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Myocardial Protection of Warm Blood Cardioplegic Induction during Cardiopulmonary Bypass

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Abstract: In his prospective randomized clinical study, we evaluated the myocardial protection of warm blood cardioplegic induction and cold blood cardioplegic induction, respectively, during cardiopulmonary bypass. Twenty-eight adult patients who underwent valve replacement were randomly divided into two groups: group T (14 cases) received cold (6–8°C) blood cardioplegic induction after ECG showed straight line induced by warm (35–37°C) blood cardioplegia; whereas, group C (14 cases) received cold blood cardioplegic induction only. The effects of myocardial protection of both cardioplegic inductions were evaluated by clinical outcomes, myocardial biochemistry index (cardiac troponin T, cTnT), and myocardial automorphology. The ratio of myocardial auto resuscitation was significantly higher in group T (93%) than that in group C (50%). Only one case in group T (7%) and three cases in group C (21%) needed temporary pacemakers. No case in group T (0%) and five cases (36%) in group C received dopamine. The postoperative mechanical ventilation time and ICU stay time of group T were shorter than those of group C. Myocardial biochemistry index—plasma level of cTnT in group T was lower than that of group C immediately and 6 h after cardiopulmonary bypass. Myocardial morphology—group T had comparably better outcomes than group C. We concluded that warm blood cardioplegic induction during cardiopulmonary bypass, compared with cold blood cardioplegic induction, provides better myocardial protection.
Keywords: myocardial protection, blood cardioplegia, warm blood cardioplegic induction. *JECT. 2001;33:106–110*

Blood cardioplegia, compared with crystalloid cardioplegia, has shown much better effect on myocardial protection for adult patients undergoing cardiovascular surgery (1–4). Since 1993, there have been more than 12,000 adult cases that received cold (6–8°C) blood cardioplegia during cardiopulmonary bypass (CPB) in Fu Wai Hospital. In our previous investigations, both clinical outcomes and experimental indexes demonstrated that intermittent cold blood cardioplegia could reduce myocardial oxygen consumption, provide necessary substratum and oxygen of phosphorylation, and, therefore, alleviate ischemia and reperfusion injury (5).

Recently, more and more studies suggest that cold blood cardioplegia inevitably produces side effects, some of which are severe. Cold fluid flow in coronary circulation results in "cold contracture" of microvascular smooth muscle in myocardium (6). Contracture of microcirculation in coronary arteries causes heterogeneous distribution of hyperpotassium blood cardioplegia, and leads to an additional ischemia and reperfusion injury. Erythrocytes undergoing the attenuation of their deformation attributable to hypothermia can jam in capillaries and aggravate the myocardial ischemia. Therefore, some authors presented the conception of "warm heart surgery" (7–9). They preferred continuous warm (35–37°C) blood cardioplegia (antegrade or retrograde) perfusion during CPB and got better outcomes than intermittent cold blood cardioplegia.

However, in our hospital, a large number of cases (about 500–800 per year) are rheumatic valve disease and have to receive open-heart operations. Standard warm heart surgery cannot provide clean operative fields for surgeons in these cases. We designed a modified warm blood cardioplegic-perfusing program. First, patients receive warm blood cardioplegia, and then, as soon as the electrocardiogram (ECG) monitor shows straight line, receive cold blood cardioplegia until the amount of induced cardioplegia reaches 15–20 ml/kg. Cold blood cardioplegia is used as subsequent intermittent (every 30 min) maintenance. This program is labelled "warm blood cardioplegic induction" during open-heart surgery (10–12).

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The objective of this prospective clinical study was to evaluate the myocardial protective effect of warm blood cardioplegic induction and cold blood cardioplegic induction, respectively, during adult valve replacement surgery.

MATERIALS AND METHODS

Staff

All surgeons, anesthetists, perfusionists, and physicians in this clinical research group were constant. This was to attenuate systematic errors.

Cardiopulmonary Bypass

The cardiopulmonary bypass circuit included a Stockert-II roller pump (Stockert, Munich, Germany), a Duroflo-II membrane oxygenator (Jostra Bentley Corp., Irvine, CA), tubing pack with a cardioplegia delivery (blood: crystalloid = 4:1) system (Perfect, Beijing, China), and an arterial filter (Xi Jing, Beijing, China). All patients received moderate (34°C) hypothermia. Nonpulsatile CPB was used at a flow rate of 2.6–3.0 L/min/kg. Mean arterial pressure was maintained (50–70 mm Hg) by adjusting blood flow rate. Oxygen and airflow to the oxygenator were titrated to maintain physiologic blood gases (ph 7.35–7.45, PCO_2 35–45 mm Hg, and PO_2 100–200 mm Hg). No patient received a homologous blood transfusion throughout the study period.

