Original Article

Cold Crystalloid Versus Warm Blood Cardioplegia for Coronary Artery Bypass Surgery

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Purpose: Intermittent cold crystalloid cardioplegia by antegrade route to arrest the heart for coronary artery bypass grafting (CABG) is a commonly used technique. The aim of this study is to compare the intermittent antegrade warm blood cardioplegia with cold crystalloid cardioplegia by means of measuring myocardial injury markers CKMB and troponin T. We also compared the results with antegrade and retrograde warm blood cardioplegia.

Materials and Methods: Patients (n=30) undergoing CABG were prospectively randomized into group 1 (n=10) which received cold crystalloid cardioplegia by antegrade route, group 2 (n=10) which received warm blood cardioplegia by antegrade route and group 3 (n=10) which received antegrade/retrograde warm blood cardioplegia.

Results: Preoperative and intraoperative variables were equal in all three groups. Control levels of troponin T and CKMB were in a normal range. Postoperative troponin T was significantly lower in group 3 compared to group 2 (*p*"=0.008") and to group 1 (*p*"=0.005"). CKMB is significantly higher in group 1 compared to group 2 (*p*"=0.013") and higher in group 2 than that in group 3 (*p*"=0.043").

Conclusion: Antegrade with retrograde warm blood cardioplegia is a simple delivery method. Troponin T and CKMB levels were significantly lower, suggesting that this offered better myocardial protection than antegrade cold crystalloid and warm blood cardioplegia. We recommend its wider use. (Ann Thorac Cardiovasc Surg 2005; 11: 382–5)

Key words: coronary artery bypass surgery, cardioplegia, troponin T

Introduction

The optimal delivery of cardioplegia, multiplicity of cardioplegia solutions available, patient selection, and the methods used to determine myocardial injury have made it difficult to accurately determine which form of cardioplegia is best.[1] There is some clinical evidence however that showed warm blood cardioplegia to be superior in metabolic and functional recovery over crystalloid cardioplegia.[2-4] Blood cardioplegia is superior to crystalloid cardioplegia in inhibiting proteins responsible for ischemia-reperfusion-induced apoptosis.[5] Homogeneous perfusion of all segments of myocardium may be limited by applying antegrade cardioplegia to badly collateralized coronary artery stenosis. Retrograde administration through the coronary sinus seems to offer a solution for this problem.[6,7] Combination routes of antegrade and retrograde intermittent blood cardioplegia allows better results in left main stenosis, with increased ventricular mass and impaired micro vascular circulation.[8] Troponin T was shown to be a more specific marker of myocardial muscle damage then other ischemic markers.[9] Therefore troponin T should be sensitive to detect minor injuries due to inhomogeneous myocardial protection.

We therefore investigated the differences of our previous method of cold crystalloid antegrade cardioplegia with warm blood antegrade cardioplegia and also compared it with antegrade and retrograde warm blood cardioplegia, all given intermittently.

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Materials and Methods

Thirty patients admitted for elective isolated, primary coronary artery bypass grafting (CABG) were prospectively randomized into three groups. In group 1, antegrade cold crystalloid cardioplegia (Martindale) was given intermittently. In group 2, intermittent warm blood cardioplegia (4:1) was given by antegrade route, and in group 3, warm blood cardioplegia was given by antegrade and retrograde route with intermittent means. Exclusion criteria were redo CABG and recent MI (raised preoperative troponin T). Operation was performed by one surgeon (MID). Anaesthetic and cardiopulmonary bypass (CPB) techniques were standardized. The bypass circuit used a hollow fibre membrane oxygenator, nonpulsatile flow generated by a roller pump, and 40 μm arterial line filter. Flow was 2.4 L/min/m^2 at 37ºC falling to 1.8 L/min/m^2 at 32°C, arterial pressure was maintained between 50-70 mmHg, haematocrit between 0.20 and 0.25, and alpha stat blood gas management was used.

A cardioplegia delivery cannula with vent line (DLP® Medtronic Inc., Minneapolis, MN, USA) was inserted into the ascending aorta of all patients. In the retrograde group an additional coronary sinus catheter with autoinflating silicon cuff (DLP® Medtronic Inc., Minneapolis, MN, USA) was positioned by a close trans-atrial technique.

