Comparing del Nido and Conventional Cardioplegia in Infants and Neonates in Congenital Heart Surgery

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Background. **The aim of this study was to evaluate outcome measures after the use of del Nido (dN) cardioplegia compared with conventional multidose high-potassium (non-dN) cardioplegia in neonates and infants.**

Methods. **We retrospectively analyzed data in patients, aged younger than 1 year, undergoing cardiopulmonary bypass (CPB) from January 2012 to August 2015. We changed our cardioplegia protocol from non-dN to dN administered in a single or infrequently dosed strategy in September 2013. The outcomes of the dN group (n = 107) are compared with the non-dN group (n = 118). We analyzed variables for demographic, intraoperative, early postoperative, and discharge variables.**

Results. **The two groups were similar in age, weight, height, CPB, and cross-clamp time; preoperative and postoperative echocardiographic systolic functions; first 24-hour postoperative urine output and inotropic score; length of stay; and mortality rate. The Society of Thoracic Surgeons/European Association for Cardio-Thoracic Surgery Congenital Heart Surgery (STAT) mortality category was significantly higher in the dN group ($p = 0.03$). The cardioplegia dosing interval was lower for the non-dN group ($p < 0.001$). The volume and doses of cardioplegia per patient were significantly higher in the non-dN group ($p < 0.001$). In a subanalysis, when the Norwood patients were excluded from both groups, the overall STAT mortality category difference was no longer significant. The demographic, early postoperative, and discharge variables still showed no significant difference when the two groups were compared.**

Conclusions. **Similar outcomes can be achieved with less frequent interruption of the operation and lower volume of cardioplegia when using dN cardioplegia solution compared with conventional cardioplegia. The dN cardioplegia with extended ischemic interval can be used as an alternative strategy in the neonatal and infant population during cardiac operations.**

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Over the years, myocardial preservation in adults and children alike has been generally achieved by delivering solutions containing high potassium as cardioplegia and by inducing hypothermia for metabolic support during the ischemic period [1–7]. There has been a steady focus to develop more-specific myocardial preservation for an immature heart [1, 3, 8–13]. Areas of interest have included studying the important role of intracellular calcium ion accumulation and regulation, high-energy phosphate and lactate production, and buffering mechanisms during ischemia in the immature myocardium [1, 3, 8–15]. Despite this progress, a variety of cardioplegia solutions are currently used in the pediatric population, suggesting continued lack of consensus about the best cardioplegia strategy [16]. The del Nido (dN) cardioplegia solution, the most commonly used cardioplegia, developed with some of the above-mentioned specific focus, is used by a third of the pediatric cardiac surgeons [2, 4, 17]. Despite its increasing adoption, there remains a paucity of reporting of its clinical efficacy in infants and neonates unlike that in the adult literature [18–23]. The aim of this study was to compare outcome measures in infants and neonates who received dN cardioplegia solution with those who received conventional multidose high-potassium (non-dN) cardioplegia.

Patients and Methods

Study Subjects

The study protocol was reviewed by the institutional review board that issued an exempt status. We retrospectively collected and analyzed data in all patients, aged younger than 1 year, undergoing cardiopulmonary bypass (CPB) with cardiac arrest from January 2012 to August 2015.

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Abbreviations and Acronyms

CPB = cardiopulmonary bypass
CPS = cardiopulmonary support
DHCA = deep hypothermic circulatory arrest
dN = del Nido
ICU = intensive care unit
IQR = interquartile range
LOS = length of stay
STAT = Society of Thoracic Surgeons/European Association for Cardio-Thoracic Surgery Congenital Heart Surgery
TEE = transesophageal echocardiography

In September 2013, we switched our cardioplegia protocol from non-dN cardioplegia exclusively to dN cardioplegia solution in all cardiac operations in our institution. The dN and the previous conventional cardioplegia solutions are prepared at our pharmacy (Table 1) [1]. To assess the safety and efficacy of the dN cardioplegia solution, we compared the clinical in-hospital outcomes of infants and neonates undergoing congenital heart operation with those who received non-dN cardioplegia. dN cardioplegia solution was used in 107 patients (from September 2013 to August 2015) and non-dN cardioplegia was used in 118 patients (from January 2012 to August 2013). All patients in this study underwent modified arteriovenous ultrafiltration. Types of operations performed in each group are shown in Table 2.

