



MYOCARDIAL DAMAGE; FREQUENCY OF PATIENTS UNDERGOING CABG RECEIVING INTERMITTENT ANTEGRADE WARM BLOOD CARDIOPLEGIA AT EXTENDED INTERVAL

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INTRODUCTION

The concept of Warm blood cardioplegia was for the first time introduced by Salerno and associates¹ and Liechtenstein and associates². Many studies have demonstrated that continuous warm blood cardioplegia is superior to cold blood cardioplegia in preserving myocardial metabolic and functional recovery^{3,4}. Before that intermittent cold crystalloid and cold blood cardioplegia were used for myocardial protection. The theory which favored warm blood cardioplegia was that the O₂ consumption of the heart is reduced to 90% below the baseline values when it is arrested by K⁺ enriched normothermic blood, while there

ABSTRACT... Background: Intermittent antegrade warm blood cardioplegia is routinely used as a mean of myocardial protection since its introduction. There is a considerable debate on the longest time off cardioplegia interval during aortic cross clamping. **Objective:** To see the frequency and extent of myocardial damage in patients undergoing CABG receiving intermittent antegrade warm blood Cardioplegia at LTOC (longest time off cardioplegia) 11-15 minutes (Group I) and 16-20 minutes (Group II). **Patients and Methods:** A randomized prospective study involving 94 patients was arranged to see the safe periods of intermittency. There were two groups of patients having LTOC of 11-15 minutes (Group I) and 16-20 minutes (Group II). 20 minutes was the upper limit. The duration of study was from 1-09-2013 to 10-02-2014. Data was analyzed using SPSS Version 16. Independent sample t-test and chi-square were applied to see the significance. **Results:** Mean age was 54.1±9.36 years. There were more males as compared to females. More than 50% of the patients had Hypertension and Diabetes. There was no urgent surgery. Triple vessel disease (TVD) was present in 48.9% patients and 40.4% had Double vessel disease (DVD). Average blood flow during CPB was 2.4±0.14 (L/min.m²). Average body temperatures were 31.7±2.3°C. Cardioplegia temperature was 36-37°C. According to Left Ventricular Function Classification, 43.6% of the patients were of LV grade II and 10.6% of LV grade III. There was no significant increase in the levels of CK-MB in two groups. 77.8% patient in Group I and 66.7% in Group II gained spontaneous rhythm (p-value 0.16). IABP was inserted in 5.4% patients in group I and 5.6% in group II (p-value 0.97). There was no failure to wean off from bypass and no peri-operative mortality. The levels of inotropes viz dopamine and epinephrine on weaning were also almost the same. Perioperative MI occurred only in 7 patients (ruled out by biochemical evidence). **Conclusions:** A reasonable margin of safety exists with intermittent antegrade warm blood cardioplegia in these two groups. So the LTOC (longest time off cardioplegia) up to 20 minutes is unlikely to lead to adverse clinical outcomes and is clinically acceptable.

Key words: Warm blood cardioplegia, Coronary artery bypass grafting, Intra-aortic Balloon Pump, Myocardial infarction.

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is only a slight reduction in O₂ consumption (7-8%) when the temperature is lowered to about 11°C⁵. The gradual evolution of continuous warm blood cardioplegia then led to the development of intermittent antegrade warm blood cardioplegia as a mean of myocardial protection in 1995⁶. Intermittent antegrade warm blood cardioplegia is now used worldwide and in Pakistan to arrest and protect the heart. Because Warm blood cardioplegia cannot protect the heart for extended intermittency therefore this study was conducted to see the frequency of myocardial damage and to find whether the extended intermittency is harmful to the myocardium or not.

PATIENTS AND METHODS

A randomized prospective study of 94 patients was performed at Punjab Institute of Cardiology, Lahore. Duration of study was from 1-09-2011 to 10-02-2012. There was a follow up of three days after surgery. There were two groups of patients having LTOC (longest time off cardioplegia) of 11-15 minutes (Group I) including 36 patients and 16-20 minutes (Group II) including 54 patients.

The data was analyzed using SPSS 16 software. Independent sample t-test was applied to compare quantitative variables and Chi-square test was used to analyze the qualitative variables.

