Technique Article

Use of del Nido Cardioplegia Solution and a Low-Prime Recirculating Cardioplegia Circuit in Pediatrics

Richard M. Ginther, Jr., CCP; Ronald Gorney, PA-C, CCP; Joseph M. Forbess, MD

Division of Pediatric Cardiothoracic Surgery, University of Texas Southwestern Medical Center and Children’s Medical Center, Dallas, Texas

Abstract: The evolution of myocardial protection techniques has been both the source of milestone advancements and controversial debate in cardiac surgery. Our institution has modified a low-prime cardioplegia system (CPS) and adopted a single-dose cardioplegia solution (del Nido cardioplegia) for our congenital heart disease population. The goal of this article is to describe our CPS and outline our myocardial protection protocol. These techniques have allowed us to minimize circuit surface area, operate uninterrupted, and safely protect the myocardium during extended ischemic periods. Keywords: pediatric, myocardial protection, cardioplegia, del Nido, circuit miniaturization.

Protecting the myocardium is a multifaceted component of successful cardiac surgery. Cardioplegia, one of the major protection techniques, has evolved in many different directions since the first report of elective cardiac arrest by Dr. Melrose in 1955 (1). In the United States, depolarizing solutions are the most common type of cardioplegia (2). These hyperkalemic solutions offer sufficient electromechanical arrest, but postoperative ventricular dysfunction is still observed (3,4). It has been widely reported that intracellular calcium loading resulting from potassium-induced membrane depolarization is related to the development of ventricular dysfunction (5–8). These findings have spawned many modified depolarizing solutions, which contain membrane-stabilizing additives (e.g., magnesium or lidocaine) that directly or indirectly control intracellular calcium concentrations (9–12). To further complicate the goal of finding an optimal cardioplegia solution, differences in the mature and immature myocardium and congenital variations must be considered (13,14). Despite numerous advancements and an extensive body of research, most myocardial protective techniques continue to be classified as institutional- and experience-based (15).

In 2005 our pediatric congenital heart surgery program abandoned the Buckberg cardioplegia solution and adopted a modified depolarizing solution commonly referred to as del Nido cardioplegia. The developmental history and use of del Nido cardioplegia was recently described in the September 2012, Volume 44, Number 3 Guest Editorial of JECT (16). This cardioplegia solution is quickly gaining national recognition among congenital heart surgery programs because of its observed effectiveness at protecting the myocardium without the need for multiple doses.

The purpose of this report is to illustrate our updated low-prime modified cardioplegia system (CPS), describe the components of this modified depolarizing solution, and outline our delivery protocol.

METHODOLOGY

Modified Cardioplegia Circuit

In 1994, our perfusion group published a novel technique for incorporating the Terumo Sarns Conducer (Figure 1;
Terumo Cardiovascular Systems Corporation, Ann Arbor, MI) heat exchanger in a low-prime recirculating cardioplegia system (17). Since then, we have made several updated modifications and have simplified the recirculating technique because of our single-dose cardioplegia solution.

The Conducer has a prime volume of 7 mL and is typically available as a part of a premade cardioplegia set. The blood and water travel countercurrent within thin stainless steel bellows. The housing is a clear polycarbonate and comes equipped with barbed ¼-inch inlet and outlet connectors. Its low-prime volume and high heat exchange efficiency while recirculating make it suitable for any sized patient.

Our cardioplegia set requires a custom order from the manufacturer, and four steps are needed for assembly (Figure 2). First, the custom Conducer set is removed from the sterile peel pack. This set, from tip to tip, includes: priming spike, ¼-inch tubing for bubble sensor, Conducer, ¼- to 3/16-inch stepdown for raceway tubing, large-bore double stopcock, and a priming spike. The set then spikes into the outer ports on one of three different sized Baxter Viaflex Containers (Baxter Healthcare Corporation, Deerfield, IL): 250-mL, 500-mL, and 1000-mL bags. These bags are chosen based on the anticipated initial cardioplegia dose described in the delivery protocol section. The middle port of the Viaflex Container is an ⅛-inch line, referred to as a pigtail, with a fluid transfer adapter. The fluid transfer adapter is cut off with a sterile blade, and the male end of a large-bore three-way stopcock is inserted into the ⅛-inch pigtail. Next, the crystalloid cardioplegia solution line and shunt from the oxygenator are connected to the three-way stopcock. The final step is connecting a transducer and delivery line (handed off from surgical field) to the large-bore double stopcock. This CPS, with zero volume in the Viaflex bag and including the ¼-inch delivery line, primes with approximately 25 mL.

