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# COMPARISON BETWEEN DEL NIDO CARDIOPLEGIC SOLUTION AND ST. THOMAS CARDIOPLEGIC SOLUTION IN CORONARY ARTERY BYPASS GRAFTING (CABG) SURGERY - A PROSPECTIVE SINGLE CENTRE STUDY

Cardiology

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## ABSTRACT

The aim of study is Comparision between single dose Del Nido cardioplegic solution and repeated doses St. Thomas cardioplegic solution in the group of the patients who underwent to coronary artery bypass surgery.

This Prospective, descriptive and observational study was conducted from August 2017 to December 2019. Total number of patients in this study were 136 and devided on the basis of cardioplegia into two groups one is Del Nido(DC) group [n=68] and other is St. Thomas (ST) group [n=68] . A single dose of Del Nido solution was administered . Parameters were cross clamp time, total CPB time, DC shocks given, Postoperative troponin levels and postoperative left ventricular ejection fraction, post op ionotropic supports, duration of ventilation in ICU and total hospital stay. In DC group the aortic cross clamp time (62.78±8.46 vs. 56.82±7.23) was significantly shorter, Total CPB time was shorter (85.84±9.99 vs. 78.18±7.90) and requirement of DC shocks was less (23 (33.8)% vs. 11 (16.2)%) . Inotropic requirement was significantly less in immediate post-operative period in DC group. Prolong intubation (>48 hours ) was significantly less in DC group 9 (13.2)% vs 5 (7.4)%. In post operative period ejection fraction improved more( 49.63±3.01 vs. 51.10±3.26 ) and Troponin level (0.027±0.004 vs. 0.027±0.004) significantly reduced in DC group.

Conclusion of this study is that myocardial protection was superior with Del Nido cardioplegic solution compared with St. Thomas solution. Outcomes were better with Del Nido cardioplegic solution intra operatively and immediate post-operatively.

## KEYWORDS

Coronary artery bypss surgery, Del nido cardioplegia, St. Thomas cardioplegia

## 1. INTRODUCTION

With an increase in cardiac surgery procedures for treatment of cardiac diseases, various new and improved methods for myocardial preservation invented. Cardioplegia is an integral part of myocardial preservation. Most of the cardiac surgeries are performed on cardiopulmonary bypass, CPB furnish reproducible and safe methods for administration of cardioplegia. Energy consumption by myocardial cells is significantly lower in cardioplegic arrest, even at normothermia. [1]

### 1.1. Del Nido cardioplegia –

Dr. Pedro Del Nido developed Del Nido cardioplegia at the University of Pittsburgh in 1990 and which has been used initially for pediatric cardiac surgery and since 2003 has been used for adult cardiac surgery [2]. In the adult cardiac surgery, use of DN cardioplegia has been expanded because cardioplegic arrest achieved upto 90 minutes with only a single dose, as compared with conventional multi-dose blood cardioplegia (BC), doses must be repeat every 15–20 min. Limited studies validating the safety margins and effectiveness of Del Nido in adults. [3]

In our study, we compared the use of DN cardioplegia with BC for isolated coronary artery bypass grafting (CABG) surgeries , performed by a single surgeon at our institution.

Del Nido cardioplegia is an extracellular solution mixed with autologous blood, the crystalloid: blood ratio is 4: 1. A Single dose at 20 ml/kg is sufficient to achieve optimal myocardial protection upto 90 minutes. The administration flow is 200–300 ml/min. The Pressure at which cardioplegia administered is 100–200 mm Hg. The delivery temperature is 8–12°C. The blood provides buffering capabilities and improves coronary perfusion and supports aerobic metabolism during the delivery. Hypothermia reduces both the metabolism and oxygen consumption. [2]

The basic crystalloid solution is Plasma-Lyte A. [Table 1].

