Review Article

Recent advances in paediatric cardiac anaesthesia

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ABSTRACT

Paediatric cardiac anaesthesia involves anaesthetizing very small children with complex congenital heart disease for major surgical procedures. The unique nature of this patient population requires considerable expertise and in-depth knowledge of the altered physiology. There have been several developments in the last decade in this subspecialty that has contributed to better care and improved outcome in this vulnerable group of patients. The purpose of this review is to present some of the recent advances in the anesthetic management of these children from preoperative evaluation to postoperative care. This article reviews the role of magnetic resonance imaging and contrast-enhanced magnetic resonance angiography in preoperative evaluation, the use of ultrasound to secure vascular access, the use of cuffed endotracheal tubes, the optimal haematocrit and the role of blood products, including the use of recombinant factor VIIa. It also deals with the advances in technology that have led to improved monitoring, the newer developments in cardiopulmonary bypass, the use of centrifugal pumps and extracorporeal membrane oxygenation and the role of DHCA. The role of new drugs, especially the α-2 agonists in paediatric cardiac anesthetic practice, fast tracking and effective postoperative pain management have also been reviewed.

Key words: Cardiopulmonary bypass, congenital heart disease, monitoring, paediatric cardiac anaesthesia, recent advances

INTRODUCTION

Writing about advances in the field of paediatric cardiac anaesthesia is a real daunting task. The review of literature for advances with a scientific outlook can sometimes be frustrating, as we often find some statements and techniques that are scientifically invalidated but are practiced widely. Advances in invasive monitoring, cardiopulmonary bypass (CPB) techniques and an increasing number of skilled paediatric cardiac surgeons and paediatric cardiac anaesthesiologists have enhanced the surgical management of children with complex congenital heart disease. New clinical and laboratory research has not only improved our knowledge of the effects of the anaesthetic drugs on the paediatric myocardium, but also led to the improved survival rates and better neurological outcomes, even in the sickest of the infants. The following is the review of important advances in paediatric cardiac surgery and anaesthesia.

PREOPERATIVE EVALUATION

In the recent times, advances in cardiac imaging had influenced significantly, the science and practice of paediatric cardiology and cardiac surgery. The echo lab has become a true morphologic and hemodynamic laboratory and transthoracic echocardiography has become the "working horse" of the paediatric cardiology. The development of matrix ultrasound probes made 3D echocardiography possible in paediatric patients. Detailed 3D images of cardiac structures can now be easily obtained, even in small babies. Along with the routine clinical examination and the echocardiography, the information provided by magnetic resonance imaging (MRI) and contrast-enhanced magnetic resonance angiography (CE-MRA) have reduced the need for invasive procedures such as cardiac catheterization. Cardiac MRI can provide accurate information on anatomy, ventricular function, shunt quantification and tissue characterization. CE-MRA is

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a useful diagnostic tool for the preoperative evaluation of the morphology of pulmonary arteries and blood supply in neonates with pulmonary atresia.[1]

CUFFED ENDOTRACHEAL TUBES: A NEW PRACTICE IN PAEDIATRIC ANAESTHESIA

The use of cuffed endotracheal tubes (ETTs) in infants and children is still a matter of debate. The evidence in the recent literature suggests no major advantages of using uncuffed ETTs in children. Many recently published reports suggest usage of high volume low pressure cuff and microcuff tubes in children and they provide a number of advantages such as low fresh gas usage, reduced gas pollution, a decrease in repeated laryngoscopies, considerably reduced aspiration risk and improved gas monitoring. Cuffed ETTs also offer the advantages of reliable capnography and reduced risk of dislocation/accidental extubation after patient positioning.[2]

