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Recent Experience in the use of Del Nido Cardioplegic Solution in Pediatric Patients

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Abstract

Background: The interest in Del Nido cardioplegia for myocardial protection in pediatric cardiac surgery is growing. Research hitherto supports the use of Del Nido cardioplegia in providing myocardial preservation as well as reducing surgery time.

Objectives: To contribute to the literature, we sought to share our own experiences and outcomes of 86 pediatric patients who underwent cardiac surgery at our centre in whom this cardioplegic solution was used.

Methods: In a retrospective study, we evaluated 86 pediatric patients with congenital cardiac defects who underwent corrective cardiac surgery in whom Del Nido cardioplegic solution was used.

Results: The mean age of the patients was 55.1 ± 48.6 months and the mean weight was 16.2 ± 11.4 kilograms. Repair of tetralogy of Fallot and closure of atrial septal defect or ventricular septal defect represented 44% of the operations. Mean cross clamp time was 75.5 ± 38.6 minutes. In five patients (5.8%), cardioversion defibrillation was used to regain sinus rhythm after cross clamp release. Only one patient needed inotropic support grade 3 (epinephrine dose equal or more than 0.1 mcg/kg/min), while the remainder were in grade 2 or less.

Conclusion: We think that the use of Del Nido cardioplegia in our patients was associated with clinical benefits and decreased morbidity. It can provide appropriate myocardial protection for longer cross clamp times with decreased repeat dosing. However, the preferred cardioplegic solution in congenital cardiac surgery remain highly variable among centers.

Keywords: myocardium; heart surgery; cardioplegic solutions; myocardial ischemia; myocardial stunning

Introduction

Cardioplegia is the intentional, temporary and reversible cessation of cardiac activity, and it is necessary during a vast number of cardiac operations [1]. Whilst global ischemia is the easiest way to induce cardioplegia, it causes a range of reversible and irreversible ischemic injuries. Hence, cardioprotective procedures have been developed to delay the onset of irreversible injury and increase the period of reversible injury [2]. Whereas previously whole-body systemic hypothermia and circulatory arrest were used to protect and reduce detrimental effects, more sophisticated methods are now used. Chemical cardioplegia is now the gold standard for myocardial protection during cardiac surgery and helps reduce morbidity and mortality [2, 3]. This pharmacological diastolic arrest results in a relaxed, non-beating heart within a bloodless field allowing surgeons to operate more freely [3]. For the past 40

years, it has been, and remains the primary method of myocardium protection during cardiac operations where the heart must be stopped [1, 4]. It is used to prevent injuries such as ischemia-reperfusion injury, cell apoptosis and infarction [5, 6].

Cardioplegic solutions work based on the principal of creating a more positive resting membrane potential. This is generally established by a hyperkalemic solution causing depolarization [2]. There are two main types: Cold crystalloid cardioplegic solutions and blood cardioplegia [5]. The search for the best cardioplegic solution however, is still continual with a multitude of options available [3,5,7]. Pedro Del Nido and his team at the University of Pittsburgh developed Del Nido cardioplegia in 1990s. This blood-based solution has been used for pediatric cardiac surgery in Boston's Children Hospital since 1994 [3, 4]. The needs and differences of the pediatric and therefore immature heart were recognized and a specific cardioplegic

solution was produced [4,8]. It has the ability to induce prolonged periods of cardiac arrest with a single dose unlike other therapies which require multiple doses [3,8].

Del Nido cardioplegia is an extracellular solution combined with blood obtained from the extracorporeal circuit of the patient. There is a crystalloid: blood ratio of 4:1. This means the crystalloid solution makes up 80% and is mixed with blood of a 20% volume. A single dose of this solution confers optimal myocardial protection for approximately 90 minutes. An administration pressure of 100-200 mmHg and an administration flow of 200-300 ml/min is recommended. The achieved myocardial temperature is <15°C (usually between 8-12°C). At this temperature, there is reduced metabolism and oxygen consumption [3, 4]. The crystalloid solution includes Plasma-Lyte as a basic solution, mannitol, magnesium sulfate, bicarbonate, potassium and lidocaine. There are various preparations distributed which contain different volumes and concentrations of the components. Therefore, the formula at times needs to be modified to obtain the correct ingredient concentration. Each ingredient in the solution plays an important role in the cardioprotective strategy as discussed below:

