Original Article

Myocardial Protection in Cardiac Surgery: Del Nido versus Blood Cardioplegia

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Abstract

Objectives: del Nido cardioplegia which was traditionally used for myocardial protection in pediatric congenital heart surgery is now being extensively utilized in adult cardiac surgery. The aim of this study was to compare the safety and efficacy of del Nido cardioplegia (DNC) with blood cardioplegia (BC). **Materials and Methods:** This is a historical cohort study using secondary data. Two hundred and eighty six patients who underwent coronary artery bypass graft (CABG) or valve surgery were included. They were divided into 2 matched cohorts of which 143 patients received BC and 143 patients received DNC. **Results:** There was no difference in cardiopulmonary bypass time (P = 0.516) and clamp time (P = 0.650) between the groups. The redosing of cardioplegia was significantly less for DNC (1.13 vs. 2.35, P = <0.001). The post bypass hemoglobin was higher for DNC (9.1 vs. 8.7, P = 0.011). The intraoperative and postoperative blood transfusion was comparable (P = 0.344) (P = 0.40). The incidence of clamp release ventricular fibrillation (P = 0.207) was similar. The creatine kinase-MB isotype levels for the CABG patients were comparable on all 3 days (P = 0.104), (P = 0.106), and (P = 0.158). The postoperative left ventricle ejection fraction was lesser but within normal range in the DNC group (53.4 vs. 56.0, P = <0.001). The duration of ventilation (P = 0.186), ICU days (P = 0.931), and postoperative complications (P = 0.354) were comparable. There was no 30-day mortality or postoperative myocardial infarction in both the groups. **Conclusion:** DNC provides equivalent myocardial protection, efficacy, and surgical workflow and had comparable clinical outcomes to that of BC. This study shows that DNC is a safe alternate to BC in CABG and valve surgeries.

Keywords: *Blood cardioplegia, Del Nido, efficacy, myocardial protection*

Introduction

Adequate myocardial protection is essential for a successful clinical outcome during cardiac surgery. The main principles of myocardial protection are reduction of metabolic activity by hypothermia and diastolic arrest of the electrical activity of the heart by administering cardioplegia.[1] This provides the surgical team with a still, bloodless field essential for their surgical precision.

There is no clear consensus on the optimal composition of cardioplegic solutions.[2] The composition varies based on institutional preferences. The two main types that have gained widespread acceptance are diastolic arrest induced and maintained with potassium added to either blood-based solution or a crystalloid-based solution.[1,3] There are several types of blood cardioplegia that differ in their electrolyte and drug additives which are supplemented to stabilize the membrane potential. Some examples are Buckberg solution, Plegisol solution, and St. Thomas solution.[4] Del Nido is a crystalloid-based cardioplegia known to have a prolonged arrest time due to the lignocaine and magnesium additive but can inherently cause hemodilution.[5] Although originally designed for a child's immature heart,[6] del Nido is now used as a new alternative to protect the adult ischemic myocardium in a wide range of surgeries.[7]

In our institution, modified St. Thomas blood cardioplegia (BC) has been the standard solution for cardiac arrest in adult cardiac surgery. We transitioned to del Nido crystalloid cardioplegia (DNC) from May 2017. The purpose of our study was to compare the efficacy and safety of del Nido with the conventional blood cardioplegia in different cardiac surgical groups.

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Materials and Methods

Our institution is a tertiary care center where all our patient data is stored in an easily retrievable form. The study design is a historical cohort using secondary data from January 2017 to August 2017 inclusive of the period of transition. The Institutional Ethics Committee approved the study (IRB no. 10998). The requirement for informed consent from individual patients was waived because of the study design. We extracted all patient information and clinical data from perfusion charts, anaesthesia records, postoperative intensive care unit (ICU) charts, and the in-house hospital information system. A sample size of 122 (61 in each group) was calculated based on the study by Mishra *et al*.[8] to test the mean difference of 21 and with standard deviation of 42 for the time duration of cardiopulmonary bypass (CPB) with 80% power and at 5% level of significance. Given that we are using secondary data, we took a larger number of cases. Two hundred and eighty six patients were included in the study. They were divided into 2 matched cohorts of which 143 patients received BC and 143 patients received DNC.

