Original Article

Nepalese Heart Journal 2020; Vol 17 (1), 23-27

Comparative study between the use of St. Thomas' II cardioplegia and del Nido cardioplegia in patients who underwent open-heart surgery.

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Cite this article as: Vaidya S, Adhikari AB, Karmacharya R, et al. Comparative study between the use of St. Thomas' II cardioplegia and del Nido cardioplegia in patients who underwent open-heart surgery. Nepalese Heart Journal 2020; Vol 17 (1), 23-27

Submitted date: 9th February 2020
Accepted date: 8th April 2020

Abstract

Background and Aims: Cardioplegia is used to arrest the heart after the application of an aortic cross-clamp that interrupts the coronary circulation. Commonly used St. Thomas'II cardioplegic solution has to be repeated at short intervals, which may cause additional myocardial injury. So, this study is done to determine whether del Nido (DN) cardioplegia, which has a longer duration of arrest with a single dose, provides equivalent or better myocardial protection as compared to St. Thomas' II Cardioplegia. **Methods:** A prospective observational study was done among 100 patients who underwent open-heart surgery with myocardial protection, between September 2016 to August 2018 in Bangabandhu Sheikh Mujib Medical University, Bangladesh. Patients were divided into two groups, group A (n=50) for del Nido cardioplegic and group B (n=50) for St. Thomas' II cardioplegia. We compared the amount of cardioplegic solution, Aortic cross-clamp time, cardiopulmonary bypass (CPB) time, ischemic time, arrhythmia, spontaneous sinus rhythm after declamping, intraoperative DC shock requirement, postoperative left ventricular ejection fraction, serum potassium level, low cardiac output, cardiac Troponin level I and CK-MB release after 12 hours and 24 hours, presence of myocardial infarction and death. **Results:** The per-operative variable suggested spontaneous activity during a cardiac arrest was 2% in del Nido and 14% in St. Thomas' II group (p=0.044). Similarly, during intraoperative phase spontaneous restoration of cardiac activity after the procedure in del Nido was 2.90 ± 1.16 minutes and in St. Thomas' II was 1.8 ± 0.615 minutes (p=0.001). However total bypass time and ischemic time were not significant. During the postoperative period, Troponin I and CKMB were measured at 12 hours and 24 hours which were not statistically different in two groups. Postoperatively, low output syndrome was seen among 3 patients in del Nido Group and 4 patients in St. Thomas' II group (p-value=0.341). **Conclusion:** This study showed with the use of del Nido cardioplegia provides equivalent myocardial protection to St. Thomas' II cardioplegia, with the use of only single-dose cardioplegia.

Keywords: delNido solution; St. Thomas'II Solution; Cardioplegia; Myocardial Protection.

DOI: https://doi.org/10.3126/njh.v17i1.28802

Introduction

Cardioplegia is used to arrest the heart after the application of an aortic cross-clamp that interrupts the coronary circulation.[1] Aortic cross-clamping without the use of cardioplegia results in anaerobic metabolism and depletion of myocardial energy stores. Thus, without a reduction in myocardial metabolism, either by hypothermia or by chemical-induced cardiac arrest, aortic occlusion producing ischemic arrest for more than 15-20 minutes would result in severe myocardial dysfunction.[2] In 1955, Melrose first described the use of potassium citrate to achieve electro-mechanical diastolic arrest of the heart during cardiac surgery,[1,3] hence cardioplegia or chemical induced arrest of heart was introduced as a method of myocardial protection.[4] In the context of cardiac surgery, myocardial protection refers to the strategies and techniques used during the surgery to prevent ischemic reperfusion injury.[5,6] These strategies help lower the heart's metabolic demands, minimizing myocardial stunning and perioperative necrosis.[5] In 1975 Hearse and associates at St. Thomas' hospital in London took a slightly different approach to chemical cardioplegia. Rather than using an intracellular solution, these investigators developed a predominantly extracellular formula based on sodium as the primary cation. Emphasis was placed on making the solution as physiological as possible. Specific additives were included to arrest the heart and maintain membrane integrity. The St. Thomas' solution has been used clinically since 1975 and has gained widespread acceptance.[7] However, it must be administered repeatedly at short intervals during the surgery. In the early 1990s, Dr. Pedro del Nido and his team at the University of Pittsburgh developed a cardioplegic solution to address the specific needs of immature myocardium encountered in neonatal and pediatric cardiac surgery. The solution, now commonly referred to as del Nido cardioplegia, induces a depolarizing arrest during cardiac surgery. Del Nido's potential practical advantage is the fact that it provides a long period of arrest before a subsequent dose is needed.[7,8]

