

Experimental Evaluation of Bretschneider's Solution for Myocardial Preservation in Cardiac Transplantation

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ABSTRACT

Myocardial preservation by Bretschneider's solution (BR solution, Group I) with an intracellular like electrolyte and histidine buffer action was compared with EC-Bi solution (Group II) which has an extracellular like electrolyte and bicarbonate buffer action in the mongrel dogs. The PH and PCO₂ of the effluent from the coronary sinus were maintained during myocardial ischemia for 3 hr but the lactate rose gradually in group I. The oxygen and lactate up-take ratio of the myocardium after re-perfusion was satisfactory and LV max dp/dt was also maintained at a high level in group I. Morphologically, myelin figure and mitochondrial deformation were more found in group II on electron microscopy.

A donor heart preserved for 3 hr in cold BR solution was transplanted in the left thoracic cavity in four mongrel dogs by the technique of the heterotopic cardiac transplantation. Resuscitation of cardiac pulsation was smooth and maintenance of the systemic circulation after transplantation was possible in every case. From these findings, it might be concluded that myocardial preservation using cold BR solution was useful for cardiac transplantation.

Bretschneider's solution (BR solution) which has the intracellular like electrolyte content and the histidine buffer action has been evaluated as one of the ideal cardioplegic solution for cardiac surgery in Europe. It is supposed that BR solution might be effective also in myocardial preservation for cardiac transplantation. Then, this study was done to see whether BR solution is superior as the myocardial preserving fluid in heterotopic cardiac transplantation that is one of the cardiac transplantation studies in our department^{6,7)}.

MATERIALS AND METHODS

(1) Fundamental experiment of myocardial

preservation

26 mongrel dogs weighing 8-18kg were divided into 2 groups, i.e., Group I: group administered BR solution (10 dogs, 5 pairs) and Group II: group administered EC-Bi solution (16 dogs, 8 pairs), which has an extracellular like electrolyte and bicarbonate buffer solution. Each myocardial preserving fluid was infused (20ml/kg) from the aortic root for cardioplegic arrest and myocardial protection. The heart was removed after cardiac arrest and left in ischemic state for 3 hr. During ischemia, the myocardial preserving fluid was infused by intermittent coronary perfusion every 30 min and myocardial temperature was maintained at 4°C. During

coronary perfusion, effluent from the coronary sinus was collected and PH, PO₂, PCO₂, lactate value of the fluid were measured. After reperfusion of the ischemic heart by Mann's method⁵, the myocardial contractility and microscopic findings were evaluated at 30 min later.

(2) Experimental application for heterotopic cardiac transplantation after preservation in BR solution

A donor heart preserved for 3 hr with cold BR solution was transplanted by an improved technique¹⁰ of heterotopic cardiac transplantation. After transplantation, the ascending aorta of the recipient dog was ligated and the systemic circulation of the recipient dog was maintained by the donor heart as shown in Fig. 1.

In this heart-transplanted dog, short term hemodynamic study was performed.

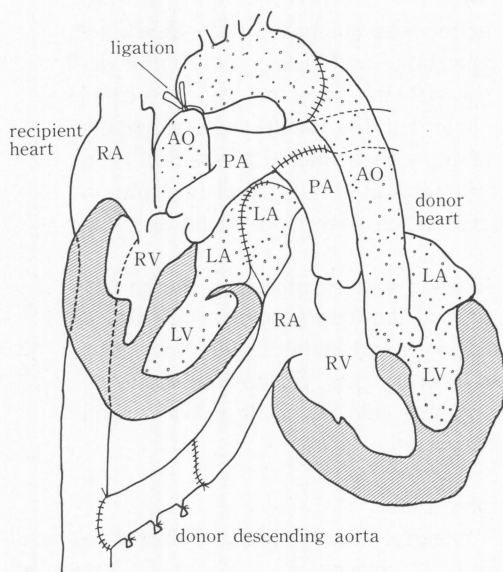


Fig. 1. Experimental model of heterotopic myocardial transplantation

RESULTS

(1)-a. Examination of the effluent from the coronary sinus.

PO₂ of BR solution itself was 131.0 ± 12.5 mmHg and that of EC-Bi solution was 193.9 ± 28.2 mmHg. After coronary infusion, the change of PO₂ values in the coronary effluent showed same decrease in two groups (Fig.2).

