Advances In Myocardial Protection

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Citation

R Yao, J An. *Advances In Myocardial Protection*. The Internet Journal of Anesthesiology. 1998 Volume 3 Number 2.

Abstract

In 1975, anesthesiologists at the Cardiovascular Institute and Fu Wai Hospital began myocardial protection by perfusing cold crystalloid cardioplegic solutions into the ascending aorta. Since then, both clinical and basic research has been directed toward optimal myocardial protection. Current efforts have focused on the components of the arresting solution, the cardioplegic perfusate temperature, and perfusate methods.

I. COMPONENTS OF THE ARRESTING SOLUTION

a) Blood cardioplegia:

(4/5 blood added to 1/5 crystalloid solution with a final KCL concentration of 24 mmol/L)

Blood cardioplegia has been used in Fu Wai Hospital since 1994 and provides benefits over cold crystalloid cardioplegia [formula consists of KCl 20 mmol/L, MgCl2 16 mmol/L, CaCl2 1.2 mmol/L, Procaine 0.9 mmol/L, pH 6.9, osmoality 340 mOsm/L]. More than 5,000 open-heart operations have been performed with blood cardioplegia in the years of 1994 to 1996. A special perfusion device has been developed to provide cold blood cardioplegia, hyperkalemic warm blood cardioplegia or simple oxygenated blood perfusion.

To evaluate the effects of blood cardioplegia, 496 patients undergoing open-heart surgery were randomized into two groups. Each group either received cold crystalloid cardioplegia (n=165) or cold blood cardioplegia (n=331). Cardioplegic solution was infused in an intermittent anterograde fashion in both groups. The results demonstrated no significant difference in myocardial oxygen consumption. The blood cardioplegia did, however, result in more prompt resumption of lactate extraction and lower levels of released myocardial-specific isoenzyme, creatinine phosphokinase (CK-MB), during reperfusion. Tissue samples were taken from the right atrium 5 minutes before the heart was arrested and 15 minutes after cross clamp removal. Pathological studies in these two groups demonstrated more severe damage to the myocardial ultrastructure in the crystalloid group. Ultrastructure damage was mainly detected in the part of myocardial mitochondria. Myocardium perfused with blood cardioplegic solution demonstrated a more rapid establishment of cardiac rhythm (65%) compared to the crystalloid solution (45%).

b) Leukocyte filtered blood cardioplegia (LCBC)

To investigate the effects of leukocyte filtered blood cardioplegia on cardiac tissue, a prospective randomized study was performed on 20 patients undergoing valve replacement with myocardial protection by blood cardioplegia (BC) (n=10) or LCBC (n=10). Both groups had adequate cardiac arrest during the procedure. Plasma levels of CK-MB were significantly lower in LCBC group than in BC group. Ultrastructure analysis of the myocardium demonstrated damage in the BC group while the LCBC group demonstrated little damage. LCBC may provide superior myocardial protection to blood cardioplegia.

Figure 2

Changes of CK-MB in the leukocyte filtered plegia:

	BC	LCBC
before arrest	3.2 +/- 1.9	2.8 +/- 3.12
2 hours after opening	26.6 +/- 8.3	14.3 +/- 3.14
4 hours after opening	31.8 +/- 11.5	16.2 +/- 5.9

P between groups < 0.05

Figure 3

Malondialdehyde results:

	Crystalloid	Puerarin
prior to arrest	4.11 +/- 1.77	4.04 +/- 1.46
removal of cross clamp		
5 mins	4.54 +/- 1.47	4.26 +/- 0.65
10 mins	5.02 +/- 1.16 *	4.16 +/- 0.84 #