*Table 1. Del Nido cardioplegia solution*

| Components | Volume |
|---|---|
| Plasmalyte A | 1000 ml |
| Mannitol 20% | 16.3 ml |
| Mg Sulphate 50% | 4 ml |
| NaHCO3 | 13 ml |
| Lidocain 1% | 13 ml |
| KCL 2meq/ml | 13 ml |
| Ph | 7.4 |

Every ingredient plays an important role in the myocardial protection.

### 1.2. Plasma-Lyte A contains:-

Na: 140 mmol/l, K: 5 mmol/l, Cl: 98 mEq/l, Mg: 3 mmol/l, acetate: 27 mEq/l and gluconate: 23 mEq/l with pH: 7.4.

Mannitol scavenging free radicals and reduces the edema due to hyperosmotic capabilities [4].

Magnesium improve myocardial recovery by blocking the calcium channels. Magnesium (Mg++) ions inhibits a myosin phosphorylase, which protects Adenosine Triphosphate (ATP) reserves for postischemic activity and help to stabilize the myocardial membrane [5].

Rapid depolarized arrest achieved by potassium chloride with potassium concentration >25 meq/L.

Sodium ions ($Na^+$) maintain ionic integrity of myocardial tissue which is essential. The chloride ions ($Cl^-$) maintain the electroneutrality of the solution.

Bicarbonate ($HCO_3^-$) anions act as a buffer to make the cardioplegic solution slightly alkaline and compensate with metabolic acidosis that occurs due to ischemia.

Lidocaine is a class Ib antiarrhythmic agent and sodium channel

blocker which prevents the negative effect of hyperkalemic depolarized arrest by polarizing the cell to some degree and reducing intracellular sodium and calcium influx [6].

Mixing of blood in cardioplegic solution supports in aerobic metabolism and improves coronary perfusion during the delivery, it is also protects from reperfusion injury by preserving myocardial metabolism and reducing ischemic stress. [7].

### 1.3. St Thomas cardioplegia –

*Table 2. St Thomas cardioplegia Solution II*

| Components | Concentration (mmol/l) |
|---|---|
| Na | 110 |
| K | 16 |
| Cl | 128 |
| Ca | 1.2 |
| Mg | 16 |
| $NaHCO_3$ | 10 |
| Ph | 7.8 |

The St Thomas (ST) cardioplegic solution was developed at London in 1975.

St Thomas Hospital Solution II developed in 1981, it is an refined version of St Thomas cardioplegic solution I in which the concentration of potassium, sodium and calcium are low. It has been a popular and well established, crystalloid cardioplegia however, it must be administered in repeated dose every 20 to 30 min during the surgery [Table 2] [8, 9].

### 1.4. Rationale for use of del Nido -

Because of poor tolerance due to ischaemia Del Nido cardioplegia was launched for immature myocardium. It reduces troponin T release and intracellular calcium during arrest and reperfusion which protects from reperfusion injury [6]. It preserves myofibrillar architecture which is responsible for better preservation of cardiac index as compared to St. Thomas cardioplegia and reduces Troponin I release in pediatric patient [10]. The fibrillation rates on declamping are low hence the use of electric defibrillation are less with Del Nido cardioplegic solution. [11-13]

With widespread use of Del Nido cardioplegia, its efficacy has been established in pediatric cases. Recently, it is being used as cardioplegia solution in adult cardiac surgery. Its usefulness in various clinical scenarios have been demonstrated in few retrospective studies. It provides prolonged period of cardiac arrest with a single dose administration which is favourable conditions for the operating surgeon by non-interruption of surgical workflow.

## 2. Methodology

This study was conducted in the cardiovascular and thoracic surgery department, Sawai Man Singh Medical College and Hospital, Jaipur. The study protocol was reviewed by institutional board and need for consent was waived off. Here we are presenting our experience with Del Nido cardioplegia solution in CABG. Aim of this study was to compare its efficacy and safety with St. Thomas solution in all adult patients specially who were undergoing Coronary Artery Bypass Surgery.