Once assembled, the circuit is primed with the crystalloid cardioplegia solution before initiating cardiopulmonary bypass (CPB). The ⅛-inch delivery line is kept empty and is primed up to the surgical field after the blood is added to the cardioplegia circuit and recirculated. To calculate the crystalloid priming amount, add 80% of the final delivery volume + 20 mL (to account for 80% of the 25-mL cardioplegia system prime volume) to the Viaflex bag (see delivery protocol). When the bag is filled with the desired amount, the roller head is turned on and the CPS easily primes (the same way a dry patient circuit is primed with an intact A-V loop). This setup differs from a typical recirculating system in that is does not recirculate up to the surgical field. With one of the large-bore stopcocks turned off to the cardioplegia delivery line, the system recirculates by pulling the solution down through the Conducer and pumping it back to the Viaflex bag. Conceptually, the Viaflex bag functions as a cardioplegia reservoir. To deliver cardioplegia, the delivery line stopcock is simply turned off to the bag and opened to the patient. Before initiating CPB, the crystalloid cardioplegia is kept cold by constantly...
recirculating the solution with a heater cooler water temperature of 2°C. Once on CPB, oxygenated blood is shunted to the Viaflex bag through the pigtail stopcock and recirculated to mix. To calculate the volume of blood, add 20% of the final delivery volume + 5 mL (to account for 20% of the 25-mL cardioplegia system prime volume) to achieve the one part blood to four parts crystalloid cardioplegia ratio. Next, the delivery line is primed to the surgical field and then slowly trickled as the surgeon connects the delivery line to the cardioplegia catheter. Figure 3 illustrates the cardioplegia circuit primed, mixed with blood, and ready to deliver del Nido cardioplegia.

Modified Depolarizing Solution
The Society of Thoracic Surgeons congenital heart surgery database defines a modified depolarizing cardioplegia as: a solution that combines a depolarizing agent (e.g., potassium) with additional membrane stabilizing additives (e.g., magnesium or lidocaine) to arrest the heart. The crystalloid component of del Nido cardioplegia is intended to have no calcium and uses Plasma-Lyte A (Baxter Healthcare Corporation) as the base solution. Our institutional pharmacy prepares the crystalloid com-ponent, and it is kept refrigerated for up to 48 hours (Table 1).

Cardioplegia Delivery Protocol
The final delivery composition of this cardioplegia, mixed 1:4 blood to crystalloid cardioplegia, is prepared after initiation of cardiopulmonary bypass (Table 2). Our hematocrit management protocol for all patients is to maintain a resultant hematocrit ≥30% (18), and this protocol allows us to achieve a resultant cardioplegia hematocrit of at least 6%. The patient’s oxygenated blood is shunted to the cardioplegia infusion bag and is mixed with the crystalloid cardioplegia solution until cold. Precise measurements of oxygenated blood can be achieved by drawing blood through a manifold syringe and injecting this volume into the Viaflex bag. It is also possible to passively shunt the oxygenated blood into the Viaflex bag and use the volume markers on the bag to measure large volumes of infused blood. On placement of the aortic crossclamp, a single, cold (4 to 6°C; measured at delivery bag), 20-mL/kg antegrade dose (1200 mL maximum dose) of cardioplegia is delivered through the aortic root. For neonates and infants, we deliver at an aortic root pressure between 30 and 40 mmHg. For children and small adults, we deliver at an aortic root pressure between 40 and 50 mmHg. Generally, the target aortic root pressure during

| Table 1. Crystalloid formula of modified depolarizing solution. |
|---------------------|---------|
| Plasma-Lyte A*      | 1000 mL |
| K-Cl                | 26 mEq  |
| Na-HCO₃ 8.4%        | 13 mEq  |
| Mannitol 25%        | 3.25 g  |
| Lidocaine 2%        | 130 mg  |
| Mg-SO₄ 50%          | 2 g     |

*Baxter Healthcare Corporation, Deerfield, IL.

<table>
<thead>
<tr>
<th>Table 2. Composition of mixed cardioplegia.*</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
</tr>
<tr>
<td>pCO₂, mmHg</td>
</tr>
<tr>
<td>pO₂, mmHg</td>
</tr>
<tr>
<td>HCO₃, mmol/L</td>
</tr>
<tr>
<td>BE, mmol/L</td>
</tr>
<tr>
<td>Na, mmol/L</td>
</tr>
<tr>
<td>K, mmol/L</td>
</tr>
<tr>
<td>Cl, mmol/L</td>
</tr>
<tr>
<td>iCa, mmol/L</td>
</tr>
<tr>
<td>Mg, mmol/L</td>
</tr>
<tr>
<td>Glucose, mmol/L</td>
</tr>
<tr>
<td>Hb, g/dL</td>
</tr>
</tbody>
</table>

*The values shown represent the final concentration when mixed one part blood to four parts crystalloid and were calculated by averaging 10 different samples.