P between groups < 0.05

c) Crystalloid cardioplegic solution containing puerarin

Puerarin (C12H20O9) is the extract of the root of kudzu vine (a Chinese herb). In a randomized controlled study in 20 adult patients undergoing cardiac valve replacement, we investigated the myocardial protective effects of puerarin. Ten patients received cold crystalloid cardioplegia and 10 received cold crystalloid cardioplegia enhanced with 2mg/kg of puerarin. Arterial and coronary venous sinus blood samples were collected simultaneously for the measurement of oxygen, lactate, malondialdehyde (MDA), CK and CK-MB levels. Biopsy samples of the left atrium for electron microscopy were obtained before cross-clamping and 10 minutes after aorta opening. The result demonstrated that crystalloid cardioplegic solution containing puerarin may significantly reduce myocardial metabolism and reduce postoperative myocardial enzymes release. Damage of the myocardial ultrastructure (mitochondria) following ischemia and reperfusion is also less with the puerarin group. The damage to the mitochondria was estimated by means of Flameng (J Thorac Cardiovasc Surg,1980, 79:413-418). Before cardiac arrest, changes in the mitochondria of both groups were graded 0-1. Ten minutes after removing the aortic cross clamp, the puerarin group changed to a grade 2-3 where as the crystalloid group had more severe damage with a grade 3-4. There was also noted more severe damages in the cell nucleus in the crystalloid group.

{image:3}

* compared to prior arrest group P 0.05

compared to crystalloid group P 0.05

In order to understand the mechanism of myocardial protection of puerarin, the effects of puerarin on membrane ionic channel currents were investigated using using patch clamp whole cell recording techniques. The results indicated that 0.6 mM puerarin solution can inhibit Na+ currents in guinea-pig ventricular myocytes with no effects on K+ and Ca ++ currents. It appears that the mechanism of crystalloid cardioplegic solution containing puerarin against myocardial ischemia-reperfusion injury might be due to its Na+ channel blocking effects which results in the reduction of Na+ influx, decreasing of Na+ and Ca++ exchange thus avoiding intracellular calcium overload.

II. PERFUSATE TEMPERATURE

Thirty-two isolated hearts of white rats were randomly divided into two groups to investigate the effects of normothermic and hypothermic induction of cardioplegia. Normothermic induced cardioplegia proved to reduce the leak of myocardial enzymes, protect coronary circulation and myocardial function.

In another randomized controlled study, 15 dogs were equally divided into 3 groups. In group I (n=5), hypothermic crystalloid cardioplegic induction was undertaken followed by intermittent hypothermic crystalloid cardioplegia every 30 minutes during the CPB period. In group II (n=5), the hearts were identically treated as group I except that a single normothermic dose of blood cardioplegia was given before aortic opening. In group III, normothermic blood induction cardioplegia was performed followed by intermittent hypothermic crystalloid cardioplegia every 30 minutes and a single normothermic blood cardioplegia dose prior to aortic cross clamp removal. Myocardial metabolism, cardiac function and coronary circulation were evaluated. The study demonstrated a reduction in myocardial metabolism and improved systolic function in group II compared with group I. Group III demonstrated a superior protective effect not only in myocardial metabolism but also in cardiac function (both systolic and diastolic) and coronary circulation. The normothermic blood cardioplegia before aortic opening may increase the washout of intracellular calcium while normothermic arrest may prevent coronary spasm thus resulting in improved cardiac function. A clinical randomized controlled study in 20 patients undergoing valve replacement also demonstrated that normothermic blood cardioplegia had significant better protection in myocardial metabolism, enzyme release and myocardial ultrastructure.

III. PERFUSATE METHODS

Anterograde cardioplegic delivery may be impaired by coronary occlusion. Combined anterograde and retrograde cardioplegia has been developed and utilized clinically. A retrospective study in patients undergoing CABG at the Fu Wai Hospital showed better recovery (return of spontaneous heart rate) of arrested hearts that received cardioplegia in an intermittent fashion (90%, compared with that treated by simple anterograde delivery, which was 70%).

Recently, studies on pediatric myocardial protection have been carried out. They have proven that myocardial protection techniques used in adult patients do not have the same positive results in pediatric patients. The reasons are undoubtedly multifactorial but we have been focusing on the calcium concentrations and temperature of the cardioplegic solutions in these studies. Results are pending.

References

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