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Potassium Concentration in Cardioplegic Solutions in Pediatric Patients Undergoing Tetralogy of Fallot Repair: Impact on Myocardial Protection

Mohamed Ahmed Ali[1*], Sayed Kaoud Abd-Elshafy[1], Ahmed Mohammed Mandour[1], Esam M. Abdalla[1], Ehab A. Zahran[2], Mahmoud F. Sherif[3], Hany A. Elmorabaa[1], Ayman A. Abou Glalah[1] and Amr M. Sleem[1]

[1]*Department of Anesthesia and Intensive Care, College of Medicine, Assiut University, Assiut, Egypt*

[2]*Department of Cardiothoracic Surgery, College of Medicine, Assiut University, Assiut, Egypt*

[3]*Department of Pathology, College of Medicine, Assiut University, Assiut, Egypt*

[*]**Corresponding author:** Mohamed Ahmed Ali, Department of Anesthesia and Intensive Care, College of Medicine, Assiut University, Assiut, Egypt, Tel: +201008707460; E-mail: drmohamedali1984@yahoo.com

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Abstract

Objective: We investigated the cardioprotective effects of two different potassium concentrations in crystalloid cardioplegic solutions in pediatric patients undergoing tetralogy of Fallot (TOF) repair under cardiopulmonary bypass (CPB).

Methods: Eighty seven pediatric patients with Tetralogy of Fallot (TOF) were randomly allocated into two groups according to the type of cardioplegic solution. Group L received large volume with low potassium concentration (K^+ 10 mmol/L) cardioplegia; 30 ml/kg for induction of arrest and repeated every 20 min at a dose of 15 ml/kg. Group S received small volume with high potassium concentration (K^+ 30 mmol/L) cardioplegia; 10 ml/kg for induction of arrest and repeated every 20 min at a dose of 5 ml/kg.

Results: Group L showed earlier return of cardiac rhythm (33.8 ± 4.9 sec) compared to 38.9 ± 5.6 sec in group S with most of the cases had sinus rhythm. The maximum Inotropic Score in the first 24 h was lower in group L; 13 (5) compared to group S; 15 (10). Less increase in cardiac troponin I (cTnI) in all postoperative readings, shorter duration of mechanical ventilation, ICU length, and hospital stay in group L. No changes in hemodynamic parameters between both groups.

Conclusion: Better myocardial protection in pediatric cardiac patients perfused by cardioplegia with low potassium concentration.

Keywords: Myocardial protection; Pediatric cardiac surgery; Potassium cardioplegia; Tetralogy of Fallot; Cardiac troponin I

Introduction

Despite major advances in the technical aspects of surgical repair of congenital heart diseases, perioperative myocardial damage with the low cardiac output (along with imperfect surgical repair) remains the most common cause of morbidity and death after repair of the congenital lesion [1-3]. So, optimal myocardial protection is as important as an excellent technical repair in achieving the best long-term outcome with surgical correction. Cyanotic patients are particularly vulnerable to myocardial injury and should receive even greater attention than those without cyanosis [4]. A variety of myocardial protection techniques exists, and despite this variation, cardioplegia remains the most significant tool used to increase myocardial protection [5]. Hypothermic depolarizing hyperkalemic (K^+>20 mmol/L) cardioplegia is currently the "gold standard" in cardiac surgery [6]. However, high potassium concentration has been associated with deleterious consequences against myocardial protection. A significant number of studies have shown a link between exposure to high potassium and post-cardioplegia ionic and metabolic imbalances, myocardial stunning, arrhythmia, ischemic injury, tissue edema, endothelial damage, free radical production, and functional loss during reperfusion [7,8]. Our hypothesis was testing whether the lower concentration of potassium in large volume cardioplegia could be used with similar or even better outcomes regarding myocardial protection.

Materials and Methods

Eighty-seven pediatric patients on the elective waiting list for TOF repair aged between 2-6 years undergoing elective cardiac surgery with cardiopulmonary bypass were included in the study.

