Original Article

Antegrade Versus Antegrade with Retrograde Delivery of Cardioplegic Solution in Myocardial Revascularisation. A Clinical Study in Patients With Triple Vessel Coronary Artery Disease

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The effects of antegrade and antegrade with retrograde delivery of cardioplegic solution were evaluated in 60 patients who underwent myocardial revascularisation. All patients had triple vessel coronary artery disease and underwent revascularisation using arterial and vein grafts. Myocardial protection consisted of administration of the St.Thomas' Hospital cardioplegic solution, topical slushed ice and systemic hypothermia (28°C-30°C). The patients were categorised into: group A (n=30), who received antegrade cardioplegia alone, and group B (n=30), who received antegrade and retrograde cardioplegia. With the exception of the total dose of cardioplegic solution ('p'=0.02), there was no significant difference between the two groups. Cardiac function was assessed before and after the patient was weaned from the cardio-pulmonary bypass. There was a significant increase in the right atrial pressure and a significant decrease in the mean arterial pressure from the baseline ('p'<0.05), 10 minutes after cardiopulmonary bypass in group A. All patients in-group B had a spontaneous return to sinus rhythm after release of the aortic cross clamp, whereas 3 patients in group A required defibrillation to restore sinus rhythm. Intra aortic balloon pump support was necessary in 4 patients in group A, as against 1 patient in group B to terminate the cardiopulmonary bypass. The clinical outcome was similar in both groups. We conclude that the use of a combination of retrograde and antegrade cardioplegia facilitates early recovery of left ventricular function after coronary artery bypass grafting. **(Annals of Cardiac Anaesthesia 2003; 6: 143–148)**

Key words: – Myocardial preservation, Cardioplegia, CABG, Retrograde cardioplegia

Optimal myocardial protection relies on adequate delivery of the cardioplegic solution to all parts of the heart, and critical stenosis of the coronary arteries limit this delivery by the antegrade route. Retrograde administration of cardioplegia through the coronary sinus offers a good alternative for myocardial protection during coronary bypass operations.[1-3] Experimental studies have shown that there is superior myocardial protection of the left ventricle with the use of retrograde cardioplegia, even with patent coronary arteries but there is less favourable protection of the right ventricle.[4,5] In cases where there is a critical stenosis of the left main coronary artery or the presence of a left main equivalent, where the proximal circumflex and the left anterior descending (LAD) coronary artery disease is present, antegrade cardioplegia alone may be sub-optimal and retrograde cardioplegia may offer additional benefit to the myocardial preservation.

This report is a prospective, clinical trial comparing the effects of antegrade and antegrade with retrograde cardioplegia in terms of myocardial performance in patients with triple vessel coronary artery disease undergoing coronary artery bypass grafting (CABG).

Methods

Sixty patients undergoing CABG were included in the study. All the patients had a triple vessel

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coronary artery disease with a varying degree of occlusion of the LAD. Patients having a left main or left main equivalent coronary artery disease were also included in the study. Exclusion criteria included the following: reoperations, combined procedures, poor left ventricular function (Ejection fraction < 30%) and emergency CABG. The patients were divided into two groups: Group A (n=30) received antegrade cardioplegia through the aortic root, and Group B (n=30) received antegrade with retrograde cardioplegia. An informed consent was obtained from all the patients prior to surgery after obtaining institutional ethical committee approval.

Table-1 shows the preoperative patient data. Obesity was defined as more than 10% excess body weight; diabetes was defined as per WHO criteria as fasting blood glucose levels >140 mg/dL and the use of oral anti-diabetic medications or insulin dependency; hypertension, as a systolic blood pressure of more than 160 mm Hg or a diastolic blood pressure of more than 100 mm Hg; hyperlipidaemia, as a cholesterol level of more than 200 mg/dL or a triglyceride level of more than 160 mg/dL. All medications such as calcium channel blockers and beta-blockers were continued until the night before surgery. Nitrates were continued even on the morning of surgery. Anti platelet drugs were stopped a week prior to the surgery.

