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ORIGINAL ARTICLE

Comparative Study between Bretschneider Cardioplegia and Warm Blood Cardioplegia on Myocardial Protection in Patients with Ischemic Mitral Regurgitation

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Abstract

Background: ***The ideal approach for myocardial preservation during ischemic cardiac arrest remains controversial. One dosage of cardioplegia for preservation of the myocardium is advocated in protracted surgeries.***

Aim: ***To explore the effects of Bretschneider cardioplegia and warm blood cardioplegia on myocardial protection in patients with ischemic mitral regurgitation following coronary artery bypass graft surgery with mitral valve replacement.***

Patient and Methods: ***This prospective study included 60 patients from the cardiothoracic surgery department at El-Hussein University Hospital and the National Heart Institute. The patients were divided into two groups: (A) thirty patients received Bretschneider cardioplegia, and (B) thirty patients received warm blood cardioplegia. Data from both groups were assembled and compared.***

Results: ***The mean CPB time in the Bretschneider group was 103.67 ± 30.57, while in the warm blood cardioplegia group, it was 121.73 ± 33.98 minutes. The mean of intensive care unit stays in the Bretschneider group was 2.70 ± 0.75 days, whilst in the warm blood cardioplegia group was 3.40 ± 1.07 days, the mean period of the mechanical ventilation in the Bretschneider group was 7 (6 – 9) while in warm blood cardioplegia group was 12 (10 - 18) hours. Troponin elevated: The Bretschneider group was in 3 patients (10%), while the warm blood group was in 19 patients (63.3%).***

Conclusion: ***Bretschneider's cardioplegia solution showed superiority in myocardial protection, reducing CPB and CCT, fewer inotropes used, less mechanical ventilation time, and less elevation of cardiac enzymes, resulting in reduced ICU and hospital stay.***

Keywords: Cardioplegia; Bretschneider; Warm blood; myocardial protection; Ischemic Mitral Regurgitation

1. Introduction

Ischemic mitral regurgitation (IMR) is a common complication following acute myocardial infarction (AMI) and is linked with a worse prognosis. IMR is one kind of secondary mitral regurgitation that arises from ischemic heart disease. There are two types of valvular involvement: primary (organic) and secondary (functional).

Primary IMR arises after the mitral subvalvular apparatus ruptures following an AMI. When the left ventricular geometry is altered, an imbalance between the closing and tethering forces on the mitral valve causes secondary IMR, while the chordae and valve leaflets remain structurally normal .[1] The best strategy for myocardial preservation during ischemic cardiac arrest is still being debated, particularly in open-heart surgery that necessitates a considerable cross-clamp time. Cardioplegic arrest and cardiopulmonary bypass are central points of myocardial injury during cardiac surgery .[2] Cardioplegia prevents osmotic and electrolyte imbalances, buffers acidosis, and preserves myocardial energy reserves to improve tolerance to ischemia and reperfusion .[3] Bretschneider cardioplegia is favored for cardiac operations because it is directed at one dosage and offers myocardial preservation for up to three hours, enabling multiple techniques without disruption. Bretschneider first described histidine tryptophan ketoglutarate (HTK) in the 1970s .[4]

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The extracellular mechanism of crystalloid cardioplegia results in sudden cardiac collapse due to abnormally high potassium and magnesium concentrations. HTK solution is an intracellular crystalloid cardioplegia with low calcium and sodium concentrations in the form of a solution that buffers intracellular acidosis and stocks the ancestors essential for anaerobic metabolism, in addition to reducing sodium concentration because of the hyperpolarized myocyte membrane, which causes cardiac arrest in the diastolic time .[5] This study pursued to compare the effects of Bretschneider cardioplegia and warm blood cardioplegia on myocardial protection in patients having ischemic mitral regurgitation following coronary artery bypass graft (CABG) surgery with mitral valve replacement.

2. Patients and methods

Ethical consideration:

Following a clear description of the potential adverse outcomes, all patients presented acceptance prior to the commencement of the study.

Design and patients:

Sixty patients with ischemic mitral regurgitation undergoing CABG surgery and mitral valve replacement at El-Hussein University Hospital and National Heart Institute were included in this prospective comparative study, carried out from March 2020 to December 2023. The patients were randomly divided into two groups based on the type of cardioplegia they received during surgery:

Group A encompassed 30 patients who received Bretschneider cardio, and Group B encompassed 30 patients who received warm blood cardioplegia. We excluded cases with rheumatic mitral regurgitation, patients with heart failure and hepatic failure, ischemic patients with aortic valve disease, patients in need of an emergent procedure, Redo patients with ischemic heart disease, and patients with a severe degree of pulmonary hypertension.

