Original Article

EFFECT OF ROUTE OF CARDIOPLEGIA DELIVERY ON MYOCARDIAL PROTECTION

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ABSTRACT

OBJECTIVE: To evaluate myocardial protection using cardioplegia solution infused only antegradely or through a combined antegrade and retrograde route in patients undergoing surgery for ischemic or valvular heart disease.

MATERIALS & METHODS: This Prospective comparative study included 108 consecutive patients who underwent cardiac surgery from March 2013 to October 2014 at Punjab Institute of Cardiology, Lahore Pakistan. Patients requiring coronary artery surgery, aortic valve replacement or combined aortic and mitral valve surgery were included. Patients requiring emergency surgery, undergoing CPR pre-operatively, requiring early re-exploration or patients with LV EF ≤30% were excluded. Data was analyzed using SPSS 20. P-value ≤ 0.05 was taken as significant.

RESULTS: Out of 108 patients 70(64.81%) were male. The mean age of the patients was 39.62±16.15 year. Patients included 36 in CABG group, 36 in AVR and 36 in DVR group. Half of the patients in each group were delivered cardioplegia through antegrade route only and the other half were infused cardioplegia through combined antegrade and retrograde route. Significantly lower aortic cross clamp and cardio pulmonary bypass times were observed for both AVR and DVR. (p-value< 0.05). There was a significant difference between immediate, early (after 24 hours) and post-operative (after 48 hours)mean CKMB in AVR, DVR and CABG with respect to the cardioplegia delivery groups (p-value <0.05). In all 3 surgical procedures the difference between echocardiographic characteristics of both groups was insignificant (P-value >0.05). The time of ventilation, ICU stay and total hospital stay were also found to be lower for the retrograde group.

CONCLUSION: Myocardial protection using a combined antegrade and retrograde cardioplegia delivery is superior to antegrade cardioplegia used alone for Coronary artery bypass surgery and aortic valve surgery with or without mitral valve replacement. It is associated with shorter cross clamp time, shorter ventilation time, ICU and hospital stay and lower CKMB levels.

KEY WORDS: CKMB, AVR: aortic valve replacement, DVR: double valve replacement, CABG: coronary artery bypass grafting, Antegrade cardioplegia, retrograde cardioplegia, left ventricular ejection fraction.

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INTRODUCTION

Strategies for myocardial protection vary among surgeons according to their training or experience. These strategies have evolved over time and a consensus on the most effective strategy is still awaited. However, surgeons' preferences are usually based on their operative sequence, conviction of safer myocardial management and at times costs, in addition to their training and environment[1].Cardioplegic arrest of the heart in diastole is currently the most common myocardial protection technique used worldwide though opinions vary about the route of delivery, vehicle of cardioplegia and the temperature of the cardioplegia solution. However, all techniques ensure that a rapid and effective diastolic arrest is achieved to keep myocardium relaxed and to minimize the use of energy.[2] Cardioplegic solution may be carried in crystalloid solution or in blood at various ratios. The route of delivery of cardioplegia solution also varies. Effective intra-operative myocardial protection requires adequate distribution of cardioplegic solution to all myocardial segments to be accomplished in a safe, simple, and rapid fashion.

The two most favoured approaches are antegrade route or a combination of antegrade and retrograde route[3]. Antegrade route is the delivery ofcardioplegic solution through the aortic root,

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after aorta is cross-clamped. This is the most common mode of administration of cardioplegia, to protect the myocardium for cardiac operations. The retrograde route is administration of cardioplegia solution via a special catheter placed in coronary sinus through a purse-string guarded small opening made in right atrial wall. A combination of ante-grade with retrograde cardioplegia is known to give a better myocardial protection in high-risk patients.[4-6]

This study was carried out to see whether delivery of cardioplegia through a combination of antegrade and retrograde route or the antegrade route alone affects early outcomes for patients undergoing open heart surgery.

MATERIALS & METHODS:

This Prospective comparative study included 108 consecutive patients who underwent cardiac surgery from March 2013 to October 2014 at Punjab Institute of Cardiology, Lahore Pakistan. Patients requiring coronary artery surgery aortic valve replacement or combined aortic and mitral valve surgery were included. Patients requiring emergency surgery, preoperative CPR, re-exploration or with Left Ventricular Ejection Fraction ≤30% were excluded. Data was analyzed using SPSS 20. A P-value ≤ 0.05 was taken as significant.

Cardiopulmonary bypass was established using ascending aortic cannulation and a single two-staged venous cannulation, with membrane oxygenator and roller pump, keeping the perfusate temperature at 28-30^{0}C and hematocrit between 21-25%. Blood cardioplegia was administered prepared in a 4:1 ratio with St Thomas's solution using blood from cardiotomy reservoir at 28- 30^{0}C.

