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Single Dose of Del Nido Cardioplegic Solution in Comparison with St Thomas Hospital Solution in Mitral Valve Surgery: A Propensity Matched Comparison

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Abstract

Background: The aim of the study was to compare efficacy and safety of use of a single dose of Del Nido Cardioplegic solution (DN) and repeated doses of St. Thomas Hospital II cardioplegic solution (ST) in the group of patients operated due to mitral valve defect as a single or complex cardiac procedure.

Methods: The study was performed between 11/2014 and 02/2018. All 117 consecutive procedures were performed by a single surgeon. Of these first 53 patients (ST group) were given ST solution and the rest 64 patients (DN group) received DN cardioplegy. The ST group was operated between 11/2014 and 10/2016 and the DN Group between 10/2016 and 02/2018. Propensity score matching was performed using logistic regression model with Hooke-Jeeves algorithm.

Results: The patients from the ST group had higher morbidity in comparison to the DN group (Euroscore II 8.3 vs. 3.3) before and after matching. The patients from the DN group had significantly shorter times of operation, aorta cross-clamping, anesthesia and Extracorporeal Circulation (ECC). Also postoperative troponin levels were lower in this group; however, the difference did not reach a level of statistical significance. In the DN group a rate of defibrillation after aorta de-clamping was lower comparing with the ST group, however, a rate of temporary heart pacing was higher.

Conclusion: Del Nido Cardioplegic solution can be used effectively and safety in comparison with St Thomas II in adult mitral valve surgery performed as a single or complex cardiac procedures.

A single dose of DN allows decreasing surgery, aorta cross-clamping and ECC times what yields lower postoperative tropine levels.

The use of a single dose of DN compared with repeated doses of ST due to lower crystalloid load results with decreased hemodilution effect what is reflected in significantly higher hemoglobin concentration both during the operation and postoperatively. This is followed by lower rate of intra-operative hemoconcentration use, as well as postoperative red cells transfusions. However, the last two effects were not statistically significant.

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Introduction

Del Nido (DN) cardioplegia was developed by Pedro del Nido at the University of Pittsburgh in 1990 and firstly has been used for pediatric cardiac surgery and since 2003 has been used for adult cardiac surgery [1]. Del Nido cardioplegia is an extracellular solution mixed with autologous blood, the crystalloid: blood ratio is 4:1. Single dose of 20 ml/kg obtain optimal myocardial protection for 90 min. The crystalloid solution includes Plasma-Lyte as a basic solution, mannitol, magnesium sulfate, bicarbonate, potassium and lidocaine (Table 1).

Each ingredient plays an important role in the cardioprotection strategy. Plasma-Lyte A as a basic commercial solution 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 has capabilities of both scavenging free radicals and reducing edema due to hyperosmotic capabilities [2]. Magnesium additive blocks the calcium channels and improve myocardial recovery. Magnesium (Mg^{++}) ion may help stabilize the myocardial membrane by inhibiting a myosin phosphorylase, which protects Adenosine Triphosphate (ATP) reserves

Table 1: The Del Nidocardioplegia solution.

Ingredient	Volume (ml)	Role
Plasma-Lyte A	1000	Basic solution (Na: 140 mmol/l, K: 5 mmol/l, Mg: 3 mmol/l, pH-7.4)
Mannitol 15%	20	Osmotic pressure
$MgSO_4$ 20%	10	Calcium channel blocker, improved myocardial recovery
$NaHCO_3$ 1 mEq/ml	13	pH buffer
KCl 2 mEq/l	13	Myocardia depolarization
Lidocaine 2%	6.5	Sodium channel blocker, hyperpolarizing agent

Table 2: St Thomas Hospital cardioplegia solution.

