

MYOCARDIAL PROTECTION USING DEL NIDO CARDIOPLEGIA SOLUTION COMPARED TO ON-PUMP BEATING MITRAL VALVE REPLACEMENT IN CHRONIC SEVERE MITRAL INCOMPETENCE

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ABSTRACT:

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Introduction: *Del Nido cardioplegia is widely used nowadays in adult cardiac surgery. Beating heart valvular surgery is gaining more popularity and used by many cardiac centers nowadays. Both is used currently in cases of chronic mitral valve incompetence with left ventricle impairment.*

Aim of the work: *To compare the outcome of Del Nido cardioplegia and beating surgery in cases of mitral valve replacement and left ventricular impairment.*

Patients and methods: *This is a clinically randomized trial conducted in National Heart Institute during the period from June 2020 till December 2021. It contains sixty patients with chronic severe mitral incompetence indicated for isolated mitral valve replacement using two different modalities of myocardial protection. Patients were divided into two groups: group (A) containing 30 patients receiving Del Nido (ND) cardioplegia , and group (B) containing also 30 patients underwent mitral valve replacement through beating heart surgery.*

Results: *Del Nido cardioplegia has a shorter surgical time than beating heart surgery, yet it has the same ventilation time , intensive care unit stay and need for inotropic support during weaning from bypass. Beating heart surgery had a lower level of post operative troponin release.*

Conclusion: *Del Nido cardioplegia is a safe and effective method of myocardial protection during mitral valve replacement with left ventricular impairment.*

Key Words: *Del Nido cardioplegia, Beating heart surgery, left ventricular impairment.*

INTRODUCTION:

Myocardial protection is the most important step in cardiac surgery. Numerous techniques and delivery methods have been evolved in the last few decades. The Del Nido (DN) cardioplegia was initially used in pediatric cardiac surgery. It has been used for almost twenty years in Boston, USA. Its use is widely expanding in adult cardiac surgery in many institutes over the last decade with promising outcomes⁽¹⁾. It has a

unique formula with one blood component and four crystalloid components, providing single dose administration that gives protection for 60-90 minutes. Owing to its advantage of providing long time protection and less interruption of the surgical procedure due to single dose administration, it was found to be attractive to many surgeons and adopted in many centres especially during complex or redo operations and minimal invasive

procedures⁽²⁾. In cases of chronic severe mitral incompetence the left ventricle systolic function and contractility is markedly affected after failure of the primary stage of compensation. These cases are categorized as a very high risk patients for surgery even they may be not amenable for surgical correction owing to their false high ejection fraction⁽³⁾. Other echocardiographic measurements as LV end systolic volume and dimensions are better used to estimate the function as they are not depending on the preload⁽⁴⁾.

The efficiency of DN cardioplegia in complex risky cases which mandates a long time of arrest is uncertain. Many studies were found to compare the myocardial protective effect DN to other cardioplegic solutions.⁽⁵⁾ On the other hand, many authors studied several myocardial protective techniques trying to decrease the deleterious effects of myocardial ischemia which may be caused by aortic clamp, cardioplegic solution and reperfusion injury⁽⁶⁾. With the wide spread of beating heart coronary artery bypass grafting surgery, many studies elicited the possibility of applying the same concept and performing beating heart surgeries for valve surgeries^(7&8). Despite this techniques mandates the use of bypass, but it abolishes the myocardial ischemia caused by arresting the heart through continuous perfusion of the heart, optimizing pH, prevents accumulation of metabolites and subsequently reperfusion injury^(9&10). So we performed this study to compare the efficacy and outcome of Del Nido cardioplegia compared to beating heart technique used in mitral valve replacement in cases of chronic severe mitral incompetence.

PATIENTS AND METHODS:

This is a clinically randomized trial conducted in National Heart Institute during the period from June 2020 till December

2021. It contains sixty patients with chronic severe mitral incompetence indicated for isolated mitral valve replacement using two different modalities of myocardial protection. Patients were divided into two groups: group (A) containing 30 patients receiving Del Nido (ND) cardioplegia, and group (B) containing also 30 patients underwent mitral valve replacement through beating heart surgery. Patients with redo surgeries, concomitant cardiac procedures, Infective endocarditis and severe other system co-morbidities were excluded from the study. An informed consent was taken from all patients. All patients received routine preoperative preparation.

Surgical procedure: All patients received a median sternotomy incision, aorto-bicaval cannulation for CPB, LV vent through left atriotomy.