Crystalloid cardioplegia (group 1): after aortic cross-clamping 10 ml/kg of antegrade of crystalloid cardioplegia (Martindale 20 ml) was added to one litre of ringer solution (each 1,000 mls contained calcium chloride 0.32 g, potassium chloride 0.30 g and sodium chloride 8.60 g, Otsuka Pharmaceutical Co., Ltd., Japan) was given at 4°C with aortic route pressure kept between 80-100 mmHg. A second or third shot of crystalloid cardioplegia was given every 15-20 min, with half of the initial dose (5 ml/kg) of the first dose. Blood cardioplegia (groups 2 and 3): warm (37°C) blood cardioplegia was prepared by adding 20 ml of Martindale solution (magnesium chloride 3.253 g, potassium chloride 1.193 g, procaine hydrochloride 272.8 mg also contain disodium edetate, sodium hydrochloride and water, Martindale Pharmaceuticals, Romford, Essex, UK), 180 ml of ringer solution and 800 ml of oxygenated blood to make it one litre by the ratio of 4:1 blood and crystalloid delivered in group 2 with same protocol as used for group 1. For antegrade and retrograde group (group 3) 37°C warm blood cardioplegia was used with 20 ml of Martindale solution added with one litre of blood and ringer solution to make the ratio of 4:1 with blood and crystalloid. Dose of 10 ml/kg was used, 60% of the dose given antegradely and the remaining 40% given retrogradely. During retrograde delivery, the coronary pressure was maintained at around 40 mmHg. Further doses were given every 15-20 min in the same manner but the dose was reduced to half of the initial dose.

The distal and proximal anastomosis were performed during the same period of a single aortic cross clamp time in all the three groups.

All patients were weaned off from CPB with a small dose of adrenaline, used routinely as an anaesthetic protocol in our hospital.

Troponin T (Roche Diagnostics GmbH, Mannheim, Germany) and CKMB (Roche Diagnostics GmbH, Mannheim, Germany) were measured by commercially available assay. Control samples were taken at the time of elective admission within 24 hrs prior to surgery. Subsequent samples were taken 12 hrs postoperatively to determine troponin T levels and 24 hrs postoperatively to determine CKMB activity.

Ethical committee approval was obtained, and all patients gave written informed consent.

Data are presented as mean with standard deviation and statistical comparisons are by paired samples T-test and Wilcoxan signed ranks test with a probability of less then 0.05 considered significant.

Results

Ten patients were randomized into each cardioplegia group. The preoperative and intraoperative variables were equally represented in three groups in Tables 1 and 2 respectively. Control levels of troponin T and CKMB were within normal range. Postoperatively troponin T levels were significantly lower in group 3 compared to groups 1 and 2 (mean measurements were 0.13±.02 μg/L compared to 0.32±.04 μg/L and 0.44±.03 μg/L respectively). Producing a *p* value was less than 0.008 in group 3 compared to group 2 and less than 0.005 for group 3 compared to group 1 (Fig. 1).

Post operative CKMB levels were also significantly higher in group 1 than groups 2 and 3. Mean measurements were 29±13 IU/L in group 1, 13±4 IU/L in group 2 and 11±2 IU/L in group 3. Producing a *p* value of less than 0.013 in group 2 compared to group 1, less than 0.043 in group 3 compared to group 2 and less than 0.005 in group 3 compared to group 1 (Fig. 2). No patient showed any severe haemodynamic instability or the need for IABP.

Table 1. Preoperative variables in groups 1-3

Variables	Group 1 (n=10)	Group 2 (n=10)	Group 3 (n=10)
Age (years)	60±9	59±9	59±6
Male	8 (80)	8 (80)	7 (70)
Diabetes mellitus	5 (50)	2 (20)	4 (40)
NYHA class I	1 (10)	2 (20)	1 (10)
II	3 (30)	3 (30)	2 (20)
III	6 (60)	4 (40)	7 (70)
IV	Nil	1 (10)	Nil
Hypertension	3 (30)	2 (20)	3 (30)
Left main stem lesion	2 (20)	3 (30)	2 (20)
Ejection fraction (%)			
Good (>60%)	2 (20)	2 (20)	Nil
Moderate (30-60%)	7 (70)	7 (70)	8 (80)
Poor (<30%)	1 (10)	1 (10)	2 (20)

Data is shown as number followed by percentage in parentheses or mean with standard deviations.
NYHA, New York Heart Association; Nil, 0 (zero).

