy. Recently, the Boston group demonstrated improved outcome in pediatric patients undergoing open heart surgery (OHS) with higher hematocrit during CPB.[16] In our experience, at least on two occasions, low hematocrit (~20%) on CPB was associated with poor neurologic outcome in cyanotic patients. In both the patients hemodynamic parameters were well maintained during prebyapss, postbypass and postoperative periods and there were no obvious causes

for the neurologic injury except low hematocrit (~20%) during CPB. In patients with cyanotic lesions, bronchial and aorto-pulmonary collaterals can reroute up to 30 to 40% of the pump flow and return it directly to the left heart[17] and severely compromise the perfusion of the brain.In our present practice, hematocrit of ~30% is standard in all neonates, infants and cyanotic patients and using this practice we have not come across poor neurologic outcome in short term in patients who had reasonably good hemodynamics in the perioperative period. While using higher hematocrit (~30%) during CPB, if we have to use low flows or DHCA, we reduce hematocrit to ~20% by adding crystalloids. In postbypass period ultrafiltration is usually not required if higher hematocrit is maintained during bypass.

With miniaturization of oxygenators, the priming volume of current oxygenators for neonatal perfusion have static volumes of 43 mL (Capiox RX 05, Terumo, Japan), 52 mL (Safe Micro, Polystan, Denmark), and 60 mL (Lilliput I, Dideco, Italy). With the availability of a reliable oxygenator, cannula and circuit with very small prime and circuit volume, many of the problems of the conventional CPB such as hypothermia and hemodilution, need for adding blood and blood products in CPB prime are significantly reduced.

The need for hemodilution, hypothermia and hemofiltration is being reviewed and redefined. Recently, Miyaji *et al*.[18] reported transfusion-free procedures in 45 of 70 infants weighing four to seven kg who underwent various types of OHS. They achieved this feat by using Baby Rx oxygenator with a custom designed CPB system. They monitored mixed venous O_2 saturation (SvO_2) and regional cerebral oxygenation (rSO_2) using near-infrared spectroscopy (INVOS 5100; Somanetics, Inc, Troy, Mich) during CPB and maintained the values above 70 and 50%, respectively. During CPB, patients were transfused if the plasma lactate increased above 4.0 mmol/L or the SvO_2 and rSO_2 could not be maintained (above 70 and 50% respectively) despite increasing the pump flow or O_2 concentration. Postoperatively the patients were transfused if they showed hemodynamic instability despite sufficient inotropic support even when the hematocrit was above 25%. They did not transfuse platelets or fresh frozen plasma before red blood cell transfusion. The mean follow-up period was 621 days (range 86 - 1283 days), and no postoperative neurologic deficits, including seizure activity, delirium or delusion, or significant motor dysfunction, were found by the cardiologists or parents.

Indeed the pediatric CPB is safer than before because of the improvements in extracorporeal technology and better understanding of CPB related adverse effects. The safety of the CPB has been increased by various online monitors. However, despite advances the neonates and infants continue to remain susceptible to short and long term adverse neurologic outcome. The present efforts aim to reduce neurologic adverse outcome by minimizing neuronal edema by 1) keeping the physical characteristics of CPB prime close to normal by adding blood and colloids or fresh frozen plasma, 2) minimizing systemic inflammatory response and reperfusion injury by avoiding or minimizing addition of blood and blood products to prime, and 3) minimizing DHCA time and ensuring oxygen delivery every 15-20 minute during DHCA. Miniaturization of oxygenators and the extracorporeal circuit components significantly reduce the priming volume for neonatal perfusion and might achieve the objectives of keeping the physical characteristics of prime close to normal as well as avoidance of addition of blood and products to the prime and likely to reduce many of the problems of the conventional CPB. Using miniaturized ECC and mixed venous oxygen saturation and regional oxygen saturation monitoring guided transfusions during and after CPB have been shown to reduce transfusions without affecting the neurologic outcome.

WHERE DO WE GO FROM HERE?

The use of low flow and DHCA will continue. Apart from surgical reasons, world over, particularly in west and Europe, there is a growing concern and demand to avoid use of blood and blood products during and after surgery. It will become imperative to monitor cerebral oxygenation during low flows and DHCA and ensure that all is well with the brain. Several investigators reported the importance and usefulness of cerebral monitoring during cardiac surgery;[6,19] especially during low-hematocrit bypass.[20] The present monitoring techniques include superior vena cava or jugular venous oxyhemoglobin saturation regional oxygen saturation, electroencephalography (EEG), and processed EEG during CPB. These techniques monitor either global or regional oxygenation directly or by surrogates. Only techniques that monitor oxygenation in vulnerable brain areas of a neonate and infant would be able to ensure complete neuroprotection.

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