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Research Article

A REVIEW OF CURRENT STATUS OF DELNIDO CARDIOPLEGIA AND IT'S VARIATIONS IN CARDIAC SURGERY

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ABSTRACT

Del Nido cardioplegia is a favored choice in pediatric cardiac surgery, known for its unique composition with lidocaine to counteract potassium-induced depolarization, minimizing interruptions and enhancing surgical efficiency. Recent research extends its application to adult cardiac surgery, affirming its safety, efficacy, and cost-effectiveness. Limited availability of the standard base solution, Plasmalyte-A, in some regions hinders its use. An alternative approach with lactated Ringer's solution has been explored. This review investigates Modified Del Nido cardioplegia, focusing on myocardial protection and early clinical outcomes. In cardiac surgeries, myocardial protection is critical, as inadequate protection can lead to adverse outcomes. Traditional approaches minimize ischemic damage when the aorta is clamped. Del Nido cardioplegia, with its unique composition, demonstrates effectiveness in pediatric and adult cases, including enhanced cardiac index, shorter hospital stays, and reduced troponin release. Modified Del Nido, using lactated Ringer's, offers promise where Plasmalyte-A is unavailable, maintaining cardiac index and myocardial protection. In conclusion, Del Nido and Modified Del Nido cardioplegia represent significant advances in myocardial protection during cardiac surgery. Their effectiveness and cost-efficiency make them appealing options for various cardiac procedures, with the potential for further improvements in patient outcomes. In this review study we aim to investigate the outcomes of this modified Del Nido cardioplegia, assessing its impact on myocardial protection and early clinical results.

INTRODUCTION

Cardiopulmonary bypass (CPB) uses a heart-lung machine and oxygenator to support heart and lung functions during surgery temporarily. CPB redirects blood flow, creating a bloodless, motionless field for safe access to the heart during surgery. Halting the heart's activity reduces metabolic demands, revolutionizing cardiac operations for enhanced safety and control. The heart's vulnerability during this critical period underscores the importance of effective myocardial protection. Since the beginning of cardiac surgery, people have been looking for the perfect cardioplegic solution. There are numerous commercial and homemade options available, del Nido cardioplegia, also known as cardioplegia, is one of these [1]. Plasmalyte-A is the usual base solution for del Nido cardioplegia; nevertheless, its wider use may be limited in certain areas due to its unavailability. To expand the benefits of del Nido cardioplegia to a wider range of patients, a different method uses lactated Ringer's solution as the base or there are changes made to the del Nido cardioplegia composition. The goal of our review study is to examine the effects of this modified del Nido cardioplegia, specifically focusing on how it affects early clinical outcomes and myocardial protection.

Origin of del Nido cardioplegia

Del Nido cardioplegia is a cardioplegic solution used in cardiac surgery to induce cardiac arrest during procedures like coronary artery bypass grafting (CABG) or valve surgery. It was developed by Dr. Pedro J. del Nido, a pediatric cardiac surgeon, in the early 1990s.

Dr. del Nido, who worked at the Boston Children's Hospital and Harvard Medical School, recognized the need for a cardioplegic solution that would provide a longer period of myocardial protection without the need for repeated doses. Traditional cardioplegic solutions require intermittent re-administration during the surgery to maintain cardiac arrest, but this can potentially lead to interruptions in the surgical procedure and increase the risk of complications.[2]

The Del Nido cardioplegia solution is unique because it offers single-dose, long-lasting myocardial protection. It contains a lower concentration of potassium and higher concentrations of

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magnesium and lidocaine compared to conventional cardioplegic solutions. The lower potassium cardioplegia concentration reduces the risk of myocardial edema, while the higher magnesium concentration enhances cellular protection.
The use of Del Nido cardioplegia has become more widespread, especially in pediatric and adult congenital cardiac surgeries. Its development represents an advancement in cardiac surgical techniques, aiming to improve patient outcomes and streamline surgical procedures.

Usage and Safety of del Nido

What is del Nido cardioplegia? it's dose, route, timing

Del Nido cardioplegia is a low calcium solution with extracellular crystalloid characteristics that make up the cardioplegia solution itself. Magnesium sulfate, mannitol, sodium bicarbonate, potassium, lidocaine, and Plasmalyte-A are all components of the crystalloid solution. As shown in Table 1.

Table 1: Supplies for Del Nido Cardioplegia Solution Preparation (Weight/Volume [w/v])

Supplies	Initial concentration	Volume (mL)
Plasma-Lyte A 7.4[a]	—	1000 (1 bag)
Sodium bicarbonate USP	8.4% w/v (1 mEq/mL)	13
Mannitol USP	20% w/v (0.2 g/mL)	16.3
Magnesium sulfate USP	50% w/v (0.5 g/mL, 4 mEq/mL)	4
Lidocaine USP	1% w/v (0.01 g/mL)	13
Potassium chloride USP	2 mEq/mL	13
	Final compounded volume	1059

[a]Baxter Healthcare Corporation, Deerfield, Illinois.

