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Antegrade Intermittent Cold Cardioplegia in Comparison to Antegrade Intermittent Warm Cardioplegia in Heart Valve Surgery

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Abstract

Background: The cardioplegic arrest is essential for motionless and bloodless heart valve surgery. The objective of this work was to compare antegrade cold versus warm blood cardioplegia during valve surgery.

Methods: This randomized controlled study included 100 patients who had mitral valve surgery. Patients were randomly assigned into two groups; the warm cardioplegic group (n= 50) and the cold cardioplegic group (n= 50). Study endpoints were creatine kinase myocardial band, lactate dehydrogenase, and troponin levels.

Results: There was no significant difference in age and sex between groups (p= 0.51 and 0.56, respectively). Cardiopulmonary bypass was significantly longer in the cold group (85.66 ± 22.9 vs. 72.34 ± 25.09 minutes; P= 0.01); however, there was no difference in ischemic time (p= 0.32). The number of DC shocks given for each patient is less in the warm group with a median of 1.5 (range 1-3 times), while in the cold group, the median was 2 (range 2-4 times); p= 0.02. The amount of blood loss was significantly lower among the warm group (645.4 ± 464.93 ml vs. 404 ± 252.7 P< 0.01). warm group had significantly lower postoperative CK (532.78 ± 249.08 vs. 638.14 ± 344.01 IU/L; P< 0.01), CK-MB (78.64 ± 34.58 vs. 103.18 ± 82.11; P< 0.0.01), LDH level (805.3 ± 322.71 vs. 1060.88 ± 500.94 mg/dl; P< 0.01) and (0.4148 ± 0.226 vs. 0.6404 ± 0.411 ng/ml; P< 0.01).

Conclusion: Antegrade warm blood cardioplegia may provide better myocardial protection during valve surgery compared to the cold cardioplegia. A larger study is recommended.

KEYWORDS
Mitral valve replacement; Cardioplegia; Heart valve surgery; Blood cardioplegia

Introduction

The cardioplegic arrest is essential for motionless and bloodless heart valve surgery, in addition to myocardial protection during the ischemic period. Cardioplegia can be administered as a warm or cold solution, antegrade, or retrograde. Warm cardioplegia provides a more physiological environment and a protective effect against ischemia-reperfusion-induced apoptosis [1-2]. However, cold crystalloid cardioplegia decreases oxygen consumption because of the associated hypothermia.

Antegrade cardioplegia may not perfuse all myocardial segments homogeneously in patients with poor collaterals. The combination of antegrade and retrograde cardioplegia could overcome this problem and achieve better results [3].

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It is still debatable, which cardioplegia offers better protection and less cardiac injury reflected by postoperative troponin levels [4]. The objective of this work was to compare antegrade cold versus warm blood cardioplegia during valve surgery.

Patients and Methods:

This work was conducted according to the Code of Good Practice and the guidelines of the Declaration of Helsinki. The local Ethical Committee approved the study, and informed consent was obtained from all participants.

The study included 100 patients who had isolated mitral valve surgery between 2015 and 2018. Patients were randomly assigned to either cold or warm groups. Patients in the cold group (n= 50) received cold intermittent antegrade blood cardioplegia at moderate hypothermia (28ºC). The warm group patients (n= 50) received warm intermittent antegrade blood cardioplegia at normothermia.

Randomization was done using computer-generated random number tables and opaque sealed envelopes containing the patients' group allocation. All patients were blinded to the assignment.

We excluded patients with ischemic mitral valve regurgitation, concomitant cardiac surgery, patient with severe pulmonary hypertension pulmonary artery pressure (PAP) > 60 mmHg, low ejection fraction (EF) < 50%, and those required urgent or re-operative surgery.

Anesthetic technique

Induction of anesthesia was performed using fentanyl citrate and sodium thiopental. Patients were monitored using five-leads electrocardiography (ECG), invasive blood pressure line, and central venous pressure. Urine output was monitored via an indwelling Foleys catheter, and the esophageal temperature was monitored.

Cardiopulmonary Bypass Technique

The mean perfusion pressure was maintained between 60 and 90 mmHg. In the cold cardioplegia group, patients were cooled to 28ºC. The systemic flow was 2.2 L/m2 /min at 37ºC and 2 L/m2/min at 28ºC. In the warm group, the temperature was drifted to 34ºC, and the systemic blood flow was maintained at 2.2 L/m2 /min all the time.

Surgical technique

All patients had median sternotomy with aorto-bicaval cannulation. Exposure of the mitral valve was performed through the Sondergaard's groove.

Warm cardioplegia group

Normothermic blood (37◦c) was drawn from the oxygenator then infused into the aortic root. Syringe pump containing K+ in a concentration of 2 mEq/ml was connected to the cardioplegia line. The first dose of cardioplegia was 600 ml in 2 minutes; further doses of cardioplegia were given every 15-20 minutes.