This prospective, randomized, double-blinded, controlled clinical trial was conducted at Assiut University Orman Cardiology Hospital from August 2017 to April 2018. Patients with acyanotic congenital heart disease, needing preoperative inotropic support, known renal or hepatic dysfunctions, planned off-pump cardiac surgery or emergency cardiac surgery were excluded from the study. The study was approved by the local ethics committee of the faculty of Medicine, Assiut University and registered with ClinicalTrials.gov (ID: NCT03229980). A written informed consent has been taken after discussing a detailed description of the study with the parents. Patients were allocated randomly according to the cardioplegic solution used into two groups; Low potassium high volume group (group L) and High potassium low

volume group (group S), by computer programs and were contained in sealed opaque envelopes.

In both groups, all children received premedication with oral midazolam (0.5 mg/kg) and intramuscular atropine (10 mcg/kg) 30 min before the operation. Intravenous access was introduced under EMLA cream. Induction of anesthesia performed by ketamine (2 mg/kg) plus fentanyl (5 mcg/kg) and cisatracurium (0.1 mg/kg) and maintained with sevoflurane in addition to fentanyl (1-2 mcg/kg/hr) and cisatracurium (0.05 mg/kg per dose every 30 min). Pressure-controlled ventilation was instituted, and ventilation parameters were set to maintain normocarbia. Oxygen and air were adjusted to maintain the arterial oxygen saturation at a value equal to or greater than the baseline SaO_2 of the patient. Five leads electrocardiogram (ECG), invasive blood pressure (IBP), central venous pressure (CVP), nasopharyngeal temperature, pulse oximetry and end-tidal capnography ($ETCO_2$) were continuously monitored during the procedure. The degree of muscle relaxation was monitored intermittently by train of four. Cerebral oximetry was used to monitor the adequacy of brain oxygenation. Transesophageal probe (TEE) was inserted after intubation. In all patients, a median sternotomy and aortic-bicaval cannulation were done. CPB was standardized in all patients according to our institute protocol except for technique of cardioplegic solution which was used according to group randomization. In both groups, after aortic cross-clamping, the heart was arrested using intermittent doses of cold cardioplegic solutions infused into the aortic root according to the study groups. Cardioplegia was prepared by the clinical pharmacy department in the hospital but with different composition concentration and volume according to group randomization. The first dose of cardioplegia, (arresting dose) was given over 3-5 min, and subsequent doses were given every 20 min over 2-3 min. The cardioplegic solution was delivered at a temperature of 4°C-10°C and perfusion pressure between 80-100 mmHg. During the cardioplegic infusion, the right atrium was opened, and the solution was almost completely removed. It should be noted that every patient has received the same amount of cardioplegia components but with different dilutions.

Group L (45 patients): The composition of cardioplegic solution was K^+ (10 mmol/L), Lidocaine (50 mg/L), magnesium sulphate (1 gm/L), dextrose 25% (10 mL/L), and sodium bicarbonate 8.4% (10 mL/L) added to one liter of ringer acetate. It was given at a dose of 30 ml/kg as arresting dose and 10 ml as subsequent doses.

Group S (42 patients): The composition of cardioplegic solution was K^+ (30 mmol/L), Lidocaine (150 mg/L), magnesium sulphate (3 gm/L), dextrose 25% (30 mL/L), and sodium bicarbonate 8.4% (30 mL/L) added to one liter of ringer acetate. It was given at a dose of 10 ml/kg as arresting dose and 5 ml as subsequent doses.

Core body temperature during CPB was maintained between 28°C-30°C. Alpha-stat blood gas strategy was used. $PaCO_2$ between 35 mmHg and 45 mmHg and oxygen partial pressures of 150 mmHg-250 mmHg were maintained during CPB. A mean arterial pressure (MAP) was maintained between 30-60 mmHg during CPB by adjusting pump flow rates and occasionally by using vasopressors/vasodilators.

After completion of repair, aortic cross-clamp was removed, and conventional mechanical ventilation was resumed. Weaning from CPB was done at 37°C after completion of surgery. Perfect surgical repair was confirmed by transesophageal echocardiography (TEE) after weaning from CPB in all studied patients. Patient hemodynamics and arterial blood gasses were stabilized. Heparin was reversed by protamine. After the end of the surgery, the patients were transferred to the intensive care unit (ICU). Extubation in ICU was done if the patients were fully conscious, hemodynamically stable, no arrhythmias, good airway reflexes, acceptable blood loss and accepted arterial blood gas analysis.