Solution	Concentration	Role
Na^+	110 mmol/l	Ionic integrity of myocardial tissue
K^+	16 mmol/l	Myocardia depolarization
Mg^{2+}	16 mmol/l	Calcium channel blocker improved myocardial recovery
Ca^{2+}	1.2 mmol/l	Low concentration is included in the solution to maintain integrity of cell membrane to ensure that there is no likelihood of calcium paradox during reperfusion.
$NaHCO_{3.}$	10 mmol/l	pH buffer

for postischemic activity [3]. Potasium chloride provides rapid depolarization arrest. Potassium (K^+) ion concentration is responsible for prompt cessation of mechanical myocardial contractile activity. The immediacy of the arrest thus preserves energy supplies for postischemic contractile activity in diastole.

The Chloride (Cl^-) and Sodium (Na^+) ions have no specific role in the production of cardiac arrest. Sodium is essential to maintain ionic integrity of myocardial tissue. The chloride ions are present to maintain the electroneutrality of the solution.

Added Bicarbonate (HCO_3-) anion is included as a buffer to render the solution slightly alkaline and compensate for the metabolic acidosis that accompanies ischemia.

Lidocaine, class Ib antiarrhythmic agent, sodium channel blocker, prevents the negative effect of hyperkalemic depolarized arrest by polarizing the cell to some degree and reducing intracellular sodium and calcium influx [4].

Del Nido cardioplegic solution is given together which blood with is supporting an aerobic metabolism and improving coronary perfusion during the delivery, preserving myocardial metabolism and reducing ischemic stress along with reperfusion injury [5].

The St Thomas (ST) cardioplegic solution was developed at London in 1975. This was improved upon by reducing potassium, sodium and calcium concentration and named St Thomas Hospital Solution II in 1981, has been a popular, well established, crystalloid cardioplegia however, it must be administered repeatedly every 20 to 30 min during the surgery (Table 2) [6,7].

The buffered admixture contains the following electrolytes (per liter): Ca^{++}: 2.4 mEq, Mg^{++}: 32 mEq, K^+: 16 mEq, Na^+: 120 mEq, Cl^-: 160 mEq and bicarbonate ($HCO_{3.}$): 10 mEq; osmolar concentration, 324 mOsmol/liter (calc.); pH: 7.8 (approx.).

Calcium (Ca^{++}) ion in low concentration is included in the solution to maintain integrity of cell membrane to ensure that there is no likelihood of calcium paradox during reperfusion.

The comparison between del Nidonad St Thomas II solution was performed by Mishara et al., [8] The study included 100 patients who underwent coronary artery revascularization or double valve surgery. The aortic cross clamp and bypass times were shorter in del Nido group and the postoperative left ventricular ejection fraction was better preserved in del Nido group.

Material and Methods

Between 11/2014 and 02/2018 all 117 consecutive patients underwent mitral valve surgery alone or simultaneously with other procedures. All procedures were performed by the same surgeon. Of these first 53 patients (ST group) were given ST solution and the rest 64 patients (DN group) received DN cardioplegy. The ST group was operated between 11/2014 and 10/2016 and the DN Group between 10/2016 and 02/2018. Preoperative data of patients from both groups are displayed in Table 3 (before matching) and Table 4 (after matching).

Surgical Technique

Conventional general anesthesia was used in all patients. All patients were operated in mild hypothermia 32 to 34 st C. St Thomas solution in general was administered antegrade first dose 1000 ml and every 20 min to 30 min additional 500 ml antegrade or retrograde. Del Nido solution was given in a single dose, antegrade, 1000 ml per patient. Intraoperative use of inotropes, fluid administration and transfusion were carried out at the discretion of the anesthesiologists.

Data Analysis

All analyses were performed with the Statistica 13.1 software. Propensity score matching was performed using logistic regression model with Hooke-Jeeves algorithm. The variables selected for matching were: age, creatinine level before operation, EF% before operation, CRP-level, hemoglobin level and presence of asthma. The patients were matched with 1:1 ratio. For pair-wise comparison of matching parameters between cardioplegia methods χ^2 tests and Welch t-tests were performed for categorical and continuous variables, respectively. A two-sided $p<0.05$ was considered statistically significant.