Cold cardioplegia

We infused antegrade cold blood cardioplegia at a temperature of 4°C, into the aortic root. Cardioplegia solution was used, which is composed of 20 mmol/L of potassium, 144 mmol/L of sodium, 16 mm of magnesium, and one mmol/L of procaine. Blood was withdrawn from the cannula and mixed with the cardioplegia solution in a ratio of 1:4. The first dose of cold blood cardioplegia was 110 ml/kg; further doses of cardioplegia were 5 ml/kg and were given every 25-30 minutes. Systemic cooling was done up to 28°C. Topical cooling the arrested heart was done using ice slush.

Data collection

Preoperative and operative data were collected. The study outcomes were postoperative creatine kinase level (CK-MB), troponin, and lactate dehydrogenase (LDH).

Statistical Analysis

Continuous data were presented as mean, range, median, and standard deviation (SD) and categorical data as number and percent. The comparison of the continuous variables was performed using the Student t-test for parametric data. The Chi-square X^2 test or Fisher exact test was used for categorical data. P-value was significant if < 0.05. All statistical calculations were done using Microsoft Excel version 7 and SPSS version 20 (IBM Corp- Chicago- IL- USA).

Results

Baseline data

The mean age of patients in the cold group was 39.82 ± 13.74 years, and in the warm group was 44.06 ± 13.06 years. The number of males to female's ratio in the warm group was 1.3: 1, and in the cold group was 1:1. There were no significant differences between groups in age and sex. (Table 1)

Table 1: Age and sex among studied patients. Data expressed as frequency (percentage), mean (SD).

		Warm group (n= 50)	Cold warm (n= 50)	P
Age (year)		39.82 ± 13.74	44.06 ± 13.06	0.51
Sex	Male	28 (56%)	25 (50%)	0.56
	Female	22 (44%)	25 (50%)	

Operative data

Cardiopulmonary bypass (CPB) time was significantly higher in the cold group (85.66 ± 22.9 vs. 72.34 ± 25.09 minutes; P= 0.01). While the aortic cross-clamp time was insignificantly shorter in the cold group.

The need for DC shock to regain sinus rhythm was significantly lower in the warm group (8% vs. 34%; P= 0.01). Temporary ventricular pacemaker support was required in two patients in the cold group. The number of DC shocks given for each patient is less in the warm group with a median of 1.5 (range 1-3 times), while in the cold group, the median was 2 (range 2-4 times). The warm group required lower doses and duration of inotropic support. (Table 2)

Postoperative Data

The mean amount of postoperative bleeding was significantly higher in the cold group (645.4 ± 464.93 ml vs. 404 ± 252.7 P< 0.01). One case had left-sided hemiparesis in the warm group with no neurological events in the cold group. The time needed for extubation was significantly higher in the cold group.

The warm group had significantly lower postoperative CK (532.78 ± 249.08 vs. 638.14 ± 344.01 IU/L; P< 0.01), CK-MB (78.64 ± 34.58 vs. 103.18 ± 82.11; P< 0.0.01), LDH level (805.3 ± 322.71 vs. 1060.88 ± 500.94 mg/dl; P< 0.01) and troponin (0.4148 ± 0.226 vs. 0.6404 ± 0.411 ng/ml; P< 0.01). (Table 3)

Discussion

During periods of hypothermia, an imbalance between oxygen demand and supply may exist. Hypothermia is associated with reduced oxygen consumption, but a leftward shift of the oxygen dissociation curve and extracellular alkalosis may impair oxygen delivery to tissues [5]. Hypothermia has many effects on myocardial function; it inhibits calcium sequestration and myocardial enzymes, disrupts cellular membranes, decreases energy production, and reduces oxygen delivery. These effects can lead to poor recovery of cardiac performance after surgery [6].

The age of our population was lower compared to other published series [7]. This difference could be explained by the inclusion of patients with rheumatic pathology who are younger compared with patients with ischemic mitral valve disease.

Table 2: Operative data among studied patients. Data expressed as frequency (percentage), mean (SD).

		Warm group (n= 50)	Cold warm (n= 50)	P
Bypass time (minutes)		72.34 ± 25.09	85.66 ± 22.9	< 0.001
Aortic cross clamp time (minutes)		49.5 ± 19.34	44.24 ± 15.29	0.32
DC shock	Frequency (%)	4 (8%)	17 (34%)	< 0.001
	Median (range)	1.5 (1-3)	2 (2-4)	0.02
	Joules	25 ± 5.77	28.23 ± 14.24	0.12
Inotropes	Dose (mic/kg/min)	0.0482 ± 0.058	0.0842 ± 0.063	< 0.001
	Duration (hours)	13.68 ± 26.01	26.52 ± 25.66	< 0.001

Table 3: Post-0perative data among studied patients. Data expressed as frequency (percentage), mean (SD).