Primary outcome: Time and type of cardiac rhythm after aortic de-clamping. (It should be noted that the time elapsed from the last cardioplegia was same in 2 groups before declamping)

Secondary outcomes: Hemodynamic changes, vasoactive-inotropic score (VIS) or inotropic score (IS), Serum cardiac troponin I (cTnI), and 30-day mortality.

Study measurements: Beside recording various socio-demographic data, we recorded invasive blood pressure, heart rate, CVP, temperature, oxygen saturation, ECG, and respiratory rate at baseline, on reperfusion (1 min and 15 min after de-clamping of aorta), post-CPB (10, 30, 60, and 120 min) and every hour in ICU. We also recorded the initial (after weaning from CPB) and maximum VIS or IS during the first 24 h after cardiac surgery and duration of vasopressor/inotropic support.

VIS was calculated as follows: dopamine dose, (μg/kg/min) +dobutamine dose, (μg/kg/min)+100 × epinephrine dose, (μg/kg/min) +10 × milrinone dose, (μg/kg/min)+10,000 × vasopressin dose, (U/kg/min)+100 × norepinephrine dose (μg/kg/min) [9,10].

We also recorded the total amount and frequency of administered cardioplegic solution.

Arterial and coronary sinus blood sample was taken to assess different parameters of blood gases and serum potassium. Transthoracic echocardiography (TTE) was done for assessment of the cardiac function 24 h after surgery. Samples for troponin I levels were obtained 6 h, 12 h and 24 h after aortic cross-clamping as a marker of myocardial ischemia and injury

Duration of cross-clamping, total CPB, operation, mechanical ventilation, ICU length, and hospital stay was also recorded.

Statistical analysis

For sample size calculation data were collected from a previous study [11]. It was estimated that 40 patients were required per group to compare the cardioprotective efficacy of the two cardioplegic solutions with 80% power and 5% probability of Type I error. So, we included 87 patients in our study. All statistical analyses were performed using IBM SPSS Statistics version 22.0 (SPSS Software, Chicago, IL, USA). The Shapiro-Wilk test assessed the normality of the data distribution. Continuous data were presented as mean ± SD or median (interquartile range). Categorical data were showed as numbers (%) and were tested using the Chi-square test or Fisher exact test as appropriate. A two-tailed $p<0.05$ was considered statistically significant.

Results

After reviewing the inclusion and exclusion criteria, 87 patients were allocated and divided randomly into two groups. All allocated patients completed the study protocol and were finally analyzed (Figure 1).

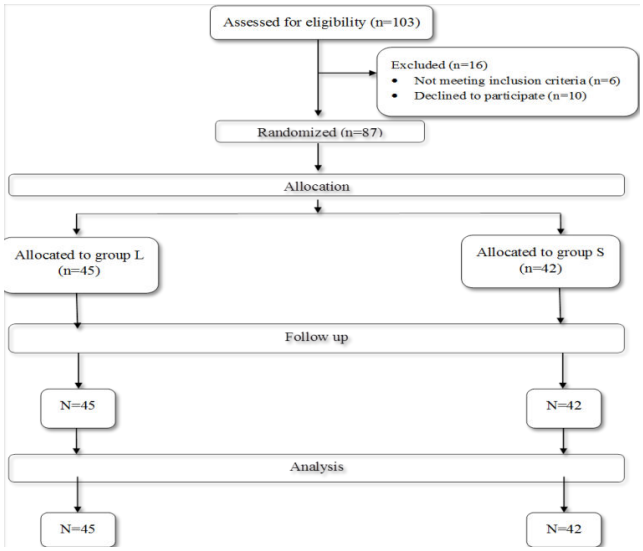

Figure 1: Consort Flow Diagram. Group L=Low potassium concentration large volume group; Group S=High potassium concentration small volume group.

Patient characteristics, duration of CPB, aortic cross-clamp time, and operative time demonstrated insignificant differences between the two studied groups (Table 1).