Results

The patients from the ST Group had higher morbidity rate preoperatively, both before and after matching. Significantly higher rate was observed for the following diseases; fresh myocardial

Table 3: Before matching.

Type of cardioplegia	ST. Thomas II Cardioplegia	Del Nido Cardioplegia	p-value
No. of patients	M=38, F=15	M=36, F=28	0.0845
Age (mean ± SD)	63.92 ± 9.23	62 ± 12.54	0.024
Previous heart surgeries (median, IQR)	0.1026 (4)	0.0938 (6)	0.1208
CCS			0.1381
No angina	17 (32.08)	15 (23.44)	
CCS I	12 (22.64)	26 (40.63)	
CCS II	12 (22.64)	15 (23.44)	
CCS III	12 (22.64)	7 (10.94)	
CCS IV	0 (0.0)	1 (1.56)	
NYHA			0.4856
No heartfailure	1 (1.89)	4 (6.25)	
NYHA I	2 (3.77)	2 (3.13)	
NYHA II	17 (32.08)	26 (40.63)	
NYHA III	25 (47.17)	27 (42.19)	
NYHA IV	8 (15.08)	5 (7.81)	
Cardiac infarctions	0.2453	0.0781	0.0476
PCIs before	0.2308	0.1563	0.3679
Body mass	73.55	72.57	0.6976
Height	171.77	167.05	0.0105
Smoking (1-Never, 2-Former, 3-Current)			0.0041
Never	12 (22.64)	31 (48.44)	
Former	28 (52.83)	28 (43.75)	
Current	13 (24.53)	5 (7.81)	
Diabetes mellitus	7 (13.21)	12 (18.75)	0.4184
Hypertension	38 (71.70)	47 (73.44)	0.8336
Hyperlipidemia	32 (60.38)	31 (48.44)	0.1972
Creatinine before surgery (mg/dl)	10.108	0.8884	0.2679
Asthma	7 (13.21)	2 (3.13)	0.0416
Heart rhytm before surgery			0.6423
sinus rhytm	36 (67.92)	46 (71.88)	
abnormal	17 (32.08)	18 (28.13)	
Renal impairment			0.2845
no impairment (CC>85 ml/min	23 (43.40)	32 (50.00)	
moderate impairment (85>CC<50 ml/min)	22 (41.51)	28 (43.75)	
severe impairment (CC<50 ml/min)	8 (15.09)	4 (6.25)	
Extracardiac arteriopathy	13 (24.53)	7 (10.94)	0.0519
Chronic lung disease	12 (22.64)	8 (12.50)	0.1469
Poor mobility	15 (28.30)	7 (10.94)	0.0167
Endocarditis	6 (11.32)	3 (4.69)	0.1801
Critical state	2 (3.77)	1 (1.56)	0.4513
Fresh myocardial infarction	8 (15.09)	2 (3.13)	0.0212
Pulmonary hypertension			0.0007
absent	9 (16.98)	29 (45.31)	
moderate (31 mmHg to 55 mmHg)	26 (49.06)	28 (43.75)	
severe (>55 mmHg)	18 (33.96)	7 (10.94)	
Surgery type (1-elective, 2-urgent, 3-emergency)			
elective	42 (79.25)	55 (85.94)	
urgent	5 (9.43)	0 (0.00)	
emergency	6 (11.32)	9 (14.06)	
Mitral Stenosis (0-No, 1-Yes)	5 (9.43)	9 (14.06)	0.4426
Mitral Regurgitation grade			0.4414
None	0 (0.00)	2 (3.13)	