Patients

This study was approved by The Ethics Committee of Fuwai Hospital, Beijing, China. Twenty-eight adult patients undergoing valve replacement were randomly divided into two groups: group T (14 cases) received warm blood cardioplegic induction; whereas, group C (14 cases) received cold blood cardioplegic induction.

Blood Cardioplegia

The potassium concentration of blood cardioplegia for all patients was 21–23 mmol/L. The amount of induced blood cardioplegia for all patients was 15 mL/kg. The amount of subsequent intermittent cold blood cardioplegia for all patients was 8 mL/kg. The integrated coils were used to control the temperature of blood cardioplegia.

Evaluation Index

Preoperative clinical indexes of patients in both groups were recorded as follows: age, weight, cardiac-thoracic ratio (CTR), left ventricular ejection fraction (LVEF).

Perioperative clinical indexes of each group were recorded as follows: CPB time, coronary circulation arrest time, amount of blood cardioplegia when ECG showed straight line, ratio of myocardial autoresuscitation, ratio of requirement for temporary pacemaker, ratio of postoperative requirement of inotrope (dopamine), postoperative ventilation support time, ICU stay time, and postoperative hospitalization.

Plasma level marker of myocardial damage (cardiac troponin T, cTnT) was measured before anesthesia, immediately, 6 h and 24 h after CPB. Measurement of cTnT was performed with a recently developed enzyme immunoassay (ELISA) (13). All cTnT data were corrected for blood dilution according to hematocrit.

In addition, right atrial biopsy specimens obtained immediately before aortic declamping (ischemic period) and 10 min after crossclamp removal (reperfusion period) were examined with a H-7000 transmission electron microscope after operation.

Statistical Analysis

MS-SPSS software was used for statistical analysis. Normal distribution data were presented as "mean ± standard error" and received *t*-test; whereas, probability data were presented as "%" and received χ^2 test between the two groups. Results were significant when $p < .05$.

RESULTS

Preoperative Clinical Indexes

No significant preoperative differences were presented between the two groups (Table 1).

Perioperative Clinical Indexes

There were no significant differences in nasopharyngeal temperature, CPB time and coronary circulation arrest time between the two groups (Table 2). The amount of blood cardioplegia when the ECG showed straight a line in group T (8.4 ± 1.1 mL/kg) was larger ($p < .05$) than that (3.9 ± 0.9 mL/kg) of group C. The myocardial autoresuscitation ratio of group T (13 cases, 93%) was much higher ($p < .05$) compared with the ratio (7 cases, 50%) of group C. In group T only one case (7%) required a temporary pacemaker; whereas, three cases in Group C (21%) required temporary pacemakers. No case in group T (0%) and five cases (36%) in group C received dopamine ($p < .05$). The postoperative ventilation support time (11 ± 5 h) and ICU stay time (21 ± 0.7 h) of group T were considerably shorter ($p < .05$) than those (16 ± 6 h, 24 ± 3.5 h, respectively) of group C. Group T tended to have less postoperative hospitalization (8.7 ± 0.7 days) than group C (9.4 ± 1.1 days), but no obvious differences were presented.

Table 1. Preoperative clinical indexes.

	Group C	Group T
Age (year)	46 ± 5	43 ± 7
Weight (kg)	61 ± 5	65 ± 9
CTR	0.60 ± 0.04	0.60 ± 0.03
LVEF (%)	60 ± 7	60 ± 6

Table 2. Perioperative clinical indexes.

		Group C (14 cases)	Group T (14 cases)
Nasopharyngeal temperature	(°C)	33.9 ± 0.4	33.8 ± 0.3
CPB time	(min)	63 ± 20	63 ± 17
Coronary circulation arrest time	(min)	41 ± 16	40 ± 16
Amount of blood cardioplegia when ECG showed straight line	(ml/kg)	3.9 ± 0.9	8.4 ± 1.1*
Ratio of auto-resuscitation		7 cases, 50%	13 cases, 93%*
Ratio of requirement for temporary pacemaker		3 cases, 21%	1 case, 7%
Ratio of postoperative requirement of dopamine		5 cases, 36%	0 case, 0%*
Postoperative ventilation support time	(hour)	16 ± 6	11 ± 5*
ICU stay time	(hour)	24 ± 3.5	21 ± 0.7
Postoperative hospitalization	(day)	9.4 ± 1.1	8.7 ± 0.7

* = $p < .05$ vs. Group C

Cardiac Troponin T

There was no significant difference in cTnT levels between the two groups before anesthesia (Table 3). Plasma level of cTnT in both groups rose after CPB. In group T, cTnT were lower ($p < .05$) than those in group C immediately (0.70 ± 0.14 vs. 0.99 ± 0.15 mg/L) and 6 h (0.49 ± 0.10 vs. 0.65 ± 0.17 mg/L) after cardiopulmonary bypass. The increased cTnT level tended to decrease and there was no distinct difference.

