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ORIGINAL ARTICLE

Self-constituted modified del Nido cardioplegia solution in pediatric congenital heart defect surgery.

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ABSTRACT… Objective: To present our experience of modified del Nido Cardioplegia for chemical arrest and myocardial protection during congenital heart defect repair pediatric cardiac surgeries. **Study Design:** Retrospective Cross Sectional. **Setting:** Department of Cardiac Surgery, PAQSJIMS, Gambat, Khairpur. **Period:** 15th March, 2021 to 10th October, 2022. **Material & Methods:** del Nido solution is generally constituted in plasma lyte A solution, not available in Pakistan; therefore, we constituted del Nido solution in ringer lactate solution. We had collected our data retrospectively for our study to assess the safety and efficacy of modified del Nido cardioplegic arrest during the open heart surgeries for congenital heart defects. We report clinical outcomes of our patients that include spontaneous rhythm, ionotropic score and duration of mechanical ventilation in patients underwent open heart surgeries. **Results:** During the study period we had performed 102 surgeries for correction or palliation of congenital heart defects. We have included 54 patients in our study with 28 (52%) male and 26 female (48%) patients; had a mean age 8.9 (±3.7) years and mean weight 22.4 (±12.7) kg. Majority of patients 29 (54%) belonged to Category 2 on RACHS-1 scale. Our average cross clamp time was 39.7min, and 37(68%) patients required a single dose of cardioplegia. Spontaneous sinus rhythm was established in 48(89%) patients; average ionotropic score of patients at the time of PICU arrival was 8.6 (±5.6) with 31(57%) have score of less than 10, while 2(4%) patients were received without the ionotrope. All the patients were shifted on mechanical ventilators with average time of 253.6 (±219.6) min of mechanical ventilation. **Conclusion:** Our results show modified del Nido solution is safe, with added benefits of fewer interruption in surgery, greater magnitude of spontaneous sinus rhythm and fewer ionotropic requirements

Key words: Congenital Heart Defects, Cardiac Surgery, Cardiopilegia, del Nido Solution, Pediatric Cardiac Surgery, Ringer Lactate.

INTRODUCTION

Myocardial protection is integral to open heart surgeries. During pediatric open heart surgeries potassium rich cardioplegia invokes chemically induced cardiac arrest that decreases myocardial metabolic demand further added with induced hypothermia[1] to achieve myocardial protection. Cardioplegic arrested heart generates quiescent bloodless field, a prerequisite for repairing intra-cardiac defects. Finding an ideal cardioplegia solution with consensus is till far from desired.[2] Several types of solutions are available with different electrolytic compositions to achieve diastolic arrest, which include Buckberg, Plegisol, and St. Thomas solutions.[3,4] These solutions enhance myocardial protection and membrane stabilization from ischemia reperfusion injury. Nevertheless, release of troponin[5], and minor ventricular dysfunction resulting low cardiac output from reperfusion requires ionotropic support[6] during postoperative period.

Differences in cardioplegia solutions, customized or commercially used[7,8], during pediatric cardiac surgery differ in electrolytic composition, dilution, favored chemical substances, doses and their intervals. Irrespective of the type of cardioplegia, every cardioplegia solution require a carrier solution like ringer solution, ringer lactate solution, Plasma lyte A and blood. These differences are dictated by surgeons and institutional practices, largely due to lack of evidence about the

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superiority of one solution over another.[9]

Recently, del Nido, Cao-Danh, Sommers, and Ohkado at the University of Pittsburgh developed cardioplegia solution for pediatric myocardial protection with the following composition; Mannitol (20%) 16.3ml, Magnesium sulfate (50%)4ml. Sodium bicarbonate (8.4%)13ml, Potassium chloride 13ml(2meq/ml), Lidocaine (1%)13ml. These all components are mixed in on l litre of Plasma-Lyte A (Baxter Healthcare Corporation, Deerfield, IL), a base solution for del Nido cardioplegia is calcium free solution with electrolyte composition similar to extracellular fluid[11] and administered with the dose of 20ml/kg with crystalloid: blood ratio of 4:1.[10]

The Plasma-Lyte A (Baxter Healthcare Corporation, Deerfield, IL), a base solution for del Nido cardioplegia is not available in Pakistan therefore to achieve the benefits of del Nido cardioplegia we used lactated Ringer's solution instead of Plasma Lyte A. Composition of both solutions are shown in Table-I and compared to human plasma.