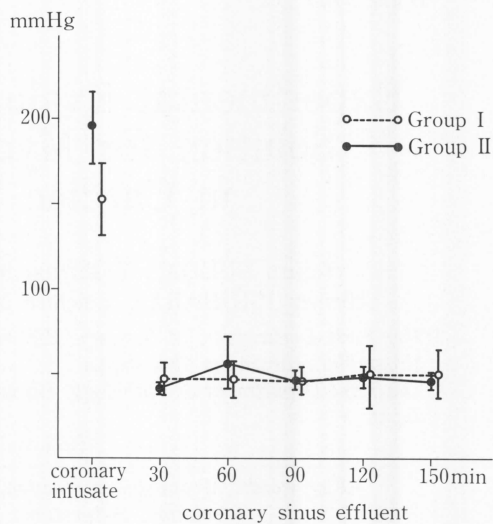


Fig. 2. PO₂ in the coronary sinus effluent following each supplementary infusion of the preserving fluid.

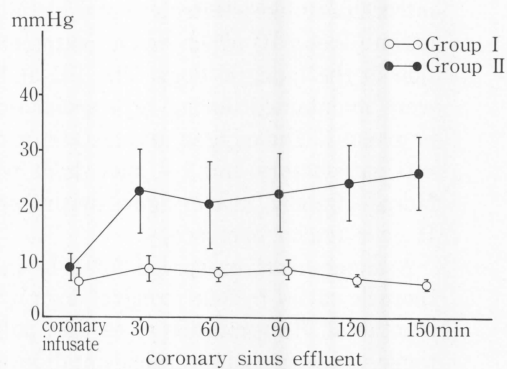


Fig. 3. PCO₂ in the coronary sinus effluent following each supplementary infusion

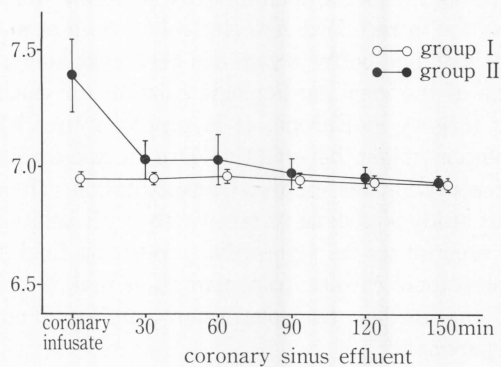


Fig. 4. pH in the coronary sinus effluent following each supplementary infusion

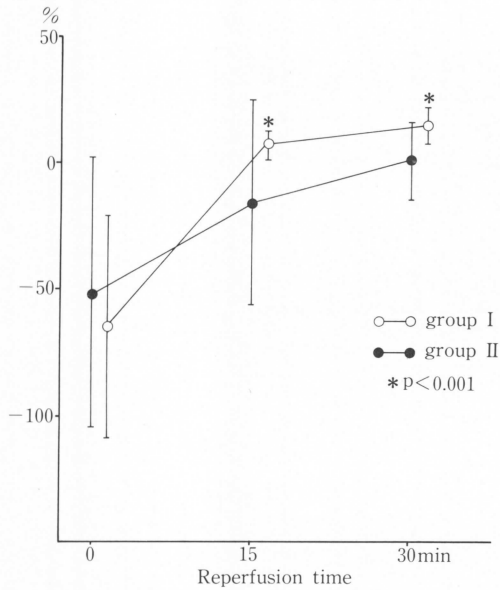


Fig. 5. myocardial lactate extraction during reperfusion following 3 hr ischemia

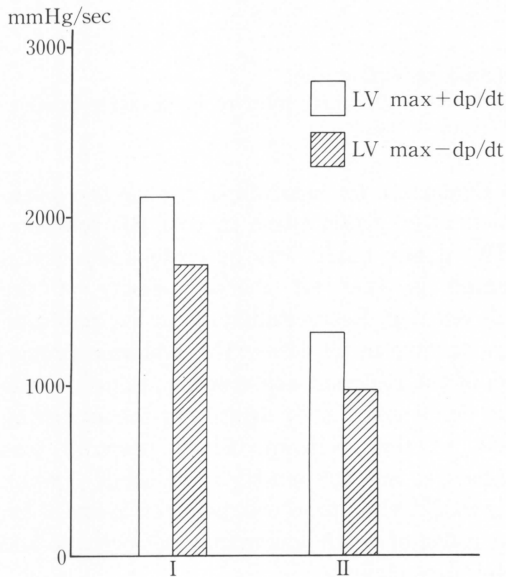


Fig. 6. LV max +dp/dt and LV max -dp/dt during reperfusion following 3 hr ischemia

