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Original Article

del Nido versus St. Thomas Cardioplegia Solutions: A Single-Center Retrospective Analysis of Post Cross-Clamp Defibrillation Rates

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Abstract: There are many cardioplegia solutions currently in use for pediatric cardiopulmonary bypass (CPB). The most common being del Nido solution. Another common cardioplegia solution used for pediatric CPB is St. Thomas. In October 2014, Children's Mercy Kansas City changed from the use of modified St. Thomas to del Nido. This study compared rates of post cross-clamp fibrillation requiring defibrillation between del Nido solution and modified St. Thomas solution stratified by weight at Children's Mercy Kansas City. This retrospective study consisted of 394 patients who underwent cardiac surgery requiring cardioplegia between January 1, 2014 and July 31, 2015. The outcome measured was defibrillation upon cross-clamp removal. Statistical significance was determined using Fishers exact test with a two-sided significance level of .05. Incidence of defibrillation post cross-clamp removal was 4.4% in the del Nido group and 26.8% in the St. Thomas group ($p < .0001$). Analysis by weight stratifications displays a reduction in post cross-clamp defibrillation rates in groups using the del Nido solution. The 0- to 6-kg category had an incidence of fibrillation of 1.23% in the del Nido group and 17.5% in the St. Thomas group ($p < .0003$). The 6- to 15-kg category had an incidence of defibrillation of 1.82% in the del Nido group and 14% in the St. Thomas group ($p < .0198$). The 15- to 60-kg category had an incidence of defibrillation of 8.9% in the del Nido group and 61% in the St. Thomas group ($p < .0001$). The >60-kg category had an incidence of defibrillation of 16.7% in the del Nido group and 63% in the St. Thomas group ($p < .0623$). This study demonstrates a 6-fold decrease in the overall rate of defibrillation post cross-clamp removal between St. Thomas and del Nido cardioplegia solutions. Analyses of weight stratifications demonstrate a decrease in the rate of defibrillation post cross-clamp removal in all categories within the del Nido group.
Keywords: cardioplegia, defibrillation, del Nido, St. Thomas.
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Today, a variety of cardioplegia solutions are used in pediatric open heart surgery and the choice of a preferred solution varies from institution to institution (1). Cardioplegia solutions are categorized as either extracellular or intracellular solutions based on their ion composition and the cellular environment that they reflect (extracellular or intracellular) (2). Extracellular cardioplegia solutions include St. Thomas, Buckberg, and del Nido while Custodiol® HTK Solution (Essential Pharmaceuticals, Ewing, NJ) is an intracellular solution. Commonly, institutions modify these solutions to suit their preferences.

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The goal of this study is to retrospectively compare rates of fibrillation post cross-clamp removal for patients receiving del Nido cardioplegia solution vs. modified St. Thomas cardioplegia solution. In October 2014, following a change in cardioplegia solution from St. Thomas to del Nido, anecdotal observation of reduced rates of defibrillation post cross-clamp removal were observed. Therefore, it was hypothesized that a significant decrease in the rates of post cross-clamp fibrillation among all patients and weight categories that received del Nido cardioplegia over St. Thomas solution would be appreciated.

MATERIALS AND METHODS

"A retrospective analysis comparing del Nido cardioplegia solution to modified St. Thomas cardioplegia solution" was approved on October 26, 2015 by Children's

Mercy Kansas City (IRB no.: 15,090,442). This retrospective study examined the rates of fibrillation post cross-clamp removal comparing del Nido cardioplegia solution to St. Thomas cardioplegia solution. Inclusion criteria were all patients who underwent cardiac surgery requiring cross-clamping of the aorta and the delivery of cardioplegia between January 2014 and July 2015.

The patient population was organized into two groups. In group 1, patients were administered modified St. Thomas cardioplegia solution. In group 2, patients were administered del Nido cardioplegia solution. These groups were then stratified by weight ranges in the following categories: 0–6, 6–15, 15–60, or >60 kg. In terms of Society of Thoracic Surgeons (STS) surgical risk category, both populations were similar (Table 1).

Cardioplegia Administration Protocol

The cardioplegia circuit used at our institution includes a CSC 14 cardioplegia delivery and heat exchanger (Sorin, Arvada, CO), and a roller pump with tubing in 1–4 dimensions (Sorin).

From January 1, 2014 to October 10, 2014 at our institution, a modified version of St. Thomas solution with an additional 60 mEq/L of potassium chloride was used. The modified St. Thomas solution was given in a 4:1 ratio of blood to crystalloid. The arresting dose delivered was 40 mL/kg with a typical re-dose time of 20 minutes. Maintenance doses were 20 mL/kg.