Base Fluids in Del Nido cardioplegia with a neutral pH, such as Plasmalyte-A solution (pH 7.4), which are isotonic and contain electrolyte ions that are similar to those found in human plasma, are considered balanced crystalloids. In Plasmalyte-A solution, which contains magnesium (an intracellular cation) that is crucial for cardiac ATP metabolism as well as acetate and gluconate for the synthesis of bicarbonate

- Mannitol can scavenge free radicals and reduce edema due to its hyperosmotic properties.
- Magnesium serves as a calcium channel blocker, enhancing myocardial recovery.
- Sodium bicarbonate scavenges hydrogen ions and helps maintain intracellular pH.
- Potassium chloride provides rapid depolarized arrest, though research suggests it may impair myocardial recovery due to intracellular sodium and calcium accumulation. The potassium concentration in the del Nido cardioplegia solution is 24 mEq/l.
- Lidocaine acts as a sodium channel blocker and a class Ib antiarrhythmic agent. It prolongs the myocyte refractory period, counteracting the negative effects of hyperkalemic depolarized arrest by polarizing the cell and reducing intracellular sodium and calcium influx.[1]

Del Nido cardioplegia is administered in a 1:4 ratio, using 4 parts of the cardioplegia solution and 1 part of oxygenated pump blood. Depending on the procedure being performed and the degree of aortic valve insufficiency, del Nido cardioplegia may be administered antegrade through an aortic root catheter, directly through the coronary ostia, or retrogradely via the coronary sinus. To check the distal anastomosis if coronary bypass grafting is necessary, 5–10 mL of del Nido cardioplegia is injected into the saphenous vein or radial artery graft. One dose of 20 mL/kg is calculated to obtain optimal myocardial protection for 90 minutes. The administration pressure is 100 to 120 mm Hg and the administration flow is 200 to 300 mL/min. The blood has its effect in supporting aerobic metabolism, providing buffering capabilities, and improving coronary perfusion during the delivery. The blood addition is the only source of calcium ions in the Del Nido cardioplegia solution. This ensures that only a trace of calcium is given. The delivery temperature is 4°C. Hypothermia reduces metabolism and oxygen consumption.

Table 2: Comparison of del Nido with other cardioplegia solutions [3]

Component	DNC	HTK	CBC
Na+ (mmol/l)	150	15	136-152
Cl- (mmol/l)	132	50	126-132
K+ (mmol/l)	24	9	13-24
Mg2+ (mmol/l)	6	4	2-13
Ca2+ (mmol/l)	0.4	0.02	0-1
Lidocaine (mg/l)	140	-	27
Mannitol (mmol/l)	14.5	30	0-12
Osmolality (mOsmol/kg)	294	300	304-320
Ketoglutarate (mmol/l)	-	1	-
Tryptophan (mmol/l)	-	2	-
Histidine (mmol/l)	-	198	-

CBC – cold blood cardioplegia, DNC – Del Nido cardioplegia, HTK – Bretschneider histidine-tryptophan-ketoglutarate solution

Comparison of del Nido cardioplegia with other cardioplegia solutions in pediatric patients

In pediatric cardiac centers, Del Nido cardioplegia stands out as the preferred choice for myocardial protection during cardiac surgery, a status supported by various clinical studies. O'Brien's pioneering study in 2009 highlighted its superiority in managing calcium levels and reducing troponin T levels compared to conventional cardioplegia methods [4]. Charette's study further emphasized its efficacy, demonstrating comparable outcomes in terms of surgical risk factors and intraoperative parameters while revealing significant differences in cardioplegia dosing and perioperative glucose levels [5].

Surgeons in North America predominantly favor Del Nido cardioplegia, with its single-shot administration being the most common strategy, irrespective of cross-clamp duration [6]. Comparative studies have consistently shown favourable outcomes for Del Nido over other solutions. A randomized trial comparing Del Nido with St Thomas cardioplegia showcased superior cardiac index, shorter ventilation, ICU, and hospital stays, along with reduced troponin release and myofibrillar disarray [7]. Similarly, in studies comparing Del Nido with modified St Thomas solution, Del Nido demonstrated comparable inflammatory response but higher lactate levels postoperatively, potentially attributed to its administration intervals [8].