We included all adult patients from age group of 18 to 80 years who underwent elective cardiac surgery under CPB requiring cross-clamping of the aorta and the administration of cardioplegia. The surgeries included were coronary artery bypass grafting (CABG), aortic (AVR) and mitral (MVR) valve replacement, double valve replacement (DVR), mitral valve replacement with tricuspid annuloplasty (MVR + TAP), and double valve replacement with tricuspid annuloplasty (DVR + TAP). We excluded pediatric and adult congenital cardiac surgeries, CABG with valve surgeries, arch surgeries, and redo and emergent surgeries.

We analyzed three categories of variables in each group: Patient demographics, intraoperative variables, and postoperative variables. In order to assess the efficacy, we compared the aortic cross clamp (ACC) times and CPB times and the number of doses of cardioplegia required. In addition, we looked at intraoperative hemoglobin (Hb) values to observe if there was an increased risk of blood transfusion with DNC. The safety was evaluated by analyzing the adequacy of myocardial protection and presence of postoperative myocardial injury. This was done by assessing the incidence of ventricular tachyarrhythmias or fibrillation (VT/VF) necessitating electrical defibrillation post ACC removal. We also compared creatine kinase-MB isotype (CK-MB) in CABG patients and left ventricular (LV) function for all patients by transthoracic echocardiography (TTE) done on fifth postoperative day. Moreover, we looked into frequency and duration of temporary pacing in each group. Postoperative clinical outcome variables like incidence of new arrhythmia, myocardial infarction (MI), ICU stay, hospital stay, and postoperative complications were also looked at.

All patients selected for the study were operated within a period of 8 months and, therefore, the effect of changes and advances in surgical care in this short interval can be considered minimal and the standardized protocols in our center were not altered. Because of the study design, we attempted to minimize inherent selection bias by including consecutive patients and equal number of patients in each surgical group. Patients were operated by the same set of surgeons. All patients were given a standard general anesthesia protocol employing CPB with mild systemic hypothermia (30°C to 34°C). Myocardial protection consisted of administration of one of these cardioplegic solutions through antegrade route along with topical slushed ice.

Cardioplegia preparation and administration [Table 1]

Modified St. Thomas blood cardioplegia

The BC solution is given as two doses: Induction dose and maintenance dose. Induction dose was prepared by adding 2 ampoules of St. Thomas cardioplegia concentrate to 500 ml Ringers Lactate (RL). St Thomas concentrate solution contains procaine hydrochloride, potassium chloride (KCL), and magnesium chloride. It was modified by adding extra KCL and 8.4% sodium bicarbonate ($NaHCO_3$). Maintenance dose was made by adding 1 ampoule of the cardioplegia concentrate to 500 ml RL with additional 8.4% $NaHCO_3$. The BC was given in a 4:1 ratio of patient's blood to crystalloid (cardioplegia). The arresting dose was 20 ml/kg and a redose of 10 ml/kg was given every 20–25 min.

Del Nido cardioplegia

The DNC solution was prepared in 1000 ml of Plasma-Lyte A to which KCl, 8.4% $NAHCO_3$, 20% mannitol, 50% magnesium sulphate, and 2% lignocaine were added. The final composition is given in the ratio of 1:4 patient's blood to crystalloid (cardioplegia). The initial arresting dose is 20 ml/kg up to a maximum of 1200 ml. A redose of 10 ml/kg was given at 60 min if the anticipated duration of ischemia is more than 90 min.

The DNC solution was cooled to 4°C–6°C and BC to 8°C–10°C and administered at 300–350 cc/min. Hb was maintained at 7–8 gm% during CPB. Retrograde autologous priming (RAP) and venous antegrade priming (VAP) was done in the patients who were hemodynamically stable. The volume removed varied with each patient. All the blood volume in the CPB circuit was reinfused prior to removal of the aortic cannula. We did not use cell salvage. Pump flows were maintained at 2.2 to 2.4 L/min/m^2 (based on height, weight, and body surface area) and mean arterial pressure targeted between 50 and 70 mmHg. After surgery, patients were transferred to the ICU and provided standardized postoperative care. Patients were shifted to step down ICU after extubation and weaning from inotropic supports.