PCO₂ of BR solution and EC-Bi solution were 6.4 ± 2.1 mmHg and 9.0 ± 2.7 mmHg before coronary infusion. After coronary perfusion, PCO₂ of the effluent became elevated to 23.0 ± 7.9 mmHg at 30 min in Group II (p < 0.05). But the change of PCO₂ was not sig-

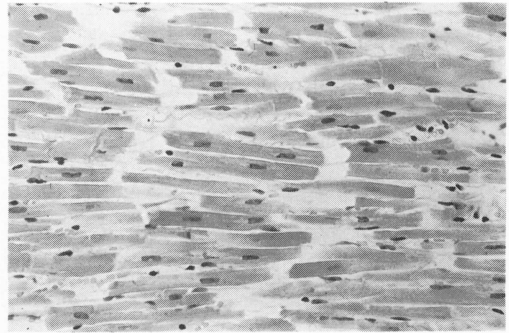


Fig. 7. Left ventricular myocardium of reperfused heart in Group II (H.E.stain). Fragmentation of myocardial cells is appeared.

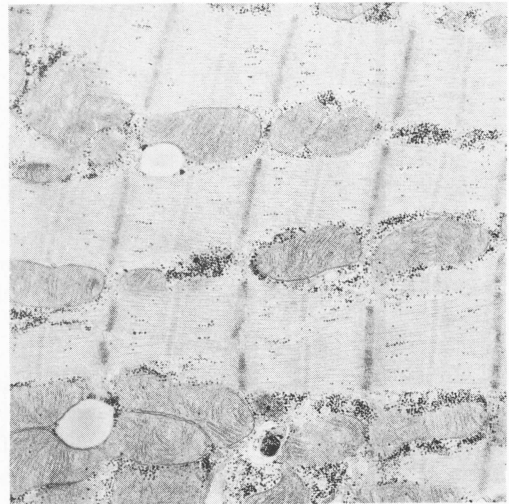


Fig. 8. Electron microscopic appearance of myocardial cell in Group I. Myelin figure are appeared less frequently compared with Group II.

nificant in the effluent of Group I (Fig.3).

PH change of the coronary effluent was different between Group I and Group II. PH of the effluent dropped significantly in Group II (Fig.4). (1)-b. Measurement after reperfusion

Oxygen uptake ratio after reperfusion improved gradually in group I as 22.0 ± 10.0% immediately after reperfusion → 21.6 ± 10.9% after 15 min → 33.4 ± 12.0% after 30 min. It showed no improvement of oxygen uptake ratio in Group II as 34.4 ± 17.7% immediately → 28.6 ± 5.6% after 15 min → 34.7 ± 14.8%

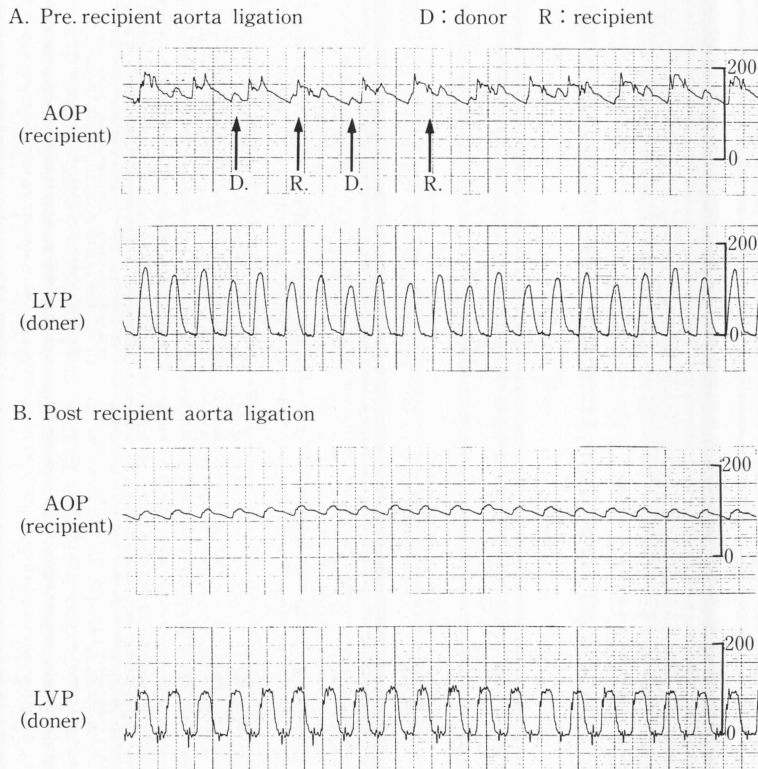


Fig. 9. Hemodynamics of the heterotopic myocardial transplantation. Doner heart could maintain the systemic pressure to 90–100 mmHg after recipient aorta ligation.

after 30 min.