Trivial	2 (3.77)	2 (3.13)	
Mild	0 (0.00)	2 (3.13)	
Moderate	3 (5.66)	5 (7.81)	
Severe	48 (90.57)	53 (82.81)	
Hg before	13.1 ± 1.59	13.64 ± 1.42	0.0591
CRP before	9.13 ± 12.29	3.1 ± 3.46	0.0324
FA before	12 (30.77)	15 (40.54)	0.3737
EF before (%)	51.92 ± 14.83	53.77 ± 12.64	0.4767
Euroscore before operation	8.72 ± 14.36	3.45 ± 5.63	0.0143
Intra and post operation parameters before matching			
Type of cardioplegia	**Cold Crystalic Cardioplegia**	**Blood Cardioplegia**	**p-value**
Mitral valve operation type			0.9531
Replacement	13 (24.53)	16(25.00)	
Repair	40 (75.47)	48 (75.00)	
Coronary surgery	17 (32.08)	15 (23.44)	0.2968
Aortic valve surgery	4 (7.55)	4 (6.25)	0.7819
Tricuspid valve surgery	11 (20.75)	9 (14.06)	0.3385
Ascending aortic surgery	4 (7.55)	4 (6.25)	0.7819
Peripheral artery bypass	0.27 ± 0.45	0.2 ± 0.4	0.4692
Peripherial venous bypass	0.49 ± 0.76	0.3 ± 0.63	0.1787
Operation time (min)	246.6 ± 65.92	213 ± 63.68	0.0066
EF after (%)	48.13 ± 13.30	48.00 ± 12.14	0.1391
Total extracorporeal circulation time (min)	122.43 ± 41.17	119.44 ± 29.59	0.6598
Total aortic clamptime	86.04 ± 25.75	74.45 ± 19.31	0.0081
Volume of cardioplegic solution	1845.28 ± 410.71	995.31 ± 37.50	0
Reoperation for bleeding	8 (15.09)	3 (4.69)	0.0549
LVDD	57.78 ± 5.25	56.66 ± 6.97	0.3845
Hg after	8.09 ± 0.79	8.88 ± 0.87	0
Transfusion	37 (75.51)	42 (66.67)	0.3085
CRP after	153.75 ± 103.60	212.8 ± 87.94	0.0372
IABP	4 (7.55)	4 (6.25)	0.7819
Stimulation temporary	10 (18.87)	27 (46.55)	0.002
Defibrylation after crosclamping	41 (77.36)	3 (4.84)	0
Deaths	4 (7.55)	0 (0.00)	0.0834
Troponin level	1505.9 ± 992.06	1213.48 ± 1019.58	0.358
Neurological complications	2 (3.77)	1 (1.56)	0.4513
Hemofiltration	9 (16.67)	0 (0.00)	0.0007
FA after	15 (38.46)	17 (47.22)	0.4435
Intubation time >48 h	9	7	0.2427
2 inotrops (epinephrine, norepinephrine) after surgery	8 (15.09)	3 (4.69)	0.0549

infarction within 90 days before the operation (p=0.0462), extracardiac arteriopathy (p=0.0385), poor mobility (p=0.0283), pulmonary hypertension (p=0.0148). All those significant differences were reflected in significantly higher preoperative Euroscore II in the ST Group (p=0.0069). Other data did not differ significantly between the Groups.

Operation Data

Previous heart surgery, type of surgery (elective, urgent, emergency), additional coronary revascularization, number of grafts, aortic valve surgery, tricuspid valve surgery, ascending aorta surgery were similar in both groups. In the DN group a need of defibrillation after aorta de-clamping was lower comparing with the ST group (p=0.0000 after matching), however, a rate of temporary heart pacing was higher in the DN Group (p=0.0006 after matching). Overall aortic clamp, CPB time and operating room time were shorter in DN group and were confirmed before and after matching (Table 3 and 4). Need of defibrillation was significantly lower in DN group. The difference in postoperative Troponin levels between the groups was not statistically significant; however, they were lower in the DN Group what might result from a shorter overall aortic cross-clamp time in this group. Postoperative use of 2 inotropic agents was higher in ST group. Postoperative EF adjusted for preoperative EF was unaffected in both groups. Occurrence of reoperation for bleeding, IABP inserting, temporary heart stimulation, defibrillation after cross-clamping, deaths, troponin level, neurological complication after surgery, FA after surgery and prolonged ventilation time (>48) are enclosed in Table 3 and 4.