Table 1: Composition of cardioplegia solutions

Composition	Blood cardioplegia (mST) Induction dose	Blood cardioplegia (mST) Maintenance dose	del Nido
Carrier solution	Ringer lactate (500 ml)	Ringer lactate (500 ml)	Plasmalyte (1000)
Blood to crystalloid ratio	4:1	4:1	1:4
Potassium chloride (mEq)	36 (32+4)	16	26
Procaine hydrochloride (1 mmol/20 ml=272 mg)	544 mg	272 mg	nil
Lignocaine (2%) (mg)	nil	nil	130
Magnesium (g)	6.4	3.2	2
Sodium bicarbonate 8.4% (mEq)	27	13.5	13
Mannitol 20% (g)	nil	nil	16

mST: Modified St. Thomas

Arterial blood gas (ABG) analysis was done at different points in the surgery. All A samples were baseline and taken before anesthesia induction, B samples were during CPB 10–15 min after giving cardioplegia, B_1 samples were 5–10 min after ACC release, and C samples were after protamine administration. In the ICU, all blood samples were taken on arrival. Serial ABGs were subsequently done every 6 h. CK-MB and creatinine were done daily.

If VT/VF occurred after the aorta was unclamped, intravenous lignocaine was given and if the arrhythmia persisted, electrical cardioversion (20–30 joules) was administered with internal paddles. New-onset postoperative atrial fibrillation (AF) was defined as AF occurring in a patient with no history of AF. Postoperative myocardial injury was assessed by CK-MB. We do not check CK-MB preoperatively for elective cases. This is routinely done postoperatively only for the CABG patients. The normal CK–MB range is 5 to 25 IU/L. Values above 40 IU/L were considered to be significant.[9] Perioperative myocardial infarction (MI) was diagnosed with CK-MB above 40 IU/L, ST elevation or appearance of a new Q wave on the electrocardiogram.[9]

Statistical methods

Statistical analysis was performed with STATA version 15.0 (College Station, Texas 77845 USA). Continuous data with normally distributed and skewed variables were reported as mean (SD) and median (IQR) values, with categorical data as frequency and percentages. Differences between categorical variables were tested with the χ^2 test to compare the proportions, and comparison of means was carried out using Student's *t*-test for normally distributed and log-transformed data for skewed variables and compared using *t*-test. Differences were considered significant at values of $P < 0.05$.

Results

A total of 286 patients were included in the analysis with 143 in each group. In each side, 45 had CABG, 34 had AVR, 27 had MVR, 28 had DVR, 5 had MVR + TAP, and 4 had DVR + TAP. Both the groups were similar in their preoperative characteristics including age, gender, ejection fraction (EF), and cardiac risk factors. The median EF was >55% for both groups [Table 2].

There was no difference in CPB time (90 vs. 87, $P = 0.516$) and ACC time (59 vs. 57, $P = 0.650$) between the groups [Table 3]. A subanalysis comparing individual surgeries between the groups [Table 4] also did not show a significant difference between CPB time and ACC time. The number of doses of cardioplegia given was significantly less for DNC (1.13 vs. 2.35, $P = <0.001$).

The Hb values in the A (13.2 vs. 12.9, $P = 0.234$), B (8.0 vs. 7.9, $P = 0.280$), and B_1 (8.5 vs. 8.5, $P = 0.101$) samples were comparable but in the C sample (9.1 vs. 8.7, $P = 0.011$), the Hb was significantly higher in the DNC group. Considerably more amount RAP and VAP was done in the DNC group (450 vs. 250 $P = <0.001$). The intraoperative transfusion of blood and blood products was not significantly different between the groups (75 vs. 67, $P = 0.344$).

The incidence of ACC release ventricular VT/VF was comparable in both the groups (21 vs. 14, $P = 0.207$). Less number of patients who developed VF/VT needed defibrillation in the DNC group (10/21 vs. 12/14) and settled with just lignocaine bolus (11/21 vs. 2/14). Fewer patients in the DNC group required pacing on coming off bypass (15 vs. 20, $P = 0.367$) and were paced for significantly less time (2 vs. 4, $P = 0.023$) [Table 3].

The Hb in the ICU at 6 h (10.2 vs. 9.9 $P = 0.14$) and at 24 h (9.6 vs. 9.3 $P = 0.13$) was comparable and the need for postoperative transfusion of blood and products (30 vs. 36, $P = 0.40$) did not differ between the groups [Table 5].

The CKMB levels for the CABG patients in both the groups were comparable on all 3 days (16.9 vs. 20.4, $P = 0.104$), (14.8 vs. 13.0, $P = 0.106$), and (7.0 vs. 6.1, $P = 0.158$). The postoperative TTE showed that the LVEF was lesser but within normal range in the DNC group (53.4 vs. 56.0, $P = <0.001$).