In antegrade cardioplegia group the cardioplegia solution was infused through aortic root or completed vein grafts, while in antegrade and retrograde cardioplegia group, the initial 50% dose was given through aortic root, antegradely and the remaining 50% dose was given through coronary sinus cannula retrogradely. Subsequent doses were repeated at 20 minutes intervals retrogradely and via completed distal coronary grafts intermittently. Pressure in the retrograde cannula was monitored by the side arm of the coronary sinus cannula connected to a manometer ensuring that infusion pressure did not exceed 45 mm Hg. Blood cardioplegia was infused at 150-180 ml/min for an initial dose of 1 litre and subsequent doses of 500 ml each total, divided between retrograde cannula and completed vein grafts. The left ventricle was vented through the root via the Y connection in the antegrade cardioplegia cannula. For additional myocardial protection iced slush was used on the anterior surface of heart for topical cooling. An isolating pad was placed between the heart and left side of pericardium containing the phrenic nerve. Cold fluid was aspirated from pericardial cavity regularly to safeguard the phrenic nerve. Before patient was weaned from bypass (CPB) rewarming was done until nasopharyngeal temperature reached 37°C. The hematocrit was maintained between 21-25%. Arterial blood gases (ABG's) were monitored and maintained. For optimal myocardial performance optimal filling pressures were achieved. The aorta was de-cannulated at completion of half dose of protamine ensuring hemodynamic stability. Creatinine kinase(CK-MB) were determined in the morning of the operation, immediately after cessation of bypass, 24hrs and 48hrs later from venous blood sample. Post-operative support with inotropes was used as necessary. No patient required intra-aortic balloon support. Echocardiography was done within two days before the operation and on the third or fourth day postoperatively by same evaluators. Duration of ventilation, length of ICU stay, hospital stay and other outcomes were observed.

Data was analyzed by using SPSS (statistical package for social sciences) version 21. Mean ± S.D was given for quantitative variables. Frequencies, percentages were given for qualitative variables. Chi-square test was used to compare the qualitative variables with cardioplegia delivery groups; while for quantitative variables independent t-test was applied.

RESULTS:

Patient characteristics in both groups did not differ significantly in terms of demographics, Echocardiographic parameters and disease pattern. Table-1 shows the patient characteristics in both groups.

The cross clamp times were significantly shorter in the combined retrograde antegrade (A+R) group for aortic valve surgery and trend was seen for lower clamp times in double valve surgery but difference was not significant for CABG. Similarly cardiopulmonary bypass time was significantly lower for both AVR and DVR in the A+R group whereas this did not reach significant level in the CABG group. (Table-1)

Left ventricular function was not significantly different postoperatively though ejection fractions were generally higher for the retrograde group. (table-1)

Table-1: Patient characteristics in different procedure types with respect to the cardioplegia delivery.

Variables		Procedure Types	ANTEGRADE	ANTEGRADE+ RETROGRADE	P-VALUE
Gender	Male	AVR	11(30.6%)	14(41.2%)	0.47
		DVR	12(33.3%)	8(23.5%)	0.31
		CABG	13(36.1%)	12(35.3%)	1.00
	Female	AVR	7(38.9%)	4(20%)	0.47
		DVR	6(33.3%)	10(50%)	0.31
		CABG	5(27.8%)	6(30%)	1.00
Age (Years)		AVR	38.7222±20.32	28.61±11.25	0.044
		DVR	34.17±15.80	31±10.61	0.645
		CABG	53.78±8.49	51.44±8.29	0.345
Height (cm)		AVR	154±15.02	156±19.68	0.567
		DVR	157±15.39	144±27.29	0.048
		CABG	161±14.07	153±29.57	0.051
Weight (Kg)		AVR	58.22±14.47	57.08±13.89	0.333
		DVR	53.17±10.50	51.39±13.35	0.245
		CABG	71.94±11.26	73.39±16.89	0.190
BSA (m^2)		AVR	1.59±0.23	1.52±0.26	0.126
		DVR	1.51±0.18	1.47±0.23	0.423
		CABG	1.96±0.40	1.86±0.34	0.040
Blood flow (mL/ minute/g)		AVR	3.81±0.56	3.70±0.57	0.222
		DVR	3.62±0.41	3.51±0.59	0.210
		CABG	4.42±0.34	4.35±0.50	0.59
Cross clamp time (minutes)		AVR	81.41±30.19	60.24±18.16	0.034
		DVR	88.83±25.21	83.61±22.34	0.567
		CABG	59.75±30.39	59.12±21.72	0.987
Bypass time (minutes)		AVR	113±35.12	78±18.53	0.021
		DVR	130±36.27	107±20.25	0.048
		CABG	116±56.56	109±42.22	0.41
Pre Ejection Fraction (%)		AVR	53.44±8.38	57.33±6.74	0.432
		DVR	56.06±6.35	59±3.61	0.321
		CABG	50.72±12.67	54.28±7.31	0.432
Post Ejection Fraction (%)		AVR	54.6±10.8	56.3±6.7	0.456
		DVR	58.15±6.36	59.0±3.6	0.512
		CABG	49.47±12.0	52.2±7.3	0.442

Table 2:In-hospital outcome of patient characteristics in different procedure types with respect to the cardioplegia delivery.