Further comparisons with histidine-tryptophan-ketoglutarate (HTK) cardioplegia underscore Del Nido's advantages, including superior cardiac index preservation, shorter ICU and hospital stays, reduced inotropic support, and lower troponin release. Electron microscopy corroborated these findings, highlighting Del Nido's better preservation of myocardial

architecture and glycogen reserves, suggesting its suitability for pediatric cardiac surgery. Despite variations in inflammatory responses and lactate levels, Del Nido consistently emerges as a reliable option for myocardial protection in pediatric patients. Talwar's comparative analysis provides compelling evidence of Del Nido's superiority over HTK, reinforcing its position as a leading cardioplegia solution in pediatric cardiac surgery [9].

Comparison of del Nido cardioplegia with other cardioplegia solutions in adult patients

When it comes to adult patients undergoing cardiac procedures, studies comparing Del Nido cardioplegia with other solutions shed light on their efficacy and outcomes. In one study comparing Del Nido with St Thomas No. 2 solutions, the Del Nido group showed shorter aortic cross-clamp and bypass times, alongside better preservation of postoperative left ventricular function [10]. Another examination of adult patients undergoing congenital surgery using Del Nido cardioplegia revealed no ventricular electrical activity during aortic cross-clamping and minimal changes in ejection fraction postoperatively [11].

Comparisons between Del Nido and Buckberg cardioplegia solutions in adult patients undergoing aortic or mitral surgery showed similar troponin levels and postoperative ejection fractions, but the Del Nido group had shorter procedural times and lower glucose levels [12]. Retrospective studies also highlighted the advantages of Del Nido over Buckberg cardioplegia, including fewer doses required and reduced need for defibrillation, with no significant differences in postoperative events [13].

In the context of specific procedures like aortic valve surgery, Del Nido cardioplegia demonstrated shorter bypass and cross-clamp times compared to traditional whole-blood cardioplegia, with comparable postoperative outcomes [14]. Additionally, it showed promise in minimally invasive aortic valve surgery, reducing procedural times and maintaining stable cardiac parameters [15].

Studies assessing Del Nido cardioplegia in redo surgery scenarios found it to be as effective as blood cardioplegia in maintaining myocardial protection and patient outcomes [16]. Del Nido cardioplegia also proved its efficacy across a range of ventricular masses and ischemic durations, with fewer incidences of ventricular fibrillation and comparable troponin levels to blood cardioplegia.

While some studies noted higher CK-MB levels with Del Nido at certain time points, it also demonstrated advantages such as reduced postoperative atrial fibrillation incidence compared to whole blood cardioplegia. Overall, these findings support the safety and effectiveness of Del Nido cardioplegia in adult cardiac surgery, offering comparable or even superior outcomes compared to traditional solutions [17,18].

A study comparing del Nido (DN) and histidine-tryptophan-ketoglutarate (HTK) cardioplegia solutions in complex valve surgeries with prolonged ischemic durations demonstrates that DN is a viable alternative to HTK. The findings suggest that DN provides comparable myocardial protection, as evidenced by satisfactory cardiac arrest effects and similar levels of cardiac biomarkers postoperatively. Moreover, DN offers several advantages over HTK, including a higher rate of return to spontaneous rhythm, reduced incidence of severe arrhythmias, improved postoperative hemodynamics, fewer transfusions, and shorter ICU stays. These benefits make DN an attractive option for cardiac surgeons performing complex valve surgeries, particularly in cases with expected prolonged ischemia [19].

Modification to the fundamental approach in Del Nido cardioplegia

Reviewing Base Fluids in Del Nido Cardioplegia

In Del Nido cardioplegia, the choice of base fluid with a neutral pH is essential. Plasma-Lyte solutions with a pH of 7.4, resembling the electrolyte composition of human plasma and maintaining isotonicity, are considered balanced crystalloids. However, the widespread availability and cost-effectiveness of Plasma-Lyte A in developing countries remain limited. As an alternative in such instances, Ringer's Lactate can be utilized.
Ringer's Lactate, with a pH of 6.6, incorporates lactate as a source of bicarbonate. Nevertheless, caution is warranted when administering significant volumes of lactate-containing fluids to diabetic patients due to the potential in vivo conversion of lactate to glucose via the gluconeogenic pathway. This article provides a comprehensive examination of the various base fluid options for Del Nido cardioplegia, considering their pH, electrolyte composition, and practical considerations.

Table 3 Discrepancy in the composition of two solutions.