All patients underwent routine lab investigations, echocardiography, electrocardiogram, coronary angiography, and carotid duplex. General anesthesia and median sternotomy incision were performed during surgery on all patients in both groups, followed by pericardium opening, mammary artery, and SVG harvested. Moreover, both aortic and double venous cannulation were done in all cases. The cardioplegic arrest was carried out after establishing cardiopulmonary bypass and aortic cross-clamping. Cardioplegia was given to all the patients according to each group; mitral valve replacement was performed in all cases, while CABG surgery was performed according to the number of grafts needed. When homeostasis was accomplished, field closure was performed on layers, and the patients were admitted to the ICU on mechanical ventilation.

Statistical analysis

Data were assembled, reviewed, verified, and entered into the Statistical Package for Social Science (IBM-SPSS) version 23. The quantitative data are represented as mean, standard deviations, and ranges. Moreover, the qualitative variables were displayed as numbers and percentages. The Chi-square test was employed to compare the qualitative data between groups. Also, with quantitative data and a parametric distribution, the independent t-test was utilized to compare two independent groups. The confidence interval was 95%, while the acceptable margin of error was 5%. As a consequence, the following p-values were taken into account:

$p > 0.05$ indicates non-significant (NS)

$p < 0.05$ indicates significant (S)

$p < 0.01$ indicates highly significant (HS)

3. Results

This study encompassed sixty patients, 25 of them were males (38.3%) and 5 (16.7%) were females in (A) group (Bretschneider cardioplegia), while 26 patients (86.7%) were males and 5 (13.3%) were females in (B) group (Warm blood cardioplegia). In group (A) the mean of patients age was 51.53 ± 8.14 years and 51.83 ± 10.21 years for group B (Table 1).

24 patients (80%) had diabetes mellitus in (A) group, while 27 patients (90%) had diabetes mellitus in (B) group. Group (A) included 23 hypertension patients (76.7%) while Group (B) had 28 (93.3%).

The mean of ejection fraction in Group A was 38.10 ± 4.34, while 36.13 ± 4.23 in Group B, End diastole of patients in group A was 6.17 ± 0.26 and in Group B was 6.15 ± 0.35, the mean of the left ventricular end systolic diameter (LVESD) was 4.33 ± 0.62 in Bretschneider group and 4.97 ± 0.56 in the warm blood group; with no significant difference between the two groups. The left atrium (LA) was mild dilated in both groups. The mean of the LA size in Bretschneider group was 4.3 ± 0.5 and in the warm blood group was 4.4 ± 0.6; with no significant difference between the two groups. Regarding pre-operative NYHA classification: all patients in the 2 groups were classified as grade IV, with no significant difference between the 2 groups. Regarding number of grafts in group A patients 2.91 ± 1.091 and in group B 2.85 ± 0.937 (Table 2).

The results revealed that, cardiopulmonary bypass time mean in (A) group was 103.67 ±

30.57 while in (B) group B was 121.73 ± 33.98 minutes, and a cross-clamp time of 85.67 ± 18.13 in (A) group and 97.80 ± 21.85 in (B) group. Regarding re-dosing of cardioplegia one patient in group A needed re dosing (3.3%) while 30 (100.0%) needed re-dosing of cardioplegia in group B. regarding DC shock one patient (3.3%) used it in (A) group, whilst 24 patients in group B (80.0%) (Table 3).

The use of inotropic supports (adrenaline - levophed - doubtrix) early intraoperative and ICU supports (Adrenaline - Levophed - doubtrix) had significant variations between both groups with p-value 0.015, 0.017, 0.028, 0.010, 0.032 and 0.037 respectively (Table 4).

There was a slight increase in use of early post operative IABP in group B (6 patients 20%), and just one patient in group A used it (3.3 %), due to severe impairment of LV function. Arrhythmias occurred in group B in 10 patients (33.3 %) in the form of: atrial fibrillation (AF) occurred in 3 patients due to electrolyte disturbance and ischemia; ventricular fibrillation (VF) occurred in 6 patients due to ischemia; supraventricular tachycardia (SVT) occurred in 1 pateint due to ischemia. There was no arrhythmias happened in patients with group A 0.0%.