VARIABLES	Procedure Types	ANTEGRADE	ANTEGRADE+ RETROGRADE	P-value
Post-operative creatinine (mg/ dL)	AVR	0.76±0.158	0.83±0.19	0.48
	DVR	0.86±0.26	0.77±0.19	0.45
	CABG	1.03±0.27	0.74±0.18	0.047
Immediate Post-operative CKMB	AVR	61.47±23.82	54.33±19.91	0.045
	DVR	67.78±18.24	62.06±12.09	0.044
	CABG	59.28±16.34	44.67±23.29	0.003
After 24hrs Post-operative CKMB	AVR	52.35±17.00	44.78±20.22	0.027
	DVR	55.44±247.27	44.50±29.11	0.035
	CABG	69.78±60.80	40.56±31.42	0.027
After 48hrs Post-operative CKMB	AVR	47±16.18.0	42±9.22	0.047
	DVR	56.44±19.0	37±5.00	0.001
	CABG	38±4.00	37±5.00	0.0237
Duration of ventilation (Hours)	AVR	36±23.78	8.19±3.97	0.001
	DVR	26.17±20.28	11.72±4.71	0.001
	CABG	16.35±17.70	14.06±8.16	0.058
Total ICU stay (Days)	AVR	7.89±5.00	4.0±2.00	0.024
	DVR	5.33±2.00	3.89±0.76	0.037
	CABG	5.89±2.63	4.44±1.76	0.578
Hospital stay (Days)	AVR	12.89±9.05	10.11±8.53	0.480
	DVR	9.72±7.36	8.67±2.35	0.462
	CABG	12.17±5.71	8.72±3.04	0.030
Post-op inotropes used	AVR	16(53.3%)	14(46.7%)	0.371
	DVR	18(56%)	14(43%)	0.034
	CABG	18(50%)	18(50%)	1.000
Mortality	AVR	2 (11.1%)	0 (0.0%)	0.146
	DVR	2 (11.1%)	0 (0.0%)	0.146
	CABG	1 (5.6%)	0 (0.0%)	0.310

Table 2: shows the postoperative comparison of the two groups. Immediate and early post-operative CKMB levels were significantly lower for retrograde group. This group also showed significantly shorter ventilation time in all subgroups and a significantly lesser need for inotropes in the double valve replacement subgroup.

The time of ventilation, ICU stay were also significantly lower for both AVR and DVR in the retrograde group whereas this did not reach significant level in the CABG group. (Table-1) while total hospital stay was significantly lower for CABG in the retrograde group.

Postoperative creatinine was significantly lower in the CABG (A+R) group. Also there were no deaths in the retrograde group compared to 5 deaths in the antegrade group though the difference did not reach significant level.

DISCUSSION:

Our results support the notion that the combination of antegrade and retrograde cardioplegia is a safe and effective method for myocardial protection in AVR, DVR and CABG patients. There is lesser release of enzymes in the immediate and early postoperative period indicating better protection. Part of this effect may be due to a more even distribution of cardioplegia with dual route.[7] The limitations of antegrade cardioplegia alone are well recognized as the myocardium beyond tight coronary lesions remains at jeopardy[8]. In the presence of diffuse coronary disease, this inadequacy of cardioplegia distribution becomes accentuated.[9] The superiority of retrograde cardioplegia over antegrade cardioplegia in protecting cardiac muscle that cannot receive antegrade cardioplegic flow is well established.[10]

Our study indicates that a combined technique of antegrade and retrograde cardioplegia is associated with shorter cross clamp times. This technique allows surgical procedure to continue without interruption especially in aortic valve surgery with or without mitral valve replacement. This advantage of the technique has been demonstrated by

most workers using this technique for myocardial preservation in patients undergoing CABG and valve replacement. [9-12] Another advantage of the technique is that it avoids trauma to coronary ostia by repeated antegrade cardioplegia infusion. It avoids opening the ascending aorta in cases of mild Aortic incompetence. There is sufficient evidence now that combined technique allows good biventricular protection.[13-16] There are minimum chances of injury to the coronary sinus provided coronary sinus perfusion pressures are kept below 60 mmHg17 as shown in our study.

Value of CKMB as a prognostic marker of myocardial injury is also well known.[18-19] Cardiac surgery is associated with universal rise in CKMB and values more than 3-5 times normal indicate myocardial infarction. Higher CKMB is associated with long term worse outcomes too. CK MB values in our study remained below three times the normal values in all patients but were significantly higher in the antegrade group compared to combined antegrade and retrograde group showing better protection with the latter technique.

CONCLUSION:

Myocardial protection using a combined antegrade and retrograde infusion of blood cardioplegia provides improved clinical outcomes compared to antegrade cardioplegia alone. It is associated with shorter aortic clamp time, lower levels of CKMB and a shorter hospital stay after open heart surgery for valvular or ischemic heart disease.

Author's Contribution

AHK: Data analysis, manuscript writing and wrote the article.
SA: Helped in manuscript writing and reviewed the article
AUKN: Data collection reviewed the article.
MI: Data collection and data analysis

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