Institutional report - Cardiopulmonary bypass

Warm induction cardioplegia and reperfusion dose influence the occurrence of the post CABG TnI level

Bingyang Ji, Mingzheng Liu, Feng Lu, Jinping Liu, Guyan Wang, Zhengyi Feng, Qiang Hu

Abstract

As a new biochemical marker cardiac troponin-I (CTnI) is a more sensitive and specific marker for detection of differences in myocardium injuries than other chemical enzymes. This study investigates the effect of warm induced and reperfusion blood cardioplegia on the release of troponin-I during the CABG. In our research, 24 three-vessel coronary artery disease (CAD) patients underwent CABG and were divided into two groups randomly: Group of warm induction and reperfusion blood cardioplegia (Group W N=12); Group of simple warm induction and no reperfusion (Group C N=12). The effect of myocardium protection of the two methods of myocardium protection were evaluated by clinical outcome, CTnI. Serial venous blood samples were obtained before and after surgery. In both groups, there were no differences in operative parameters. The level of CTnI increased from postoperative 6 h (P<0.05), reached peak in 24~72 h and recovered postoperatively on 6th day in both groups. Compared with group C, the plasma concentrations of CTnI in group W were significantly lower at 6 h, 24 h and 72 h (P<0.01). The results suggest that the method of warm induction and reperfusion blood cardioplegia reduces the leakage of CTnI than group of simple warm blood cardioplegia in CABG patients.

Keywords: Myocardial protection; Troponin-I; Cardioplegia; Cardiopulmonary bypass

1. Introduction

In a previous prospective randomized study [1] involving 28 patients with myocardial protection undergoing an elective first cardiac operation, we evaluated the myocardial protection of warm blood cardioplegia induction and simple cool blood cardioplegia induction during cardiopulmonary bypass and using cardiac troponin T (CTnT) as the criteria for evaluating the adequacy of myocardial protection. The results clearly showed, compared with cold blood cardioplegia induction, that warm blood cardioplegia induction provides better myocardial protection during cardiopulmonary bypass. Then we tried to find out another way to do it better. We applied both the warm induction and reperfusion during the CABG, compared with the simple warm induction without reperfusion and using troponin-I as the marker for evaluating the results of the myocardial injury during CABG.

Warm blood cardioplegia using the antegrade intermittent technique was more recently proposed to overcome the disadvantage of a continuous blood flow in the operative field.

1.1 Patients selection

The study was approved by Fuwai Heart Hospital, Beijing, China. All the patients were operated by the same group in Fuwai hospital, including the surgeons, anesthesiologist and perfusionist. From May 2002 to October 2002, 24 CAD patients operated on CABG were randomized to warm blood cardioplegia (group W; n=12), simple warm blood cardioplegia induction (group C; n=12). Preoperative and operative clinical parameters are shown in Table 1. Randomization was performed by the method described by Altman and Bland [4]. All the patients were three-vessel coronary artery disease without valve disease with normal left ventricle function, and the first time to receive CABG. Not included were patients with an ejection fraction below...
0.30 and recent myocardial infarction (≤2 months). The left internal mammary artery was used in all patients.

2.2. Cardiopulmonary bypass

The Stockert-II heart-lung machine with roller pump and Medtronic membrane oxygenator Affinity was used. Tubing pack with cardioplegia delivery (blood: crystalloid=4:1) system (Perfect, Beijing, China), and an arterial filter (Xi Jing, Xi an, China). Non-pulsatile CPB was used at a flow rate of 2.6–3.0 l/min/kg. Mean arterial pressure was maintained 65–85 mmHg) by adjusting blood flow rate. Anesthesia Standard general anesthesia was achieved in all groups with fentanyl, isofurane and enflurane.

