ORIGINAL ARTICLE

Clinical outcomes of intermittent antegrade warm versus cold blood cardioplegia

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Abstract

Objectives: To compare clinical outcome in patients undergoing conventional coronary artery bypass graft surgery who received intermittent antegrade warm blood cardioplegia or intermittent antegrade cold blood cardioplegia for myocardial protection.

Methods: The observational, prospective non-randomised analytical comparative study was conducted at the Punjab Institute of Cardiology, Lahore, and Chaudhry Pervaiz Elahi Institute of Cardiology, Multan, from September 2012 to October 2013, and comprised patients undergoing coronary artery bypass graft surgery. They were divided into two groups, with Group I having those who received intermittent antegrade warm blood cardioplegia, and Group II having those who received intermittent antegrade cold blood cardioplegia. SPSS 16 was used for statistical analysis.

Results: Of the 215 patients, 94(44%) were in Group I, and 121(56%) in Group II. Total surgical time in Group II was 119.26±22.24 minutes compared to 105.73±31.34 in Group I ($p > 0.0001$). Spontaneous resumption of sinus rhythm and peri-operative myocardial infarction was statistically insignificant ($p>0.05$). There were 21(17.4%) patients in Group II to whom peri-operative myocardial infarction occurred compared to 9(9.6%) in Group I ($p=0.10$).

Conclusion: Intermittent antegrade warm blood cardioplegia showed better myocardial protection in early postoperative period compared to intermittent antegrade cold blood cardioplegia.

Keywords: Intermittent antegrade warm blood cardioplegia, Intermittent antegrade cold blood cardioplegia, Myocardial protection. (JPMA 65: 593; 2015)

Introduction

Variety of cardioplegia composition, route of delivery and related myocardial protection strategies are well established in clinical practice.[1] The concept of warm blood cardioplegia was introduced first.[2,3] And then the safety and efficacy of intermittent antegrade warm blood cardioplegia (IAWBC) was proven.[4] Before that intermittent cold crystalloid and cold blood cardioplegia was the most widely used methods of myocardial protection. The basic concept which favoured the use of warm blood cardioplegia was that the oxygen (O_2) consumption of the heart is reduced to 90% below the baseline values when it is arrested by K^{+-} enriched normothermic blood, while there is only a slight reduction in O_2 consumption (7-8%) when the temperature is lowered to about 11°C.[5] Cold blood cardioplegia (10°C) protects the myocardium from ischaemic injury but inhibits mitochondrial respiration and raises coronary vascular resistance, resulting in delayed recovery of postoperative ventricular function.[6]

Both cold and warm cardioplegia are widely used methods of myocardial protection. Some studies have demonstrated the superiority of one cardioplegia temperature over the other.[7-9] Other studies have been unable to demonstrate any difference. Which of these two has better clinical outcome profile is important from the clinical standpoint.

The current study was planned to compare the clinical outcomes in patients undergoing conventional coronary artery bypass graft surgery (CABG) who received IAWBC or intermittent antegrade cold blood cardioplegia (IACBC) for myocardial protection.

Patients and Methods

The observational, prospective non-randomised analytical comparative study was conducted at the Punjab Institute of Cardiology, Lahore, and Chaudhry Pervaiz Elahi Institute of Cardiology, Multan, from September 2012 to October 2013, and comprised patients undergoing CABG surgery. They were divided into two groups, with Group I having those who received IAWBC, and Group II having those who received IACBC.

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The sample size was calculated using the results of a previous study.[4] At level of significance (α) of 5% and Power of the test (1-β) of 80%, the calculated sample size was 68 individuals in each group. We took more individuals in each group to make the study more reliable.

Patients having acute myocardial infarction (MI) less than 7 days before surgery, concomitant cardiac procedure (valve repair/replacement or congenital heart disease repair) and those who needed carotid end-arteractomy, peri-operative cardiac massage and patients with major immediate post-operative stroke after surgery were excluded.

Cardiopulmonary bypass was instituted using two-stage single venous cannula and a straight tip ascending aortic cannula. An antegrade aortic root cardioplegia cannula was used to administer cardioplegia. Manual cardioplegia system (using pressure bag) was used for warm blood cardioplegia delivery. Cardioplegia delivery system (myotherm, medtronic inc.) was used for cold blood cardioplegia delivery. Membrane Oxygenator and roller pump were employed during standard cardiopulmonary bypass. Blood flow during surgery was maintained at ~2.0-2.4 $l/min.m^{-2}$ at mild hypothermia. Arterial pressure was maintained at about 55-65mmHg. Haematocrit was maintained between 25%-30%. Systemic temperature was maintained between 30-32°C during surgery.