### 2.1. Patient population-

The period of study is from August 2017 to December 2019. Data collected for patients who were undergoing coronary artery bypass surgery with use of Del Nido cardioplegia (n=68) in the cardiovascular and thoracic surgery departement. Operating surgeon and his team was the same to reduce surgeon bias and data of the patients are collected. They were compared to prospective group of patients in whom St Thomas solution was used (n=68).

Outcomes measured were aortic cross clamp time, total bypass time, electric defibrillation rate, use of inotropes, post operative ejection fraction, post-operative troponin levels, duration of ventilation, ICU and Hospital stay.

In all surgeries, surgical approaches were midline sternotomy under standard general anaesthesia, cardiopulmonary bypass with mild hypothermia, antegrade method was used for delivery of cardioplegia . Repeated dose of St Thomas cold blood cardioplegia was given in every 20 minutes interval whereas of Del Nido cardioplegia was given in single dose.

### 2.2. Exclusion criteria-

- Congenital cardiac lesions
- Reduced ventricular function (<40% Ejection Fraction)
- Other associated diseases which are requiring intervention
- Preoperative inotropic or mechanical support
- Redo surgeries

## 3. Data Analysis

***Statistical Analysis***

SPSS was used to analyse the data. Categorical variables were reported as frequency and percentage of total and compared using chi-square or fisher's exact test where applicable. Continuous variables were described as mean+ standard deviation and compared by using independent samples t-test. All p values < .05 were considered significant.

## 4. RESULTS

Demographic features of patients are presented in table 3. There were 136 patients in our study, 68 patients were in Del Nido cardioplegia group (DC) and remaining 68 patients were in St. Thomas cardioplegia group. Baseline of demographic features of patients were similar in both groups.

*Table 3. Demographic features of patients*

| Variables | St Thomas N= 68 | Del Nido N=68 | Total N=136 | (P value) |
|---|---|---|---|---|
| Sex n (%) | | | | |
| Female | 22 (32.3) | 11 (16.1) | 33 | 0.02* |
| Male | 46 (67.6) | 57 (83.8) | 103 | |
| NYHA Class n (%) | | | | |
| 1 | 45 (66.1) | 60 (88.2) | 105 | 0.0021* |
| 2 | 23 (33.8) | 8 (11.7) | 31 | |
| CCS Score n (%) | | | | |
| 1 | 25 (36.8) | 19 (27.9) | 44 | 0.36 |
| 2 | 43 (63.2) | 49 (72.1) | 92 | |
| Smoking n (%) | | | | |
| Yes | 50 (73.5) | 60 (88.2) | 110 | 0.0291* |
| No | 18 (26.4) | 8 (11.7) | 26 | |
| | Mean±SD | Mean±SD | | (P value) |
| Age (Mean±SD) | 61.09±6.03 | 63.15±6.97 | | 0.068 |
| Height (Mean±SD) | 162.49±5.24 | 165.44±6.83 | | 0.005* |
| Weight (Mean±SD) | 58.66±7.24 | 66.50±5.73 | | .000*** |
| BSA (Mean±SD) | 1.62±0.12 | 1.73±0.10 | | .000*** |

*Significant (p value<0.05), *** highly Significant (<0.001).

*Table 4. Intra operative variables*

| Variables | St Thomas N= 68 | Del Nido N=68 | Total N=136 | (P value) |
|---|---|---|---|---|
| Vol. of Cardioplegia n (%) | | | | |
| 1 | 4 (5.9) | 68 (100.0) | 72 | 0.000*** |
| 1 (2) | 9 (13.2) | 0 (0.0) | 9 | |
| 1 (3) | 53 (77.9) | 0 (0.0) | 53 | |
| 1 (4) | 2 (2.9) | 0 (0.0) | 2 | |
| Electric defibrillation (Yes) | 23 (33.8) | 11 (16.2) | 34 | 0.017* |
| Aortic_cross_clamp_time (min.) (Mean±SD) | 62.78±8.46 | 56.82±7.23 | | 0.000*** |
| Total_bypass_time_min (Mean±SD) | 85.84±9.99 | 78.18±7.90 | | 0.000*** |

*Significant (p value<0.05), *** highly Significant (<0.001).