		Warm group (n= 50)	Cold warm (n= 50)	*P*
Bleeding (ml)		404 ± 252.7	645.4 ± 464.93	< 0.001
Time to recovery (hours)		8.88 ± 5.38	9.88 ± 4.11	0.95
Time of extubation (hours)		9.44 ± 6.19	10.54 ± 4.53	0.11
Laboratory data	Creatinine (mg/dl)	1.088 ± 0.21	1.19 ± 0.39	0.45
	Creatine kinase (IU/L)	532.78 ± 249.08	638.14 ± 344.01	0.03
	CK-MB (IU/L)	78.64 ± 34.58	103.18 ± 82.11	0.02
	Lactate dehydrogenase (mg/dl)	805.3 ± 322.71	1060.88 ± 500.94	< 0.001
	Troponin (ng/dl)	0.4148 ± 0.226	0.6404 ± 0.411	< 0.001

CK-MB: Creatine kinase-myocardial band

The total bypass time was higher in the cold group secondary to the time required for rewarming, which is consistent with the literature [8]. Cross-clamp time was found to be longer in the warm group because of the intermittent administration of cardioplegia.

Spontaneous recovery of sinus rhythm without DC shock was less marked in the cold group where only 17 patients (34%) of the cold group needed DC shock to return to sinus rhythm, while four patients (8 %) in the warm group needed DC shock to return to sinus rhythm. Additionally, the number of shocks given for each patient was higher in the cold group. This finding is compared to Kammerer's, who found that 10% of the warm group need DC shock to regain sinus rhythm, in comparison to 45% in the cold group [9]. Franke and colleagues noticed a higher need for defibrillation shock in the cold group, and the requirement of defibrillation was significantly lower in the warm group [10].

The cold group required more inotropic support. Our results are similar to what was reported by Nappi and coworkers, who found that the frequency of inotropic support use in the postoperative period was less in the warm group [11]. The increased need for inotropic support in the cold group is attributed to the increase in both pulmonary and systemic vascular resistance (SVR) during hypothermia, as was reported by Leslie and colleagues [12, 13].

Postoperative bleeding was significantly higher in the cold group, which is correlated with the results of Pelletier and coworkers who found that approximately 6% of the cold group required ex-exploration for bleeding versus 2% in the warm group [14]. Endothelial-associated coagulation platelet aggregation is reduced with hypothermia with increased risk of postoperative bleeding and increase the need for blood products [15]. Boldt found that postoperative bleeding and the demand for blood products were higher in the hypothermic group [16]. It was found that 10% to 20% of the cold group showed inefficient hemostasis that needed blood products transfusion, 3% required ex-exploration for bleeding [8, 17]. On the other hand, Boldt and associates found no difference in the number of platelets between both groups; however, there was thrombo-asthenia, which was higher with hypothermia [16].

We had one case of left-sided hemiparesis in the warm group with no neurological events in the cold group. The recovery of consciousness and ventilation times were lower in the warm group. This result correlates with what Craver and associates found. They reported higher incidence of postoperative neurologic sequelae in the normothermic group (4.7% versus 1.8%; p = 0.0380) [17]. Ikonomidis and associates found that the use of hyperkalemic blood avoided the need for infusing extra fluid to obtain cardioplegic arrest in the warm group. Unlike the cold group in whom a more cardioplegic volume was needed with resulting tissue and brain edema. This effect was not only reflected in the form of delayed recovery of conscious level and hence delayed extubation, but also lead to a higher total fluid imbalance in the postoperative period [18]. Singh found that stroke was not related to the systemic perfusion temperature. Still, it was related more to the preexisting cerebrovascular disease, or some alteration in the surgical techniques with dislodgment of debris and old age of patients with associated atherosclerosis [19].

The biomarkers of cardiac injury were higher in the cold group. Pelletier and colleagues found the levels of CK, CK-MB, and troponin were higher in the cold group [14]. Yau and coworkers found that CK-MB in the first two days postoperative was insignificantly lower in the warm group [8]. However, Chocorn and associates found that there was a significant increase in cardiac troponin I after cold cardioplegia in comparison to warm cardioplegia [20]. Ascione and coworkers found that the cold group had lower troponin release than the warm group and concluded that cold blood cardioplegia had less ischemic stress and myocardial damage in patients with aortic stenosis [21]. In a meta-analysis of randomized controlled trials (RCTs), there was no statistical difference between both groups regarding clinical outcomes; however, warm cardioplegia was associated with improved postoperative cardiac index with lower CK-MB and troponin [22].

Study limitations

The main limitation of the current study was the patients' number; however, we were able to find a difference in the study endpoints between groups. Moreover, all patients had mitral valve surgery, and generalization of the results to other surgeries may be an issue. Therefore, we recommend performing a larger study on more patients with different types of cardiac surgeries.

Conclusion

Antegrade warm blood cardioplegia may provide better myocardial protection during valve surgery compared to the cold cardioplegia. A larger study is recommended.

Conflict of interest: Authors declare no conflict of interest.

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