While looking at postoperative clinical outcomes, the incidence of new-onset AF was similar between both the groups (11 vs. 9, $P = 0.643$). The duration of ventilation (16.5 vs. 17.2, $P = 0.186$), ICU days (3.1 vs. 3.1, $P = 0.931$),

Table 2: Preoperative characteristics

Preoperative characteristics	del Nido (*n*=143) *n* (%)	Blood cardioplegia (*n*=143) *n* (%)	*P*
Gender			
Male	100 (69.9)	86 (60.1)	0.083
Female	43 (30.1)	57 (39.9)	
Age†	48.2 (13.1)	46.7 (13.5)	0.337
Ejection Fraction¶	57.0 (54.2, 58.8)	56.5 (54.8, 58.5)	0.842
Cardiovascular Risk Factors			
Hypertension	46 (32.2)	43 (30.1)	0.702
Diabetes	47 (32.9)	45 (31.5)	0.800
Smoking	21 (14.7)	17 (11.9)	0.486
COPD	9 (6.3)	6 (4.2)	0.426
Dyslipidemia	46 (32.2)	45 (31.5)	0.899
PAD	1 (0.7)	0	0.316
Cerebral Vascular Event	4 (2.8)	6 (4.2)	0.520
Arrythmias	22 (15.4)	30 (21.0)	0.220
Preoperative Hb†	13.2 (1.9)	12.9 (1.7)	0.157
Creatinine¶	0.88 (0.73,1.01)	0.86 (0.70, 1.01)	0.206

Reported with *n* (%) for categorical variables with Chi-square *P*. †Mean (SD) for the continuous normally distributed variables and ¶Median (IQR) for continuous skewed variables. Comparison of means was carried out using Student's *t*-test for normally distributed and log-transformed data for skewed variables and compared using *t*-test. *P*<0.05 is significant. COPD: Chronic obstructive pulmonary disease, PAD: Peripheral arterial disease, Hb: Hemoglobin

Table 3: Intraoperative data

Intraoperative variable	del Nido (*n*=143) Mean (SD)	Blood cardioplegia (*n*=143) Mean (SD)	*P*
Cardiopulmonary bypass time (min)¶	90.0 (74.0, 116.0)	87.0 (76.0, 108.0)	0.516
Cross clamp time¶ (min)	59.0 (48.0, 75.0)	57.0 (47.0, 70.0)	0.650
Number of Doses of cardioplegia	1.13 (0.3)	2.35 (0.5)	<0.001
Hb a (g/dL)	13.2 (2.1)	12.9 (1.8)	0.234
Hb b (g/dL)	8.0 (2.0)	7.9 (2.1)	0.280
Hb b_1 (g/dL)	8.5 (1.2)	8.5 (5.9)	0.101
Hb c (g/dL)	9.1 (1.5)	8.7 (1.0)	0.011
RAP/VAP¶	450 (300, 500)	250 (0, 300)	<0.001
Blood Products	75 (52.5)	67 (46.9)	0.344
Red Blood Cells#			0.716
1	35 (48.6)	36 (54.6)	
2	23 (31.9)	20 (30.3)	
3	13 (18.1)	10 (15.2)	
4	1 (1.4)	0	
Fresh Frozen Plasma#			0.264
1	1 (16.7)	1 (50.0)	
2	1 (16.7)	1 (50.0)	
3	4 (66.7)	0	
Platelets#			
3	8 (100.0)	7 (100.0)	-
VT/VF	21 (14.7)	14 (9.8)	0.207
No. of defibrillations#			
1	8 (80.0)	9 (75.0)	
2	1 (10.0)	3 (25.0)	0.388
3	1 (10.0)	0	
Lignocaine#	21 (100.0)	13 (92.9)	0.214
Pacing#	15 (10.5)	20 (14.0)	0.367
Number of hours pacing¶	2.0 (1.0, 4.0)	4.0 (1.5, 75.5)	0.023

Reported with Mean (SD) for the continuous normally distributed variables and ¶Median (IQR) for continuous skewed variables, #*n* (%) for categorical variable with the Chi-square *P*. Comparison of means was carried out using Student's *t*-test for normally distributed and log-transformed data for skewed variables and compared using *t*-test. *P*<0.05 is significant. Hb: Hemoglobin; RAP/VAP: Retrograde autologous priming/venous antegrade priming; VT/VF: Ventricular tachyarrhythmia/ventricular fibrillation