Adequate protection of the myocardium during an ischemic arrest is essential for a successful clinical outcome. The optimal method for cardioplegia and myocardial preservation is still under debate, despite the substantial number of experimental and clinical studies that have been published over the years. Myocardial protection during open-heart surgery has been the focus of clinical research for many decades, but the debate regarding the ultimate cardioprotective strategy and the search for the ideal cardioplegic solution is still ongoing. St. Thomas' II cardioplegia has been used in many cardiac institutes in Bangladesh and also worldwide. However, as the conventional cardioplegic solution it has to be given more frequently to maintain myocardial protection every 25 minutes, which may lead to obscuring of the surgical field by blood, and also increases the ischemic time and procedure time. The study aims to see whether the new del Nido cardioplegic solution provides good myocardial protection with a single dose cardioplegia and helps avoidance of the need for repetitive interruption of the procedure to administer multiple doses of St. Thomas' II cardioplegia, which leads to shorter cross-clamp times.

Table 1: Composition of St Thomas and del Nido cardioplegia solutions[5]

St. Thomas II Cardioplegia	Del Nido Cardioplegia
Na^+ 110 mmol/l	Mannitol 20%, 16.3 ml, 3.26g/L
K^+ 16 mmol/l	Magnesium sulfate 50%, 4 ml, 2g
Mg^{2+} 16 mmol/l	Sodium bicarbonate 8.4%, 13 ml, 13 mEq
Ca^{2+} 1.2 mmol/l	Lidocaine 1%, 13 ml, 130 mg
$NaHCO_3^-$ 10 mmol/l	Potassium chloride (2 mEq/ml) 13 ml, 26 mEq

Materials and Methods

Patient Population

This was a prospective observational study conducted at Bangabandhu Sheikh Mujib Medical University, Bangladesh. This study protocol was viewed and reviewed by the Institutional Review Committee for ethical clearance. The sample size for this study was calculated using two proportional methods. A cross-sectional study was done for study design and a systemic randomize sampling method was used to collect the sample. The study includes 100 patients who underwent aortic valve replacement, mitral valve replacement and congenital heart disease cases between September 2016 and August 2018. The patients were divided into two groups based on the type of cardioplegia administration, Group A (n=50) for del Nido cardioplegic and group B (n=50) for St. Thomas' II cardioplegia.

Cardioplegia Administration

All procedures were performed using a standard general anesthesia protocol, median sternotomy approach, and cardiopulmonary bypass with moderate systemic hypothermia (28 to 32°C). Myocardial protection was achieved with either St. Thomas' II or del Nido cardioplegia. In both groups, the heart was arrested with an induction dose (20 ml/kg) cardioplegia using antegrade delivery. In addition, repeated doses at 10 ml/kg of ST Thomas' II cardioplegia were given to St. Thomas' II patients usually after 25 minutes of cardiac arrest. A second dose of del Nido was provided only when the cross-clamp time exceeded 90 minutes.

Comparison variables

We compared per-operative cardiopulmonary bypass (CPB) time, aortic cross-clamp (CC) time, spontaneous activity during cardiac arrest, spontaneous restoration of activity after cardiac surgery in two modalities and cardiac troponin I and CKMB as a marker for myocardial damage, low cardiac output syndrome which was measured using parameters such as a decrease in cardiac index <2.0 L/min/m^2, systolic blood pressure <90 mmHg and hypoperfusion (cold periphery, clammy skin, confusion, and oliguria)[9] and in-hospital mortality postoperatively.

Statistical Analysis

The data were analyzed using SPSS version 23.0. Continuous variables were reported as mean ± standard deviation and compared using the independent samples t-test. Categorical variables were reported as frequency and percentage of the total group and compared using the χ^2 test or Fisher's exact test where applicable. All p-values ≤ 0.05 were considered significant.

Results

Fifty patients were studied in each group. There were no statistical differences in demographic variables among both groups (Table 2). In St. Thomas' II group 45% of patients underwent aortic valve replacement, 25% underwent mitral valve replacement, 20% underwent double valve replacement and 10% underwent intra-cardiac repair for congenital heart disease. In the del Nido group, 35% of patients underwent aortic valve replacement, 35% underwent mitral valve replacement, 15% underwent double valve replacement and 15% underwent intra-cardiac repair for congenital heart disease. The overall mean age of the patients was 41.75 ± 12.07 years and 40.35 ± 8.66 with a p-value of 0.676.