Group (A) Del Nido cardioplegia:

After establishing of CPB and applying of cross clamp, Del Nido cardioplegia was administered antegradely into the aortic root through cardioplegia cannula, Only one single dose was sufficient in all cases with no need for re-administration, left atriotomy was done parallel to Sondergaard groove. Any case with repairable valve was excluded. Preservation of posterior mitral leaflet was done in all cases, with implantation of mechanical prosthetic valves in all cases. Closure of the left atriotomy and removal of cross clamp after deairing. Tricuspid valve repair, if indicated, was done on beating heart. Weaning from CPB after stabilization of hemodynamics.

Dosage of Del Nido cardioplegia: Induction dose mixing with 1/4 blood, 20 ml/kg, up to 1000 ml, Temperature (°C) 4–15, Pressure (antegrade/retrograde) 140/45 mmHg, Perfusion speed (minutes) 3–5, Reinfusion interval (minutes) 60–90, Maintenance dose 200–300 ml. Crystalloid component of Del Nido cardioplegia solution: 1 litre of plasma lyte A base

solution to which the following are added: Mannitol 20% 16.3 ml, Magnesium sulphate 50%, 4 ml. Sodium bicarbonate 8.4%, 13 ml. Potassium chloride 2meq/l, 13 ml, and Lidocaine 1 % 13 ml⁽¹¹⁾.

Group II (On- pump beating heart technique):

Aorto-bicaval cannulation in the usual manner, insertion of pulmonary vent through main PA and LV vent through right upper pulmonary vein. A double lumen cannula was inserted in the aortic root in which one port was connected to the arterial line to maintain coronary continuous perfusion at time of aortic cross clamping, while the other port is connected to a low suction line throughout the procedure and used in deairing after removal of LV vent. After establishing the CPB, aorta is not clamped, left atrial is opened in an empty, non ejecting heart, taking care not to induce aortic insufficiency with the atrial retractor leading to coronary hypo-perfusion, distended heart and bloody field. LV vent is passed through the mitral valve to ensure empty heart and more incompetence and bloodless field so as to prevent air embolism. Several maneuvers were used to avoid air embolism as: An LV vent is passed through the mechanical valve during its implantation and till closure of left atrial wall, to disturb the isometric contraction phase of cardiac cycle and render the LV as an open chamber. Also used to empty the heart during momentary cross clamp appliance preventing its distension and used for deairing. Momentary aortic clamping is used three times: At opening left atrium, implantation of mechanical valve, and finally at time of left atrial wall closure. Secondly one port of double lumen cannula is connected to low suction. Thirdly maintaining the patient at Trendelenburg position with mean systolic perfusion

pressure kept at 70-78mmhg during CPB. low cardiac output refers to the need for a high dose of inotropics (Dopamine > 15 µg /kg/ min, Epinephrine > 0.1 µg/ kg /min, norepinephrine > 0.1 µg/ kg/min) to maintain a systolic blood pressure greater than 90 mmHg or the need for mechanical circulation support [extracorporeal membrane oxygenation (ECMO) or intra-aortic balloon pump (IABP)] after the operation

Statistical Analysis:

Statistical presentation and analysis of the present study were conducted, using the mean, standard deviation and chi-square test by SPSS V.16. P value is considered significant when the test value equals to or less than 0.001.

RESULTS:

There was no statistically significant difference between the two groups regarding the demographic data as shown in table (1). Demographic data of the patients pre-operatively showed that group (A) contained 20 males (66.7%) and 10 females (33.3%) while group (B) contained 17 males (56.7%) and 13 females (43.3%) with a P value of 0.462 NS. Mean age in group A was 32.50±7.94 years while in group B it was 31.36±9.18 years, P value = 0.611 NS. In Group (A) there was 4 patients in sinus rhythm (13.3%) and 26 patients were in atrial fibrillation (AF) while in group (B) 5 patients were in sinus rhythm (16.7%) and 25 patients were in AF (83.3%) with a P value 0.718 NS. In group (A) 3 patients presented in NYHA class II (10%) and 27 patients presented in class III (90%) while in group (B) 7 patients presented in NYHA class II (23.3%) and 23 patients presented in class III(76.7%) with a P value 0.166 NS.