Table 4: After matching.

Type of cardioplegia	St Thomas II Cardioplegia	Del Nido Cardioplegia	p-value
No. of patients	M=38, F=15	M=33, F=20	0.3018
Age (mean ± SD)	63.93	63.38	0.7827
Previous heart surgeries (median, IQR)	0,1026 (4)	0,0727 (4)	0.4483
CCS			0.1079
No angina	17 (32.08)	10 (18.87)	
CCS I	12 (22.64)	23 (43.40)	
CCS II	12 (22.64)	12 (22.54)	
CCS III	12 (22.64)	7 (13.21)	
CCS IV	0 (0.0)	1 (1.89)	
NYHA			0.3754
No heartfailure	1 (1.89)	1 (1.89)	
NYHA I	2 (3.77)	0 (0.00)	
NYHA II	17 (32.08)	23 (43.40)	
NYHA III	25 (47.17)	25 (47.17)	
NYHA IV	8 (15.08)	4 (7.55)	
Cardiac infarctions	0.2453	0.0943	0.0818
PCIs before	0.23	0.151	0.3478
Body mass	73.550	73.77	0.9313
Height	171.77	168.19	0.0537
Smoking (1-Never, 2-Former, 3-Current)			0.0374
Never	12 (22.64)	22 (41.51)	
Former	28 (52.83)	26 (49.06)	
Current	13 (24.53)	5 (9.43)	
Diabetes mellitus	7 (13.21)	9 (16.98)	0.5874
Hypertension	38 (71.70)	41 (77.36)	0.5036
Hyperlipidemia	32 (60.38)	26 (49.06)	0.2417
Creatinine before surgery (mg/dl)	1.0108	0.8979	0.3038
Asthma	7 (13.21)	2 (3.77)	0.0815
Heart rhytm before surgery			0.8339
sinus rhytm	36 (67.92)	37 (69.81)	
abnormal	17 (32.08)	16 (30.19)	
Renal impairment			0.137
no impairment (CC>85 ml/min	23 (43.40)	26 (49.06)	
moderate impairment (85>CC<50 ml/min)	22 (41.51)	25 (47.17)	
severe impairment (CC<50 ml/min)	8 (15.09)	2 (3.77)	
Extracardiac arteriopathy	13 (24.53)	5 (9.43)	0.0385
Chronic lung disease	12 (22.64)	8 (15.09)	0.3207
Poor mobility	15 (28.30)	6 (11.32)	0.0283
Endocarditis	6 (11.32)	2 (3.77)	0.1413
Critical state	2 (3.77)	0 (0.00)	0.1534
Fresh myocardial infarction	8 (15.09)	2 (3.77)	0.0462
Pulmonary hypertension			0.0148
absent	9 (16.98)	19 (35.85)	
moderate (31 mmHg to 55 mmHg)	26 (49.06)	27 (50.94)	
severe (>55 mmHg)	18 (33.96)	7 (13.21)	
Surgery type (1-elective, 2-urgent, 3-emergency)			0.0713
elective	42 (79.25)	47 (88.68)	
urgent	5 (9.43)	0 (0.00)	
emergency	6 (11.32)	6 (11.32)	
Mitral Stenosis (0-No, 1-Yes)	5 (9.43)	6 (11.32)	0.7501
Mitral Regurgitation grade			0.2688
None	0 (0.00)	1 (1.89)	

