Original Article

Myocardial Protection by Retrograde Application of Bretschneider Cardioplegia during Heart Valve Surgery

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Background: Bretschneider or Histidine-Tryptophan-Ketoglutarate (HTK or Custodiol) cardioplegic solution provides protection for more than 2 hours of myocardial ischemia. It is convenient to require only single dose.

Objective: To present outcomes of using single dose of retrograde HTK solution for double valve replacement [DVR] and tricuspid valve annuloplasty [TVA] surgery at Khon Kaen University.

Materials and Methods: Twenty-two patients were treated by DVR and TVA using single dose of retrograde HTK solution between January 2013 and April 2017. Data included demographics, operative data, early outcomes, serum cardiac enzyme markers, complications and peri-operative mortality.

Results: The mean age of patients was 49.27±10.6 years and 50% were female. Left ventricular ejection fraction was 53.52±16.3%, aortic cross clamp time was 94.8±13.3 minutes, cardiopulmonary bypass time was 125.13±20.3 minutes, spontaneous ventricular fibrillation was 40.9%, and no mortality.

Conclusion: The use of single dose of retrograde HTK cardioplegia for DVR and TVA surgery is feasible, convenient and acceptable early outcomes. HTK solution may be applicable to a broader range of cardiac surgery compared with multiple doses of cold blood cardioplegia.

Keywords: Cardioplegia, Custodiol, DVR, HTK, TVA

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Myocardial protection during cardiac surgery is defined as the set of strategies aiming at decreasing myocardial oxygen consumption adapting it to the momentary tissue supply and/or at making cardiac cells more resistant to ischemic episodes. The goals were to reduce the magnitude of ischemia-reperfusion-induced injuries and their noxious early and late consequences, such as acute myocardial infarction [AMI], arrhythmias, ventricular dysfunction, cardiogenic shock and increased perioperative mortality[1,2]. Cardioplegia with histidine–tryptophan–ketoglutarate (HTK–Custodiol; Koehler Chemi, Alsbach-Haenlien, Germany) or Bretschneider solution for cardiac arrest during cardiac operations has been widely used more than 700,000 cases of open cardiac surgery. The use is very convenient, administered for only single dose, and this is claimed to give sufficient myocardial protection for more than 2 hours during cardiac arrest[1-8].

Antegrade route of HTK solution is used widely, but retrograde route of HTK solution has very limited data. No studies present the effects of retrograde HTK cardioplegia on myocardial injury in patients having valve surgery have been reported.

This study describes intra and perioperative complication, procedural details, and serum cardiac enzyme as end points.

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Materials and Methods

All patients with valvular heart disease were treated with double valve replacement and tricuspid anuloplasty (DVR and TVA) between January 1, 2013, and April 30, 2017 were included. Data were recorded retrospectively included demographics, procedural details, and early outcomes. The study protocol was approved by the ethics committee of Faculty of Medicine Khon Kaen University.

HTK solution

One liter of HTK solution contains the following components: 15 mmol/L sodium chloride, 9 mmol/L potassium chloride, 4 mmol/L magnesium chloride, 18 mmol/L histidine hydrochloride, 2 mmol/L tryptophan, 30 mmol/L mannitol, 0.015 mmol/L calcium chloride, 1 mmol/L potassium hydrogen 2-ketoglutarate, osmolarity 310 mOsm/kg, pH 7.02 to 7.20. The cardioplegic solution was delivered at a temperature of 4 to 8 degree celcius.

Dosing of HTK was 40 to 50 ml of solution per kilogram of body weight. Solution was infused retrogradely driven by hydrostatic pressure only (from approximately 2 m height) over a time span of 6 to 8 minutes as recommended by the manufacturer.

Venous blood samples were collected just after operation and 24, 48, 72 hours postoperatively. The upper normal reference limit is less than 14 mg/l for serum cardiac troponin-T.

Results

In total, 22 patients were treated (between January 2013 and April 2017) with DVR and TVA and a single dose of retrograde HTK solution was used for preservation of myocardium. The mean age of patients was 49.27±10.6 years. 50% were female (Table 1). Most (14; 63.6%) patients were categorized as NYHA class II (Figure 1). Mean LVEF was 53.52±16.3%. Most (14; 63.6%) patients had LVEF >49% (Figure 2).

The mean aortic cross-clamp time was 94.8±13.3 (72 to 134) min, mean cardiopulmonary bypass time was 125.13±20.3 (94 to 187) min, incidence of ventricular fibrillation was 9 (40.9%) cases. Re-operation was required in one case (4.5%) to release pericardial effusion. Pneumonia occurred in one case (4.5%), and two patients (9%) experienced a new onset of atrial fibrillation. Mean ICU length of stay was 4.64±1.8 (2 to 11) days. Hospital length of stay was 16.7±9.8 (8 to 45) days and no 30-day mortality. Only one case needed implantation of a temporary pace maker, which was removed before discharge to home (Figure 4).

Table 1. Demographic data

	n = 22
Age, years	49.27±10.6
Female, n (%)	11 (50)
AF, n (%)	16 (72.7)
Smoking, n (%)	7 (31.8)
COPD, n (%)	1 (4.5)
Hypertension, n (%)	1 (4.5)
Dyslipidemia, n (%)	1 (4.5)
LVEF, %	53.52±16.3
Serum creatinine, mg/dl	0.9±0.2

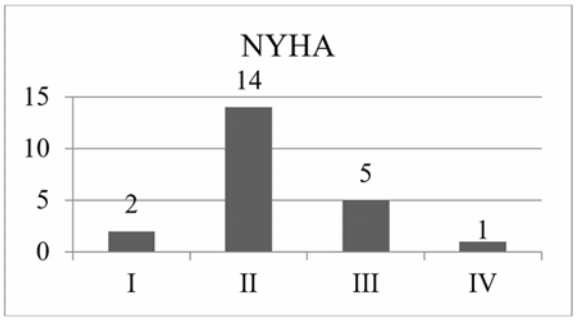

Figure 1. NYHA classification.