2.3. Method of myocardium protection

Institution cardioplegia was administered in both groups. The cardioplegia were administered every 30 min for a period of 2 min with the same infusion rate as the first time. Group of warm induction and reperfusion blood cardioplegia (Group W, n=12); Group of simple warm blood cardioplegia induction (Group C, n=12). The route of delivery was exclusively antegrade in the two groups. The temperature of cardioplegia ranged from 4 to 6 °C in groups and was applied during clamp off. In both groups the heart was induced by the warm blood cardioplegia (35 °C) into the line, during clamping using the cold blood cardioplegia maintaining. Also before clamp off, in Group W the warm reperfusion was applied. Warm reperfusion was started immediately after the last distal anastomosis, and was performed with a constant flow rate of 150 ml/min. Warm reperfusion was carried out in two steps and took 6 min: (1) during the first 2 min, the blood hyperkalemic mixture defined above was injected and progressively rewarmed to 20 °C, and (2) during the last 4 min, the infusate used was exclusively composed of oxygenated blood, which increased to 35 °C at the end of the reperfusion.

2.4. Laboratory assay

Plasma level marker of myocardial damage (CTnI) was obtained from serial venous blood samples before induction, after cardiopulmonary bypass CPB), postoperative 6 h, 24 h, 72 h and 6th day, respectively. Cardiac troponin-I concentrations were measured by a specific immunoenzymometric assay developed. Test sample was incubated with monoclonal antibody BE1 for 15 min. After washing, following the addition of a substrate (tetramethylbenzidine), enzyme activity was measured. The reaction was stopped by adding H2SO4, and the absorbance was read at 450 nm on the status spectrophotometer.

2.5. Electrocardiogram

A 12-lead electrocardiogram was recorded preoperatively at 2 h, at 2 h postoperatively and then daily postoperatively. The electrocardiographic diagnosis criteria for perioperative myocardial infarction (PMI) were new Q-waves >0.04 ms or a reduction in R-waves >25% in at least two leads.

2.6. Statistical analysis

Statistical analysis was performed with SPSS statistical software. One-way analysis of variance (ANOVA) was performed to test the effect of the type of cardioplegia and time on CTnI concentration. Two-way analysis of covariance with repeated measures was performed to test the effect of the type of cardioplegia on CTnI concentration. Statistical significance was accepted at a P<0.05. All data are expressed as mean ± standard deviation (S.D.) (Table 2).

3. Results

Preoperative, operative, and postoperative data are shown in Table 1. The preoperative status was nearly identical in the two groups according to age, sex ratio, weight, C/T and EF%.

In the operative data there was no significant difference between the two groups in cardiopulmonary bypass time, clamp time, graft number, total amount of cardioplegic solution, lowest temperature during bypass and auto-resuscitation.

All patients survived, and no differences were observed in groups with regard to postoperative incidences of renal, upper and lower gastrointestinal bleeding, postoperative wound infection.

### Table 1

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group W</th>
<th>Group C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Age (years)</td>
<td>58±8.2</td>
<td>58.6±7.6</td>
</tr>
<tr>
<td>Women/men</td>
<td>5/7</td>
<td>5/7</td>
</tr>
<tr>
<td>C/T</td>
<td>0.49±0.06</td>
<td>0.51±0.04</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>80±11</td>
<td>75±15</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>56±7</td>
<td>59±8</td>
</tr>
<tr>
<td>Clamp time (min)</td>
<td>68±9</td>
<td>71±13</td>
</tr>
<tr>
<td>CPB time (min)</td>
<td>102±18</td>
<td>99±14</td>
</tr>
<tr>
<td>Total amount of cardioplegia</td>
<td>1640±445</td>
<td>1741±562</td>
</tr>
<tr>
<td>Auto-resuscitation</td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td>Lowest temperature during CPB</td>
<td>30.9±0.9</td>
<td>30.7±1.2</td>
</tr>
<tr>
<td>during bypass (°C)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Graft number</td>
<td>3.8±0.4</td>
<td>3.7±0.6</td>
</tr>
</tbody>
</table>

1: All the variables are not significantly (P<0.05) different in the two groups.

2. Cardiopulmonary bypass

3. Method of myocardium protection

4. Laboratory assay

5. Electrocardiogram

6. Statistical analysis
respiratory, and neurological complications. The level of CTnI in both groups (group W 5.21±0.48 μg/l and group C 6.20±1.15 μg/l) increased from postoperative 6 h (P<0.05) compared with before induction (group W 0.43±0.27 μg/l, group C 0.40±0.29 μg/l), and this indicates that in both groups the myocardium was injured. The value reached peak in 24~72 h and recovered on the postoperative 6th day. Compared with group C, the plasma concentration of CTnI in group W was significantly lower at 6, 24 and 72 h (P<0.01) (Fig. 1).