ULTRASOUND-GUIDED CENTRAL VENOUS ACCESS

Central venous cannulations (CVC) are performed routinely to monitor central venous pressure and to allow infusion of vasoactive drugs in infants and children undergoing cardiac surgical procedures. The National Institute for Clinical Excellence (NICE) has recommended ultrasound guidance as the preferred method for insertion of central lines.[3] Studies have shown that ultrasound-guided CVC decreases the overall time required to cannulate the vessel by increasing the probability of successful cannulation, decreasing the number of skin punctures to obtain access, eliminating the need to change sites for access, and decrease the likelihood of untoward effects including but not limited to severe hematoma, requiring attempts at additional sites and inadvertent puncture of the wrong vessel or hemothorax/pneumothorax.[4,5]

CARDIOPULMONARY BYPASS IN INFANTS AND CHILDREN

Since the development of mechanical CPB circuits in late 1950s, the extra corporal perfusion circuits have come long way from monkey lungs, film and bubble oxygenators to modern miniature membrane oxygenators with centrifugal pumps and vacuum-assisted venous drainage with an in-line gas monitoring.[6] For congenital cardiac surgery, the extracorporeal circuit must be adjusted to a wide range of age groups and size variations, from 1.5 kg premature infants to 100 kg adults. Infants and children have smaller circulating blood volumes, higher oxygen consumption rates and often, highly reactive pulmonary vascular beds. In addition, neonates and infants have labile thermoregulation and immature organ systems with multiple implications for ischemic tolerance and inflammatory response.

Haemodilution

The relatively large CPB prime volumes compared with circulating blood volumes in infants and children lead to significant haemodilution. The benefits of improved viscosity at low temperatures clearly outweigh the disadvantages of haemodilution such as anaemia with decreased oxygen carrying capacity, reduced levels of plasma proteins and clotting factors leading to tissue oedema and coagulopathy, electrolyte imbalance and exaggerated release of stress hormones and compliment activation. With the newer technology, the minimum priming volumes for CPB circuits allowing full support in neonates at normothermia is 220 mL (180 mL if the arterial filter is excluded).

Optimal haematocrit on CPB and role of blood products

The optimal haematocrit (HCT) on bypass remains controversial, particularly for neonates. Some recent studies in infants have demonstrated negative effects on perioperative outcomes and neurological development when lower HCT (20% vs. 30%) was used.[7] The potential advantage of adding clotting factors and antithrombin III to the prime must be weighed against the negative effects associated with blood storage and activation of inflammatory pathways. To minimize the lung injury associated with reactive oxygen species, re-inflation of lungs with air and keeping the PaO_2 less than 150 mmHg and possibly lower for cyanotic infants is suggested.

pH management

Many centres use pH stat for neonatal surgery involving deep hypothermic circulatory arrest (DHCA) or combined strategies with crossover during cooling phase. Despite increased intracellular acidosis and enzyme dysfunction, experimental studies have shown some advantages of pH stat, including improved cerebral perfusion, more homogenous cooling and better oxygen delivery.

Systemic inflammatory response

The relatively large circuit size, blood prime and need for increased flow rates, all these factors are well known for triggering systemic inflammatory response. Immature and developing organ systems are particularly vulnerable to these inflammatory injuries. Current anti-inflammatory strategies include use of steroids, serine protease inhibitors, modified ultrafiltration and heparin-bonded circuits.[8]

Deep hypothermic circulatory arrest versus low flow perfusion

Recent publications suggest worse outcomes with increased cerebral oedema, pulmonary dysfunction and neurological injury after prolonged exposure to low flow perfusion.[9] Probably, short periods of DHCA are better tolerated than continuous low flow perfusion. The recommendations for safe DHCA are pre-bypass treatment with steroids and anti-inflammatory agents, hyper oxygenation before the initiation of DHCA, adequate duration of cooling (minimum of 20 min), maintenance of higher haematocrits during cooling, using pH stat blood gas management during the cooling phase, limiting the duration of DHCA exposure by providing intermittent cerebral perfusion for 1-2 min at 15-20 min intervals and usage of ultrafiltration techniques.