From October 11, 2014 to July 31, 2015 at our institution, del Nido solution was given in a 1:4 blood to crystalloid ratio. The initial arresting dose was 20 mL/kg with a typical re-dose time of 40 minutes. Maintenance doses were 10 mL/kg.

Measures

The outcome measure for this study was the incidence of ventricular fibrillation necessitating electrical defibrillation post cross-clamp removal. Patients were stratified by weight categories, 0–6, 6–15, 15–60, and >60 kg, commonly seen in pediatric heart surgery literature. These data were collected using a secure department database.

Statistical Analysis

Statistical analysis of our patient population was done using the Cochran–Mantel–Haenszel test. Analysis of defibrillation rates was done using Fisher's exact test with a two-sided significance level of .05. The analysis was done using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY) and GraphPad Inc. (San Diego, CA).

RESULTS

This retrospective study consisted of 394 patients who underwent cardiac surgery requiring cardioplegia between January 1, 2014 and July 31, 2015, at Children's Mercy Kansas City. Patients were categorized by weight and type of cardioplegia solution administered. The St. Thomas group included 190 patients who underwent cardiac surgery between January 1, 2014 and October 10, 2014. The del Nido group included 204 patients who underwent cardiac surgery between October 11, 2014 and July 31, 2015. The incidence of defibrillation post cross-clamp removal was 4.4% in the del Nido group and 26.8% in the St. Thomas group ($p < .0001$). Analysis by weight stratifications demonstrates a reduction in post cross-clamp defibrillation rates in all groups using the del Nido solution. The 0- to 6-kg and 15- to 60-kg stratifications displayed the most significance in difference of defibrillation rates although the >60-kg stratification displayed the least amount of difference in fibrillation rates. See the clinical data in Table 2.

DISCUSSION

It was hypothesized that del Nido solution would result in lower defibrillation rates post cross-clamp removal when compared to a modified St. Thomas solution. These retrospective data support this observation. Analysis over all weight categories demonstrates significance ($p < .05$) in every weight stratification with the exception of >60 kg, possibly due to the small sample size in that weight category.

In 1976, a cardioplegia solution was introduced at St. Thomas Hospital in London, England, and coined "St. Thomas solution" (3). St. Thomas solution is an extracellular, potassium-based cardioplegia solution that can be administered as a crystalloid solution or combined with a blood component. At the time, the addition of magnesium

Table 1. Patients grouped by surgical risk category.

STAT Score	del Nido (*n*)	del Nido Row (%)	St. Thomas (*n*)	St. Thomas Row (%)	Row Mean Scores Difference
5	10	4.93	11	5.79	0.3188
4	37	18.23	44	23.16	
3	36	17.73	29	15.26	
2	50	24.63	46	24.21	
1	70	34.48	60	31.58	

STAT score is a complexity stratification method used for the STS Congenital Heart Surgery Database. With this stratification system, a 5 is considered the most complex case and a 1 is considered the least complex.

Table 2. Defibrillation rate data by cardioplegia type and weight stratification.

	del Nido			St. Thomas			
Weight	*n*	Defibrillation	%	*n*	Defibrillation	%	*p*
All patients	204	9	4.4	190	51	26.8	<.0001
<6 kg	81	1	1.23	66	14	17.5	<.0003
6–15 kg	55	1	1.82	64	9	14	<.0198
15–60 kg	56	5	8.9	38	23	61	<.0001
>60 kg	12	2	16.7	8	5	63	<.0623

was unique to St. Thomas solution. The magnesium ion functions as a calcium channel blocker. As St. Thomas solution was further investigated, improvements were made to the solution (potassium concentration was increased, whereas sodium and calcium concentrations were both decreased) and in 1981, it became known as St. Thomas no. 2 also known as Plegisol (3). The components of the unmodified St. Thomas no. 2/Plegisol solution are listed in Table 3.

Many centers that use St. Thomas no. 2/Plegisol add extra potassium to the solution and combine it with a blood component, typically in a ratio of 4 parts blood to 1 part crystalloid. This is an example of a modified St. Thomas solution. Combining St. Thomas solution with blood enables a depolarized electrical arrest with less crystalloid administration, thereby decreasing the degree of hemodilution on cardiopulmonary bypass. Furthermore, adding blood to cardioplegia allows for the natural acid–base buffers to be used, improved oxygen delivery to the myocardium, increased colloidal oncotic pressure to prevent cellular edema, and improved preservation of high-energy phosphates, such as adenosine triphosphate (ATP) (4).

Modified St. Thomas solution has been used effectively in both adult and pediatric cardiac surgery programs to achieve electrical arrest and myocardial protection. Typically, modified St. Thomas solution is administered every 20 minutes while the aorta is cross-clamped to maintain electrical arrest and provide myocardial protection.