Trivial	2 (3.77)	0 (0.00)	
Mild	0 (0.00)	2 (3.77)	
Moderate	3 (5.66)	4 (7.55)	
Severe	48 (90.57)	46 (86.79)	
Hg before	13.1 ± 1.59	13.64 ± 1.53	0.0826
CRP before	9.13 ± 12.29	2.99 ± 3.49	0.0298
FA before	12 (30.77)	14 (42.42)	0.3049
EF before (%)	51.92	53.47	0.5715
Euroscore II before oparation	8.72 ± 14.36	3.09 ± 2.93	0.0069
Intra and post operation parameters after matching			
Type of cardioplegia	**Cold Crystalic Cardioplegia**	**Blood Cardioplegia**	**p-value**
Mitral valve operation type			0.6425
Replacement	13 (24.53)	11(20.75)	
Repair	40 (75.47)	42 (79.25)	
Coronary surgery	17 (32.08)	13 (24.53)	0.3884
Aortic valve surgery	4 (7.55)	4 (7.55)	1
Tricuspid valve surgery	11 (20.75)	9 (16.98)	0.6195
Ascending aortic surgery	4 (7.55)	4 (7.55)	1
Peripheral artery bypass	0.27 ± 0.44	0.21 ± 0.41	0.5504
Peripherial venous bypass	0.49 ± 0.76	0.26 ± 0.53	0.0919
Operation time (min)	246.6 ± 65.92	218.62 ± 66.69	0.0321
EF after (%)	48.13 ± 13.30	51.22 ± 12.08	0.2212
Total extracorporeal circulation time (min)	122.43 ± 41.17	122.29 ± 29.40	0.9841
Total aortic clamptime	86.04 ± 25.75	76.90 ± 19.45	0.0434
Volume of cardioplegic solution	1845.28 ± 410.71	994.34 ± 41.21	0
Reoperation for bleeding	8 (15.09)	3 (5.66)	0.1113
LVDD	57.78 ± 5.25	57.00 ± 6.92	0.562
Hg after	8.09 ± 0.79	8.82 ± 0.93	0
Transfusion	37 (75.51)	34 (65.38)	0.2657
CRP after	153.75 ± 103.60	208.83 ± 88.86	0.0564
IABP	4 (7.55)	4 (7.55)	1
Stymulator temporary	10 (18.87)	25 (51.02)	0.0006
Defibrylation after crosclamping	41 (77.36)	3 (5.88)	0
Deaths	4 (7.55)	0 (0.00)	0.1262
Troponin level	1497.18 ± 947.58	1211.98±893.48	0.1698
Neurological complications	2 (3.77)	0 (0.00)	0.1534
Hemofiltration	9 (16.67)	0 (0.00)	0.0007
FA after	15 (38.46)	15 (46.88)	0.4752
Intubation time >48	9	7	0.5339
2 inotrops (epinephrine, norepinephrine) after surgery	8 (15.09)	3 (5.66)	0.1113

Discussion

This study demonstrates no disadvantages of use single dose of DN solution in mitral valve surgery performed also with concomitant procedures. Use of DN solution has several advantages. Operative time were shorter, the reduction in time might be due to no need to interruption in the surgical repair. The similar conclusions were drawn by other investigators comparing the use of a single dose of DN cardioplegic solution with other cardioplegic solutions [8-11]. The both groups had preoperatively relatively high Euroscore II; the ST Group -8.72+-14.36 and the DN Group 3.09+-2.93 after matching. In spite of this, 30-days mortality was lower than predicted in the both groups, with no death in the DN Group. The cost of preparing a single dose of 1000 ml of DN and ST solution is similar and is about 15 Euros per portion. It is difficult to estimate a total cost of the use of ST solution. It requires higher use of fluids, more frequent use of hemoconcentration during the operation, as well as more extensive blood transfusions postoperatively, although the difference was not statistically significant. In spite of increased rate of hemoconcentration and transfusion use in the ST Group, finally the postoperative hemoglobin concentration was higher in the DN Group. Generally, relatively low cost of the use of DN results from using only a single dose of this, as well as less frequent need of hemoconcentration and similar transfusions rate in the DN Group. Need of defibrillation was significantly lower in DN group, but postoperative, temporary use of pacemaker was higher in DN group what might be due to use lidocaine in DN solution. Ramanathan retrospectively studied 142 adult patients who received either del Nido or Buckberg cardioplegia fewer dose of cardioplegia and fewer defibrillations were noted in

del Nido group [12]. Coronary artery bypass surgery was proven to be safe with del Nido solution with similar results but required less defibrillations and blood transfusion when compared with blood cardioplegia [13]. Postoperative Troponin level was not differ in both group but were lower in the DN Group that might result from a shorter overall aortic cross-clamp time in this group. Postoperative use of 2 inotropic agents was higher in ST group. Postoperative EF adjusted for preoperative EF was unaffected in both groups.