Right Atrial Biopsy

Well-organized myocardial fibers in each group and no obvious difference between the two groups were presented immediately before aortic declamping (ischemic period) (Figures 1–4). Ten minutes after crossclamp removal (reperfusion period), group T got comparably better outcomes than group C.

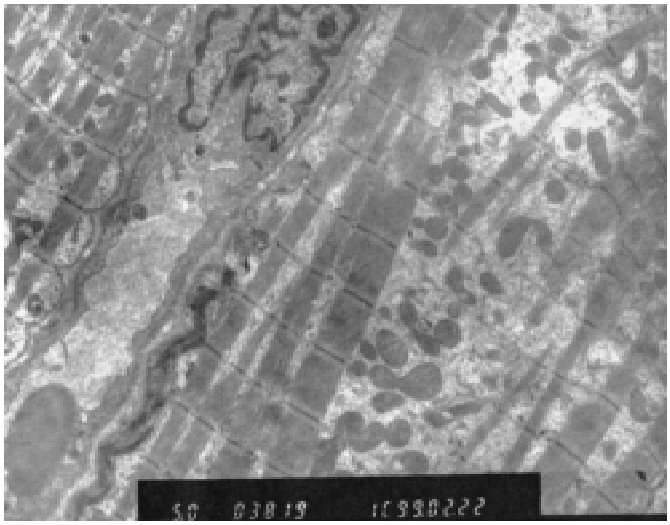

Figure 1. Group T before myocardial ischemia (5000×, no. 3819), well-organized myofibers. There is no abnormality in the interstitial stroma and vessels.

DISCUSSION

In the whole study, we tried to control all experimental conditions between the two groups to be the same as possible in order to attenuate systematic errors. All patients in this study received the same operative procedure, anesthetic procedure, CPB procedure, cardioplegic formula, and ICU management. We could also consider from the results that the clinical backgrounds of the two groups were almost identical: age, weight, CTR, LVEF, nasopharyngeal temperature, CPB time, and coronary circulation arrest time.

Table 3. Plasma level of cTnT perioperatively.

	Group C	Group T
Before anesthesia	0.21 ± 0.14	0.15 ± 0.10
Immediately after CPB	0.99 ± 0.15	0.70 ± 0.14*
6 h after CPB	0.65 ± 0.17	0.49 ± 0.10*
24 h after CPB	0.40 ± 0.11	0.35 ± 0.10

* = $p < .05$ vs. Group C

Intermittent cold blood cardioplegia, compared with intermittent cold crystalloid cardioplegia, has been shown to be more beneficial to adult cardiac muscle by many reports. Not only does it reduce myocardial cell oxygen consumption during coronary circulation arrest period, but it also provides necessary oxygen and substratum of the tricarboxylic acid cycle during perfusion and reperfusion periods and, therefore, attenuates myocardial ischemia and ischemia-reperfusion injury. But inevitably, cold blood cardioplegia leads the capillaries in the myocardium to a "cold contracture" status during the first perfusion period, and causes an additional myocardial injury. Also, the injured erythrocytes responding to hypothermia tend to clump in capillaries. One solution to this problem is the presentation of "warm heart surgery." However, it seems difficult for continuous warm blood cardioplegia to provide a clean and quiet operative field in open-heart surgery. So a modified cardioplegic program taken as "warm

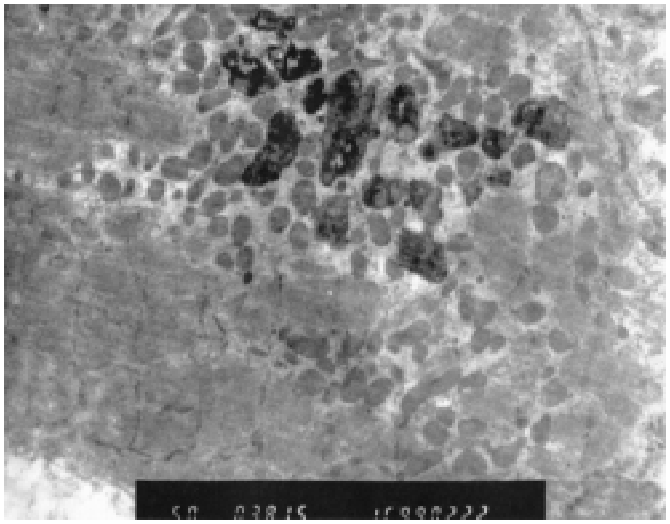

Figure 2. Group C before myocardial ischemia (5000×, no. 3815), well-organized myofibers with several lysosomes.