4. Discussion

Cardiac troponin-I is a specific and sensitive marker of myocardial injury. CTnI was found exclusively in cardiac muscle and clearly was different from skeletal isoforms, so making it a specific marker for myocardial damage. This specificity is particularly beneficial for patients undergoing cardiac surgery because the value of measurements of serum creatinine kinase and lactate dehydrogenase is limited by enzyme release from noncardiac tissues [5,6]. The CTnI increases in all patients after cardiac surgery. This fact shows the inevitable myocardial damage caused by myocardial arrest. The CTnI measurements can detect these small differences in myocardial tissue damage. We have already used it to assess the myocardium injury in our research [7]. The purpose of our present prospective randomized study was to determine the extent to which warm induction and reperfusion cardioplegia, and simple cool blood cardioplegia, contribute to the improvement of myocardial protection using CTnI as the criteria for evaluating the adequacy of myocardial protection.

In a previous study, cold blood cardioplegia with warm induction was clearly better than simple cool blood cardioplegia induction [1]. In our present study, we add the warm reperfusion before the clamp off. Comparison of the results of these two methods shows that with the addition of warm reperfusion to simple warm cardioplegia induction makes it as effective.

Therefore, it is acceptable that hypothermia has been routinely used as it reduces oxygen demand by decreasing the basal metabolic rate. However, hypothermia may have side effects like ‘cold contracture’ of microcirculation in coronary arteries to cause additional ischemia and reperfusion injury [8], rapid cooling during cardioplegia increas-

Fig. 1. CTnI concentration time course in W group (warm induction and reperfusion) and C group (simple warm induction). Concentrations of CTnI are significantly higher in the group C than in the group W at 24 h and 72 h (P<0.01).

ing left ventricular pressure, [Ca²⁺], and coronary resistance, and is energy consuming [9] inhibiting the sodium pump to cause edema, and shifting the oxygen-hemoglobin dissociation curve leftward [10]. So warm induction reduces damage by avoiding cool contracture. In our previous study we learnt that warm induction is better than the cool blood induction. We could hypothesise that with the additional warm reperfusion before the clamp off, the better the result we could get, because of washing out the substances produced by the anaerobic metabolism and by bringing free radical scavengers to a heart at rest. Kawasuzu’s results suggest that terminal warm blood cardioplegia also may enhance myocardial reoxygenation and optimize the oxygen supply/demand balance of the myocardium during reperfusion [11].

In Teoh’s study [12] he compared cold blood cardioplegia (11 patients) to cold blood cardioplegia followed by a ‘hot shot’ (9 patients). They showed that with the hot shot, myocardial metabolic recovery was improved, high-energy phosphates were better preserved, metabolic response to stress was normal, and diastolic function was preserved. Reperfusion damage is thought to be caused in part by oxygen free radicals produced during the early phases of reoxygenation. For Teoh and colleagues, the hot shot improves cold blood cardioplegia protection by washing out the products of anaerobic metabolism. In Caputo’s study [13], thirty-five patients undergoing primary elective coronary revascularisation were randomized to one of two different techniques of myocardial protection. The data suggest that warm blood hyperkalemic reperfusion hot shot prevents myocardial metabolic derangement seen during coronary artery surgery.

Our data showed a significant higher grade of myocardial protection exerted by warm induction and reperfusion in comparison to simple warm blood cardioplegia induction. This finding supports the hypothesis of a high protective effect of warm induction and reperfusion. Warm reperfusion accelerated myocardial metabolic recovery, preserved high-energy phosphates, improved the metabolic response to postoperative hemodynamic stresses, and reduced left atrial pressures.

In summary, our study showed that with the additional warm reperfusion to simple warm cardioplegia induction offers advantage in low risk patients. This conclusion cannot be extended to high risk patients (e.g. redo CABG, combined surgery, ejection fraction under 0.30, unstable angina). Whether the higher release of CTnI in both the groups might be predictive of an adverse clinical outcome in a larger patient population or in higher-risk patients remains to be investigated.

References