Cold blood cardioplegia was prepared by mixing four parts of blood with one part of crystalloids (4:1). Warm blood cardioplegia was containing blood only. Initially 15ml/kg high dose K^{+-} enriched blood cardioplegia containing 25meq/L of K^+ in cold cardioplegia and 30meq/L of K^+ in warm cardioplegia was utilised to arrest the heart in first cardioplegia dose. Subsequently arrest was maintained by using low K^{+-} in both warm and cold blood cardioplegia (10-15meq/L). Cardioplegia was repeated after every graft or after 20 minutes if the graft time prolonged. Graft patency was checked by giving 20ml of cardioplegia through it. Left internal mammary artery graft and saphenous vein were used as conduit.

The total doses of Epinephrine (Ug/kg/min) on weaning from cardiopulmonary bypass (CPB), spontaneous resumption of sinus rhythm after release of aortic cross clamp and need for Intra-aortic Balloon Pump (IABP) support were noted. Serial blood sample for Creatinine Kinase Myocardial Band (CK-MB) were taken at shifting to intensive care unit (ICU), 12 and 24 hours after surgery. Peak levels of CK-MB were noted in both groups. Enzymatic criteria were used to identify peri-operative MI. A fivefold increase in the levels of CK-MB above baseline values i.e. above 125 IU/L was considered MI.

Data was analysed using SPSS 16. Shapiro-Wilk's test was used to check the skewness in quantitative variables. Independent sample t-test was used to compare normally distributed quantitative variables and Mann-Whitney U test was used to compare skewed variables. Chi-square test and Fisher's exact test were used to compare qualitative clinical outcomes between the groups.

Results

Of the 215 patients, 94(44%) were in Group I with a mean age of 54.61±7.85 years, and 121(56%) in Group II with a mean age of 53.85±9.32 years (Table-1). Total surgical time in Group II was 119.26±22.24 minutes compared to 105.73±31.34 in Group I ($p > 0.0001$). Spontaneous resumption of sinus rhythm and peri-operative myocardial infarction was statistically insignificant ($p > 0.05$). There were 21(17.4%) patients in Group II to whom peri-operative myocardial infarction occurred compared to 9(9.6%) in Group I (p=0.10).

Aortic cross clamp time in Group II was 65.71±13.58 minutes versus 62.52±13.38 minutes in Group I (p=0.08). Doses of epinephrine on weaning were significantly low in Group II (p=0.006). Frequency of IABP use and post-operative peak CK-MB levels were significantly high in Group II ($p < 0.05$). IABP was inserted in 14(12.6%) patients in Group II compared to only 4(4.3%) in Group I (p=0.03).

Table-1: Comparison of Demographic, Echocardiographic and Angiographic Characteristics of Patients of Group I and Group II.

Variable	Group I IAWBC n=94	Group II IACBC n=121	P-Value
Mean Age (years)	54.61±7.85	53.85±9.32	0.51
Gender			
Male	71 (75.5%)	107 (88.4%)	0.01
Female (%)	23 (24.5%)	14 (11.6%)	
Diabetes history (%)	36 (38.3%)	42 (34.7%)	0.58
Smoking history (%)	33 (35.1%)	53 (43.8%)	0.19
Hypertension (%)	55 (58.5%)	57 (47.1%)	0.09
Coronary Artery Disease TVD*			
DVD**	80 (85.1%)	110(90.9%)	
TVD+LMS*** Disease (%)	10 (10.6%)	8 (6.6%)	0.42
	4 (4.3%)	3 (2.5%)	
Mean Ejection Fraction (EF)	51.94±10.16	51.73±10.03	0.88
Left Ventricular Function			
Grade I	69 (73.4%)	85 (70.2%)	
Grade II	16 (17.0%)	16 (13.2%)	0.28
Grade III	9 (9.6%)	20 (16.6%)	

*TVD: Triple Vessel Disease, **DVD:Double Vessel Disease, ***LMS:Left main stem
Criteria for Left Ventricular Functional Grades;
Grade I= E.F >50%, Grade II=E.F 50-35%, Grade III= E.F <35%.