Table 2. Intraoperative variables in groups 1-3

Variables	Group 1 (n=10)	Group 2 (n=10)	Group 3 (n=10)
No. of grafts	3±0.7	3.2±0.8	3±0.7
X-clamp (min)	44±12	52±13	46±11
CPB (min)	71±8	87±20	69±13

Data is shown as number in mean with standard deviations.
CPB, cardiopulmonary bypass.

Discussion

The results of this trial suggest improved myocardial protection with warm blood antegrade, retrograde, intermittent cardioplegia for coronary artery bypass grafting surgery. We used troponin T and CKMB for perioperative ischemic myocardial injury marker. Release of troponin T is recognized marker for ischemic myocardial injury[9] and peak levels reached at 8-12 hours.[10] troponin T release has functional significance as it is closely related to ischemic time and reflects delayed recovery of left ventricular function and oxidative metabolism and is useful in assessing myocardial protection strategies.[11]

Blood cardioplegia facilitates aerobic myocardial metabolism during cross clamp period and reduces anaerobic lactate production,[12] it improved oxygen carrying capacity, enhanced myocardial oxygen consumption and preserved myocardial high energy phosphate stores.[13,14] Intermittent warm blood cardioplegia preserve systolic function and improved systolic and diastolic chronotropic responses. Normalization of the chronotropic responses post cardiopulmonary bypass is likely due to effects of successful revascularization and subsequent relief of ischemia.[15] Randomized trial showed less myocardial cell damage with intermittent antegrade warm blood cardioplegia.[3] Another large retrospective study demonstrated that warm blood cardioplegia is associated with better short and long term freedom from cardiac morbidity and mortality.[4] However, when advanced coronary artery disease is considered (LMS, increase LV mass, impaired microvasculature) it can result in an uneven distribution and consequently delayed functional recovery.[8] Myocardial areas distal to complete occlusion are poorly protected by the antegrade route alone. The combined route of administration allows better results and more homogeneous myocardial protection,[16] with superiority in metabolic and functional recovery. In patients with unstable angina and non-ST segment elevation myocardial infarct, isolated antegrade blood cardioplegia showed higher mortality, preoperative infarction, delay in recovery of wall motion score index and higher troponin I release compared to warm blood combined antegrade and retrograde cardioplegia.[17]

In conclusion; antegrade, retrograde, intermittent and warm blood cardioplegia is safe and effective. It produces better myocardial protection as assessed by is-

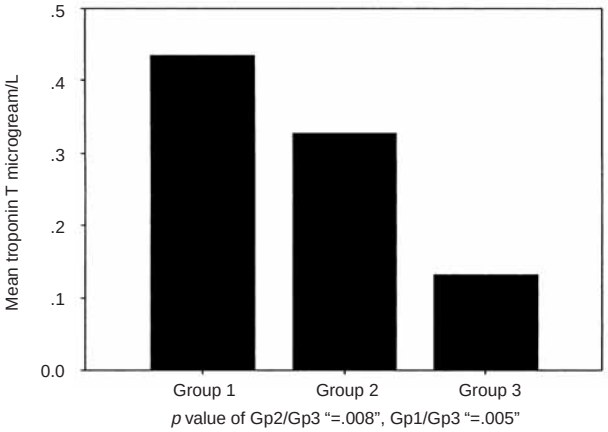

Fig. 1. Bars of mean release of troponin T with *p* values.

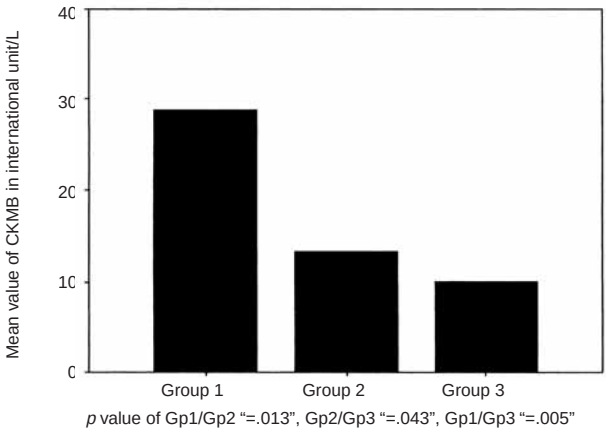

Fig. 2. Bars of mean release of CKMB with *p* values.

chemic myocardial injury marker troponin T and CKMB. Retrograde insertion is a simple to learn technique. In our set up, where small coronary vessels, diffuse disease and left main stem are common; this technique improved myocardial protection. We recommend its widespread use.

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