

Original Research Article

Use of del nido cardioplegia versus St. thomas solution 2 in adult mitral valve replacement surgery at a tertiary care hospital in Kolkata, India

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ABSTRACT

Background: del Nido cardioplegia has been historically used in paediatric cardiac surgery. However it's use in adults has also been documented. It has the advantage of 90 minutes of cardiac inactivity over St. Thomas solution no.-2, which requires repeated dosing at 20 minutes interval. Aim of this study to find out whether del Nido cardioplegia with longer duration of arrest is advantageous over St. Thomas solution no. 2 in adult mitral valve replacement.

Methods: Total 60 patients of severe mixed mitral valve disease of comparable patient profiles, underwent mitral valve replacement with preservation of anterolateral and posteromedial chordae. Half the patients received del Nido cardioplegia and other half received St. Thomas solution no 2. (ST-2). The two groups were compared.

Results: del Nido group had lesser CPB time (70.73 ± 12.15 min) as compared to ST-2 group (81.76 ± 20.03 min) with $p=0.01$; lesser Cross clamp time (del Nido- 68.8 ± 10.64 min; ST-2- 75.83 ± 14.00 min) with $p=0.02$; lesser time taken to arrest heart (del Nido- 21.58 ± 13.37 sec; ST-2- 25.26 ± 5.27 sec) with $p=0.04$ and lesser time taken for normal ECG activity to manifest after release of cross clamp (del Nido- 19.86 ± 6.10 min; ST-2- 31.03 ± 5.28 min) with $p=0.02$. All other parameters did not reach statistical significance.

Conclusions: del Nido cardioplegia group of patients required significantly less CPB time; Cross-clamp time; Mean time taken to arrest the heart; as well as that taken to manifest normal ECG morphology when compared to ST-2 group.

Keywords: del Nido, Mitral, St. Thomas

INTRODUCTION

Currently in adult cardiac surgery, variety of cardioplegic solutions are being used worldwide. These solution could be extracellular or intracellular (depending on their ionic composition).¹ St. Thomas Solution no.2 (ST-2) and del Nido are two such extracellular cardioplegic solutions. Both are hyperkalemic solutions and cause potassium induced membrane depolarising cardiac arrest. However, in order to reduce the ventricular dysfunction that occurs due to intracellular calcium loading during potassium

induced membrane depolarisation, membrane stabilising additives like magnesium and lignocaine have been added in depolarising solutions as modifications which directly or indirectly control the intracellular calcium concentrations.²⁻⁵ Thus, del Nido is a modified depolarising solution because of its zero calcium and presence of lignocaine as additive.

A comparison between these two solutions is given in table 1. Moreover, del Nido has the advantage of no need for repetition of cardioplegia till 90 minutes of infusion.

Hence, in this study, authors have tried to find out the superiority of one solution over the other in terms of certain intraoperative parameters as well as postoperative inotrope requirements, duration of ventilation and ITU stay.

Table 1: Comparison between St. Thomas solution no 2 (ST-2) and del Nido.

Composition	ST -2	del Nido
Na+	110mmol/l	150mmol/l
K+	16mmol/l	26mmol/l
Mg ⁺⁺	16mmol/l	16mmol/l
Ca+	1.2mmol/l	-----
NaHco ₃	10mmol/l	26mmol/l
Lidocaine	-----	140mg/l
Mannitol	-----	2.6g/l

Objective of study to find out, whether del Nido cardioplegia is advantageous over St.Thomas solution no.2, in adult mitral valve replacement in terms of : CPB Time, Cross Clamp Time, Time taken to Arrest the heart, Time taken for normal ECG Morphology to manifest after cross clamp release, Ventricular fibrillation after cross clamp release, Defibrillation requirement, Temporary pacemaker requirement, Blood transfusions requirement during CPB, Haematocrit on CPB, Blood Mg²⁺ level after cross clamp release, Blood Lactate level after decannulation, K⁺ and Ca²⁺ levels after decannulation, post operative requirement of inotropes in 1st 24 hours (Adrenaline, Nor-adrenaline, Milrinone and Dobutamine), post operative Ventilation requirement in ITU and lastly duration of ITU/Hospital stay.

METHODS

This prospective analytical observational study was conducted in the CTVS department of Medical College, Kolkata between 1st January 2019 and 31st December 2019.

A total of 60 patients of rheumatic severe mixed mitral valve disease (MS/MR) were included in our study. All of them had mild TR, PASP in the range of 40-50mm Hg, preserved left ventricular ejection fraction and were in atrial fibrillation.