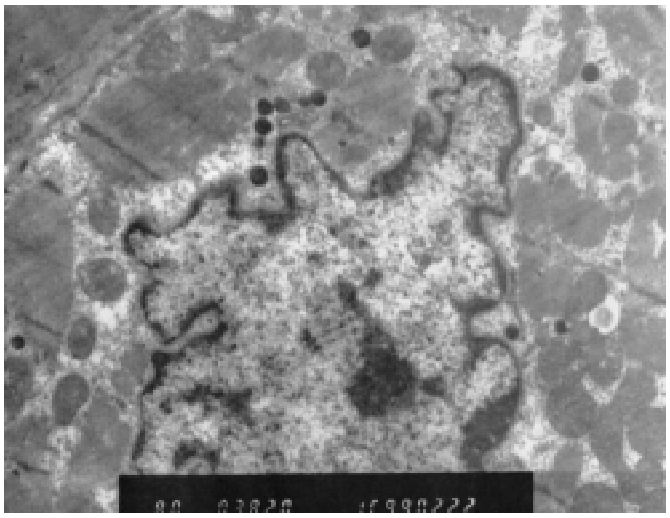

Figure 3. Group T after myocardial reperfusion (8000×, no. 3820), mild swelling of myocardiac muscle, a few neuroendocrine granules are seen in the cytoplasm.

blood cardioplegic induction" is recommended for these types operation. Patients receive warm blood cardioplegia first, and then receive cold blood cardioplegia as soon as the ECG shows straight line until the amount of induced cardioplegia reaches 15 mL/kg. Cold blood cardioplegia is used as subsequent intermittent (every 30 min) maintenance.

The results of this study indicated that warm blood cardioplegic induction had more benefits for the ischemic myocardium than cold blood cardioplegic induction, in the following aspects: myocardial electromechanical function during the reperfusion period, postoperative myocardial clinical outcomes, perioperative biochemical marker (cTnT) of myocardial injury, and myocardial biopsy after

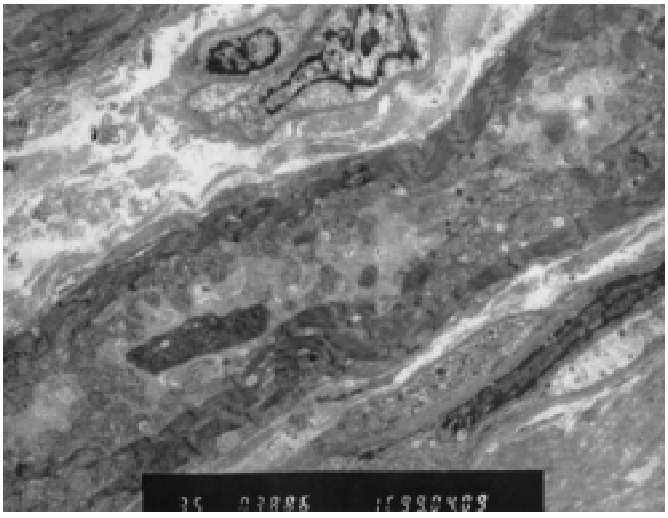

Figure 4. Group C after myocardial reperfusion (4000×, no. 3886), perinuclear swelling of myocardium, disorganization of the myofibers; a capillary with collapsed lumen, swollen endothellium, and perivascular edema is seen at the upper part of the picture.

crossclamp removal. This deduction coincides with our previous animal studies (14).

It is interesting to note that the amount of blood cardioplegia when ECG showed straight line of group T (8.4 ± 1.1 mL/kg) was greater than that in group C (3.9 ± 0.9 ml/kg). We believe that two explanations are reasonable for this phenomenon. First, hypothermia has its own cardioplegic effect (15). Second, microvascular cold contracture caused by hypothermia results in a severe myocardial ischemic status and then leads to an ischemic cardioplegia. This is just the advantage of warm blood cardioplegic induction compared with cold blood cardioplegic induction (16, 17).

In summary, warm blood cardioplegic induction during cardiopulmonary bypass, compared with cold blood cardioplegic induction, can provide better myocardial protection.

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