Table (1): Preoperative Patient’s data: NYHA, Rhythm, sex

		NYHA			Rhythm			Sex		
		II	III	Total						
					sinus	AF	Total	male	female	Total
Del Nido	N	3	27	30	4	26	30	20	10	30
	%	10.0%	90.0%	100.0%	13.3%	86.7%	100%	66.7%	33.3%	100%
Beating	N	7	23	30	5	25	30	17	13	30
	%	23.3%	76.7%	100.0%	16.7%	83.3%	%	56.7%	43.3%	100%
Total	N	10	50	60	9	51	60	37	23	60
	%	16.7%	83.3%	100.0%	15%	85%	100%	61.7%	38.3%	100%
		P-value		0.166	0.718			0.462		

Pre-operative echocardiography showed mean end diastolic diameter of 6.92 ± 0.50 in group (A) while in group (B) it was 6.81 ± 0.53 with P value 0.421 and no significant difference. End systolic diameter was 4.49 ± 0.43 in group (A) while in group (B) it was 4.94 ± 0.40 with a P value of 0.286 NS. Ejection fraction in group (A) was 45.73 ± 5.64 and in group (B) it was 46.16 ± 6.18 with a P value of 0.712 NS

The Aortic cross-clamp time the range was 25– 55 minutes in group (A) with mean 35.75 ± 4.54 but in second group aortic cross-clamp was momentary applied in certain times as mentioned before: we compensate for it statistically by the operation surgical time (from opening of the left atrium wall till its closure); it ranged from 40-65 minutes with mean 44.50 ± 9.59 in group (B), and ranged from 18 – 33 with mean 28 ± 4.59 in group (A). It was significantly longer in group (B) compared

to group (A) as $P < 0.001$. There was no significant difference between the two groups as regard to the total bypass time , it was 67.50 ± 12.64 in group (A) while it was 63 ± 12.97 in group (B) with a P value 0.441 as shown in table (2). During weaning from cardiopulmonary bypass we faced 23 patients in group (A) who needed therapeutic dosed of inotropes (76.6%) with only 7 patients needed high inotropic support more than the therapeutic dose or more than one inotrope (23.3%) while in group (B) only 3 patients needed high inotropic support (10%) with 27 patients needed therapeutic dose (90%) with a P value of 0.166 with no statistically significant difference. There were no patients needed mechanical support in the form of intra-aortic balloon pump counter pulsations in an early postoperative period in both groups .

Table 2: showing operative and post operative data.

	Del Nido	Beating	P-value
Total bypass time (min)	67.50 ± 12.64	63 ± 12.97	0.441
Operation surgical time(min)	28 ± 4.59	44.50 ± 9.59	0.001
Ischemic Clamp time (min)	35.75 ± 4.54	0	-
Ventilation hours	8.43 ± 3.01	7.86 ± 2.98	0.373
ICU stay(days)	3.60 ± 1.19	3.40 ± 0.68	0.049
Hospital stay(days)	14.87 ± 0.50	14.53 ± 0.50	0.244
Total CK 3H	2091.8 ± 574.9	1361.7 ± 155.8	0.001
LDH 3H	1182.5 ± 459.9	832.3 ± 71.01	0.001
Total CK 12H	2237.5 ± 681.5	1320.2 ± 214.3	0.001
LDH 12H	1226.2 ± 463.2	864.7 ± 126.9	0.005

EDD: End diastolic diameter
FS: Fraction shortening
ICU: Intensive care unit.

EF: Ejection fraction
LDH: Lactate dehydrogenase

ESD: End systolic diameter
CK: creatine kinase

Mechanical ventilation patients in the beating heart group had a shorter time of mechanical ventilation 7.86+2.98 hours and ICU stay 3.40+0.68 days post operatively while ventilation time of 8.43+3.01 hours and ICU stay of 3.60+1.19 days in the Del Nido group with a P value of 0.373 and 0.049 respectively with no significance. Serial measurements of cardiac enzymes (total CK,) after 3 hours, and 12 hours in both groups revealed a significant difference between two groups in favor of group (B). It

was after 3 hours 2091.8±. 574.9 in group (A) and 1361.7±155.8 in group (B) with a P value of 0.001 which is considered significant. While after 12 hours it was 2237.5 ± 681.5 in group (A) and 1320.2 ± 214.3 in group (B) with a P value of 0.001 (significant). There was no statistically significant difference regarding post operative echocardiographic data between the two groups as shown in table (3) there was no in hospital mortality in both groups .

Table (3) showing post operative echo data.

	Del Nido	Beating	P-value
EDD late	6.39+0.51	6.13+0.54	0.067
ESD late	4.74+0.48	4.52+0.46	0.084
FS late	25±3.1	26.8±3.01	0.022
EF% late	47.16±5.81	46.83±5.78	0.003

DISCUSSION:

Several factors have led to the increase and wide use of Del Nido cardioplegia nowadays in the adult cardiac surgery despite its original development as a myocardial protection solution used in congenital cardiac surgeries⁽¹²⁾. Among these factors is having a long duration of action, single shot administration , and its ability of decreasing consumption of energy and inflammatory substrates scavenger. Several studies have evaluated the outcome and benefits of usage of Del Nido cardioplegia in various adult cardiac surgeries , the simple and complex ones⁽¹³⁾.