Ultrafiltration

Neonates and infants tend to accumulate large amounts of fluid during bypass, resulting in whole body oedema with pulmonary and myocardial dysfunction. Often, the sternum has to be kept open for a few days. Several techniques such as conventional ultrafiltration (CUF), dilution ultrafiltration (DUF) and modified ultrafiltration (MUF) have been developed to handle this problem.

Conventional ultrafiltration

It is done throughout the bypass run or whenever the venous reservoir volume is sufficient to allow filtration. With the newer miniature circuits, the effective fluid removal is limited and difficult to predict.

Dilutional ultrafiltration

It is more effective for the removal of inflammatory mediators than for haemoconcentration.

Modified ultrafiltration

It is used after weaning from CPB and before protamine administration, either through arterio-venous route, directly from the aortic cannula or veno-venous route via a roller pump. To minimize the adverse effects of MUF-like prolonged bypass exposure, iatrogenic air embolism, increased heparin levels, specific end points are usually set like duration (15-20 min), haematocrit (40%) or extracted volume (750 mL/m^2).

Neurologic outcomes

With the advances in perioperative care, survival after cardiac surgery for congenital heart disease has dramatically improved, and attention is being increasingly focused on long-term functional morbidities, such as neurodevelopmental outcomes and their profound consequences to patients and society. Neuroimaging studies have shown that newborns with CHD have a higher incidence of pre-existing cerebral anomalies (20-40%), especially peri-ventricular leukomalacia. In order to minimize additional neurologic injury, all contributing factors must be taken into consideration. The newer neuromonitoring techniques such as processed electroencephalography, cerebral oximetry, and Transcranial Doppler (TCD) can minimize the problem. Other neuroprotective strategies include temperature regulation, acid–base management, degree of haemodilution, blood glucose control, and anti-inflammatory therapies. While there are many studies showing an increase in perioperative mortality and morbidity associated with hyperglycaemia, there are also studies showing that hypoglycaemia is associated with poor outcomes. Currently, there is a lack of consensus regarding perioperative glucose control in paediatric patients undergoing cardiac surgery.

Monitoring

As recent evidence suggests an association between brain immaturity and CHD, monitoring of cerebral oxygenation with the newer technologies such as TCD and near infrared spectroscopy (NIRS) may improve neurologic outcomes.[10]

Transcranial doppler ultrasound

It is a sensitive, real-time monitor of cerebral blood flow velocity and emboli during congenital heart surgery. Diaz and Andropoulos used TCD of the middle cerebral artery to determine the level of bypass flow necessary during regional low flow cerebral perfusion for neonatal aortic arch reconstruction and they have concluded that TCD is a valuable monitor to ensure adequate and not excessive cerebral blood flow during low flow cerebral perfusion.[11] Additionally, TCD is a useful monitor for detecting acute decreases in cerebral blood flow velocity and also helps in the adjustment of bypass cannulae, thereby averting a potential neurological disaster.

Near infrared spectroscopy

It is a non-invasive optical technique used to monitor brain tissue oxygenation.[11] Commercially available devices measure the concentration of oxy and deoxyhemoglobin, thereby determining the cerebral oxygen saturation. The cerebral oximetry probe is placed on the forehead below the hairline. A light-emitting diode emits near infrared light which passes through a banana-shaped tissue volume of approximately 10 mL in the frontal cerebral cortex to two or three detectors placed 3-5 cm from the emitter. A study of 26 infants and children undergoing cardiac surgery using CPB and DHCA found that three patients had acute postoperative neurological changes with low regional cerebral oxygen saturation index (rSO_2i).[12] Although it seems intuitive to conclude that low rSO_2i, as measured by NIRS, may lead to adverse neurological outcomes and therefore should be monitored and treated, more data from prospective studies using this modality in infants and children are necessary.