	Group L (N=45)	Group S (N=42)	P-Value
Age (month)	34 (58)	24 (17.25)	0.26
Sex (male/female)	26/19	26/16	0.83
Height (cm)	92.71 ± 20.27	86.93 ± 18.16	0.17
Weight (kg)	12.69 ± 4.64	12.38 ± 5.16	0.77
BSA (m^2)	0.57 ± 0.16	0.54 ± 0.17	0.48
PG (mm Hg)	74.24 ± 13.45	75.05 ± 8.61	0.74
Mc Goon ratio	2.16 ± 0.44	2.2 ± 0.48	0.63
Saturation on room air (%)	81.09 ± 8.19	82.17 ± 7.64	0.53
Preoperative Hematocrit (%)	39.84 ± 4.1	39.9 ± 4.44	0.95
Lowest Hematocrit on CPB (%)	29.33 ± 3.75	29.48 ± 4.19	0.87
Postoperative hematocrit (%)	40.49 ± 4.2	39.67 ± 3.63	0.33
Postoperative LV function (normal/impaired)	42/3	35/7	0.19
Postoperative RV function (normal/impaired)	41/4	36/6	0.51
Cardiopulmonary Bypass (minutes)	151.1 ± 33.9	162.9 ± 39.9	0.07
Aortic Cross Clamping (minutes)	98.8 ± 25	105.6 ± 26.9	0.29
Operation (hours)	5.9 ± 1	6.2 ± 0.8	0.25

Data were presented as median (IQR), mean ± SD or Number (%). EF: Ejection Fraction, BSA: Body Surface Area, PG: Pressure Gradient between right ventricular outflow tract and the pulmonary artery, LV: Left Ventricle, RV: Right Ventricle. L: Large volume group, S: Small volume group. P-value>0.05 is considered insignificant

Table 1: Patient characteristics and surgical data.

Table 2 shows the amount of cardioplegia given per kg, frequency of administration, and the time taken to arrest the heart (time measured from the start of cardioplegia infusion to complete loss of electrical and mechanical activity of the heart). The amount of cardioplegia per kg given in group L was 50.5 ± 17.1 ml, and 38.9 ± 14.50 ml in group S, with statistically significant difference between the two groups (p=0.001). On the other hand, the frequency of cardioplegia infusion was nearly equal in both groups (3 (1.5) times in group L compared to 3 (1.25) times in group S), with statistically insignificant difference between the two groups. The time taken to arrest the heart was shorter in group S (29.6 ± 6.2 seconds) compared to group L (34.9 ± 2.9 seconds) with P<0.001.

	Group (L) (N=45)	Group (S) (N=42)	P-Value
Amount of cardioplegia per kg (ml/kg)	50.5 ± 17.1	38.9 ± 14.5	0.001*
Frequency of cardioplegia doses	3 (1.5)	3 (1.25)	0.223
The time taken to arrest the heart (sec)	34.9 ± 2.9	29.6 ± 6.2	<0.001*

Data are presented as mean ± SD. L: Large volume group, S: Small volume group.

Table 2: Cardioplegic solution in the two studied groups.

	Group L (N=45)	Group S (N=42)	P-Value
Time of rhythm return after decamping (sec)	33.8 ± 4.9	38.9 ± 5.6	<0.001*
Type of rhythm:			
· Sinus rhythm	39 (87%)	29 (69%)	0.19
· VT or VF	4 (9%)	6 (14%)	
· Heart block	2 (4%)	6 (14%)	
· SVT	0 (0%)	1 (2%)	
DC shock use	4 (9%)	5 (12%)	0.45
Pacemaker use	4 (9%)	6 (14%)	0.33

Data were presented as (mean ± SD) and number (%). VF: Ventricular Fibrillation, VT: Ventricular Tachycardia, HB: Heart Block, SVT: Supraventricular Tachycardia, DC: Direct Current shock. L: Large volume group, S: Small volume group.

Table 3: Cardiac rhythm following cross-clamp removal.