On the other hand, the wide use of beating heart techniques in coronary artery bypass surgery and its good results obtained encouraged many surgeons to apply the same concept in valvular heart surgery. Several studies have shown the efficacy and outcome of beating surgery in valvular replacement surgeries. So, we conducted our study to compare two of the recent modalities used nowadays in myocardial protection in cases of chronic mitral valve insufficiency with left ventricular

dysfunction. Our main finding is that Del Nido cardioplegia patients had significantly less surgical time and consequently bypass time, which in turn was reflected on the need of high inotropic support during weaning from CPB and hence time of mechanical ventilation which was not significantly different between the two groups. This may be explained by less maneuvers needed to prevent air embolism in the beating heart group as multiple clamp application and removal, besides relatively technically more difficult dealing with the beating mitral annulus. These results are in the same line with many studies comparing beating heart mitral valve replacement with warm blood cardioplegia, they used same way of perfusing the coronary arteries during surgery, showing that surgical time was significantly lower in cases of Del Nido patients than cardioplegic patients⁽¹⁴⁾. Other studies didn't specify surgical time from bypass time⁽¹⁵⁾ and showed the same results concerning the operative time totally.

Our study showed less ventilation time similar to other studies showing nearly the same duration^(10&14) with much less

ventilation time than other studies which showed long time extending to 44 hours⁽¹⁵⁾.

Other studies showed no superiority or inferiority of Del Nido cardioplegia over warm cardioplegia with no significant difference in CPB time (97vs 103 minutes) with less aortic clamp time in Del Nido patients. They related CPB time and clamp time to be independent factors for mortality post operatively⁽¹⁶⁾.

Our study showed that there was elevated rise in cardiac enzyme troponin in the post operative period in the Del Nido group much more than beating heart group with a statistically highly significant difference. This was reported also by many studies comparing Del Nido to warm blood cardioplegia⁽⁷⁾. However, other studies concluded that mere rise of cardiac troponin post operatively is neither conclusive nor of certain significance unless accompanied with ECG and echocardiographic positive findings⁽¹⁷⁾. There was no significant difference regarding post operative low cardiac output as manifested by number of patients who needed high dose of inotropes during weaning from CPB. This was discordant with other studies which showed decrease of low cardiac output syndrome in cases of Del Nido as compared with warm cardioplegia⁽¹⁸⁾. Another randomized control study proved that Del Nido cardioplegia might be very useful especially in mitral valve surgery due to non-interruption of the procedure when administering multiple doses of cardioplegia, so surgical steps-flow is improved⁽¹⁹⁾. Another meta- analysis , recently published , showed that Del Nido has a lower bypass time, yet no difference was detected in low cardiac-output, enzyme levels or the need of inotropes between the two groups⁽²⁰⁾. They concluded that Del Nido, though is not the only one shot myocardial protective solution used in cardiac surgery, it certainly has documented many benefits in CABG and valvular surgery in this control, randomized

trial. In our study, there was no peri-operative mortality or other major complications such as cerebral strokes CVS or perioperative myocardial infarction in both group. This matches with other studies that showed one year survival rate of 96%⁽²¹⁾.

Conclusion:

Del Nido cardioplegia solution has a shorter surgical time than beating heart surgery. It offers the same ventilation time, ICU stay and incidence of low cardiac output same as beating heart surgery. Moreover, it provides some advantages over the beating heart surgery as single shot administration with no interruption of surgical flow, as well as deleting the incidence of introducing air embolism . Del Nido cardioplegia solution is a safe and effective method of myocardial protection especially in high risk patients as left ventricular dysfunction caused by chronic severe mitral incompetence.

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**محلول الديل نيدو المثبط لعضلة القلب مقارنة بطريقة القلب النابض في تغيير الصمام الميترالي للقلب
في حالات اعتلال البطين الايسر**

مقدمة: زاد استخدام محلول الديل نيدو في حالات جراحة القلب للبالغين كما ان استخدام طريقة القلب النابض اثبتت نتائج مذهلة في عمليات تغيير الصمامات للقلب

الهدف من البحث: مقارنة محلول الديل نيدو مع طريقة القلب النابض في عمليات تغيير الصمام الميترالي للقلب مع اعتلال البطين الايسر

الطريقة و المرضى: اجريت هذه الدراسة علي ستون مريضا في معهد القلب القومي و تم تقسيمهم الي مجموعتين كل مجموعة ثلاثون مريضا.

النتائج: مجموعه الديل نيدو كان لها وقت جراحي اقصر مع ارتفاع في انزيمات القلب بعد العمليه.

التوصيات: محلول الديل نيدو له نتائج مبشرة في حالات تغيير الصمام الميترالي مقارنة بطريقة القلب النابض.