Plasma-Lyte is a commercial solution with a pH of 7.4. It contains 140 mEq/l sodium, 5 mEq/l potassium, 3 mEq/l magnesium, 98 mEq/l chloride, 27 mEq/l acetate and 23 mEq/l gluconate. Mannitol is a hyperosmotic solution that helps reduce oedema and myocardial cell swelling. It also scavenges free radicals which can cause myocardial injury [5, 9]. Magnesium blocks the calcium channel which has been proved to improve myocardial recovery [10-12]. This is due to the fact that myocardial function is tightly associated with intracellular calcium concentration. Sodium bicarbonate scavenges hydrogen ions and thus maintains the intracellular pH. It acts as a buffer with the help of the carbonic anhydrase from the red blood cells to achieve this [4]. Potassium chloride causes a rapid depolarized arrest. Care has to be taken because sole depolarised arrest has been associated with impaired myocardial recovery due to the accumulation of intracellular sodium and calcium [13]. Lidocaine is a sodium channel blocker and an antiarrhythmic agent. It helps by increasing the refractory period and also

prevents the harmful effects of hyperkalaemic depolarised arrest [14].

The blood additive supports aerobic metabolism, provides buffering capabilities and improves coronary perfusion [15]. There has been reports of it helping preserve myocardial metabolism and thus reducing ischemia along with reperfusion injury [16-18].

The interest in Del Nido cardioplegia for myocardial protection in pediatric cardiac surgery is growing. Research hitherto supports the use of Del Nido cardioplegia in providing myocardial preservation as well as reducing surgery time. It is believed to be both clinically and cost effective, however the evidence is somewhat controversial and unclear [3,5]. Techniques to ensure optimal myocardial protection are still variable among surgeons with no real consensus [15]. To contribute to the literature, we sought to share our own experiences and outcomes of approximately 90 paediatric patients who underwent cardiac surgery at our centre in whom this cardioplegic solution was used.

Materials and Methods

The study included 86 pediatric patients in whom Del Nido cardioplegia was used during corrective cardiac surgery for congenital heart defects from April 2018 to August 2019 at our center, Damascus University Cardiac Surgery Hospital, Syria. In a retrospective study, their medical records were reviewed to obtain the required data. The studied data included: age, weight, diagnosis and type of the operation, cross clamp time, the need for defibrillation after cross clamp relief, inotropes requirements immediately and during the first 24 hours postoperatively, the duration of mechanical ventilation, and the length of stay in the intensive care unit. The local ethics committee in our institution approved this study protocol.

Results

Baseline characteristics

The mean age of the patients was 55.1 ± 48.6 months (range 11 days to 16 years) and the mean weight was 16.2 ± 11.4 kilograms (range 3 to 65 kilograms). The types of the performed operations are summarized in table 1.

TFTC	15 (17.4%)
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ASD closure	13 (15.1%)
VSD closure	10 (11.6%)
CAVSD repair	5 (5.8%)
DSAS repair	5 (5.8%)
VSD closure-PDA repair	5 (5.8%)
VSD closure-RVOTO repair	4 (4.7%)
TAPVC repair	3 (3.5%)
Valvar PS repair	3 (3.5%)
PAVSD repair	3 (3.5%)
VSD closure-TV repair	3 (3.5%)
RVOTO repair	2 (2.3%)
DORV repair	2 (2.3%)
VSD closure-AI repair	2 (2.3%)
VSD closure-DSAS repair	2 (2.3%)
ASD closure-PDA closure	1 (1.2%)
ASD closure-TV repair	1 (1.2%)
ASO	1 (1.2%)
PAPVC repair	1 (1.2%)
AVR	1 (1.2%)
Ebstein anomaly repair	1 (1.2%)
Fontan	1 (1.2%)
Truncus Arteriosus repair	1 (1.2%)
VSD closure-supramitral ring repair	1 (1.2%)

TFTC: Tetralogy of Fallot Total Correction, ASD: Atrial Septal Defect, VSD Ventricular Septal Defect, CAVSD: Complete AtrioVentricular Septal Defect, DSAS: Discrete SubAortic Stenosis, PDA: Patent Ductus Arteriosus, RVOTO: Right Ventricular Outflow Tract Obstruction, TAPVC: Total Anomalous Pulmonary Venous Connection, PS: Pulmonary Stenosis, PAVSD: Partial AtrioVentricular Septal Defect, TV: Tricuspid Valve, DORV: Double Outlet Right Ventricle, AI: Aortic Insufficiency, ASO: Arterial Switch Operation, PAPVC: Partial Anomalous Pulmonary Venous Connection, AVR: Aortic Valve Replacement.