A standardised anaesthetic technique was used with oxygen, nitrous oxide and isoflurane. Pancuronium/ vecuronium (0.1mg/kg) was used for muscle relaxation, midazolam (0.1-0.2 mg/kg) was used for amnesia and fentanyl citrate (15 µg/kg) / buprenorphine (6 µg/kg) was used for analgesia. A Swan-Ganz catheter (Baxter Healthcare Corporation Irvine, CA, USA) was introduced into the pulmonary artery via the right internal jugular vein. All operations were performed by one surgeon to avoid the variability that would have arisen with multiple surgeons. The distal anastomoses were performed during a single period of cross clamping, and proximal anastomoses were performed with a partial occluding clamp. Standard bypass techniques were used with an Edward Vital TM membrane oxygenator and a roller pump (Pemco Inc. USA) while the patient was operated under moderate systemic hypothermia (naso-pharyngeal temperature of 28-30°C), and moderate haemodilution. Myocardial protection was achieved by infusion of cold (4°C) St.Thomas' Hospital cardioplegic solution in a dose of 300 ml/m^2 and was repeated in a dose of 150 ml/m^2 every 20 minutes. However, if the asystole was not produced with this dose, an additional dose was given till asystole was produced. In Group A, the cardioplegic solution was infused in the aortic root whereas in group B, 50% of the calculated dose was infused in the aortic root antegradely and the remaining 50% was given retrogradely in the coronary sinus. The coronary sinus was cannulated with an Edwards Life Sciences 14F, 27cm (RC014T) cannula. We used a DLP Inc. Grands Rapid (MI49501-0409) Y connector with a 14G, 7F(ATCO14V) cannula for the antegrade delivery of cardiolplegia. The left ventricle was vented through the aortic root by means of a Y connection in the antegrade cardioplegia cannula connected to the roller pump. Patient temperature was kept between 28°C and 30°C and slushed ice was used for topical cooling as additional myocardial protection. Before the patient was weaned from cardiopulmonary bypass (CPB) rewarming was done until the naso-pharyngeal temperature reached 38°C. The haematocrit was maintained at 21%-25%. Arterial blood gas values were maintained within normal limits. Intravenous fluid therapy was intended to achieve optimal filling pressures for the actual myocardial performance, which was monitored by frequent determinations of cardiac filling pressures and calculations of

Table 1. Preoperative patient data

	Group A (n=30)	Group B (n=30)	'p' value
Male/female	21/9	23/7	NS
Age (years)	58.2±8.1	57.6±7.8	NS
BSA (m^2)	1.86±0.18	1.88±0.14	NS
NYHA class	3.1±0.59	3.1±0.50	NS
Obesity	4	3	NS
Hypertension	12	13	NS
Diabetes	5	4	NS
Hyperlipedaemia	10	12	NS

Data expressed as mean ± standard deviation
NS: Not significant
BSA: Body surface area
NYHA: New York Heart Association classification

stroke work index and cardiac index (CI). The aorta was decannulated after 10 minutes of haemodynamic stability after cessation of CPB and infusion of 50% of the calculated dose of protamine sulphate.

The recovery of cardiac function was assessed by monitoring systolic pressure (SAP), diastolic pressure (DAP), mean arterial pressure (MAP), mean right atrial pressure (RAP), mean pulmonary artery pressure (MPAP), pulmonary capillary wedge pressure (PCWP) and heart rate (HR). Cardiac output (CO) was measured by the thermodilution technique. Derived haemodynamic indices were obtained using the formulae: Cardiac index (CI) = CO/ body surface area (L/min/m^2); stroke index (SI) = $\frac{SV}{BSA}$ mL/beat/m^2,

left ventricular stroke work index (LVSWI) = SI (MAP-PCWP). 0.0136 (g.m/m^2); right ventricular stroke work index (RVSWI) = SI (MPAP-RAP). 0.0136 (g.m/m^2); systemic vascular resistance index (SVRI) = (MAP-RAP). 80/CI (dynes.sec.cm^{-5} m^2). These haemodynamic variables were measured after the induction of anaesthesia (baseline), after the cessation of CPB following 10 minutes of stable haemodynamics and two hours later. At 12 hours after the operation creatinine phosphokinase (CPK-MB) was determined from a venous blood sample.

Intra-operative myocardial infarction was defined as a development of a new Q wave. Low CO was defined as CI of < 2.2 L/min/m^2 or a need for an inotropic support in excess of 5µg/kg/min of dopamine with or without any other inotrope to maintain the CI of > 2.2 L/min/m^2. Preoperative and postoperative ECG were compared and special attention was given to the appearance of atrioventricular conduction disturbances and the presence of fresh 'Q' waves.

The quantitative data was analysed statistically by the use of the paired students 't' test and a Willcoxon ranked sign test where appropriate and a multivariate analysis was performed. A 'p' value of less than 0.05 was considered to be significant. Data are expressed as mean ± standard deviation.

