

First Argentine Experience with Del Nido Cardioplegia in Adults. Comparison with Buckberg Cardioplegia

Primera experiencia argentina de cardioplegia de Del Nido en adultos. Trabajo comparativo con cardioplegia de Buckberg

FERNANDO M. BARBOSA¹, CLAUDIO MOYANO², DIEGO A. COLICHELLI¹, ANDRÉS E. OTERO¹, FERNANDA CASTRO¹, DAMIÁN MORELLI¹, ALEJANDRA NAZRA¹, LEANDRO GOLDTRAJ¹, NICOLÁS MENICHINNI², ANA DURET¹

ABSTRACT

Background: Traditionally, Buckberg cardioplegic solution is used for cardiovascular interventions in adult patients requiring cardiopulmonary bypass, whereas Del Nido solution is more commonly used in pediatric cardiac surgery. This is the first Argentine report of Del Nido cardioplegia in adult patients.

Methods: From November 2016 to March 2018, 267 cardiac surgeries were performed by the same surgical team in two cardiovascular surgery centers. Among the total number of patients undergoing these surgeries, 50 received Del Nido cardioplegia (DN group) and were compared with a homogeneous group of 50 patients receiving Buckberg cardioplegia (BK group).

Results: Average total operative, cardiopulmonary bypass and aortic cross-clamp times (128.80 min, 70.83 min and 55 min, respectively, in the DN group, and 167.78 min, 80.7 min and 64.71min, in the BK group) were statistically significant between groups ($p=0.001$, $p=0.0032$ and $p=0.0004$, respectively). Comorbidities and type of valve surgery were similar in both groups

Conclusions: Del Nido cardioplegia can be used in adult patients with excellent results, allowing to significantly shorten operative, aortic cross-clamp and cardiopulmonary bypass times, with all the benefits these lower times entail.

Keywords: Adult Cardiac Surgery – Cardioplegia - Myocardial Protection

RESUMEN

Introducción: Tradicionalmente, en las intervenciones cardiovasculares de pacientes adultos que requieren de circulación extracorpórea, se utiliza la solución cardiopléctica de Buckberg, mientras que en cirugía cardíaca infantil se emplea con mayor frecuencia la solución de Del Nido. Este es el primer reporte argentino de la experiencia con esta última cardioplegia en pacientes adultos.

Material y métodos: Desde noviembre de 2016 hasta marzo de 2018, el mismo equipo quirúrgico realizó 267 cirugías cardíacas en dos centros de cirugía cardiovascular; de ese total, a 50 pacientes se les realizó la cardioplegia de Del Nido (grupo DN) y se los comparó con un grupo homogéneo de 50 pacientes que recibieron cardioplegia de Buckberg (grupo BK).

Resultados: En promedio, el tiempo total de cirugía, de circulación extracorpórea y de clampeo aórtico fueron, respectivamente, 126,70 min, 70,63 min y 54 min en el grupo DN y 165,78 min, 80,5 min y 64,21 min en el grupo BK; estas diferencias fueron estadísticamente significativas ($p= 0,001$, $p= 0,0032$ y $p= 0,0004$, respectivamente). Las comorbilidades y el tipo de cirugía valvular realizada fueron similares en ambos grupos.

Conclusión: La cardioplegia de Del Nido puede utilizarse en pacientes adultos con excelentes resultados; esta permite disminuir significativamente los tiempos de cirugía, clampeo aórtico y circulación extracorpórea, con todos los beneficios que esto conlleva.

Palabras Clave: Cirugía cardíaca en adultos - Cardioplegia - Protección miocárdica

Abbreviations

AR	Aortic regurgitation	DN	Del Nido cardioplegia
AS	Aortic stenosis	MR	Mitral regurgitation
AVR	Aortic valve replacement	MS	Mitral stenosis
BK	Buckberg cardioplegia	MVR	Mitral valve replacement

REV ARGENT CARDIOL 2019;87:363-366. <http://dx.doi.org/10.7775/rac.v87.i5.12932>

Received: 02/21/2019 – Accepted: 08/28/2019

Address for reprints: Fernando Martin Barbosa, Pasteur Clinic. Cardiovascular Surgery Service. Neuquén E-mail: fernandomartinbarbosa@gmail.com

¹ Clínica Pasteur, Neuquén

² Sanatorio Juan XXIII, Rio Negro

INTRODUCTION

Traditionally, Buckberg cardioplegic solution is used for cardiovascular interventions in adult patients requiring cardiopulmonary bypass (CPB), and Del Nido solution is more commonly used in pediatric cardiac surgery since 1990, when the team led Dr. Pedro Del Nido started to use this cardioplegic solution in pediatric cardiac surgery at Boston Children's Hospital, Massachusetts. Since then, Del Nido cardioplegia has been more frequently used, even in adult patients.

The most important difference between both procedures is that with Del Nido solution, the need for reinfusion of cardioplegic solution is every 90 minutes, whereas with Buckberg cardioplegia a dose is required every 15 minutes to ensure adequate myocardial protection. The possibility of completing the operation without reinfusions of cardioplegic solution significantly shortens surgical and aortic cross-clamp times, as well as CPB time, thus reducing the times of intervention, anesthesia and use of the operating room. This situation modifies the morbidity and mortality of any type of procedure, especially in cardiovascular surgery. There are few worldwide reports of the use of Del Nido cardioplegia in adults and none in our country.