Patients with associated aortic valve pathology, coronary artery disease and those who underwent previous cardiac surgeries were excluded.

Among 30 of these patients had received ST -2 solution and 30 had received del Nido during operation. All surgeons were consultants with requisite competence for the operation.

In the ST- GROUP, 20ml/kg of St.Thomas-2 cardioplegia solution mixed with blood (4 part ST-2 crystalloid: 1 part

blood) was delivered in 3-4 minutes at a temperature of 10-12°C. Cardioplegia was repeated every 20 minutes.

In the del Nido group as well, the cardioplegia volume was 20ml/kg. However unlike ST-2 group, ratio of del Nido solution with blood was 4:1.

This solution was delivered at a temperature of 8-10°C, in 3-5 minutes. Half dose was repeated after 90 minutes when required.

In all these patients mitral valve was replaced with appropriately sized St. Jude Master series bileaflet mechanical valves in antianatomical position with preservation of anterolateral and posteromedial chordae.

There was no requirement for addressing the Tricuspid valves in any of our cases.

The following parameters were noted:- CPB Time(mean), Cross Clamp Time(mean), Time taken to Arrest, Time taken(mean) for normal ECG Morphology to manifest, ventricular fibrillation after cross clamp release(%), Defibrillation required (%), Temporary pacemaker required (%), Units of Blood transfusions required during CPB; Haematocrit (mean) on CPB - 10 minutes after administering cardioplegia, Blood K⁺, Ca²⁺ and Lactate level 15 minutes after coming off pump, Post operative requirement of inotropes for 1st 24 hours (Adrenaline, Nor-adrenaline, Milrinone and Dobutamine), Mean Ventilation required postoperatively in ITU (hours), Mean ITU stay (days) and lastly Mean Hospital stay (days).

Results were analysed using standard statistical software in Microsoft Excel (Windows-10)

RESULTS

The patient profiles in the two groups were comparable (Table 2).

Table 2: Patient characteristics in ST-2 and del Nido groups.

Patient characteristics	del Nido (N=30)	ST -2 (N=30)
Age (Years) mean±SD	54.31±6.5	56.77±4.6
Male : Female ratio	1:3.75	1:2.34
Bodyweight mean±SD	59.2±7.8	65.03±17.1
BSA(m ²)- mean±SD	1.235±0.26	1.42±0.35
EF(%)	preserved	preserved
Atrial Fibrillation n(%)	28 (93%)	29(96%)
TR	mild	Mild
PASP	40-50mmHg	40-50mmHg

The intraoperative parameters showed significantly less mean CPB time ($p=0.01$) and Cross-clamp time ($p=0.02$) in the del Nido group. The mean time taken to arrest the

heart ($p=0.04$); as well as that taken to manifest normal ECG morphology ($p=0.02$) were also significantly low in del Nido group as compared to the ST-2 group (Table 3).

Table 3: Comparison of intraoperative parameters between del Nido and St. Thomas solution no 2.

Intraoperative parameters	del Nido	ST-2	p value
CPB Time(mean)	70.73±12.15 min	81.76±20.03 min	0.01
Cross Clamp Time(mean)	68.8±10.64 min	75.83±14.00 min	0.02
Time taken to arrest	21.58±13.37 sec	25.26±5.27 sec	0.04
Time taken for normal ECG Morphology (mean)	19.86±6.10 min	31.03±5.28 min	0.02
Ventricular fibrillation after cross clamp release (%)	3(10%)	5(16.67%)	>0.05
Defibrillation given (%)	3(10%)	4(13.33%)	>0.05
Temporary pacemaker (%)	12(22.64%)	16(53.33%)	>0.05
Units of blood transfused during CPB (mean)	1.067±0.785	0.400±0.563	>0.05
Mean Haematocrit on CPB 10 minutes after cardioplegia (%)	24.21± 2.3	30.11±2.1	>0.05
Mean Lactate levels 15 minutes after coming off pump (meq/L)	2.46±0.86	2.59±0.94	>0.05
Mean K ⁺ levels 15 minutes after coming off pump (mmol/L)	4.31±0.5	4.8±1.5	>0.05
Mean Ca ²⁺ levels 15 minutes after coming off pump (mmol/L)	0.9±0.5	1.5±0.5	>0.05

Table 4: Comparison of post-operative parameters between del Nido and St. Thomas solution no 2.