In the 1990s, del Nido cardioplegia solution was developed at the University of Pittsburgh to address the needs of immature and developing myocardium particularly in neonatal, infant, and pediatric patients (5). Immature myocardium has decreased ventricular compliance which leads to less preload reserve and has higher sensitivity to intracellular calcium due to an underdeveloped sarcoplasmic reticulum which has reduced ability to store calcium (5). The del Nido solution includes a 20% blood component and an 80% crystalloid component (1 part blood to 4 parts crystalloid) that is comprised of Plasmalyte A and additives listed in Table 4.

These additives were chosen for the following reasons. Mannitol acts as an oxygen free radical scavenger and has osmotic properties that can reduce cardiac myocyte edema. Magnesium functions as a calcium channel blocker and can reduce the buildup of intracellular calcium, which can lead to diastolic stiffness resulting in poor filling and decreased cardiac function post cross-clamp removal (6). Sodium bicarbonate is a buffering solution to scavenge excess hydrogen ions that help to maintain intracellular pH since aerobic metabolism is not maintained throughout the period of myocardial arrest. This is noteworthy because excess hydrogen ion accumulation has been shown to inhibit anaerobic production of ATP. Potassium chloride is used to provide a rapid depolarized arrest, which is important to preserve intracellular levels of ATP. Lidocaine is a sodium channel blocker that is used to prevent accumulation of sodium within the cell during depolarized arrest (6). As previously described, the inclusion of blood with cardioplegia is to prolong aerobic metabolism and provide

Table 3. Constituents (mEq/L) of St. Thomas no. 2/Plegisol solution (buffered with 10 mL of 8.4% sodium bicarbonate).

K^+	16
Na^+	120
Ca^{2+}	2.4
Mg^{2+}	32
Cl^-	160
$NaHCO_3$	10

Table 4. Constituents of del Nido solution.

Plasmalyte A (mEq/L)	
Na^+	140
K^+	5
Mg^{2+}	3
Cl^-	98
Acetate	27
Gluconate	23
del Nido Additives	
K^+	26 mEq/L
Mg^{2+}	2 g
$NaHCO_3$	13 mEq/L
Mannitol	3.26 g
Lidocaine	130 mg

physiological buffering to promote anaerobic glycolysis. This important buffering role is the responsibility of the red blood cells containing carbonic anhydrase, which promotes removal of hydrogen ions by combining them with bicarbonate and eventually producing carbon dioxide and water (6).

Comparison of Cardioplegia Solutions

One advantage reported with the use of del Nido solution is the ability to have longer ischemic times between doses of cardioplegia. This allows the surgeon to have an uninterrupted work flow without having to stop and re-dose cardioplegia as frequently as other solutions (1–7). Reported protocols demonstrate re-dose times ranging between 20 and 60 minutes (1). When compared to Buckberg solution, pediatric patients receiving del Nido have lower rates of fibrillation post aortic cross-clamp removal. This has also been shown to be true by studies done in adult patients who have received del Nido solution (8–10).

Interestingly, although del Nido was developed for the needs of the immature myocardium, some adult centers have started using it. In adult populations, del Nido may be an alternative that provides some advantages seen in pediatric use such as longer lasting myocardial protection between doses thus decreasing re-dosing of cardioplegia which interrupts the surgeons work flow and it may provide superior protection for aged hearts compared to Buckberg solution (8–10).

Negative Impact of Electrical Defibrillation

In open heart surgery, ventricular fibrillation following cross-clamp removal can be a common event. Although fibrillation can be treated rapidly with electrical defibrillation, defibrillation itself may be a source of injury to the myocardium (11). It has been proposed that a correlation may exist between defibrillation and elevated troponin T levels (10–12). Elevated serum troponin T levels are specific marker of myocardial injury and an independent predictor of early death in pediatric cardiac surgery patients (13). The dysfunction of cardiac myocytes from electrical shock may be due to altered membrane permeability and disrupted calcium homeostasis (12). To prevent poor outcomes, the ability to prevent ventricular fibrillation with an effective cardioplegia management strategy is potentially more important than treating it after has occurred (11).

The vast decrease in fibrillation rate post cross-clamp removal with del Nido over modified St. Thomas suggests that del Nido is a more effective solution for providing myocardial protection specifically in patients 0–60 kg over modified St. Thomas solution. Randomized prospective trials studies may be advantageous for determining other conditions of optimal myocardial protection, such as dosing regimens and redosing intervals. Further analysis will be necessary to determine how other cardioplegia solutions compare to del Nido solution.

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