Results

The intraoperative data are shown in Table 2. The mean time to reach asystole was longer in group B as compared with group A. The total dose of cardioplegic solution was significantly higher in group B as the calculated dose of cardioplegia did not suffice to cause asystole in patients of this group and an additional dose was needed to achieve this. In all patients at least one internal mammary artery was used as a graft. The haemodynamic data are summarised in Table 3. The baseline haemodynamic parameters were similar in both the groups. There were no changes in the haemodynamic parameters during the subsequent period, except that MAP decreased from 80.2 ± 10.6 to 65 ± 9.1 mm Hg, ('p'<0.05) and RAP increased from 5.8 ± 1.8 to 9.3 ± 1.8 mm Hg ('p'<0.001), 10 minutes after cessation of CPB in group A. The RAP recovered at 2 hours after CPB but MAP continued to remain low in this group. The levels of the cardiac specific enzyme CPK MB were not different in the two groups. Troponin I and troponin C levels were not estimated in our study due to absence of the facilities in our institute. In all patients the clinical outcome was good. There were no deaths and no patient had a perioperative infarction. Five patients, four in group A and one in group B showed signs of low CO on weaning from CPB and required the use of an intra-aortic balloon pump (IABP). All these five patients were weaned off the IABP within the first six hours postoperatively. All patients in group B had a spontaneous return to sinus rhythm on release of the aortic cross clamp whereas three patients in group A required a single defibrillation of 20 joules to return to sinus rhythm. Both before and after the surgery all patients had a regular sinus rhythm. No patients in both the groups developed the presence of fresh 'Q' waves in the postoperative

Table 2. Intra-operative patient data

	Group A (n=30)	Group B (n=30)	'p' value
Cardioplegic solution (ml)	1113±130.6	1240±180.8	p = 0.02
Asystole time (sec)	50±9.5	54.3±10.2	NS
Bypass time (min)	150±22.5	162±28.5	NS
Aortic cross clamp time (min)	96±12.8	94±10.6	NS
No. of grafts	3.1±0.3	3.2±0.4	NS

Data expressed as mean ± standard deviation
NS: Not significant
Asystole time: Time to reach asystole.

Table 3. Haemodynamic data in the two groups

	A	B	A1	B1	A2	B2
HR (beats/min)	61.5±7.1	58.9±8.4	86.5±9.9	80.2±11.4	83.6±9.0	84.1±9.8
MAP (mm Hg)	80.2±10.6	78.6±9.4	65.1±9.1*	78.3±8.6	75.8±9.4 *	86.1±9.1
RAP (mm Hg)	5.8±1.8	6.1±1.2	9.3±1.8*	6.6±1.2	8.8±1.9	7.4±1.4
MPAP (mm Hg)	18.2±4.1	19.4±3.6	18.8±2.2	19.9±3.4	17.3±4.3	17.8±3.9
PCWP (mm Hg)	9.6±3.1	9.5±3.1	11.2±3.4	9.8±2.8	10.5±4.1	8.8±2.3
CO (L/min)	4.9±1.1	4.6±1.4	5.2±1.1	5.4±1.6	5.3±1.1	5.2±1.4
CI (L/min/m^2)	2.4±0.8	2.3±1.2	2.6±0.5	2.7±0.9	2.7±0.3	2.5±0.8
SI (mL/beat/m^2)	41.4±9.5	41.8±7.2	39.6±9.9	38.4±6.9	32.6±4.4	33.1±6.3
LVSWI (g.m/m^2)	36.8±8.8	38.2±7.7	31.1±7.2	31.6±4.6	35.1±9.1	34.7±9.2
RVSWI (g.m/m^2)	6.1±1.2	5.8±1.1	5.1±1.0	4.8±0.9	4.6±1.6	4.8±1.3
SVRI (dynes.sec. cm^{-5}.m^2)	1985±860	2098±812	1480±542	1364±430*	1760±564	1896±721

Data expressed as mean ± standard deviation.
A: data group A after induction of anesthesia.
B: data group B after induction of anesthesia.
A1 and B1: Data group A and B, 10 minutes after cessation of the cardiopulmonary bypass.
A2 and B2: Data group A and B, 2 hours after cessation of the cardiopulmonary bypass.
HR: Heart rate, MAP: Mean arterial pressure, RAP: Mean right atrial pressure, MPAP: Mean pulmonary arterial pressure, PCWP: Pulmonary capillary wedge pressure, CO: Cardiac output, CI: Cardiac index, SI: Stroke index, LVSWI/RVSWI: Left/Right ventricular stroke work index, SVRI: Systemic vascular resistance index, *: Significant 'p' value ('p'< 0.05 versus pre-operative value).

ECG. No technical problems related to the delivery of cardioplegic solution were noted.