Post operative parameters	del Nido	ST - 2	p value	
Inotropes	Adrenaline (1 st 24 hrs)	72.93±13.09mcg	79.67±11.78 mcg	>0.05
	Nor- adrenaline (1 st 24 hrs)	21.44±6.76mcg	32.55±12.87 mcg	>0.05
	Milirinone (1 st 24 hrs)	15.17±3.58 mcg	21.89±13.67 mcg	>0.05
	Dobutamine (1 st 24 hrs)	39.20±8.38 mcg	44.52±14.99 mcg	>0.05
Mean Ventilation time(hrs)	7.77±3.97	9.07±3.48	>0.05	
Mean ITU stay (Days)	2.20±0.48	2.60±1.22	>0.05	
Mean Hospital stay(Days)	5.17±0.48	6.03±1.52	>0.05	

Authors also found, that among the post operative parameters: the inotrope requirement in first 24 hours after operation; mean requirement of mechanical ventilation and mean ITU / Hospital stays were more in the St.Thomas solution no 2 group as compared to the del Nido group . However, these differences did not achieve statistical significance (Table 4).

DISCUSSION

St. Thomas solution was introduced at St. Thomas Hospital in London, England in 1976.⁶ St. Thomas solution 2 or Plegisol was an upgradation (year 1981) of the original St. Thomas solution, wherein potassium concentration was increased, whereas sodium and calcium concentrations were both decreased.⁶ When blood (4 parts) is added to ST-2 solution (1 part), authors have Modified St. Thomas Solution, since it gives added advantages like reduction of haemodilution due to addition of blood. Also, it acts as a natural acid-base buffer, improves oxygen delivery to myocardium,

reduces tissue edema by increasing colloidal oncotic pressure & preserves high energy phosphates (ATP).⁷

Although originally developed at the University of Pittsburgh (year 1990) for usage in immature myocardium, the application of del Nido cardioplegia in adult cardiac surgery is now known.^{8,9} Apart from the convenience of avoiding cardioplegia administration multiple times (as in ST -2), authors found that our del Nido group of patients showed significantly lower Cross clamp and CPB time. This result is in concurrence with the studies by Mick SL et al and Smigla G et al.^{9,10} Authors also found that time taken to achieve cardiac arrest on administration of cardioplegia as well as time taken to manifest normal ECG morphology was significantly less in the del Nido group as compared to the ST-2 group.

During ischaemia there is intracellular accumulation of hydrogen ions. The sarcolemmal Na⁺- H⁺ exchanger effluxes the H⁺ out of the cell, in exchange of Na⁺. Thus intracellular Na⁺ concentration increases. Now there is

activation of sarcolemmal Na⁺-Ca²⁺ exchanger (NCX); which causes influx of 1 Ca²⁺ in the cell & efflux of 3 or 4 Na⁺ to maintain Na⁺ homeostasis. Thus intracellular free Ca²⁺ increases during ischaemia. Activation of voltage dependent Ca²⁺ channels can also occur by accumulation of long-chain acylcarnitine and fatty acids in sarcolemmal membrane in ischaemic myocardium and promote intracellular influx of Ca²⁺. Upon reperfusion in presence of intracellular Ca²⁺ overload mitochondria acts as a 'Ca²⁺-sink' by activation of mitochondrial Ca²⁺-uniporter, which causes increased mitochondrial Ca²⁺ uptake. This mitochondrial Ca²⁺ overload impairs its ability to produce ATP and ultimately manifests as myocardial dysfunction.¹¹ The Mg²⁺ in this solution acts as a Ca²⁺ channel antagonist and thereby protects from high intracellular calcium. Moreover, Lignocaine in del Nido solution is a direct blocker of the fast sodium channel and prevents initiation of action potential (membrane stabilizing effect).¹²

However, another interesting finding was that, although other important parameters like: requirement of inotropes post operatively, requirement of postoperative ventilation and ITU /Hospital stay; were less in the del Nido group as compared to the ST-2 group, these differences did not reach statistical significance.

Mean lactate, K⁺ and Ca²⁺ levels, 15 minutes after coming off pump were also similar in both groups.

CONCLUSION

When compared to ST-2 group, del Nido cardioplegia group of patients showed statistically significant - less CPB time (p= 0.01); Cross-clamp time (p= 0.02); Mean time taken to arrest the heart (p= 0.04); as well as that taken to manifest normal ECG morphology (p= 0.02). However, There were no significant differences between the two groups regarding : Requirement of blood during CPB ; Mean Lactate, K⁺ and Ca²⁺ levels 15 minutes after coming off pump; requirement of inotropes post operatively; requirement of post operative ventilation and ITU /Hospital stay.

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