Primary objective: Safety and efficacy of modified solution
Secondary objective: To compare the results with standard solution as per the review of literature about standard del Nido solution.

Substance/ Variable	Plasma-Lyte A Base[12]	Ringer Lactate Base[13]	Human Plasma
Sodium (mEq/L)	140.0	130.0	135-145
Potassium (mEq/L)	5.0	4.0	4.0-4.5
Chloride (mEq/L)	98.0	108.0	94.0-111.0
Calcium (mEq/L)	0.0	2.7	2.2-2.6
Magnesium (mEq/L)	3.0	3.0	0.8-1.0
Bicarbonate(mEq/L)	0	28.0	23.0-27.0
Lactate (mEq/L)	0.0	28.0	0.8-1.8
Acetate (mEq/L)	27.0	0.0	0.0
Gluconate (mEq/L)	23.0	0.0	0.0
pH	7.4	6.0 - 7.5	7.35-7.45
Osmolarity (mOsmol/L)	294.0	278.0	275.0-295.0

Table-I. Plasma-Lyte A and ringer lactate solutions compared with human plasma

MATERIAL & METHODS

After getting approval from departmental ethical board (No. D.PAQSTIMC/CS/P:02/22) data was collected for the study. In 102 surgeries, between March 15, 2021 to October 10, 2022, pediatric patients had congenital heart defects and came for palliative and definitive intervention by open and close heart surgeries. A retrospective review of our surgical record was carried out. Out of 102 surgeries 89 patients were operated for open heart surgeries were further securitized as per our criteria as mentioned bellow for selection of our final study population.

Inclusion Criteria

1. Patient underwent open heart surgeries.
2. Diastolic arrest following cardioplegia for these patients lasted for more than 10 minutes; to avoid pitfall of making of solution.

Exclusion Criteria

1. Patients that had missing records.
2. Planned for overnight ventilation due to sever Pulmonary Artery Hypertension.
3. Delayed extubation due to mediastinal drain or had to be reopened for bleeding or tamponade.
4. Expired excluding those who suffered primarily cardiogenic low cardiac output as determined by high ionotropic support requirements during first 24 hours.

Cardiopulmonary bypass, cardioplegia and PICU management strategy

We used tepid (30 to 32 degree C) to moderate (28-32 degrees C) hypothermic cardiopulmonary bypass for all open-heart surgeries with aortic and bicaval cannulation. Myocardial protection was achieved with cold blood del Nido (self-constituted by perfusionist in Ringer Lactate solution) cardioplegia in all cases transfused via aortic root with a pressure bag at 100 mmHg, and visual assessment of aortic distension to which topical cooling with frequent cold saline irrigation was carried out. Cardioplegia dose was repeated for minimum 40 minutes and maximum 60 minutes. Patients were weaned off from bypass with selected ionotropic support with adrenaline, further added inotrope support

if required then add-on with milrinone (milrinone was part management of patients with pulmonary hypertension irrespective of ionotropic requirement) and add on noradrenaline in order of our preference for inotropic support.