*Table 5. Early post-operative variables*

| Variables | St Thomas N= 68 | Del Nido N=68 | Total N=136 | (P value) |
|---|---|---|---|---|
| Number of ionotrops after surgery n (%) | | | | |
| 1 | 26 (38.2) | 49 (72.1) | 75 | 0.000*** |
| 2 | 35 (51.5) | 16 (23.5) | 51 | |
| 3 | 7 (10.3) | 3 (4.4) | 10 | |

| | | | | |
|---|---|---|---|---|
| Intubation time >48 hours n (%) | | | | |
| Yes | 9 (13.2) | 5 (7.4) | 14 | 0.398 |
| No | 59 (86.8) | 63 (92.6) | 122 | |
| EF%_Before (Mean±SD) | 49.99±3.98 | 47.09±4.01 | | 0.000*** |
| EF%_After ( Mean±SD) | 49.63±3.01 | 51.10±3.26 | | 0.007* |
| Troponin T_Level_Preop. (Mean±SD) | 0.027±0.006 | 0.030±0.028 | | 0.484 |
| Troponin T _Level_Postop. (Mean±SD) | 0.027±0.004 | 0.022±0.021 | | 0.104 |

Significant (p value<0. 05), *** highly Significant (<0.001).

Details of intra operative variables of both groups are mentioned in Table 4 and early post-operative variables of both groups are mentioned in Table 5.

The aortic cross clamp time and total CPB time were less in DC group as compared to ST group and it is statistically significant. After declamping for return to normal rhythm the requirement of electrical defibrillation was less after declamping, in DC group as compared to St Thomas group. [Table 4]

Requirement of number of inotropic supports in early post operative period was less in DC group which is statistically significant. Ejection fraction was improved more in DC group as compared to St Thomas group which was statically significant. Troponin T levels decreased in DC group. Mechanical ventilation duration in post operative period was shorter in DC group. ICU and hospital stay were also shorter in DC group as compared to St Thomas group. [Table 5]

## 5. DISCUSSION

Adequate myocardial protection should be the mainstay of all cardiac surgeries. Cardioplegia have a central role to protect the myocardium of heart from myocardial injury during on pump cardiac surgery. For years, St Thomas cold blood cardioplegia has been used for this purpose allowing various cardiac surgeries. The main drawback of St Thomas cardioplegia, it needs to be given in repeated dose at fixed and short intervals during surgery which interrupts surgical workflow. Increases in myocardial acidosis between the doses, affecting the postoperative outcome adversely. In our study, we present our experience with Del Nido cardioplegic solution in patients underwent elective Coronary Artery Bypass surgeries and compare it prospectively with St Thomas group in which patients underwent Coronary Artery Bypass surgeries with St Thomas cardioplegic solution.

Del Nido cardioplegia was instituted for immature myocardium because of poor tolerance of ischemia,. It reduces troponin T release and intracellular calcium during cardiac arrest and reperfusion. [6]

It preserves myofibrillar architecture which is responsible for superior preservation of cardiac index as compared to St. Thomas cardioplegia and reduces Troponin I release in pediatric patient. [10] The fibrillation rates on declamping are low hence the use of electric defibrillation are less with Del Nido cardioplegic solution [11-13]

Several animal studies confirmed the safety of Del Nido cardioplegia. Govindapillai et al., stated that Del Nido cardioplegia prevents superior contractions during arrest, reduced troponin release and preserves myocardial function. He also proved the superiority of single dose Del Nido over multi dose Del Nido. [14, 15].

The Del Nido cardioplegic solution has been used successfully in paediatric cardiac surgeries, however its use in adult cardiac surgery has only recently been described.