All patients undergoing on-pump CABG surgery were included in the study regardless of age and gender. In exclusion criteria, patients having MI less than 15 days before surgery, having carotid artery stenosis of <70%, and the patients undergoing any other surgery along with CABG (e.g. Valvular surgery or ASD or VSD closure) were excluded from this study.

Operative outcomes: The dose of Dopamine and Epinephrine on weaning was noted. Serial blood sample for CK-MB were taken at 0, 12 and 24 hours after surgery. Samples were analyzed in the laboratory of the hospital. Enzymatic criteria were used to identify Peri-operative MI. A five fold increase in the levels of CK-MB above baseline values i.e. above 125 IU/L was considered as MI.

RESULTS

In Table I demographic, angiographic and operative characteristics of the patients are given. And in Table II the operative and post-operative outcomes of the patients of Group I and Group II.

Criteria for LV Grade was set on the basis of ECHO using the estimated ejection fraction values (Grade I= E.F >60%, Grade II= E.F 40-59%, Grade III= E.F 20-39%, Grade IV= E.F <20%).

More than 50% of the patients were diabetic and hypertensive. 29.8% of the patients had a family history of Ischemic Heart Disease. The average temperature during surgery, blood flow, number of

Mean age	54.1±9.36
Male sex (%)	75.5 %
Female sex (%)	24.5 %
Vessel Involvement	
Single vessel	10.6 %
Double vessel	40.4 %
Triple vessel	48.9 %
LV Grade (Ejection Fraction)	
Grade I	44.7 %
Grade II	43.6 %
Grade III	10.6 %
Grade IV	1.1 %
Peri-Operative Characteristics	
Average temp. during surgery (°C)	31.7±2.3
Blood flow (L/min/m ²)	2.42±0.14
Total no. of grafts	2.6±0.91
Total no. of Anastomoses	4.5±1.84
Table-I. Demographic, angiographic & operative characteristics	

grafts constructed, and total no. of anastomoses were almost the same in these two groups.

LTOC=longest time off cardioplegia, MI= Myocardial Infarction, IABP= Intra-aortic Balloon Pump, CK-MB= Creatinine Kinase MB. Enzymatic criteria for peri-operative MI is a five fold increase in the levels of CK-MB above baseline values i.e. above 125 IU/L.

There were no significant differences in the outcomes of Group I and Group II. Total Bypass time and total X-clamp time were significantly higher in Group II (p-values 0.003 and 0.006 respectively). There were small differences in the amounts of Dopamine and Epinephrine on weaning. Rate of Spontaneous Rhythm, Peri-operative MI, and IABP used were almost same (p-values 0.82, 0.92, 0.38 respectively). CK-MB levels were little high in Group II patients but the p-value was insignificant (0.35). And these outcomes were within the acceptable limits of myocardial damage during surgery. So we found almost similar outcomes in Group I and Group II.

	LTOC 11-15 Minutes	LTOC 16-20 Minutes	p-values
Mean LTOC (min)	14.3±1.33	18.4±1.48	
Total Bypass time (min)	94.5±27.8	113±31.09	0.003
Total X-clamp time (min)	44.3±17.18	55.7±18.8	0.006
Dopamine on weaning (ug/kg/min)	5.15±2.0	5.32±2.9	0.85
Epinephrine on weaning (ug/kg/min)	0.13±0.2	0.09±0.06	0.21
Spontaneous Rhythm (%)	77.8%	66.7%	0.16
Peri-operative MI (Enzymatic criteria)	3 (8.1%)	4 (7.5%)	0.95
IABP used (%)	2 (5.4%)	3 (5.6%)	0.97
Post-op. CK-MB levels (IU/L)	43.8±21.14	48.6±25.47	0.35

Table-II. Comparison between the means of two groups

LTOC=longest time off cardioplegia, MI= Myocardial Infarction, IABP= Intra-aortic Balloon Pump, CK-MB= Creatinine Kinase MB. Enzymatic criteria for peri-operative MI is a five fold increase in the levels of CK-MB above baseline values i.e. above 125 IU/L.