Following surgery, the patients were transferred to the Pediatric Intensive Care Unit (PICU) with Propofol infusion, planned for fast tract extubation (6 hours). Nevertheless, if patient was planned for prolong intubation, then our choice was intermittent or infusion of Attracurium with Nalbuphine. Patients remained in PICU till discharge. Demographic and clinical data were collected from medical notes and included age, diagnosis, surgical procedure, perioperative use of inotropic and vasoactive medications. We used Wernovsky IS[14], for calculation of ionotropic score of patients, measured duration of CPB and aortic cross clamp and doses of cardioplegia, spontaneous rhythm after removal of cross clamp and duration of mechanical ventilation. In addition, patients were categorized on Risk Adjustment in Congenital Heart Surgery (RACHS-1).[15]

Statistical analysis

Retrospective data was collected of selected patient population on excel sheet. All continuous variables are expressed as Mean with Standard deviation and qualitative variables are expressed as number with percentage while using excel formulas.

RESULTS

We had 89 open hearts surgeries. Our final study population included 54 patients. The demographic and cardiopulmonary bypass and PICU related characters are shown in table 2 and diagnosis of our patient population are shown in Figure-1.

Table-II Demographic and cardiopulmonary bypass and PICU related characters

Male: Female 28(52%):26(48%)
Age 8.9±3.7 years
Weight 22.4±12.7 kg
Pump time 104.4±56.2 min
Cross clamp time 49.7±35.8 min
Ionotropic score 8.6±5.6
Ventilation time 253.6±219.6 min

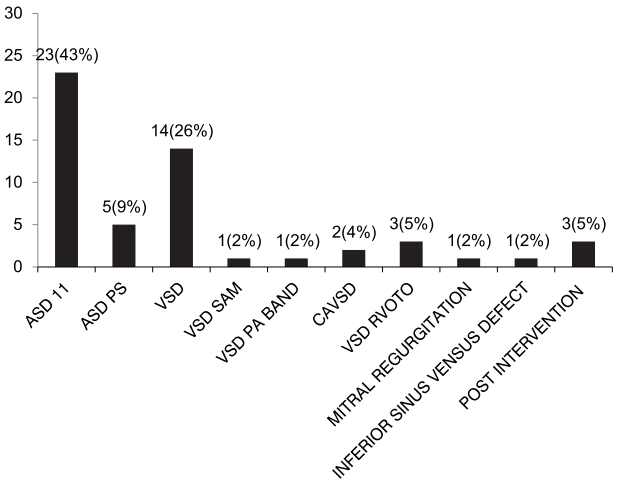

Figure-1. Diagnosis

ASD (Atrial septal defect), PS (Pulmonary stenosis), VSD (Ventricular Septal Defect), SAM (Sub Aortic Membrane), PA (Pulmonary Artery), CAVSD (Complete Atrioventricular Septal Defect), RVOTO (Right Ventricular outflow Tract Obstruction)

Majority of the patients 29(54%) belonged to risk Category 2 on RACHS 1 scale followed by Category 1; 22(44%) and Category 3; 1(2%). We repeated our cardioplegia solution after 40-60 minutes. In most cases 37(68%) we used a single application of del Nido cardioplegia while double dose in 9(17%) and three dose in 8(15%) in patients respectively. On average we repeated cardioplegia at 48 minutes, and cross clamp time was as shorter as 18 minutes. Spontaneous sinus rhythm at the removal of cross clamp of aorta was observed in 48(89%) patients while arrhythmias requiring intervention were occurred in 6(11%) patients. Ventricular fibrillation requiring cardio version were developed in 3(5%) patients; two of these patients had visible air in coronaries while one patient with ventricular septal defect (VSD) with moderate aortic regurgitation operated for VSD closure developed left ventricular distension at the removal of clamp and required cardiac massage and cardio version. Premature ventricular contraction causing hemodynamic instability developed in one patient with VSD with right ventricular our flow obstruction underwent

VSD closure and right ventricular overhaul; cardio version was unsuccessful as well as lidocaine and amiodarone loading. That patient shifted to PICU with atrial overdrive pacing for 24 hours. Heart block developed in 2(4%) patients operated for VSD closure. In one patient with type two block the VSD patch was undone and defect was closed with interrupted suture technique; patient rhythm changes to type one block with occasional missed beats and our second patient developed type one block while maintaining the hemodynamics. On the arrival of PICU two (4%) patients had no ionotropic support while the rest of patients with their ionotropic score-based group[16], are shown in Table-II.