Intra- and Post-Operative Outcomes

We used Del Nido cardioplegia solution with an initial dose of 20 ml/kg. We administered another dose of 10 ml/kg only when the cross-clamp time exceeded 70 minutes. Data was recorded for cross clamp and cardiopulmonary bypass times, dosage of cardioplegia administered, the need for DC shock to regain regular rhythm after cross clamp release, and inotropic support.

Mean cross clamp time was 75.5 ± 38.6 minutes (range 17 to 204 minutes). We administered a second dose of cardioplegia only in 23 patients (26.7%) in whom we gave half the initial dose after 70-80 minutes from the initial dose. After cross clamp release the heart started beating in sinus rhythm in 81 patients, and in ventricular fibrillation in five patients (5.8%) in whom DC shock was used to regain sinus rhythm. We used Milrinone at a dose of 0.5-0.75 mcg/kg/min for the majority of patients, starting infusion at the time of rewarming the patient. In 42 patients, epinephrine was also required. We graded the inotropic requirements

immediately postoperatively, and in the first 24 hours postoperative period according to the dose of epinephrine needed as follows:

Grade 0: no inotropes needed.

Grade 1: epinephrine dose equal or less than 0.05 mcg/kg/min.

Grade 2: epinephrine dose more than 0.05 but less than 0.1mcg/kg/min.

Grade 3: epinephrine dose equal or more than 0.1mcg/kg/min.

The results are summarized in table 2.

Grade of inotropic requirements	Number of patients (%)
0	44 (51%)
1	33 (38.4%)
2	8 (9.5%)
3	1 (1.1%)

Table 2

Mean mechanical ventilation duration was 7.9 ± 4.6 hours (range 2 to 28 hours), and mean intensive care unit stay was 2.3 ± 5.3 days (range 1 to 50 days). Pre- and post-repair echocardiography was performed to

evaluate the adequacy of surgical repair, and to discover any changes in myocardial function, or any new findings. All the patients had satisfactory surgical repair without any residual lesions, and no deterioration of cardiac function was noted in any patient.

We had three hospital mortalities (one patient who underwent an arterial switch operation died directly postoperatively, another TF patient died 4 days postoperatively due to respiratory failure after severe infection, and another CAVSD patient with Down syndrome died 50 days postoperatively due to neurologic injury).

Discussion

Myocardial protection techniques during cardiac surgery remains highly variable among congenital heart surgery centers. In this article, we aimed to share our experience with Del Nido cardioplegia in pediatric patients. All the patients included in this study were operated on by a single surgeon, and therefore we were not able to compare the outcomes with other cardioplegic solutions used in operations performed by different surgeons. The interest in this kind of cardioplegia is growing. Kotani et al revealed that Del Nido solution was used by approximately 40% of surgeons in a North American multiinstitutional survey. The use of Del Nido cardioplegia solution is associated with significantly less frequent cardioplegic dosages as it provides myocardial protection for longer intervals, and this advantage facilitated the introduction and dissemination of this newly developed cardioplegic solution [15, 19].

The first clinical study about Del Nido cardioplegia was carried out in Halifax by O'Brien in 2009. The study proved that Del Nido cardioplegia results in lower troponin T levels and better calcium management in pediatric patients as compared to adult cardioplegia [14].

We found a rate of post cross-clamp fibrillation requiring cardioversion defibrillation of 5.8%. This ratio is similar to that when Del Nido cardioplegia solution was used in a previously reported study (4.4%), in which there was a 6-fold decrease in the overall rate of defibrillation post cross-clamp removal compared to St. Thomas solution (26.8%) (20).

Mechanical ventilation duration and intensive care unit stay were 7.9 ± 4.6 hours and 2.3 ± 5.3 days respectively. These values are consistent with those in

comparative studies [21]. We think that the use of Del Nido cardioplegia in our patients was associated with clinical benefits and decreased morbidity as it has been reported previously in a study that also included electron microscopic studies which showed better preservation of myofibrillar architecture in the Del Nido group [21].

Conclusion

We think that the use of Del Nido cardioplegia in our patients was associated with clinical benefits and decreased morbidity. It can provide appropriate myocardial protection for longer cross clamp times with decreased repeat dosing. However, the preferred cardioplegic solution in congenital cardiac surgery remain highly variable among centers.

Limitations

Our study is a retrospective one, and its value is limited. A prospective, randomized trial is required to prove the feasibility or superiority of Del Nido cardioplegia over other solutions for myocardial protection. Moreover, it seems that the most appropriate study is one that correlates markers of postoperative myocardial function with myocardial preservation strategies.

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