Regarding organ failure: no cases recorded in group A while 2 cases in group B complained from renal failure and needed dialysis mostly due to hypotension and HD instability. Moreover, stroke occurred in 1 case mostly due to cerebral embolism, HD instability and arrhythmia (VF type), with no statistically significant differences between the two groups.

Elevation of (cardiac enzymes) troponin early & after 12 h is recorded in 3 patients with group A 10% and 19 patients with group B 63.3% (Table 5).

Mechanical ventilation duration in group A median IQR 7h (6h – 9h) and in group B 12h (10 - 18).

In terms of postoperative echocardiography: it was done to all cases during hospital stay before discharge and there were no significant differences between the 2 groups regarding ED, ES, LA diameter with p values (0.4, 0.3, 0.6; respectively). There were statistically significant variations between the two groups, including ejection fraction (EF), myocardial preservation with group (A) was better than group (B), EF with group (A) was 37.57 ± 5.38 and with group (B) was 26.57 ± 7.16; with a high significant variation between the two groups (P-value 0.000). Staying on ICU with group A was decreased than group B (2.70 d± 0.75d, 3.40d ± 1.07d respectively), Hospital stay was prolonged with group B than group A (↑↑7.90 d± 1.88d, 6.67 d± 1.15 d respectively). Regarding post operative NYHA classification: 18 patients in A group and 8 patients in B group were classified as grade I and there was a significant difference between the 2 groups, p value (0.037). 7 patients in A group and 6 patients in B group were classified as grade II with no significant difference between the 2 groups, p value (0.07). 4 patients in A group and 7 patients in B group were classified as grade III with no significant difference between the 2 groups, p value (0.085). 1 patient in A group and 6 patients in B group were classified as grade IV and there was a significant difference between the 2 groups, p value (0.044). No cases recorded mortality with group A, while just 3 cases were recorded with group B with no significant differences (Table 6).

Table1. demonstrates no statistically significant change between Bretschneider and warm blood groups in terms of mean age and sex of the studied patients with p-value = 0.900 and 0.718 respectively.

		Cardioplegia		Test value	P-value	Sig.
		Bretschneider	Warm blood			
		No. = 30	No. = 30			
Age	Mean ± SD	51.53 ± 8.14	51.83 ± 10.21	-0.126•	0.900	NS
	Range	36 – 68	35 – 70			
Sex	Female	5 (16.7%)	4 (13.3%)	0.131*	0.718	NS
	Male	25 (83.3%)	26 (86.7%)			

Table 2. demonstrates no statistically significant change between Bretschneider and warm blood groups regarding HTN, DM, EF, ED) p-value = 0.071, 0.278, 0.081 and 0.836 respectively, NYHA classification all cases were classified as grade IV

		Cardioplegia		Test value	P-value	Sig.
		Bretschneider	Warm blood			
		No. = 30	No. = 30			
HTN	No	7 (23.3%)	2 (6.7%)	3.268*	0.071	NS
	Yes	23 (76.7%)	28 (93.3%)			

DM	No	6 (20.0%)	3 (10.0%)	1.176*	0.278	NS
	Yes	24 (80.0%)	27 (90.0%)			
Ejection fraction	Mean ± SD	38.10 ± 4.34	36.13 ± 4.23	1.777•	0.081	NS
	Range	30 – 46	27 – 45			
End diastole	Mean ± SD	6.17 ± 0.26	6.15 ± 0.35	0.208•	0.836	NS
	Range	5.7 – 6.7	5.4 – 6.9			
End systole	Mean ± SD	4.33 ± 0.62	4.97 ± 0.56	0.182	0.399	NS
	Range	3.7 – 4.9	4.32 – 5.62			
Left atrium	Mean ± SD	4.3 ± 0.5	4.4 ± 0.6	0.258	0.145	NS
	Range	3.8 – 4.8	3.8 – 5.0			
Mitral valve	Severe Regurge	30 (100.0%)	30 (100.0%)	NA	NA	NA
CA (number of grafts)	1	0 (0.0%)	4 (13.3%)	6.619*	0.085	NS
	2	12 (40.0%)	15 (50.0%)			
	3	17 (56.7%)	11 (36.7%)			
	4	1 (3.3%)	0 (0.0%)			
			0			NA
NYHA cassification	Grade I	0	0	NA	NA	NA
	Grade II	0	0	NA	NA	NA
	Grade III	0	30	NA	NA	NA
	Grade IV	30		NA	NA	

Table 3. demonstrates a significant variations between Bretschneider and warm blood groups in terms of CPB time, CCT and High statistically significant differences regarding Re-dosing , DC Shock with P-value = 0.035, 0.023, 0.000 and 0.000 of the studied patients respectively.