Newer technologies such as pulse pressure analysis and non-invasive cardiac output measurement are available for paediatric population also. Few studies have shown that pulse pressure variation is less reliable in predicting fluid responsiveness in children as their chest wall and lung compliances are high. The increased use of peri-operative transesophageal echocardiography (TEE) has resulted in better surgical outcomes and has made a significant contribution to Reduction in a number of re-operations due to residual lesions.

Echocardiographic measurements of response to anaesthetics

Recently, detailed echocardiographic techniques have been used to evaluate the ventricular function response to anaesthetics in patients with congenital heart disease. The combined myocardial effects of fentanyl and midazolam in two different dose regimens for induction and the pre-bypass period in children undergoing congenital heart surgery were studied in a recently published article. Cardiac output and contractility were measured by echocardiography. The high dose regimen of fentanyl and midazolam resulted in a significant decrease in cardiac output, predominantly because of decrease in the heart rate.[13] Recently, the myocardial performance index (MPI) has been validated as an accurate assessment of ventricular function for all ventricular configurations including functional single ventricle. MPI is a numerical value, defined as sum of isovolumetric contraction time (ICT) and isovolumetric relaxation time (IRT) divided by ejection time (ET). The smaller the index, the better is the ventricular function. MPI provides a very good global measure of both systolic and diastolic ventricular function.

Pharmacology

Availability and increasing usage of volatile anaesthetic agents such as sevoflurane and short-acting opioids such as *remifentanil* made fast tracking feasible in paediatric cardiac surgery. *Remifentanil* is a synthetic, ultra-short-acting narcotic with a half-life of 3-5min, independent of duration of infusion, which is metabolized by non-specific plasma esterases. Donmez *et al.* reported a series of 55 children who underwent cardiac catheterization using remifentanil infusion of 0.1 mcg/kg/min, with minimal changes in heart rate, blood pressure or oxygen saturation. About half of the patients required additional sedation with midazolam or ketamine. Apnoea was infrequent, and time to recovery after discontinuation of infusion was only 2-4 min.[14]

Many case reports have been published on usage of newer inodilator *levosimendan* in complex cases. The new α-2 agonist *dexmedetomidine* is being increasingly used in paediatric population. Apart from its sedative properties, it provides effective pain relief with an opioid sparing effect.[15] Inhaled nitric oxide, prostacyclin analogues and phosphodiesterase inhibitors play a key role in controlling pulmonary hypertension associated with various congenital cardiac diseases. Intravenous immunoglobulins have been used prophylactically in neonates undergoing complex congenital surgeries such as the Norwood procedure to minimize the sensitization to allograft.

Blood conservation and recombinant factor VIIa

Use of antifibrinolytics has made blood conservation possible by minimizing bleeding, especially in severely cyanotics and re-do surgeries. Tranexamic acid and epsilon aminocaproic acid are typically administered at induction of anaesthesia, on initiation of bypass, and with administration of protamine and have been shown to be quite effective in reducing bleeding and transfusion in cyanotic children when compared with control patients.[16] Bojan *et al.* have shown that prophylactic usage of high dose aprotinin in neonates and infants had no effect on blood product transfusion or short-term outcomes. High CPB priming volumes and the ultrafiltration were found to be associated with increased use of packed cells and platelet transfusions; however, this study is limited by its retrospective design.[17]

The rFVIIa is being used in paediatric cardiac surgery for managing post-bypass coagulopathy bleeding.[18] A recent review, evaluating rFVIIa use in paediatric cardiac surgery patients, also demonstrated a statistically significant reduction in blood loss after rFVIIa. However, issues such as lack of an agreed dosing protocol in children and a laboratory assay to predict its clinical efficacy still remain unanswered. Apart from being expensive, there are no adequately powered studies available to determine the safety of rFVIIa in children undergoing cardiac surgery. These considerations, along with the theoretical risk of thrombosis, suggest that rFVIIa should be used only as last resort. Prospective, randomized, controlled trials in children are needed to obtain more comprehensive information before this therapy can be recommended for widespread use.[19,20]

Advances in paediatric mechanical circulatory support

Although a variety of mechanical circulatory support (MCS) devices currently exist for providing prolonged support as a bridge to either myocardial recovery or transplantation, present options remain limited for children who are less than 20 kg.[11] Many centres are now using extracorporeal membrane oxygenation (ECMO) support as a rescue therapy for infants and children who require preoperative stabilization, failure to wean from CPB or for those who have low cardiac output postoperatively in the ICU.