Table 4: Comparison between CPB Time and ACC time in the different surgeries

Surgery	Cardioplegia	CPB time	*P*	ACC time	*P*
AVR	del Nido	75.0 (65.0, 91.0)	0.427	52.5 (45.0, 62.0)	0.212
	BC	79.0 (71.0, 88.0)		54.5 (48.0, 68.0)	
MVR	del Nido	81.0 (72.0, 91.0)	0.225	54.0 (50.0, 60.0)	0.294
	BC	77.0 (65.0, 83.0)		50.0 (43.0, 58.0)	
CABG	del Nido	90.0 (77.0, 116.0)	0.766	56.0 (40.0, 67.0)	0.704
	BC	91.0 (76.0, 105.0)		50.0 (43.0, 60.0)	
DVR	del Nido	118.0 (100.0, 137.0)	0.322	91.5 (76.0, 101.0)	0.203
	BC	109.5 (102.5, 122.5)		84.5 (77.0, 92.5)	
MVR+TAP	del Nido	106.0 (96.0, 124.0)	0.468	79.0 (76.0, 81.0)	0.509
	BC	105.0 (95.0, 111.0)		81.0 (66.0, 82.0)	
DVR + TAP	del Nido	141.0 (127.0, 153.0)	0.481	114.5 (104.0, 122.5)	0.491
	BC	130.0 (110.5, 149.0)		105.5 (94.5, 118.0)	

Note: Median (IQR) for continuous skewed variables. log-transformed data for skewed variables and compared using *t*-test. $P<0.05$ is significant. CPB: Cardiopulmonary bypass time; ACC: Aortic cross clamp time; BC: Blood cardioplegia; AVR: Aortic valve replacement; MVR: Mitral valve replacement; CABG: Coronary artery bypass graft; DVR: Double valve replacement, MVR + TAP: Mitral valve replacement with tricuspid annuloplasty; DVR + TAP : Double valve replacement with tricuspid annuloplasty

Table 5: Postoperative data

Postoperative variable	del Nido (*n*=143) Mean (SD)	Blood cardioplegia (*n*=143) Mean (SD)	*P*
Hb ICU 6 h (g/dL)	10.2 (1.5)	9.9 (1.4)	0.140
Hb ICU 24 h (g/dL)	9.6 (1.8)	9.3 (1.3)	0.130
Blood products	30 (21.0)	36 (25.2)	0.400
Red blood cells[#]			
1	18 (66.7)	26 (78.8)	
2	4 (14.8)	5 (15.2)	0.261
3	3 (11.1)	0	
4	2 (7.4)	2 (6.1)	
Fresh frozen plasma[#]			
1	0	1 (50.0)	
2	1 (100.0)	0	0.223
3	0	1 (50.0)	
Platelets[#]	7 (100.0)	4 (80.0)	0.217
CKMB (IU/L) day 1 (CABG)[¶]	16.9 (15.0, 21.8)	20.4 (16.0, 26.5)	0.104
CKMB (IU/L) day 2 (CABG)[¶]	14.8 (11.5, 21.7)	13.0 (9.6, 19.0)	0.106
CKMB (IU/L) day 3 (CABG)[¶]	7.0 (5.2, 9.2)	6.1 (4.2, 9.5)	0.158
PO LV function[¶]	53.4 (45.1, 57.1)	56.0 (51.7, 57.6)	<0.001
New-onset AF#	11 (7.7)	9 (6.3)	0.643
Ventilation time (h)	16.5 (5.1)	17.2 (3.7)	0.186
ICU (days)	3.1 (0.8)	3.1 (0.5)	0.931
30-day mortality	-	-	-
30-day hospital Readmission	8 (57.1)	6 (42.9)	0.584
Myocardial infarction	-	-	-
PO complications[#]	8 (5.6)	12 (8.4)	0.354
PO hospital days[¶]	7 (6,8)	7 (6,9)	-
Stroke[#]	1 (0.7)	1 (0.7)	-
Creatinine day1[¶]	0.9 (0.8, 1.2)	1.0 (0.9, 1.2)	0.309
Creatinine day2[¶]	0.8 (0.7, 1.0)	0.9 (0.7, 1.0)	0.713