Table 2: Distribution of patients of both groups by demographic variables

	Group		
	del Nido	St. Thomas' II	P-value
	(n=50) N (%)	(n=50) N (%)	
**Age (In years) Mean±SD	41.75±12.07	40.35±8.66	0.676
* Sex Male	35 (70.0)	25 (50.0)	
Female	15 (30.0)	25 (50.0)	0.167
**BSA (m^2)	1.95±0.20	1.50±0.21	0.290
Cardiac Surgery	del Nido (n=50)	St. Thomas' II	p-value
*Aortic Valve Replacement	22 (45.0)	17 (35.0)	
*Mitral Valve Replacement	13 (25.0)	17 (35.0)	
*Double Valve Replacement	10 (20.0)	08 (15.0)	0.819
*Intra-cardiac Repair	05 (10.0)	08 (15.0)	
Total	50 (100.0)	50 (100.0)	

Data were expressed as number and percentage.
**Statistical analysis was done by Chi-square test χ^2 and p more than 0.05 was considered not to be significant.*
***Student's t-test and was presented as mean ± SD.*
****Fisher's Exact Test was done to analyze the data.*
The figure in parenthesis indicates the percentage.

Intraoperative and Postoperative Outcomes

Total bypass time in del Nido Cardioplegia was 119.35 ± 37.56 min while that for St. Thomas II mean extra corporeal circulation time (ECCT) time was 106.50 ± 33.34 minutes. Which is statistically not significant (p=0.206). Mean Cross clamp (XCT) was 65.45 ± 24.42 minutes and 56.75 ± 14.13 minutes respectively, which was also statistically not significant (p=0.176). Spontaneous activity during a cardiac arrest was higher in the St. Thomas group which was statistically significant (p=0.044). Spontaneous restoration of cardiac activity after the cross-clamp release was significantly higher in the del Nido group (2.90 minutes ± 1.16) compared to St. Thomas II group (1.8 minutes ± 0.6) which was statistically significant (p=0.001) (Table 3).

Similarly, in post-operative evaluation Troponin I release after 12 hours was 3.55 ± 1.84 ng/L in del Nido while in St. Thomas' II was 3.05 ± 1.69 ng/L. After 24 hours it was 3.34 ± 2.71 ng/L in del Nido and 2.30 ± 1.80 ng/L in St. Thomas' II. In both cases, the p-value was statistically not significant. Post-operative release of CKMB after 12 hours in del Nido was 16.25 ± 8.45 IU/L and in St. Thomas' II was 17.15 ± 9.35 IU/L. After 24 hours, the release of CKMB was 18.40 ± 7.82 IU/L in del Nido and in St. Thomas' II was 14.15 ± 9.33 IU/L. These differences were also statistically not significant. Low cardiac output syndrome in both groups was statistically not significant. And there was one mortality among both groups. These results are summarised in Table 4.

Table 3: Distribution of patients of both groups by Intra-operative variables

	Group		
	del Nido	St.Thomas' II	P value
	(n=50)	(n=50)	
**ECCT (Minutes) (X)	119.35 ± 37.56	106.50 ± 33.34	0.260
**XCT (Minutes) (X)	65.45 ± 24.42	56.75 ± 14.13	0.176
***Spontaneous Activity during cardiac arrest	01 (2.0)	07 (14.0)	0.044
**Spontaneous restoration of activity after surgery (minutes)	2.90 ± 1.16	1.8 ± 0.61	0.001

Data were expressed as number and percentage.
**Statistical analysis was done by Chi-square test χ^2 and p more than 0.05 was considered not to be significant.*
***Student's t-test and was presented as mean ± SD.*
****Fisher's Exact Test was done to analyze the data.*
The figure in parenthesis indicates the percentage.

Table 4: Distribution of patients of both groups by post-operative variables

	Group		
Variables	Del Nido	St.Thomas'II	P value
	(n=50)	(n=50)	
**Troponin I (12 hrs after)(ng/ml)	3.55 ± 1.84	3.05 ± 1.69	0.559
**CK-MB (12 hrs after)(IU/L)	16.25 ± 8.45	17.15 ± 9.35	0.751
**Troponin I (24 hrs after) (ng/ml)	3.34 ± 2.71	2.30 ± 1.80	0.163
**CK-MB (24 hrs after) (IU/L)	18.40 ± 7.82	14.15 ± 9.33	0.127
*Low output syndrome	03 (6.0%)	04 (8.0%)	0.341
In Hospital Mortality	1 (2.0%)	1 (2.0%)	1.000

Data were expressed as number and percentage.
**Statistical analysis was done by Chi-square test χ^2 and p more than 0.05 was considered not to be significant.*
***Student's t-test and was presented as mean ± SD.*
****Fisher's Exact Test was done to analyze the data.*
The figure in parenthesis indicates the percentage.