Lactate uptake ratio at the same time was -65.2 ± 43.7 immediately after reperfusion $\rightarrow 7.1 \pm 13.9\%$ after 15 min $\rightarrow 16.0 \pm 3.4\%$ after 30 min in Group I. However it did not improve in Group II as shown in Fig.5.

LV max $+dp/dt$ and LV max $-dp/dt$, measured when LVEDP was 0–3 mmHg, were 2170 ± 456 mmHg/sec and 1725 ± 688 mmHg/sec 30 minutes after reperfusion in Group I. The values of Group II were 1336 ± 466 mmHg/sec and 984 ± 412 mmHg/sec (Fig.6). Microscopic examination (H.E stain) revealed that degeneration of myocardial cells and appearance of contraction band were presented in Group II (Fig.7). But these cellular changes were less appeared in Group I.

By electron microscopic examination, it was found that myelin figures were less appeared in the cytoplasm and the intercalated disc of the myocardial cells in Group I (Fig.8). Appearance of myelin figures and mitochondrial deformity was prominent in the myocardial cells of Group

II.

(2) Evaluation for heterotopic cardiac transplantation after preservation in cold BR solution.

The donor heart was heterotopically transplanted in the left thoracic cavity of the recipient dog. Resuscitation of cardiac pulsation was possible in all cases. The systemic circulation of the recipient dog was maintained by the only donor heart after ligation of the ascending aorta of the recipient. Blood pressure was reached to 80–100 mmHg after aortic ligation (Fig.9). Survival time was between 2 and 9 hr. The cause of death was mainly hemorrhage and respiratory failure.

DISCUSSION

Myocardial preservation was important to inhibit the consumption of ATP in the ischemic myocardium during cardiac transplantation. The purpose of the myocardial preserving fluid is the same as that of the cardioplegic solution²⁾ which was used clinically at the time of aortic cross clamping.

Cardioplegic solutions used clinically are divided into 2 types as viewed from their electrolyte content, i.e., the extracellular like solution and the intracellular like solution. Bretschneider's solution¹⁾ and GIK solution⁸⁾ are belonged to the former type and St. Thomas Hospital solution³⁾ can be mentioned as the latter type. Opinions are divided at present as to which type of solution is preferable for an ischemic myocardium. However the Na-K pump of the myocardial cell shall stop the function during ischemia and the electronic activity of the cellular membrane will be significantly reduced⁹⁾. So it may be preferable to have the approximate electric fluid between the ischemic myocardial membrane.

As regards to the type of buffer solution, bicarbonate is generally used to maintained the ischemic myocardium somewhat alkalotic. But Bretschneider considered that it would be reasonable for the preservation of the ischemic myocardium to keep the PH of the cardioplegic solution somewhat acidotic during ischemia and he used histidine, whose PK is 6.74, as the buffer solution²⁾.

In this study, the preverving effect of two different type solution which have different electrolyte and buffer action was examined fundamentally in the ischemic myocardium. BR solution gave excellent results with respect to myocardial protection during short ischemic state. However, it was not possible to distinguish whether the electrolyte content or the buffer function of BR solution had favorable effect on the ischemic myocardium.

Then, heterotopic cardiac transplantation after short term ischemic preservation in the cold BR solution was performed. The original model of this heterotopic cardiac transplantation was developed by Matsumoto and his associates⁴⁾. The author improved their technique to make easy to anastomose IVC of the donor heart to that of the recipient heart. Following completion of cardiac transplantation, the systemic circulation of the recipient dog was maintained with the donor heart after ligation of the recipient ascending aorta and all of the subjects survived for 2~9 hr. Although some problem should be resolved to maintain the systemic circulation of the recipient permanently, long term survival will be attained nearly by this technique. We are intending to continue this experimental study.

ACKNOWLEDGEMENTS

The fundamental experiment was made by Dr. Maeda and appeared in The medical journal of Hiroshima University. The author continued this experiment and developed it for the heterotopic cardiac transplantation.

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