Note: Reported with Mean (SD) for the continuous normally distributed variables and [¶]Median (IQR) for continuous skewed variables, [#]*n* (%) categorical variable with the Chi-square *P*. Comparison of means was carried out using Student's *t*-test for normally distributed and log-transformed data for skewed variables and compared using *t*-test. $P<0.05$ is significant. Hb: Hemoglobin; ICU: Intensive care unit; CKMB: Creatine kinase-MB isotype; PO: Postoperative; LV: Left ventricle; AF: Atrial fibrillation

postoperative hospital days (7 vs. 7) and 30-day hospital readmission rates (8 vs. 6, $P = 0.584$) were comparable in both the groups. There was no 30-day mortality or postoperative MI in both groups. The incidence of stroke was alike with both groups having one patient. There was no significant difference in creatinine between the groups

on both the days (P = 0.309) (P = 0.713). Postoperative complications were lower in the DNC group (8 vs. 12, P = .354), but not statistically significant. There were 4 patients who required permanent pacemaker (PPM) insertions in the BC group and none in the DNC group.

Discussion

The optimal cardioplegia strategy is far from clear despite a substantial amount of literature on the subject. The cardioplegic solution protects the myocardium against ischemia and events during reperfusion.[1] The use of hypothermic and hyperkalemic cardioplegia solutions have evolved to become the clinical standard.[1] The main factors explored were composition (blood versus crystalloid), various substrate enhancement, the route (antegrade, retrograde, or both), the temperature (cold, tepid, or warm), and the redosing intervals.[10] A recent global survey showed that blood cardioplegia was the most commonly used.[2]

The advantages of blood cardioplegia include the benefits of the oncotic properties of blood to prevent cellular edema, superior buffering capacity, rapid arrest in an oxygen-rich environment, intermittent reoxygenation with intermittent washout of metabolites, and improved preservation of high-energy phosphates.[3]

Crystalloid cardioplegia prevents depletion of high-energy substrates and maintains ultrastructural integrity.[5] DNC is plasmalyte solution modified with magnesium and lignocaine which decrease intracellular calcium concentration, myocardial excitability, cellular metabolism, and energy consumption during and after ischemic arrest. DNC preserves intracellular high-energy phosphates. The proposed benefit of DNC is that it provides an arrest period of more than 90 min which avoids the need for repetitive interruptions during surgery to administer multiple doses as done for standard BC but at the cost of hemodilution.[11] Despite extensive research, the superiority of blood over crystalloid cardioplegia has not been established.[5]

Due to unfamiliarity with DNC, apprehensions have been present about its safety in cardiac surgeries especially in patients with LV dysfunction. Many institutions in India and worldwide are now using DNC in various surgeries but most available studies deal only with isolated surgical groups. Our study looked into its use in all CABG and valve surgeries inclusive of patients with LV dysfunction with EF ranging from 28%–68.6% for DNC and 27.7%–68.1% for BC.

The main additive in DNC was lignocaine, while it was procaine hydrochloride in our BC. Both are Class 1 sodium channel blockers that directly block the sodium channels in phase 0 depolarization of the action potential.[11,12] Compared with procaine, lignocaine has a longer half-life.[12] This gave DNC group the advantage of longer ischemic times between doses of cardioplegia. The redosing for DNC is significantly less, which allowed the surgeons to do an uninterrupted surgery with better workflow. Our study did not show difference in CPB time and ACC time similar to studies by Guajardo *et al*.[13] in their study on CABG, Sorabella *et al*.[14] in their study on redo AVR, Ad *et al*.[15] in their study on CABG and valves, and Timek *et al*.[16] in their study in CABG. However, Ota *et al*.[17] and Mick *et al*.[18] on their studies on AVR, Kim *et al*.[19] in their study on various valve surgeries, and Mishra *et al*.[8] in their study on CABG and DVR found both CPB and ACC time be significantly less with DNC.