We analyzed four categories of variables in each group: patient demographic, intraoperative, early postoperative (24-hours), and discharge data. Variables collected included age, sex, weight, height, Society of Thoracic Surgeons/European Association for Cardio-Thoracic Surgery Congenital Heart Surgery (STAT) mortality category, and hospital mortality. The intraoperative variables such as CPB, cross-clamp time, deep hypothermic circulatory arrest (DHCA) time, lowest temperature on CPB, total cardioplegia volume, number of doses, and time interval between the doses of cardioplegia were also recorded. The preoperative and postoperative transesophageal echocardiography (TEE) showing systemic ventricular function, number of post-CPB cardioversions, first 24-hour urine output (total and per kilogram), diuretic use in the first 24-hours, inotropic score [24], basic metabolic panel (Na^+, K^+, Ca^{2+}, Cl^-, blood urea nitrogen, creatinine), time to extubation, open chest, need for cardiopulmonary support (CPS), postoperative length of stay (LOS), and discharge status were also documented for analysis.

Table 1. Composition of del Nido Versus Conventional Multidose Cardioplegia Solutions (1000 mL)

Composition	dN	Non-dN
Base solution	Plasma-Lyte A	Plasma-Lyte A
Blood-to-crystalloid ratio	1:4	1:4
Potassium chloride, mEq	26	30
Sodium bicarbonate, mEq	13	55
Mannitol, g	3.3	3.8
Lidocaine, mg	130	15
Magnesium, mEq	16	4

dN = del Nido; non-dN = conventional multidose high-potassium.

Table 2. Types of Operations

Operation	dN (n = 107)	Non-dN (n = 118)
Norwood operation	21 (20)	13 (11)
Arterial switch	10 (9)	12 (10)
Aortic arch repair + VSD closure	7 (7)	6 (5)
TOF/RVOT/AVC repair	25 (23)	49 (42)
VSD closure	18 (17)	17 (14)
Glenn operation	11 (10)	7 (6)
Other	14 (13)	14 (12)

Values are n (%).

AVC = atrioventricular canal defect; dN = del Nido; non-dN = conventional multidose high-potassium; RVOT = right ventricular outflow tract; TOF = tetralogy of Fallot; VSD = ventricular septal defect.

Surgical Technique and Cardioplegia Delivery

All operations were performed using a standard general anesthesia protocol, a median sternotomy approach, and CPB with systemic hypothermia. Intraoperative TEE was routinely used before and after the termination of CPB. Two cardiologists reviewed the echocardiograms for evaluation of the systemic ventricular function according to a 4-grade scale: 0 being normal and 3 being severely impaired function. Myocardial protection was achieved with either dN or non-dN cardioplegia infused into the aortic root in an antegrade fashion. In both groups, the heart was arrested with an initial dose (20 mL/kg for dN and non-dN patients) of cold (4°C to -6°C) 1:4 mixture of blood to crystalloid cardioplegia. In addition, a repeat dose of non-dN cardioplegia was given at about 20 minute intervals in non-dN patients only. A second dose of dN cardioplegia was only given if the cross-clamp time exceeded 60 to 90 minutes (10 mL/kg) or if there was premature recurrence of activity [1]. The decision of when to re-dose cardioplegia was at the surgeon's discretion. Topical cooling with cold saline solution was used in both groups. All patients in the study underwent modified arteriovenous ultrafiltration.

Statistical Analysis

Data are presented as the median and the interquartile range or mean ± standard deviation. Variables for the two cohorts were compared using two-tailed unpaired *t* test, Fisher's exact test, and Mann-Whitney *U* test as appropriate. Our primary early outcome measures were the first 24-hour postoperative urine output and the first 24-hour inotropic score. Three different linear regression analyses were performed using first 24-hour urine output, inotropic score, and use of CPS as the dependent variable. The independent variables used in the analyses included