Myocardial Protection in Pediatric Cardiac Surgery

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Abstract: The combination of hypothermia and potassium cardioplegic arrest has become the most common method of myocardial protection in the evolution of myocardial protection. This review focuses on myocardial protection in pediatric cardiac surgery. In the 1980s, blood was added to cardioplegia solution in order to supply the myocardium with oxygen, nutrients, and for buffering purposes. Similar myocardial protection methods have been used in adult and pediatric groups for many years. However, the immature heart in the pediatric group differs in many ways from the mature hearts in adults. Low cardiac output is more often observed in pediatric patients. Most cardiac operations are performed under cardioplegic arrest in pediatric cardiac surgery. Today there are a lot of different types of cardioplegia solutions and methods used in pediatric cardiac surgery. Soon after normothermic perfusion was used in the adult cardiac surgery in the beginning of the 1990s, normothermic perfusion and cardioplegia began to be used in pediatric myocardial protection. Myocardial protection is more challenging in particular cases such as: (i) long and complex cases in which repetitive cardioplegia administration through the aortic root is difficult; (ii) newborn patients; and (iii) cases with preoperative damaged myocardium. If the mortality and morbidity rates of the centers in complex and long procedures are higher than the reported rates in literature, the myocardial protection method must be suspected and reorganized. Keywords: Myocardial—Protection—Pediatric—Infant—Newborn—Cardioplegia.
compared to mature myocardium (19), because immature myocardium has greater glycogen stores and more prolonged anaerobic utilization of glucose than in the adult heart (20,21). During ischemia in the newborn, ATP depletion is delayed due to diminished activity of 5′-nucleotidase which catalyzes the reaction of adenosine monophosphate to adenosine (21).

Hypoxic neonatal heart is more sensitive to ischemia than the adult (22). When compared with infants, children have significantly less reperfusion injury and better clinical outcome (23).

Physiologically, immature myocardium has decreased ventricular compliance, less preload reserve, decreased sensitivity to catecholamines, less inotropic reserve (with maximum adrenergic stimuli), and more (−) inotropic response to anesthetic agents (24,25).

Immature myocardium is more sensitive to extracellular calcium than mature myocardium (26,27). The sarcoplasmic reticulum is underdeveloped in the pediatric heart, has reduced storage capacity for calcium, and the activity of the sarcoplasmic calcium ATP’ase is lower than that of the adult heart (28). The antioxidant defense system is reduced in cyanotic heart defects (29,30). Cardiac output in pediatric patients is more dependent on heart rate and sinus rhythm. The increase in afterload produces significant hemodynamic impairment.

Ischemic preconditioning is ineffective in neonatal rat hearts (<7 days old) (31). However, protection by ischemic preconditioning develops after 7 days in the newborn rat heart (31).

The two contemporary myocardial protection methods used in pediatric cardiac surgery are cardioplegic arrest and on-pump beating heart. Cardioplegic arrest was used in most of the intracardiac operations. On-pump beating heart technique can be used in extracardiac and isolated right-side operations, including bidirectional cavapulmonary anastomosis, extracardiac Fontan, tricuspid, and pulmonary valve surgery.

Most of the cardiac operations are performed under cardioplegic arrest in pediatric cardiac surgery. Today there are a lot of different types of cardioplegia solutions and methods that are used in pediatric cardiac surgery. In heart transplantation in the USA, it has been reported that 167 different cardioplegic solutions have been used (32). Therefore it is not surprising to have more variety of cardioplegic solutions in pediatric cardiac surgery. The advantages of cardioplegia are diastolic arrest of the contractile components, cessation of electrical activity, reduction of metabolic activity, intermittent oxygen delivery (especially with blood cardioplegia), maintaining acid-base balance, maintaining high osmotic pressure, modifying reperfusion, reversibility, and low toxicity. The main component of cardioplegia is potassium. Cardioplegia solutions with magnesium and low calcium rates, containing glucose and buffering solutions, have been commonly used in most of the cardiac centers (33). Many other substrates including insulin, oxygen-derived free radical scavengers, procainamide, beta blockers (esmolol), NaHCO₃ exchange inhibitor (amiloride, cariporide), Na+ blocker (lidocaine, tetrodotoxin), L-Arginine, K+ channel openers (aprikalim, pinacidil, nicorandil), and Ca++ channel blockers have been used in experimental studies (2). However, most of them were not used in clinical practice (2).