Table 3 shows clinical outcomes after cross-clamp removal. Return of cardiac rhythm after aortic de-clamping was earlier in group L (33.8 ± 4.9 seconds) compared to (38.9 ± 5.6 seconds) group S; with statistically significant difference between the two groups (P<0.001). Sinus rhythm was the most common type of cardiac rhythm after de-clamping. It was higher in group L; 39 (87%) cases compared to group S; 29 (69%) cases. Ventricular tachycardia and or ventricular fibrillation were the second most common cardiac rhythm on de-clamping. Also, heart block was lower in group L. Supraventricular tachycardia was recorded in one case belonging to group S with statistically insignificant differences between the two groups, (P=0.19). DC was used in nine cases; five of them were in group S and four in group L, with statistically insignificant differences between the two groups, (P=0.45). Temporary pacemaker for heart block or sinus bradycardia were used in ten cases; four cases in group L and six cases in group S, with statistically insignificant difference between the three groups, (P=0.33).

The highest heart rate (HR), the lowest mean arterial blood pressure (MAP), and the highest CVP were nearly equal in the two groups, with statistically insignificant difference (Table 4).

	Group L (N=45)	Group S (N=42)	P-Value
Highest HR (beats/minutes)	153.6 ± 17.4	155.6 ± 18.1	0.59
Time of highest HR (hours)	4 (6.5)	5 (5)	0.4
Lowest MAP (mmHg)	62.2 ± 11.1	61.7 ± 13.2	0.85
Time of lowest MAP (hours)	6 (12)	6 (9.25)	0.99
Highest CVP (cmH_2O)	14.6 ± 2.4	15.6 ± 3.6	0.13
Time of highest CVP (hours)	5 (6.5)	4 (9.25)	0.63

Data were presented as mean ± SD and median (Interquartile Range). L: Large volume group, S: Small volume group. HR: Heart rate, MAP: Mean arterial pressure, CVP: Central venous pressure, hours: Time in hours from ICU admission.

Table 4: Highest and lowest readings of hemodynamics.

Table 5 shows various inotropic/vasopressor drugs used in this study along with both initial and maximum inotropic scores and duration of administration in the ICU. Initial IS was lower in group L; 12 (5) than in group S; 15 (8) with statistically significant difference between the two groups; (P=0.001). Also, the maximum IS in the first 24 h was lower in group L; 13 (5) compared to group S; 15 (10) with statistically significant difference between the two groups (P=0.007). There were statistically significant differences between the two groups as regards the doses of initial adrenaline, (P=0.01), maximum adrenaline, (P=0.03), initial dopamine (P=0.003) and maximum dopamine (P=0.02). There was statistically insignificant difference between the two groups as regards the use of milrinone and noradrenaline. The time at which the maximum inotropic score is reached was 1 (0) h from ICU admission in group L and 1 (0.5) in group S with statistically insignificant difference between the two groups. The duration of inotropic score was 68 (21.5) h in group L and 96 (48) h in group S, with statistically significant difference between the two groups (P<0.001).

As shown in Figure 2, the baseline serum troponin level showed statistically insignificant difference between the two groups. The cTnI in group L was 30.1 (23.1), 12.7 (18.35), and 5.6 (10.45) ng/ml measured at 6, 12 and 24 h from aortic cross-clamping respectively. Serum cardiac Troponin I levels were significantly higher in group S [48.2 (41.52), 28.75 (26), and 14.05 (13.02) ng/ml measured at six, 12 and 24 h from aortic cross-clamping respectively] compared to group L (P=0.002, P=0.001, and P=0.001) at six, 12, and 24 h respectively following aortic cross-clamping.

	Group L (N=45)	Group S (N=42)	P-Value
Initial IS	12 (5)	15 (8)	0.001*
Maximum IS	13 (5)	15 (10)	0.007*
Initial Adrenaline (ng/kg/min)	70 (30)	80 (40)	0.01*
Maximum Adrenaline (ng/kg/min)	70 (40)	80 (40)	0.03*
Initial Dopamine (mg/kg/min)	5 (6.5)	6.5 (5)	0.003*
Maximum Dopamine (mg/kg/min)	5 (7)	6.5 (5)	0.02*
Noradrenaline (ng/kg/min)	0 (0)	0 (0)	0.28
Milrinone (mg/kg/min)	0 (0.5)	0 (0.5)	0.83
Time of Maximum IS (hours)	1 (0)	1 (0.5)	0.19
Duration of IS (hour)	68 (21.5)	96 (48)	<0.001*

Data were presented as median (IQR). IS: Inotropic score, L: Large volume group, S: Small volume group.