DISCUSSIONS

CAD is a main cause of death and a major cause of morbidity and deterioration in the quality of life⁷. According to a study coronary artery disease will remain the leading cause of death in the next 18 years⁸.

The population of Pakistan in 2009 was estimated as 163 million and CAD estimated as 5.09375 million. It was more common in men than women⁹. According to a study conducted in Karachi involving urban population of age more than 40 years in 2004, prevalence of CAD was 26.9%: 23.7% in men and 30.0% in women over 40 years of age¹⁰.

Salerno et al demonstrated, if we assume that the risk of ischemia and reperfusion injury is avoided, then the continuous infusion of cardioplegia without interruption might be the ideal way to protect the myocardium. Later on many researches proved that it is possible to interrupt the cardioplegia infusion without damaging the myocardium as Calafiore and associates proposed that intermittent antegrade warm blood cardioplegia is a safe and reliable technique of myocardial protection⁶. Lichtenstein et al. concluded that shorter periods of interruptions are as safely tolerated as with cold blood cardioplegia and extended intervals may be associated with adverse outcomes. They also concluded that the LTOC of =13 minutes is a safe period of

intermittency¹¹. Fan et al demonstrated that warm blood cardioplegia resulted in significant improvement in postoperative cardiac index and reduction in postoperative enzyme release¹². Other authors also proved similar results¹³. But these authors do not commented on the longest off cardioplegia. Therefore we conducted this study to see whether extended intermittency is harmful to the myocardium or not. It was Ali and Kinley who reported that intermittent warm blood cardioplegia is as safe as cold blood cardioplegia until the X-clamp time is <90 minutes at LTOC of 15 minutes but extra precautions are needed for longer X-clamp times as it increases the risk of Global ischemia and Peri-operative MI¹⁴. In this study, there were 3 patients having X-clamp time more than 90 minutes. All of these patients were of Group II. But all of these 3 patients gained spontaneous rhythm and none of these developed peri-operative MI, nor did they require IABP support.

However, in our study there were no significant differences in the outcomes of these two groups. CKMB levels were little high in Group II (48.6±25.47) than in Group I (43.8±21.14) IU/L. The rate of Peri-operative MI in the study of Lichtenstein and associates was high in that it was 9.6% and 15.7% by enzymatic criteria at LTOC of 12-13 minutes and >13 minutes respectively. In this study, the rate of peri-operative MI was 8.1% and 7.5% in Group I and Group II respectively.

which was less than their study.

Calafiore et al and Pelletier and colleagues¹⁵ also proposed that IAWBC is a safe technique of myocardial protection. The maximum LTOC in these two studies were not more than 15 minutes. The peak CKMB levels were 38 ± 38 and 36.3 ± 5.7 IU/L.

In the study of Calafiore and associates none of the patients required IABP support among 250 patients. In this study, 5.5% of patients required IABP support. In their study the rate of spontaneous rhythm was 99.2% and in our study this rate 77.8% in Group I and 66.7% in Group II. This was considerably less than their study. Our CKMB levels were also little high as compared to their study. Our results were more closely related to the study of Pelletier et al. The rate of spontaneous rhythm and CKMB levels in GROUP I were almost the same as their study, but CKMB levels of Group II were a little high.

Christakis and associates¹⁶ also reported that IAWBC is a safe technique for myocardial protection as it is associated with a higher rate of spontaneous rhythm after unclamping the aorta. They also found that higher concentration of K^+ is required to completely stop electrical activity in patients receiving normo-thermic cardioplegia. We used higher concentrations of K^+ (30 mEq/L) and there was no incidence of spontaneous beating during X-clamp in Group I and Group II.

CONCLUSIONS

Our study showed that there is no significant difference in the peri-operative and post-operative parameters of patients in these two groups. It has been proved beyond doubt that LTOC = 15 minutes is the most widely accepted interval as reported by Lichtenstein, Ali, Calafiore and Pelletier, but we can extend it further to 20 minutes without giving any serious harm to myocardium.

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He who knows all the
Answers has not been asked
all the **Questions**.

Confucius