		Cardioplegia		Test value	P-value	Sig.
		Bretschneider	Warm blood			
		No. = 30	No. = 30			
CPB time	Mean ± SD	103.67 ± 30.57	121.73 ± 33.98	-2.165•	0.035	S
	Range	60 – 200	60 – 190			
CCT	Mean ± SD	85.67 ± 18.13	97.80 ± 21.85	-2.340•	0.023	S
	Range	50 – 130	50 – 120			
Re-dosing	No	29 (96.7%)	0 (0.0%)	56.129*	0.000	HS
	Yes	1 (3.3%)	30 (100.0%)			
DC Shock	No	29 (96.7%)	6 (20.0%)	36.274*	0.000	HS
	Yes	1 (3.3%)	24 (80.0%)			

Table 4. demonstrates a significant variation between Bretschneider and warm blood groups regarding Inotropes (Adrenaline, Levophed, Doubtrix) and ICU Supports (Adrenaline, Levophed, Doubtrix) of the studied patients with p-value 0.015, 0.017, 0.028, 0.010, 0.032 and 0.037 respectively.

		Cardioplegia				Test value*	P-value	Sig.
		Bretschneider		Warm blood				
		No.	%	No.	%			
Inotropes	Adrenaline	19	63.3%	27	90.0%	5.963	0.015	S
	Levophed	14	46.7%	23	76.7%	5.711	0.017	S
	Doubtrix	6	20.0%	14	46.7%	4.800	0.028	S
ICU supports	Adrenaline	17	56.7%	26	86.7%	6.648	0.010	S
	Levophed.	15	50.0%	23	76.7%	4.593	0.032	S
	Doubtrix	9	30.0%	17	56.7%	4.344	0.037	S

Table 5. demonstrates a significant variation between Bretschneider and warm blood groups in terms of IABP with p-value=0.044, and highly significant difference regarding Arrhythmias & Cardiac enzymes with P-value = 0.001, 0.000 respectively and there was no statistically significant variation regarding organ failure of the studied patients with p-value = 0.076.

		Cardioplegia				Test value*	P-value	Sig.
		Bretschneider		Warm blood				
		No.	%	No.	%			
IABP	No	29	96.7%	24	80.0%	4.043	0.044	S
	Yes	1	3.3%	6	20.0%			
Arrhythmias	No	30	100.0%	20	66.7%	12.000	0.001	HS
	Yes	0	0.0%	10	33.3%			

Organ Failure	No	30	100.0%	27	90.0%	3.158	0.076	NS
	Yes	0	0.0%	3	10.0%			
Cardiac Enzymes	No	27	90.0%	11	36.7%	18.373	0.000	HS
	Yes	3	10.0%	19	63.3%			

Table 6. demonstrates a high significant variation between Bretschneider and warm blood groups in terms of MV Duration (hours), Post EF, ICU Stay (days), Hospital Stay (days), of the studied patients with p-value = 0.000, 0.000, 0.005 and 0.003 respectively, and also no significant variation in mortality with p-value = 0.076, echo included ED, ES, and LA with p values 0.4, 0.3, 0.6 respectively.

		Cardioplegia		Test value	P-value	Sig.
		Bretschneider No. = 30	Warm blood No. = 30			
MV Duration (hours)	Median (IQR)	7 (6 – 9)	12 (10 - 18)	-4.114‡	0.000	HS
	Range	5 – 36	6 – 27			
Post EF	Mean ± SD	37.57 ± 5.38	26.57 ± 7.16	6.729•	0.000	HS
	Range	30 – 50	15 – 40			
End diastole	Mean ± SD	6.0 ± 0.1	5.9 ± 0.45	0.81	0.40	NS
End systole	Mean ± SD	4.1 ± 0.52	4.8 ± 0.42	0.91	0.3	NS
Left atrium	Mean ± SD	4.1 ± 0.3	4.2 ± 0.4	0.12	0.6	NS
Hospital Stay (days)	Mean ± SD	6.67 ± 1.15	††7.90 ± 1.88	-3.060•	0.003	HS
	Range	2 – 8	4 – 14			
Mortality	No	30 (100.0%)	27 (90.0%)	3.158*	0.076	NS
	Yes	0 (0.0%)	3 (10.0%)			
NYHA cassification	Grade I	18	8	4.344	0.037	S
	Grade II	7	6	3.581	0.070	NS
	Grade III	4	7	1.88	0.085	NS
	Grade IV	1	6	4.044	0.044	S