Table 5: Inotropes and Vasopressors in the two studied groups.

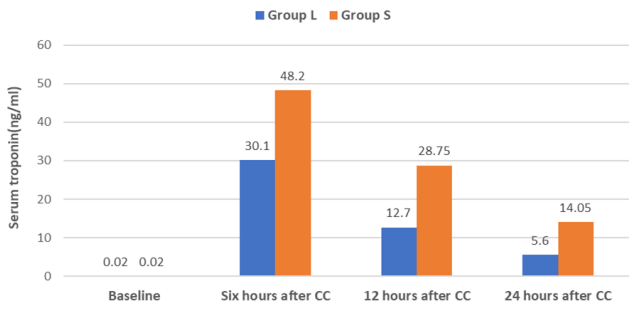

Figure 2: Serum Cardiac Troponin I (ng/ml). Data were presented as median (IQR); CC: Cross-clamping of aorta. L: Large volume group, S: Small volume group.

	Group L (N=45)	Group S (N=42)	P-Value
pH	7.01 ± 0.16	6.79 ± 0.16	<0.001*
PCO_2 (mmHg)	62.03 ± 19.54	74.05 ± 19.76	0.005*
Base deficit	-12.5 ± 4.3	-15.76 ± 3.82	<0.001*
Lactate (mmol/l)	4.94 ± 1.51	6.12 ± 1.51	<0.001*
O_2 saturation (%)	68.61 ± 14.74	54.93 ± 20.53	0.001*
Potassium (mmol/l)	7.54 ± 1.5	9.85 ± 3.39	<0.001*

Data were presented as mean ± SD. Large volume group, S: Small volume group.

Table 6: Coronary sinus blood gases.

There was statistically significant difference between the two groups as regard coronary sinus blood gases [pH (P<0.001), PCO_2 (P=0.005), base deficit (P<0.001), O_2 saturation (P=0.001), lactate (P<0.001), and K^+ concentration (P<0.001)] between the two groups (Table 6).

Although the incidence of postoperative arrhythmia was lower in group L, this difference was statistically insignificant between the two groups (Figure 3).

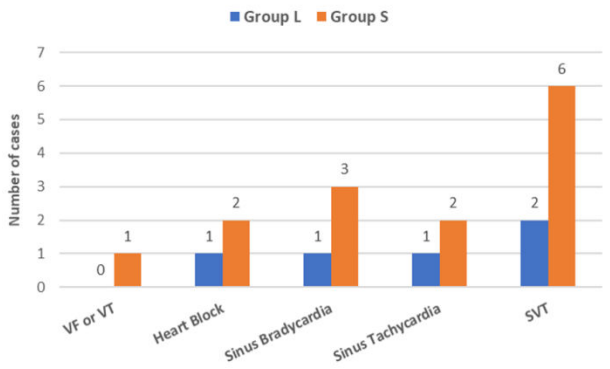

Figure 3: Postoperative arrhythmia: Data were presented as number (%). VF: Ventricular Fibrillation, VT: Ventricular Tachycardia, SVT: Supraventricular Tachycardia, L: Large volume group, S: Small volume group.

The duration of mechanical ventilation, ICU stay, and the total postoperative hospital time was lower in group L compared to group S with statistically significant difference between the two groups (Table 7). Also, mortality cases were lower in group L but without statistical significance (Table 7).

	Group L (N=45)	Group S (N=42)	P-Value
Mechanical ventilation (hours)	5 (2)	6 (1.88)	0.01*
Intensive Care Unit stay (days)	4 (1)	7 (3.5)	<0.001*
Hospital stay (days)	6 (2)	8 (3)	0.002*
30-day mortality	1 (2.2 %)	3 (7.1 %)	0.282

Data were presented as median (IQR), or Number (%). L: Large volume group, S: Small volume group.

Table 7: Postoperative outcomes.