The DNC group remarkably had higher Hb throughout and significantly higher post CPB compared to BC. Furthermore, the requirement of blood transfusion both intraoperative and postoperatively was similar to BC group. The most likely reason is significantly more amount of RAP and VAP was done for the DNC group. This was done as protocol in order to counteract the hemodilution with DNC. Hofmann *et al*.[20] and Teman *et al*.[21] in their studies demonstrated that transfusion requirements were less and postoperative Hb was higher in the patients where RAP and VAP was done. In addition, since the redosing is substantially less for DNC, the additional cardioplegia volume was not delivered like it was for BC. Mishra *et al*.[8] and Sorabella *et al*.[14] had similar findings. Guajardo *et al*.[13] and Kim *et al*.[19] surprisingly had a significant reduction in transfusions rates with DNC compared to BC.

In our study, the incidence of post ACC release VT/VF was not statistically significant between the groups. Sadeghi *et al*.[12] in a study comparing cardioplegia using lignocaine or procaine had similar findings. The study by Sellevold *et al*.[22] has shown procaine to be a good membrane stabilizer which is effective in minimizing post ischemic VT/VF. Interestingly, the DNC group required less defibrillation compared to BC group, with many settling with a lignocaine bolus. Studies by Guajardo *et al*.[13] O`Donnell *et al*.[23] on CABG patients, and Buel *et al*.[24] on pediatric cardiac patients showed post ACC release defibrillation requirement was significantly less with DNC compared with BC. Guajardo *et al*.[13] used Buckberg solution which had tromethamine and citrate phosphate, while O`Donnell *et al*.[23] and Buel *et al*.[24] used Plegisol which had magnesium and calcium. The lignocaine in DNC can be the component responsible for this outcome.

The postoperative CKMB was comparable in both the groups and did not rise above the normal range on all 3 days. This study did not show increased myocardial injury in the CABG patients receiving DNC compared to BC. Similarly, Timek *et al*.[16] along with Mick *et al*.[18] had no difference in enzyme levels. Kim *et al*.[19] and Vistarini *et al*.[25] who compared AVR and Hamad *et al*.[26] who compared valve with CABG found CKMB levels to be significantly lower in DNC, suggesting that blood cardioplegia does not confer superior myocardial protection.

Our study showed a significantly better LV function postoperatively in the BC group. Although it is statistically significant, it is not clinically relevant, because for both groups, it is in normal range of LV function. Our study was inclusive of patients with moderate-to-severe LV dysfunction (6 vs. 5) in each group. None of our patients required intra-aortic balloon pump for weaning off bypass. Studies by Mishra *et al*.,[9] Timek *et al*.,[16] Mick *et al*.,[18] and Yerebackan *et al*.[27] who looked at high-risk CABG also had preserved LV functions with DNC and did not find BC to be superior to DNC.

We had no differences in postoperative outcomes with relation to duration of ventilation, ICU stay, neurological dysfunction, or renal impairment. None of the patients had postoperative MI or 30-day mortality. Guajardo *et al*.,[13] O'Donnell *et al*.,[23] and Hamad *et al*.[26] had similar findings. Our comparable findings in relation to incidence of new-onset AF were consistent with studies by Ota *et al.,*[17] Mick *et al*.,[18] and O`Donnell *et al*.[22] Our complication rates did not differ significantly. Multiple other studies[9,14,15,19,25,26] had similar findings.

There was a higher occurrence of conduction defects requiring pacing to wean from bypass and significantly longer duration of pacing in the BC group. There was also an increased incidence of PPM insertion. This corroborates a study by Gundry *et al*.[28] where they theorized that at very low temperatures, blood undergoes rouleaux formation with potential capillary plugging and this might cause localized ischemia of the conduction system.

Study limitations

There are a few limitations that must be noted. Since this is a historical cohort study, there can be an inherent selection bias. High-risk patients like those requiring preoperative inotropic support or patients who had acute coronary syndrome have not been included. As this is a single-center study, it may limit the ability to generalize the results. The number of patients enrolled for certain surgeries was relatively small.

Conclusion

This study which comprised of a diversity of cases inclusive of CABGs and wide range of valve surgeries showed that del Nido cardioplegia provided equivalent myocardial protection and surgical workflow and had clinical outcomes that were similar to that of blood cardioplegia. We feel that the practice of RAP and VAP along with the reduced redosing lessens the hemodilution with del Nido, thus decreasing the transfusion requirements. Del Nido has the safety profile and efficacy comparable to blood cardioplegia. We can conclude that del Nido is a safe alternate to blood cardioplegia in CABG and valve surgeries. Further randomized, multicenter trials comparing different solutions in different cardiac procedures need to be done to validate these results.

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Conflicts of interest

There are no conflicts of interest.

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