Conclusion

Single dose of Del Nido solution is safe for use, with good postoperative outcomes, in mitral valve surgery as a single and concominnant with other procedures in adult. It has several advantages as shortening surgical time of aortic cross clamp, ECC time and operative time. Less need for postoperative blood supply, lower intraoperative hemodilution, less need of hemoconcentration, higher level of Hb concentration after surgery and less defibrillations, and low cost of preparing and use. The higher rate of necessity of temporary heart pacing postoperatively in the DN Group is remarkable and needs further investigations.

References

1. Matte GS, del Nido PJ. History and use of del Nido cardioplegia solution at Boston Children's Hospital. J Extra Corpor Technol. 2012;44(3):98-103.
2. Powell WJ Jr, DiBona DR, Flores J, Leaf A. The protective effect of hyperosmotic mannitol in myocardial ischemia and necrosis. Circulation. 1976;54(4):603-15.
3. Brown PS Jr, Holland FW, Parenteau GL, Clark RE. Magnesium ion is beneficial in hypothermic crystalloid cardioplegia. Ann Thorac Surg. 1991;51(3):359-66.
4. O'Brien JD, Howlett SE, Burton HJ, O'Blenes SB, Litz DS, Friesen CL. Pediatric cardioplegia strategy results in enhanced calcium metabolism and lower serum troponin T. Ann Thorac Surg. 2009;87(5):1517-24.
5. Caputo M, Modi P, Imura H, Pawade A, Parry AJ, Suleiman MS, et al. Cold blood versus cold crystalloid cardioplegia for repair of ventricular septal defect in pediatric heart surgery; a randomized controlled trial. Ann Thorac Surg. 2002;74(2):530-4.
6. Shiroishi MS. Myocardial protection: the rebirth of potassium-based cardioplegia. Tex Heart Inst J. 1999;26(1):71-86.
7. Ledingham SJ, Braimbridge MV, Hearse DJ. The St. Thomas' Hospital cardioplegic solution. A comparison of the efficacy of two formulations. J Thorac Cardiovasc Surg. 1987;93(2):240-6.
8. Mishara P, Jadhav RB, Mohapatra CK, Khandekar J, Raut C, Ammannaya GK, et al. Comparison of del Nido cardioplegia and St. Thomas Hospital solution – two types of cardioplegia in adult cardiac surgery. Kardiochir Torakochirurgia Pol. 2016;13(4):295-9.
9. Smigla G, Jaquiss R, Walczak R, Bonadonna D, Kaemmer D, Schwimer C, et al. Assessing the safety of del Nido cardioplegia solution in adult congenital cases. Perfusion. 2014;29(6):554-8.
10. Yerabekan H, Sorabella RA, Najjar M, Castillero E, Mongero L, Beck J, et al. Del Nidocardioplegia can be safely administered in high-risk coronary artery bypass grafting surgery after acute myocardial infarction: a propensity matched comparison. J Cardiothoracic Surg. 2014;9:141.
11. Mick SL, Robich MP, Houghtaling PL, Gillinov AM, Soltesz EG, Johnston DR, et al. del Nido versus Buckberg cardioplegia in adult isolated valve surgery. J Thorac Cardiovasc Surg. 2015;149(2):626-34.
12. Ramanathan R, Parrish DW, Armour TK, Brinster DR. Use of del Nido Cardioplegia in Adult Cardiac Surgery. Thorac Cardiovasc Surg. 2015;63(7):624-7.
13. Guajardo Salinas GE, Nutt R, Rodrigez-Araujo G. Del Nidocardioplegia in low risk adults undergoing first time coronary artery bypass surgery. Perfusion. 2017;32(1):68-73.