Discussion

Critical coronary artery stenosis and occlusion may result in non-homogenous distribution of antegradely delivered cardioplegic solution and consequently poor local myocardial protection.[6,7] Experimental and clinical studies have shown an increase in the myocardial energy needs in these jeopardised areas and a depression of the left ventricular function after reperfusion.[8,9,10] The experimental work of Partington et al[4,5] and the development of techniques[11] for blind cannulation of the coronary sinus have contributed to the renewal of interest in the use of retrograde cardioplegia in myocardial revascularisation.

In our study, all patients in-group B (antegrade + retrograde) returned to sinus rhythm after the release of aortic cross clamp. In addition, only 1 patient required IABP support as against 4 patients in group A (antegrade). This suggests that patients in group B had a better preservation of the myocardial function. In the majority of patients in whom antegrade cardioplegia was used, a decrease in LVSWI was accompanied by an increase in PCWP. This observation was also noticed in previously conducted clinical trials[12] and studies.[2,13]

The superior preservation of the left ventricular function in all the patients in spite of LAD occlusion in group B was observed in our study. This patient group approximates with the experimental model of Partington.[4,5] Previous clinical trials[14-16] were inconclusive concerning the superior myocardial protection achieved with retrograde cardioplegia in patients with coronary artery disease, but in none of these studies was there an extensive coronary artery disease as in our study and also the internal mammary artery was not used for grafting in all the patients. Fiore et al[14] described a mean of 2.9 diseased vessels in their study and only 65% of the patients received an internal mammary artery graft. Guiraudon et al[15] do not mention the severity of coronary artery disease or whether revascularisation was done using the internal mammary artery. The study done by Diehl et al[16] compares with our study in that all patients had isolated triple vessel coronary artery disease and a combination of antegrade and retrograde cardioplegia was used. The difference in our studies being that the internal mammary artery was used

in 100% of our study group as against 80% of the group studied by Diehl et al.[16]

Myocardial biopsy samples were not taken in our study. Studies have shown that the preservation of energy rich phosphates during ischaemic cardiac arrest is better with retrograde than with antegrade cardioplegia.[17,18]

The RVSWI was not different before and after the bypass in both the groups, which is in contrast to the results of the experimental study of Partington et al[4,5] in which the RVSWI in dogs was decreased. The less favourable protection of the right ventricle in dogs, may be related to the anatomic differences in the venous drainage of the right and left ventricles. Anatomic studies in dogs[19] have shown that most of the right ventricle and the posterior part of the inter-ventricular septum are not drained by the coronary sinus. In contrast the cardiac venous drainage in humans is more balanced. The equal distribution of the venous system over the human heart is confirmed by excellent cooling of the entire heart by retrograde cold cardioplegia as reported in this and other studies.[14,15,20 - 22]

Delay in cardiac arrest is described as a major disadvantage of giving retrograde cardioplegia.[14] In our study we did observe a difference between the two groups in the time that was needed to reach asystole, even though both the groups received a dose of antegrade cardioplegia. The total dose of cardioplegic solution was significantly higher in patients who received retrograde with antegrade cardioplegia as it was noticed that the calculated dose of cardioplegia did not suffice to cause asystole in patients of this group and an additional dose was needed to achieve this. Jasinski et al [21] reported that the incidence of ischaemic events and occurrence of ventricular fibrillation on reperfusion were significantly more frequent in patients who received purely antegrade cardioplegia. They further reported that a significantly higher percentage of patients regained sinus rhythm on aortic cross clamp release when they had received antegrade and retrograde cardioplegia during bypass. Ehrenberg et al[22] concluded that the use of retrograde cardioplegia provides more homogenous myocardial cooling than antegrade cardioplegia in patients with coronary artery occlusions and that the left ventricular function was better preserved by the use of retrograde cardioplegia. These findings are similar to those observed in our study. However a contradictory study conducted by Arom et al[23] reported that neither routes of delivery of cardioplegic solution were superior to the other.

Our study has a few limitations. Firstly it confines itself to a very short postoperative period and secondly that troponin C and I levels were not measured. The good clinical outcome in both groups in our study is also related to our patient selection along with surgical and anaesthetic strategy. Although clinical outcome was excellent in both the groups, early recovery of left ventricular function was better in patients who received antegrade with retrograde cardioplegia.

We conclude that retrograde with antegrade cardioplegia could be superior to antegrade cardioplegia alone as it facilitates early recovery of the left ventricular function in patients with triple vessel coronary artery disease undergoing CABG with the use of arterial and vein grafts.

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