Prolonged CPB times have adverse effects intra operatively and post operatively. Complications are more and duration of mechanical ventilation and ICU stay is prolong with prolonged CPB. [16]

Significant differences in the intraoperative outcomes were present in our study. Shorter Aortic cross clamp time (62.78±8.46 vs. 56.82±7.23) and Total CPB time (85.84±9.99 vs. 78.18±7.90) in the surgeries which used Del Nido cardioplegic solution as compared to St Thomas cardioplegic solution.

Duration of delivery of cardioplegia solution and Interruption of surgical workflow because repeated doses were required, increases the time in St. Thomas group.

Our intra operative outcomes supported by a study which was conducted by Marzouk et al., in 131 patients received Del Nido as compared to blood cardioplegia in combined surgical procedures, which was statistically significant. [17] Other similar studies also support these findings of decreased operative time with use of Del Nido. [18-20] These studies and their results go in line with our study.

Ad et al. published the use of Del Nido cardioplegia in adult cardiac surgeries in a randomised controlled trial which showed consistent results with these findings without reaching statistical significance. [21]

Patients who received Del Nido cardioplegia had shorter ventilation duration in our study.

Chances of return of spontaneous rhythm were higher in patients who recieved Del Nido cardioplegia . Only few patients required DC shocks in Del Nido cardioplegia group than in St Thomas cardioplegia group (16.2% vs. 33.8%), various other studies across the globe supports these findings. [22,23]

Fibrillation is a known and common event after declamping which can be stabilized by electric defibrillation. fibrillation is also known cause of myocardial injury. [24]

High inotropic support requirement was lower in DC group as compared to ST group in immediate post operative period and it was statistically significant. These findings supported by a study in paediatric patients in which inotropic requirement was lower in first 24 hours. [25] It is an indirect marker of better myocardial preservation. We performed cardiac enzyme analysis for all post-operative patients in CABG. Troponin T levels decreased significantly in DC group post operatively which is also supports that myocardial preservation is better with Del Nido cardioplegia. [6]

In post-operative period LVEF (51.10±3.26 vs. 49.63±3.01 ) improved in the DN group in our study. During on pump cardiac surgeries myocardial ischaemia occurs which causes accumulation of intracellular Ca+ through energy requiring active transport mechanisms which mediates early reperfusion injury [26-28]. The myocardial cell counteracts this high intracellular $Ca^{2+}$ and ultimately manifesting as myocardial dysfunction upon reperfusion.

Lidocaine in Del Nido cardioplegia serve as a membrane-stabilizing agent which increases Na+ channel blockade and minimizes the potential for a Na+ window current. Its $Mg^{2+}$ content acting as a $Ca^{2+}$ antagonist, these mechanisms favours that Del Nido cardioplegia protects the myocardium of heart from high intracellular $Ca^{2+}$ [6].

In our study, there was no significant difference in the post operative troponin T between two groups; however, values were slightly higher in ST cardioplegia group (0.027±0.004 vs 0.022±0.021). A study by O'Brien et al supports these findings, he used del Nido cardioplegia solution in pediatric population which showed lower troponin levels [6]

## 6. Limitations of the Study

The limitations in our study includes that it is a prospective, descriptive in nature and small cohort size. In postoperative period only hemodynamic parameters, ejection fraction and cardiac enzymes were used to assess myocardial protection.

Long-term follow-up of myocardial protection (e.g., changes in regional wall motion or ejection fraction) was not performed.

## 7. CONCLUSION

Our study explained that the use of Del Nido cardioplegia reduced the aortic cross clamp time and total CPB time, single dose was sufficient and repeated dose of cardioplegia was not required. Requirement of high inotropic support was less in immediate post-operative period.

Additionally, it provided superior myocardial protection in view of the improved LVEF values and low Troponin levels post operatively.

Del Nido cardioplegia is a superior alternative to St.Thomas cardioplegia in CABG.

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