4. Discussion

Bretschneider solution can protect the heart for over two hours with a single dosage, which saves time and prevents interruption during surgery to re-administer the cardioplegic solutions (as occur with other cardioplegic solutions, which only provide about 30 minutes of protection) .[6] Our study encompassed sixty cases that were divided into two groups: (A) group (n=30) received Bretschneider cardioplegia, and (B) group (n=30) received warm blood cardioplegia. Complete examinations and lab investigations were performed on all cases and demonstrated that:

Fifty-one cases (85%) were diabetics; hypertension was diagnosed in 85% of the cases, which was comparable with Okba et al.[7], Jacquet et al.[8], and Scrascia et al.[9]. Preoperative echocardiography was routinely requested to assess the ejection fraction and mitral aortic pulmonary valves. The ejection fraction mean was [37.12 ± 4.37], in agreement with other previous studies[10] and[11].

This study demonstrated that the cardiopulmonary bypass time in Group A was 103.67 ± 30.57, and Group B was 121.73 ± 33.98. The cross-clamp time mean in Group A was 85.67 ± 18.13, and in Group B was 97.80 ± 21.85, showing a statistically significant difference that agrees with Albadrani[11] and contrary with Okbaet al.[7] and Jacquet et al.[8].

The results revealed that the ICU stay mean in the (A) group was 2.70 ± 0.75 d. and in Group B, it was 3.40 ± 1.07 with a p-value of 0.005. Our study revealed that the mechanical ventilation time means in the Bretschneider group was seven h (6 – 9) and in the warm blood group was 12 (10 - 18) with a p-value of 0.000, indicating a high statistical variation between both groups, demonstrating that HTK solution was superior to the crystalloid cardioplegia, which was consistent with Okba et al.[7] Jacquet et al.[8], Scrascia et al.[9], Ali et al.[10], and Albadrani[11].

In terms of cardiac enzymes, troponin-T was early elevated in 3 patients who used Bretschneider cardioplegia and in 19 patients who used warm blood cardioplegia, which demonstrates a high statistically significant variation between the two groups according to cardiac enzymes with a p-value of 0.000, which is in agreement with Okba et al.[7], Jacquet et al.[8], and Scrascia et al.[9].

The echocardiography performed postoperatively indicated that the mean ejection fraction in the (A) group became 37.57 ± 5.38, whereas 26.57 ± 7.16 in the (B) group. Our results demonstrated that Bretschneider cardioplegia was better than warm blood cardioplegia with a high significant variation between the two groups with a p-value of 0.000 inconsistent with Okba et al.[7], Jacquet et al.[8], and Scrascia et al.[9] and in contrary with Ali et al.[10] and Albadrani[11] who explored that there were not any significant changes in their studies.

Our results demonstrated a significant variation between both groups, with a p-value of 0.003 in the hospital stay, since it was reduced with group A using Bretschneider cardioplegia while group B was prolonged. Our study was consistent with

Okba et al.[7], Jacquet et al.[8], Scrascia et al.[9], Ali et al. [10], and Albadrani[11].

Regarding mortality in our study, no cases were recorded in the Bretschneider cardioplegia group, while three cases died in the warm blood cardioplegia group. The first case died due to myocardial swelling and heart failure, which occurred due to progressive impairment of LV function. The second case died due to a stroke caused by cerebral embolism, which was diagnosed by CT brain, and atrial fibrillation, which was diagnosed by ECG, which led to prolonged time on mechanical ventilation, HD instability, and cardiac arrest. The third case died due to renal failure, which occurred due to a decrease in cardiac output, HD instability, and hypotension that led to cardiac arrest. There were no significant variations between both groups, with a p-value of 0.076. Our study was consistent with Okba et al.[7], Jacquet et al.[8], Scrascia et al.[9], Ali et al. [10], and Albadrani[11].

4. Conclusion

In the majority of the characteristics that were assessed, the Bretschneider cardioplegia solution was just as secure and effective as the cardioplegic solutions that were currently in use. Moreover, it showed advantages in myocardial protection, reducing CPB & CCT, less disruption during surgery as it provided two to three hours of protection every dose, less inotropic supports used, less mechanical ventilation time, less occurrence of arrhythmias, less elevation of cardiac enzymes (troponin), results in reducing ICU and hospital stay, Given its high efficiency and simple administration and decreasing hospital cost.

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

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