Table-2: Comparison of operative findings and post-operative outcomes.

Variable	Group I IAWBC n=94	Group II IACBC n=121	P-Value
Mean Total Bypass time (min)	105.73±31.34	119.26±22.24	>0.0001
Mean Total X-clamp time (min)	62.52±13.38	65.71±13.58	0.08
Mean No. of Grafts	3.26 + 0.71	3.36 + 0.53	0.430
Epinephrine on weaning (Ug/kg/min)	0.107±0.14	0.077±0.10	0.006
Spontaneous resumption of sinus rhythm (%)	81 (86.2%)	91 (75.8%)	0.06
Peri-operative MI† (%)	9 (9.6%)	21 (17.4%)	0.10
IABP used± (%)	4 (4.3%)	15 (12.6%)	0.03
Post-op. CK-MB‡ levels (IU/L) (Mean±S.D)	70.50±38.03	106.19±94.28	>0.0001

†MI: Myocardial Infarction, ±IABP: Intra-aortic Balloon Pump, ‡CK-MB:Creatinine Kinase Myocardial Band.
SD: Standard deviation.

Peak post-operative CK-MB levels in Group II were 106.19±94.28 IU/L and 70.50±38.03 in Group I (p >0.0001) (Table-2).

Discussion

Warm blood cardioplegia came into clinical use by the warm heart surgery investigators group.[2,3] The idea of warm blood cardioplegia was based on a study that found that normothermic arrested heart requires 80-90% less oxygen than does the normal working heart and from reports that indicated that 'Hot Shot' has significantly positive effects on myocardial recovery.[10,11] The deliberate use of IAWBC was for the first time reported in a retrospective study.[4]

One study concluded that warm and cold cardioplegia result in similar short-term mortality. It also concluded that large studies have shown that warm cardioplegia reduces adverse postoperative events.[12] Almost similar results were also reported in another study.[13] One research demonstrated that IACBC is better in patients with long aortic cross clamp times.[8] Difficulties in reaching a definitive conclusion regarding the optimal cardioplegia temperature are that different patient populations may benefit from different cardioplegia regimens. Therefore, we conducted this study to compare clinical outcomes in patients who received IAWBC with patients in which IACBC was used for myocardial protection during aortic cross clamp times to find out which technique is better for our population.

In this study, the IAWBC technique was modified by lowering the cardioplegia temperature to the systemic perfusion temperature of 30-32°C. Because body temperature during CPB is another controversial issue.[14,15] Some studies have clearly reported a higher incidence of neurologic events during normothermic CPB.[16] In our study, total bypass time was significantly high in Group II but the cross clamp time was not significantly different.

A study described a failure rate of 13% to achieve sustained electromechanical arrest by use of warm blood cardioplegia.[17] However, higher K+ concentration in IAWBC can prevent this failure. Ventricular arrhythmia, low operative mortality, less frequency of IABP use and less demand of inotropes on CPB weaning is reported with IAWBC compared to IACBC. Another study found similar results regarding per-operative MI, requirements for defibrillation (spontaneous rhythm) and lower mortality rates, and reduced post-operative ventilation time in IAWBC group.[9] Biochemical markers of myocardial injury i.e. CK-MB and Troponin T, have shown better laboratory profile while using IAWBC.[9,18-20]

Less than optimal myocardial protection with IACBC is assumed to be caused by disturbance of cardiac metabolism in response to hypothermia. Adenosine tri-phosphate dependent reactions are impaired and result in negative influence on membrane stability, energy production, enzymatic functions, aerobic glucose utilisation, adenosine tri-phosphate generation and its utilisation, cyclic adenosine mono-phosphate production, and osmotic homeostasis.[4,21] IAWBC is free of above-mentioned effects on myocardial metabolism. In this study, better myocardial metabolic milieu created by IAWBC over IACBC become apparent with better clinical outcome intra-operatively and in early postoperative period.

The small sample size is a limitation of our study. Intra-operative myocardial temperature was not measured during cardioplaegic arrest. Utilisation of similar operative strategies in both groups overcome these limitations.

Conclusion

IAWBC showed better myocardial protection with less frequent use of IABP and less peak CK-MB level in early postoperative period compared to IACBC.

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