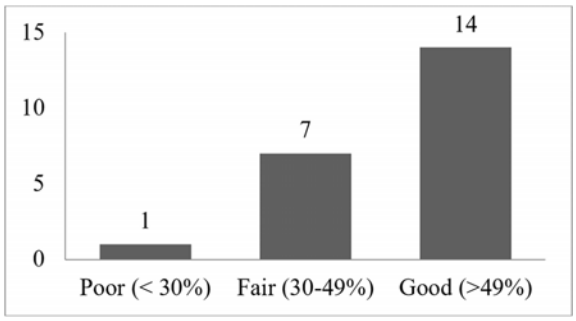

Figure 2. LVEF.

Mean serum troponin-T levels at 0, 24, 48, and 78 hours after operation were 0.78, 0.8, 0.69 and 0.52 µg/L respectively. Mean serum CK-MB levels at 0, 24, 48, and 78 hours after operation were 67.63, 56.6, 31.56 and 21.7 µg/L respectively

Discussion

During cardiac surgery, myocardial damage is caused for concern. While ischemia is the most likely major cause of intra-operative myocardial damage,

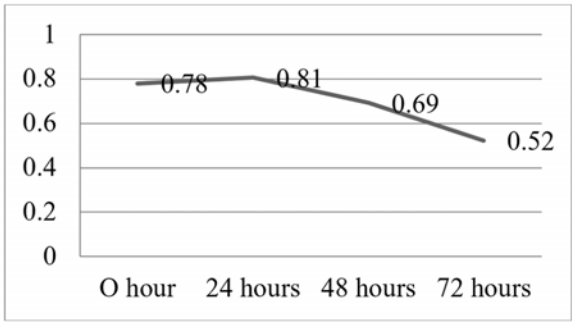

Figure 3. Serum troponin-T.

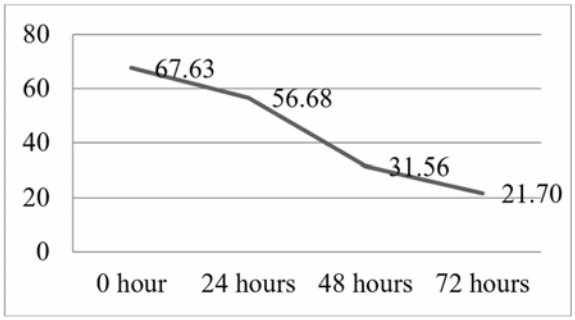

Figure 4. Serum CK-MB.

Table 2. Peri-operative data

Aortic cross clamp time (min)	94.8±13.3 (72 to 134)
CPB time (min)	125.13±20.3 (94 to 187)
VF after cross clamp, n (%)	9 (40.9)
Temporary pace maker, n (%)	1 (4.45)
PRC (day 1) (unit)	0.86±0.83 (0 to 3)
Post op Cr (mg/dl)	0.8±0.3 (0.4 to 1.8)
ICU LOS (day)	4.64±1.8 (2 to 11)
Hospital LOS (day)	16.7±9.8 (8 to 45)
Thirty-day mortality, n (%)	0

harmful mechanical and pharmacological factors must also be taken into account[1-6].

Myocardial protection during cardiac surgery is most commonly provided by the infusion of hypothermic cardioplegic blood or crystalloid solution[1,3,4,6,8].

HTK is an intracellular cardioplegic solution containing a low sodium concentration (to arrest the heart by inhibiting the rapid phase of the action potential), histidine as buffer, tryptophan to stabilize the cell membrane, ketoglutarate (to improve the ATP energy production during reperfusion), and mannitol to decrease the cellular edema[1-3,5].

HTK is usually administered by antegrade infusion into the aorta, proximally to the heart, after aortic clamping, or by direct infusion into ostia of the coronary arteries, especially in the presence of associated aortic valve disease[1,3,4,7]. It has been recently proposed that the retrograde infusion of cardioplegia into the coronary sinus ostium provided a possibility of maintaining uninterrupted infusion and the distribution of cardioplegia to regions irrigated by stenotic coronary vessels, improving sub-endocardial protection[8]. There is an overall lack of data concerning use of HTK by the retrograde route.

Ventricular fibrillation [VF] after removal of the aortic cross-clamp was the major concern with administration of HTK. Braathen et al, comparing Custodiol-HTK and cold blood cardioplegia in mitral valve surgery[1], found 71% of patients receiving antegrade HTK resumed VF after release of aortic cross clamping. Also specific markers of myocardial injury in clinical use, troponin-T and CK-MB, did not show any differences compared with this present[1].

We found clinical outcome such as mortality, low cardiac output syndrome or other major complications, to be similar in our study to levels reported in all reviewed literature.

Conclusion

A single retrograde administration of HTK cardioplegia provides a level of myocardial protection similar to that of cold blood cardioplegia solution. Absence of any requirement to re-administrer cardioplegia is convenient and improves the flow of the operation in DVR and TVA patients. No difference was identified in mortality rate and other clinical outcomes, except that VF was frequent during the reperfusion period without clinical impact.

Limitations of the study

This study was a case series. A study with comparison would be helpful.

What is already known on this topic?

HTK solution can be used in valvular heart disease surgery by the antegrade route. Need for a single use only is the important advantage.

What this study adds?

Retrograde administration of HTK solution can be used in valvular heart disease patients with outcomes comparable to those of cold blood

cardioplegia.

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Potential conflicts of interest

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