Discussion

Cardioplegic solutions have a key role in protecting the heart from myocardial injury during open-heart surgery.[7,8,10] Del Nido solution has been used successfully in pediatric cardiac surgery; however, its use in adult cardiac surgery has only recently been described.[11] In this study, demographic variables, risk factors for heart disease, and other preoperative variables were found not significant among two groups, which was consistent with the study done by Yerebakan et al in 2014 among 48 patients.[12] Similarly, the distribution of patients with type of surgery was also not significant. There was no significant difference between the two means in case of per-operative variables: the total bypass time and total cross-clamp time. Spontaneous cardiac activity during the procedure was significantly higher in group B compared to group A which signifies the reduced requirement to administer repeated doses of cardioplegia. A similar study done by O'Blenes et al. 2011, stated that del Nido cardioplegia delayed the return of rhythm during cardiac operation, which was similar findings to our study.[13]

Time to the spontaneous restoration of activity after cardiac surgery in group A was higher compared to group B. It signifies that the restoration of cardiac rhythm after the cross-clamp release was comparatively slow in the case of del Nido cardioplegia when compared to the St. Thomas's II cardioplegia.[14] Govinda Pillai and colleagues in 2013 had done a similar study which suggested spontaneous restoration of activity after cardiac surgery in del Nido may be related to Na^+ channel blockade with lidocaine, but del Nido cardioplegia also contains slightly more potassium and magnesium, resulting in more pronounced membrane depolarization[15] which also contribute to more effective arrest. Reduced spontaneous activity during the ischemic period should limit the development of intracellular acidosis, which drives the Na^+, and subsequently Ca^{2+}, an influx that contributes to ischemia-reperfusion injury.[15] In this regard, Lucas SK et al suggested that St. Thomas' II cardioplegia due to repeated doses of a cardioplegic solution have an early spontaneous activity after cardiac surgery compared to del Nido cardioplegia which help in better ultrastructural preservation by multiple doses attributed to wash-out of metabolic end products.[16]

Cardiac Troponin I and CKMB concentration was measured in a serial venous blood sample drawn post-operatively in both groups, 12 hours and 24 hours after aortic cross-clamp release. The amount of Troponin I release and CKMB release were not statistically significant. Mick et al. in 2014 and Yerkeben et al. in 2013 supported the findings that there was no significant difference among the release in Troponin I and CKMB in del Nido cardioplegia solution and St. Thomas' II cardioplegia solution.[12;10] In post-operative variables, the low output syndrome developed in 6% in group A and 8 % in group B which was also not significant. One each post-operative mortality was present among the groups, one due to post-operative arrhythmia and another due to low cardiac output syndrome.

Lidocaine is the major component of del Nido cardioplegia which is a membrane-stabilizing agent, which causes an increment in Na^+ channel blockade and minimizes the potential for a Na^+ window current. Similarly, Mg^{2+} content acts as a Ca^{2+} antagonist, these are the suggested mechanisms by which del Nido cardioplegia protects the myocardium from high intracellular Ca^{2+}.[17] O'Blenes et al. reported that, in isolated aged rat cardiomyocytes, cardiac arrest with del Nido cardioplegia resulted in lower spontaneous activity during ischemia, lower diastolic Ca^{2+} during ischemia and reperfusion, and avoidance of Ca^{2+}-induced hyper contraction during early reperfusion in comparison with standard cardioplegia.[13] A similar study was done later in the setting of aged hearts, where single-dose of del Nido cardioplegia was associated with superior calcium handling of cardiomyocytes, reduced myocardial injury, and improved functional recovery.[15]

This study demonstrates that a single dose of del Nido cardioplegia can provide a longer duration of cardioplegic arrest compared to St. Thomas' II cardioplegia with similar myocardial protection both per-operatively and postoperatively.

Conclusion

This study showed that del Nido cardioplegia provides equivalent myocardial protection to St. Thomas' II cardioplegia during cardiac surgery, with the use of only single-dose cardioplegia it prevents spontaneous activity in the arrested heart, compared to multiple doses in St. Thomas' II. However spontaneous restoration of cardiac activity after the release of aortic cross-clamp release was slightly longer in del Nido. With regards to other post-operative variables, like the release of Troponin I and CKMB and low cardiac output syndrome were similar in the case of both the groups. So, we conclude that del Nido cardioplegia provides a better alternative to St. Thomas' II cardioplegia even in longer procedures such as DVR.

Limitation

This study was a single-center study, involving a small sample size, with a short duration of the study. It was confined only to valvular heart disease and congenital heart disease. Only adult patients were included in the study and require the overall age group to confirm the efficacy and safety of the del Nido cardioplegia.

Disclosure

The authors who were members of the editorial team were not involved in any steps in the editing/publication process.

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