Crystalloid and blood cardioplegia are both widely used in clinical practice. Crystalloid cardioplegia have some advantages such as being cheap, simple to deliver, and one single application is enough for adequate arrest (34,35). It has been demonstrated that one single dose of HTK is sufficient for myocardial protection up to more than 2 h of ischemia in pediatric heart surgery (35). The solution is also frequently used for heart preservation in heart transplantation during the long-term ischemic period (36,37). On the other hand, the advantages of blood cardioplegia are: it is more physiological, hemoglobin is used for O₂ transportation, it contains metabolic substrates, physiological buffers and provides physiological osmotic pressure, it causes less hemodilution, it contains oxygen free radical scavengers and also it has been shown that the blood cardioplegia is superior to crystalloid cardioplegia over 1 h ischemia (38–40).

Hypothermia has been used since 1950 for myocardial protection as a cornerstone (3). The methods to cool the heart are cold cardioplegia, systemic cooling with cardiopulmonary bypass, and topical myocardial cooling, which has a disadvantage of phrenic nerve damage. However, myocardial arrest is more important than hypothermia in myocardial protection. The arrested, normothermic heart requires 90% less oxygen than does the normothermic working heart (41).

Hypothermia appears to have several detrimental effects, such as impaired mitochondrial and sarcoplasmic reticulum functions (42). These effects lead to depletion of myocardial energy supplies. In 1989, Lichtenstein was the first to use normothermic continuous blood cardioplegia in a patient with complicated mitral valve replacement (43). The patient had a posterior wall rupture and the repair was successfully performed over 6 h of safe cross-clamp time.
Soon after normothermic perfusion was used in the adult cardiac surgery in the beginning of the 1990s, normothermic perfusion and cardioplegia started to be used in pediatric myocardial protection (44–47). The most important advantage of normothermic blood cardioplegia is preserving the functions of sodium–potassium, ATP’ase, and calcium ATP’ase enzyme systems of the sarcoplasmic reticulum under normothermia (33,40,48).

Today, warm and cold blood cardioplegia are used in combination. In this technique, the aortic cross-clamp is applied and the heart is arrested with the administration of warm cardioplegia, which is then switched to cold cardioplegia during induction. During the cross-clamp, cold blood cardioplegia is given every 15–20 min. The terminal warm blood cardioplegia is given as a hot shot before removing the aortic cross-clamp (40,49–51).

Antegrade, retrograde, and combined methods are used in cardioplegia delivery. Antegrade delivery is simple and the cardioplegia is equally distributed to the coronary arteries. The disadvantage of the method is risk of poor antegrade perfusion in the presence of aortic insufficiency and possible injury to the coronary ostia in open aorta. Retrograde delivery has the disadvantage of having nonphysiological and nonhomogenous distribution, risk of rupture of the coronary sinuses, and decreased flow to the right ventricle and septum. It is advantageous in aortic insufficiency and aortic root surgery. Cardioplegia is used in single or multi doses. Multi-dose cold cardioplegia is usually given every 20–30 min (50,51). However, multi-dose warm cardioplegia is usually given at shorter intervals (52).

The risk of myocardial injury is increased in some cases after surgery. Ventricular hypertrophy is a risk factor for adequate myocardial protection. Pre-ischemic conditioning, including cardiogenic shock or low cardiac output state, is also a risk factor for myocardial protection. Long aortic clamp time, ventricular distention, retraction, and ventriculotomy may lead to myocardial injury (53). The risk of reperfusion injury after cross-clamp is high in cyanotic hearts. Cardiopulmonary bypass should be instituted with a PO2 of no greater than 200 mm Hg to prevent oxidant-mediated reoxygenation injury (29,49). Coronary artery injury and air embolism to coronaries are also risk factors for adequate myocardial protection. Many factors can lead to postoperative low cardiac output state related to hypocalcemia, acidosis, hypoxia, volume overloads (residual ventricular septal defect, pulmonary and aortic regurgitation, and pressure overloads [left and right ventricular outflow obstruction]), hypovolemia, pulmonary and systemic hypertension, cardiac tamponade, and rhythm changes. Transesophageal echocardiogram is a valuable tool in identifying the etiology of low cardiac output state when metabolic events are excluded. Poor myocardial protection is still considered as a significant cause for hospital mortality in children (33,49).

**CONCLUSION**

When a medical center decides on the myocardial protection method, the most important determinants are the clinical results and the surgeons’ experiences. The method should be effective, simple and cheap, and it should be accepted by all surgeons. Myocardial protection is challenging in some cases such as long and complex operations in which recurrent cardioplegia delivery from the open aortic root is required, newborn patients, and preoperatively damaged myocardium. The medical center should evaluate the protection method with respect to the outcome in different procedures. If the morbidity and mortality rate is high in especially long and complex procedures, the myocardial protection method must also be considered as a risk factor.

**REFERENCES**

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