Discussion

The results of this study showed better myocardial protection in group L (lower potassium concentration) as evidenced clinically by the earlier return of cardiac rhythm after de-clamping with most of the cases had sinus rhythm, lower doses of inotropes/vasopressors, and shorter duration of mechanical ventilation, ICU stay, and hospital stay. This also reflected on laboratory parameters of myocardial cell damage; less cTnI level especially after six hours from aortic cross-clamping, less coronary sinus lactate and less coronary sinus PCO_2 (evidence of anaerobic and aerobic myocardial metabolism). Although this less myocardial injury and better myocardial protection in group L, this was not reflected on hemodynamic parameters. In all mortality cases, we ruled out differences in severity of TOF and confirmed that the intra-cardiac repair of TOF was perfect in all these patients.

Better myocardial protection in group L was due to the frequent infusion of the cold cardioplegic solution with lower potassium concentration resulting in more washout of anaerobic metabolites (these metabolites further inhibit anaerobic energy production if accumulated) and avoidance of myocardial warming (due to more aortopulmonary collaterals in TOF patients). So, by maintenance of cardiac cooling with low potassium and metabolites wash out, better myocardial protection is achieved with a better outcome.

The arrest time (time from start of cardioplegia infusion to electromechanical arrest) was shorter in group S when compared to group L both other groups which were statistically but not clinically significant. It seemed that the high potassium concentration infused over the shorter period had led to shorter arrest time but, at the same time, led to more negative consequences of high potassium concentration (as demonstrated in coronary sinus potassium concentration) with loss of the benefit of short arrest time.

It is well known that high-potassium cardioplegic solutions are currently used to arrest the hearts during cardiac operations in most cardiac surgery centers. The concentration of potassium is typically greater than 15 mmol/L [6]. Liu et al. [12] conducted a randomized controlled trial comparing the myocardial protective effect of a moderate-potassium (MP) cold blood cardioplegic solution (K^+ 10 mmol/L, n=37) and high potassium (HP) cold blood cardioplegic solution (K^+ 20 mmol/L, n=31) in pediatric cardiac surgery. They found no statistically significant differences between the two groups in cardiopulmonary bypass time, aorta cross-clamping time, cardioplegia volume, lowest body temperature during CPB, the total volume of cardioplegia delivered, the total mediastinal drainage volume, the postoperative inotropic drug use, the length of stay in the ICU, and the postoperative hospital time. However, there was a longer arresting time and a shorter rhythm recovery time in MP group. Also, the number of patients with a long postoperative mechanical ventilation time (>24 h) was lower in MP group. Serum concentration of cTnI after aortic de-clamping was lower in the MP group when compared with that in the HP group. These findings of better myocardial protective effects in MP group when compared with conventional HP cardioplegia in pediatric patients were in agreement with our findings regarding the use of a cardioplegic solution with lower potassium concentration. Previous studies [6,8] have demonstrated that high-potassium cardioplegia can induce myocardial ionic and metabolic imbalances during ischemia, as well as myocardial stunning, tissue edema, endothelial damage, free radical production, and functional loss during reperfusion.

More recently; non-depolarizing agents such as procaine, lidocaine, and esmolol, and hyperpolarizing agents such as adenosine and KATP channel openers (e.g., pinacidil, nicorandil, aprikalim, and cromakalim), have been suggested as a possible alternative to high potassium. They were principally experimentally and, in some cases, clinically used as adjuncts in hyperkalemic cardioplegic solutions and longer-term preservation solutions, rather than the primary arresting agents with promising results [13,14].

Sloots et al. examined the effect of varying levels of extracellular potassium in adenosine lidocaine (AL) cardioplegia (0.1, 3.0, 5.9, 10, 16 mmol K^+) on the membrane potential, coronary vascular resistance (CVR), incidence of arrhythmias, heart rate, systolic pressures, aortic and coronary flows, cardiac output, time to first beat, and stroke volume (SV) after 1 and 2 h of arrest at 32°C-33°C. They showed that warm AL cardioplegia is most efficient under normokalemic conditions when the myocardial cell membrane potential is close to its resting state. Hearts arrested using higher K^+ levels or interestingly, very lower K^+ levels had significantly higher CVR, experienced reanimation arrhythmias and were "slow-to-recover" with significant losses in left ventricular function, SV, and contractility. Left ventricular functional loss was highly correlated with high or very low potassium levels in the cardioplegia [15].