Composition (mEq/L)	Ringer Lactate	Plasmalyte-A
Sodium	130	140
Potassium	4	5
Calcium	3	0
Magnesium	0	3
Chloride	109	98
Lactate	28	0
Gluconate	0	23
Acetate	0	27
Osmolarity (mOsm/L)	275	294
PH	6.75	7.40

A randomized controlled trial conducted at AIIMS Delhi explored the substitution of Plasmalyte-A solution, often inaccessible and expensive in many developing nations, with a cost-effective Ringer Plain solution in pediatric Del Nido cardioplegia. This study found that Modified Del Nido (Ringer Plain-based) cardioplegia performed comparably to Standard Del Nido (Plasmalyte-A-based) in preserving cardiac function and myocardial protection, making it a viable alternative where the latter is scarce or unaffordable.[20]

Pathan et al. conducted a study at the Department of Cardiac Surgery, PAQSJIMS, to evaluate the safety and effectiveness of modified del Nido cardioplegia (using Ringer lactate) in pediatric open-heart surgeries for congenital heart defects. Their findings indicated that this solution restored spontaneous sinus rhythm, required lower inotropic support, and resulted in fewer surgical interruptions compared to conventional solutions [21]. Another study comparing modified del Nido with cold blood cardioplegia found no significant differences in intubation duration, ICU stay, or use of vasoactive medications post-operation, confirming the modified solution's efficacy and safety [22].

Furthermore, Kantathut et al.'s 2019 study extended this inquiry to adult cardiac surgery. Their research compared Modified Del Nido cardioplegia (utilizing Ringer lactate) to blood cardioplegia. The results indicated that Modified Del Nido cardioplegia offered superior myocardial protection, manifesting as reduced troponin-T release, lower incidence of ventricular fibrillation post-aortic cross-clamp removal, shorter

inotropic support duration, and reduced hospital and ICU stays. This suggests its effectiveness in adult cardiac surgery, showcasing its potential as an improved cardioplegia option for both pediatric and adult patients, especially where conventional solutions are limited or costly.[23]

N. Kantathut et al.'s prospective randomized controlled trial advocates for using LRS (Lactated Ringer solution) as a viable substitute for del Nido cardioplegia in adult cardiac surgeries with low-risk elective patients, particularly when the expected cross-clamp time is under 120 minutes. The study reveals LRS's comparable efficacy in myocardial preservation, intraoperative performance, and postoperative outcomes, indicating its potential to widen access to the del Nido technique without compromising safety or effectiveness, particularly in regions where PlasmaLyte A availability is limited. The study primarily focuses on low-risk patients undergoing elective surgeries for acquired heart disease, highlighting the need for future investigations to encompass urgent cases with reduced left ventricular function or specific diagnoses like CABG or aortic valve procedures. Such expansion could offer valuable insights into the suitability and efficacy of LRS-based del Nido cardioplegia in more challenging patient demographics [24].

Kantathut et al. conducted a study comparing del Nido cardioplegia (MDN) with histidine-tryptophan-ketoglutarate (HTK) solution in adult valvular surgery patients. Results showed similar patient characteristics and postoperative troponin T levels. MDN group exhibited advantages: reduced ventricular fibrillation incidence (13.51% vs. 55.88%; P<0.001), lower cardioplegia volume (1,000 mL [1,000-1,250] vs. 1,800 mL [1,500-2,000]; P<0.001), shorter hospital stays (6 days [5-8] vs. 7 days [6-10]; P=0.03), and fewer red cell transfusions (34.29% vs. 61.11%; P=0.024). Other parameters showed no significant differences. The study suggests lactated Ringer 's-based MDN cardioplegia as a safe option with comparable outcomes to HTK in valvular surgery [25].

Karaarslan et al. conducted a retrospective clinical trial comparing modified del Nido cardioplegia with Standard del Nido cardioplegia in CABG patients. Studying 70 patients, they found no notable demographic differences. Cross-clamp and bypass times were similar, and intensive care and hospital stays showed no significant variations. Key outcomes such as CK-MB, troponin T, EF change, mortality, postoperative ARF, low cardiac output syndrome, and preoperative inotropic support needs didn't differ significantly. However, the modified del Nido group exhibited no decrease in hemoglobin on the first postoperative day, indicating potential benefits in myocardial protection and reduced anemia [26].

CONCLUSION

The available studies provide optimistic findings - Del Nido cardioplegia has surfaced as a remarkably efficient and adaptable method for protecting the heart during cardiac procedures, demonstrating its effectiveness in both pediatric and adult patients. Comparative studies consistently show Del Nido cardioplegia superiority with shorter clamping times, improved ejection fraction, and lower troponin release in both pediatric and adult cases. The introduction of Modified Del Nido, a Ringer lactate-based variation, provides a promising solution for regions where Plasmalyte-A is inaccessible or cost-prohibitive, as it demonstrates non-inferiority in preserving cardiac index and myocardial protection. In summary, Del Nido cardioplegia represents a significant advancement in the field of myocardial protection during cardiac surgery. Its proven effectiveness in mitigating ischemic damage, expediting recoveries, and potentially reducing costs makes it an appealing choice for a wide range of cardiac surgical procedures. The ongoing evolution of this cardioplegia technique through further research and continuous refinements holds the promise of enhancing patient outcomes and elevating the overall quality of cardiac care.

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