Extracorporeal membrane oxygenation

It offers several advantages including ease and rapidity of implementation, flexible cannulation options, full cardiopulmonary support and most importantly no patient size limitations. Despite the advantages and versatility, ECMO has several disadvantages also, like requirement of full time supervision by trained personnel, high levels of anticoagulation, which can lead to bleeding and neurological complications and increase in transfusion requirements.

Centrifugal pumps

When used without an oxygenator in the circuit, these pumps may be used to provide either uni or biventricular support for the failing hearts. Centrifugal pumps are ideal for short-term support in infants and children who have isolated left ventricular failure and difficulty in weaning from CPB. Regardless of the type of MCS used, the indication for support appears to be a major factor that determines the outcome. The survival rates in children with cardiomyopathy or myocarditis are higher as compared with children who require support because of congenital heart defects or post-cardiotomy failure.

Total intravenous anaesthesia in paediatric cardiac surgery

The availability of new short acting drugs, new concepts in pharmacokinetic modelling and computer technology made total intravenous anaesthesia (TIVA) possible in paediatric cardiac surgery. There is a better understanding of pharmacodynamics and pharmacokinetics of intravenous anaesthetic agents in children undergoing CPB and potential beneficial effects of this technique are now well understood. In a prospective study looking at the accuracy of a paediatric target-controlled infusion of propofol using a pedfusor® children who had their pharmacokinetic data set did not show a significant change in pharmacodynamic effect such as level of consciousness. This is because even in small children the volumes of bypass circuit and reservoir are small in comparison with the volume of distribution of the central and other compartments.[14]

Pain management and fast-tracking

The use of neuraxial techniques like single shot intrathecal or caudal morphine with or without local anaesthetics and insertion of thoracic epidural catheters have all made pain management in children very effective. Apart from providing superior analgesia, epidural or intrathecal opioids have been shown to blunt the stress response to surgery and CPB, improve pulmonary function, reduce time for mechanical ventilation and consequently reduce costs.[21,22] Appropriate patient selection is important for successful fast-tracking of children undergoing surgery for congenital heart disease. When the risk adjustment for congenital heart surgery (RACHS) score is applied to assess the surgical risk, multiple studies have shown that patients listed in risk category 1-3 are frequently eligible for fast-tracking.[23] For children classified as RACHS categories 4 and 5, the anaesthesiologist could opt to choose a fast-tracking anaesthetic technique and can re-evaluate them for early extubation at the end of the procedure. RACHS category 6 children are typically considered not eligible for fast-tracking.

Despite increasing evidence that fast-tracking in surgery for CHD can be achieved safely, there still remain significant individual as well as institutional concerns about the safety of such an approach. However, with the availability of short-acting opioids, and intravenous and inhalational anaesthetics with less cardiac depressive effects, hemodynamic stability can now be safely achieved without prolonging mechanical ventilation and ICU stay. The rate of reintubation following early extubation with modern anaesthetics is low and mostly unrelated to fast-tracking.

CONCLUSION

Until about 40 years ago, clinicians could only vaguely imagine how the heart anatomically and functionally looked. Newer technical revolutions have changed the practice of paediatric cardiac anaesthesia. Better understanding of the pathophysiology of complex congenital heart diseases and availability of new drugs with improved pharmacokinetic and pharmacodynamic profiles along with advances in technology for more intricate monitoring have over all significantly contributed to better outcomes in paediatric cardiac surgery. In this era of cost containment, we must welcome any technique, tool or drug that allows maximal use of resources without jeopardizing patient safety.

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