Group	Ionotropic Score	Patient Frequency (%)
1	<10	31(57%)
2	10-14	14(26%)
3	15-19	7(13%)
4	20-24	0(0)
5	>25	0(0)

Table-II. Inotrope scores in groups of patients

2 patients shifted without ionotropic support. Our none of patient had inotropic score more than 19.

DISCUSSION

Use of cardioplegia in modern cardiac surgery, especially in children has a fundamental role in myocardial protection by decreasing metabolic activity thus enhancing its capacity to tolerate ischemia. The ideal cardioplegia strategy involving composition, dosing, blood vs. crystalloid is still far from ideal and substantial literature lacks consensus and randomized trials on the subject. Traditionally cardioplegia solution needs frequent dosing in 20 to 30 minutes resulting frequent interruption of surgical rhythm. Cardioplegia solutions with long duration effects would have two primary benefits, a single dose would avoid procedural interruptions, reducing the aortic cross-clamping time and that a single-dose would achieve better myocardial protection.[17,18]

The del Nido was developed by Pedro del Nido and his team at the University of Pittsburgh in the 1990s, having been used since 1994 for congenital heart defect surgeries at the Boston Children's Hospital and also used successfully in adults since 2003.[19] The del Nido cardioplegia with Plasma-Lyte A solution contains magnesium and lignocaine that help counteract potassium depolarization and increase intracellular calcium depletion, decrease myocardial excitability and metabolism, and energy consumption during ischemic arrest. Furthermore, it preserves intracellular high-energy phosphates and free radicals scavenging and acid base buffering. In addition to good myocardial protection it provides an arrest period of 90 minutes or more thus avoiding frequent interruption of surgery to infuse multiple doses as required while using many other marketed cardioplegia solutions but at the cost of haemodilution.[11,20] In our study with though majority of patients had shorter cross clamp requiring lesser doing of cardioplegia but as compare to marketed cardioplegia in Pakistan that requires dosing in evert 20 to 30 minutes we had single dose lasting about 40 minutes adequate for many surgeries .

Similar to our modified del Nido solution there are the sporadic report of recent literature also available with utilization of modified del Nido solution in pediatric and adult cardiac surgeries.[21]

Clinical outcomes in this study presents safety and efficacy of modified del Nido solution, which is not inferior to del Nido solution. This study showed fewer (7%) patients had ventricular arrhythmias at the release of aortic cross clamp comparable is similar to fewer (10%) patients described by Talwar and his team in their study[22] about use of del Nido solution involving complex congenital defects surgeries while we had two patients that had obvious etiology of visible coronary air embolism while the third patient underwent extensive right ventricular overhaul predisposing for ventricular arrhythmias. Similarly, our ionotropic score as well mechanical ventilation period is comparable to del Nido solution groups. Further more low ionotropic score of majorities of our patient as well early extubation supporting the safety and efficacy of solution in our patients operated for congenital heart defects.

CONCLUSION

In our small series of patients with majority of them

with short period of ischemia; modified del Nido solution has resulted good myocardial protection with achievement of spontaneous sinus rhythm, low ionotropic support with minimum interruption of surgery as compare to more frequent in every 20 minutes for more conventional solution available in market.

LIMITATION

Our study is a single Centre experience with limited number of patients. Furthermore, majority of our patients belong to low-risk RACHS 1 score while the patients in other studies about standard del Nido solution includes patient from high score complexity of congenital heart defects requiring more prolong surgeries.

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2	Jai Parkash	Critical review, Literature Review.	
3	Naresh Kumar	Contribution.	
4	Muhammad Farhan Khan	Review contribution.	
5	Naveed Nek Markhand	Drafting, Literature Research.	
6	Abid Ali Soomro	Review, Manuscript.	