BE, base excess; Na, sodium; K, potassium; Cl, chloride; Mg, magnesium, Hb, hemoglobin.
delivery will typically correlate with a normal diastolic pressure for a patient of similar age and size. After directly transducing the aortic root, we found that root pressures of 30–50 mmHg correlated with cardioplegia system pressures of 70–90 mmHg. Because we do not routinely transduce the aortic root, our surgeons are careful to palpate the aortic root during delivery to confirm root pressure. This cardioplegia solution and delivery protocol is used for our entire surgical population, regardless of age or procedure. A query of our 2010 data reveals that 90% (275 of 304) of patients requiring a crossclamp received a single dose of cardioplegia. As a general rule of thumb, multiple doses are not considered if no electrocardiographic (ECG) activity is noted, and it has not been our experience to encounter ECG activity after short ischemic periods. However, multiple doses are considered for patients with aortic insufficiency, and when the anticipated ischemic time will be greater than 120 minutes (i.e., double-switch procedure for congenitally corrected transposition of the great arteries). If a second dose is needed and the static delivery line has come to room temperature (our cardioplegia circuit does not recirculate to the surgical field), the surgeon disconnects the delivery line and has the perfusionist flush the line until cold solution reaches the surgical field. In the event of unsuccessful cardiac arrest resulting from an incompetent aortic valve, we directly cannulate the coronary arteries and deliver 10 mL/kg of cardioplegia to each coronary. Patients with hypertrophied ventricles or any other factor the surgeon feels might impede proper myocardial protection may receive a larger, 25 mL/kg, initial dose. Although we typically only prepare the 20-mL/kg dose needed for the arresting dose, we will prepare larger doses before clamping the aorta, 30–40 mL/kg, if we anticipate larger initial or subsequent doses. Although it is helpful to prepare more cardioplegia than is required, unexpected additional cardioplegia doses can be mixed quickly and even while delivering a dose. The typical arresting dose for patients larger than 50 kg is usually limited to a 1000- to 1200-mL maximum dose. The largest Viaflex bag is 1000 mL, so when we choose to deliver a 1200-mL dose, we must add the extra 200 mL while delivering cardioplegia. To do so, wait for at least 200 mL of cardioplegia to be delivered, and add 160 mL of the crystalloid del Nido solution and 40 mL of blood to the Viaflex bag through the stopcock connected to the pigtail. When we plan to give multiple doses for ischemic times greater than 120 minutes, the subsequent dose ranges from 10 to 20 mL/kg and is given approximately every 90–120 minutes.

DISCUSSION

Significant reductions in perfusion circuit prime will reduce hemodilution and surface area contact activation (19). These strategies help reduce the inflammatory response and minimize, or even eliminate, the need for allogenic blood transfusions (20). Our ultralow-prime cardioplegia system (25 mL) virtually eliminates the dilutional effect of cardioplegia, which can be seen in other systems. Blood only accounts for 20% of the cardioplegia volume, so a small degree of hemodilution will occur as the cardioplegia is suctioned back to the cardiomyotomy reservoir. The crystalloid component of the cardioplegia is quickly and easily removed on CPB during hemoconcentration. The single-dose cardioplegia protocol also simplifies and adds a degree of safety while on CPB because the perfusionist can focus on supporting the patient without distraction. Our low-prime cardioplegia circuit is versatile, easy to set up, and safe to use for any sized patient.

The key to an effective cardioplegia solution is developing a solution that quickly induces diastolic arrest, protects the myocardium, is reversible, and has no toxic effects on the heart or other vital organs (21). Our cardioplegia formula uses Plasma-Lyte A as the base solution because it contains no calcium, calcium management being critical during myocardial ischemia. The membrane-stabilizing additives, magnesium and lidocaine, both preserve electrical and mechanical inactivity by controlling calcium accumulation within the myocyte. Magnesium, a calcium antagonist, reduces intracellular calcium accumulation, inhibits L-type calcium channels, inhibits sodium calcium exchange, and competes with calcium binding to troponin (10,11). Lidocaine prevents sodium shifts by blocking fast-voltage sodium channels and in turn prevents calcium accumulation into the myocyte (9). To help minimize the calcium content of the blood cardioplegia, we do not normalize the calcium content of our perfusion circuit prime. We will occasionally add small amounts of calcium chloride in the prime to achieve a target resultant ionized calcium level of .8–1.0 mmol/L in the patient. This level will typically produce an ionized calcium of approximately .4 mmol/L in the blood cardioplegia.

Anecdotally, switching our cardioplegia regimen from Buckberg to del Nido cardioplegia did not demonstrate improvements in mortality, morbidity, or length of stay. The pre-eminent reasoning for its use is the ability to safely operate uninterrupted. Although this cardioplegia protocol suggests that multiple doses are not needed, there are instances when more than one dose is delivered. Considering the empirical manner in which this protocol has been developed, our institution follows generalized guidelines for dosing. The safe ischemic time using a single dose of del Nido cardioplegia is unclear.

The observed success of this single-dose protocol at our institution, and many others, has created a viral interest in its application. Matte et al. (16) recently described
the dosing protocol and origin of del Nido cardioplegia, but based on direct communication with several centers who have switched to del Nido cardioplegia, dosing protocols and ischemic time seem to be shaped around the surgeon comfort level and experience. Two scientific reports from Dalhousie University, Halifax, Nova Scotia, have evaluated this solution both in vitro and in vivo. Findings report that this cardioplegia strategy is associated with superior calcium management, reduced troponin T release, reduced spontaneous and inducible activity during ischemia, and helps to prevent hypercontracture during early reperfusion (22,23). Although this solution is considered to be a pediatric cardioplegia, its clinical effectiveness at protecting the immature vs. mature myocardium needs to be identified. Further investigations are also needed to determine the safe ischemic time, in all patient populations, using this single-dose protocol.

REFERENCES