Jin et al. randomly allocated 134 pediatric patients with low-risk congenital heart disease into three groups; the high-potassium (HP) group (K^+ 20 mmol/L, n=46); the high-potassium adenosine-lidocaine (HPAL) group (K^+ 20 mmol/L; adenosine 0.7 mmol/L; and lidocaine 0.7 mmol/L, n=44); and the moderate-potassium adenosine–lidocaine (MPAL) group (K^+ 10 mmol/L; adenosine 0.7 mmol/L; and lidocaine 0.7 mmol/L, n=44). Around 80% of patients had Ventricular Septal Defects (VSD), and 60% had concomitant pulmonary hypertension. There were no significant differences among the three groups in defect types, age, sex or body weight or hemodynamics before CPB. There were no significant group differences in time to arrest, cross-clamp time, cardiopulmonary bypass (CPB) time, perioperative hematocrit, fluid output at the end of the operation, mechanical ventilation time, total mediastinal drainage, ICU time and post-operative hospital time. At the end of cardiopulmonary bypass and modified ultrafiltration, the systolic and pulse pressures of the MPAL group were significantly higher compared with the respective values of the HP group. At the time points of 1 to 12 h after reperfusion, the levels of serum cardiac troponin I were significantly decreased in the MPAL group compared with those in the HP and HPAL groups. Jin et al. also reported a 30% lower use of post-operative inotropes in the MPAL group compared to HP group [16].

The outcomes assessed in our study were previously used in different studies like a meta-analysis performed by Mylonas et al. [17].

Fast return to sinus rhythm after cardioplegic arrest is generally considered an indicator of fine myocardial protection. This variable has been used in experimental and clinical studies comparing different methods of myocardial protection during cardioplegic arrest [18,19]. It has been described that the incidence and duration of reperfusion arrhythmias are related to the duration of cardioplegic arrest [18], the mass of ischemic tissue and the duration and intensity of ischemia without cardioplegia [20]. The time of spontaneous sinus rhythm return after de-clamping and percentage of patients required defibrillation for ventricular reperfusion arrhythmia were used as myocardial protection markers [21].

The percentage of patients who require postoperative inotropic support is considered a relevant factor in evaluating the efficacy of myocardial protection in both adult and pediatric cardiac surgery [4]. Numerous clinical studies [22-24] have supported the ability of intraoperative sampling of coronary sinus (CS) blood to measure changes in myocardial metabolism induced by ischemia and reperfusion. Among other changes, cardiac arrest induces a period of obligate myocardial lactate production that persists for an indeterminate amount of time after reperfusion. Coronary sinus lactate assays have been established as a standard method to compare various myocardial protection strategies [25,26].

In our study, the parameters of anaerobic metabolism and tissue acidosis were better in Group L compared to group S (less acidosis; low PCO_2 and base deficit, lower coronary sinus lactate, and potassium concentration) with statistically significant difference between the two groups.

Borowski et al. concluded that coronary sinus lactate monitoring seems to be useful in the assessment of myocardial protection quality and hence in the management of the post-ischemic heart [27].

In our study, we found that levels of cardiac troponin I (cTnI) were higher at six hours after de-clamping and then gradually decreased to reach minimum but not baseline at 24 h. These levels of cTnI at six, 12, and 24 h were significantly lower in group L and higher in group S. In the pediatric population, troponin I shows a good correlation with the extent of myocardial damage following cardiac surgery and cardiotoxic medication and can be used as a predictor of subsequent cardiac recovery and mortality [28,29].

Study Limitations

Presently in the majority of cardiac centers modified St. Thomas solution having Potassium concentration of 16 mmol/L in hypothermic blood is used for myocardial protection. We used crystalloid cardioplegia which is different than the standard practice because of unavailability of such solution. Another limitation of this study is the fact that it emanated from a single institution on one type of patients and that any validation of the findings will require prospective multicenter studies performed on patients with variable cardiac pathologies. Also, in some cases of the study, the coronary sinus blood sample taken just after cross-clamp removal was contaminated by other blood in the field with a decreased accuracy of the sample.

Conclusion

From the findings of the present study we conclude that low potassium cardioplegia may have better myocardial protection effects in pediatric cardiac surgery with better clinical outcomes. It is also simple and cost-effective formulation compared to more complex formulations with multiple additives.

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