METHODS

From November 2016 to March 2018, 267 cardiac surgeries were performed by the same surgical team in two cardiovascular centers, Clínica Pasteur of Neuquén and Sanatorio Juan XXIII of Rio Negro; Buckberg cardioplegia was routinely used in all cardiovascular surgeries at one of the institutions and Del Nido cardioplegia at the other institution. Among a total of 128 surgeries performed with CPB, simple aortic or mitral valve replacements were selected to perform a cohort retrospective study. Combined procedures (valve replacement associated with coronary artery bypass grafting), coronary revascularization (our team uses the technique without CPB) double valve replacement, Bentall de Bono surgery, aortic bypass associated with valve replacement, as well as adult congenital heart disease procedures were excluded from the study.

Thus, a sample of 50 patients receiving Del Nido cardioplegia (DN group) were retrospectively compared with the same number of cases receiving modified Buckberg cardioplegia or miniplegia (BK group); both groups were homogeneous in the statistical analysis.

Del Nido cardioplegia

After aortic cross-clamping, Del Nido cardioplegia was infused through the aortic root, in a 1:4 ratio (1 part of blood and 4 of solution), at a temperature of 4°C. During surgery, if the cross-clamp time was longer than 90 minutes a reinfusion of the cardioplegic solution was performed. In patients undergoing Buckberg cardioplegia, antegrade or retrograde infusion was performed after aortic cross-clamp, repeating this procedure every 15 minutes.

Del Nido cardioplegia uses a Plasma-Lyte A-based solution, whose composition is very similar to the extracellular fluid, with the addition of 16 ml of 20% mannitol, 4 ml of 50% magnesium sulfate, 13 ml of 8.4% sodium bicarbonate, 13 ml of potassium chloride (2 mEq/mL) and 13 ml of 1%

lidocaine to complete the cardioplegia solution. The total volume with the additives incorporated to the Plasma-Lyte solution is 1200 ml. In our surgical centers the solution is prepared before the cardiac surgery by the perfusion team, in the operating room, with the required sterile measures.

Ethical considerations

The study was performed following the recommendations for research in human subjects and legal regulations in force. No data allowing patients' identification was reported. As it was a retrospective study, no informed consent was requested. Investigators responsible for the study implemented the necessary measures to protect the privacy and confidentiality of the data, according to current legal regulations (Personal Data Protection Law 25,326).

RESULTS

Table 1 details the prevalence of comorbidities in both groups, with their corresponding statistical analysis indicating non-significant differences between groups; thus, they were considered homogeneous groups. Average preoperative left ventricular function was 56% in the DN group and 57% in the BK group. Average age was similar in both groups, 60.8 years in the DN group and 61.2 in the BK group, with a gender distribution of 54% women in the DN group and 52% in the BK group. The prevalence of resolved valve diseases was similar in both groups, without statistical differences: 78% of aortic valve replacements (AVR) and 22% of mitral valve replacements (MVR). Among the valve diseases in the DN group, 69% were aortic stenosis (AS), 12% aortic regurgitation (AR), 7% mitral stenosis (MS) and 12% mitral regurgitation (MR); while in the BK group 67% were AS, 9% AR, 10% MS and 4% MR, with non-significant differences between groups. In this way we tried to compare the same type of patients, with the same procedures, but with different cardioplegia.

Average total operative, CPB and aortic cross-clamp times were 126.70 min, 70.63 min and 54 min, respectively, for the DN group and 165.78 min, 80.5 min and 64.21 min, respectively, for the BK group, with statistically significant differences for total operative time ($p=0.001$), CPB ($p=0.0032$) and aortic cross-clamp ($p=0.0004$) times, as detailed in Table 2 and Figures 1, 2 and 3.

We estimate that in our centers Buckberg cardioplegia is performed every 15 minutes. If we assume that these surgeries had in average 64.21 min of aortic cross-clamp, 4.3 doses of cardioplegic solutions were required per procedure, which might justify the difference in operative times. The difference in total operative time could be attributed to lower electrical cardioversion requirement at CPB weaning in patients of the DN group. This could be related with greater left ventricular dysfunction, though it was not statistically significant and was not evaluated in the development of the present study (a larger sample size would be necessary to evaluate this aspect). Average total hospital stay, from surgery to hospital discharge,

Table 1. Comorbidities between both groups

	DN	BK	p value
Age (years)	60.8	61.2	0.7
Men (%)	46	48	0.8
Women (%)	54	52	0.8
Hypertension (%)	82	88	0.3
Obesity (%)	59	62	0.3
Smoking (%)	39	36	0.1
COPD (%)	6	1	0.07
Diabetes (%)	19	16	0.3
Aortic Regurgitation (%)	12	9	0.8
Aortic Stenosis (%)	69	67	0.8
Mitral Regurgitation (%)	12	14	0.8
Mitral Stenosis (%)	7	10	0.8

DN: Del Nido cardioplegia. BK: Buckberg cardioplegia. COPD: Chronic obstructive pulmonary disease.

Table 2. Total operative, cardiopulmonary bypass and aortic cross-clamp times in both groups

	DN	BK	p value
Operative time (min)	126.7	165.7	0.001
Cardiopulmonary bypass time (min)	70.6	80.5	0.0032
Aortic cross-clamp time (min)	54.8	64.2	0.0004

DN: Del Nido cardioplegia. BK: Buckberg cardioplegia.

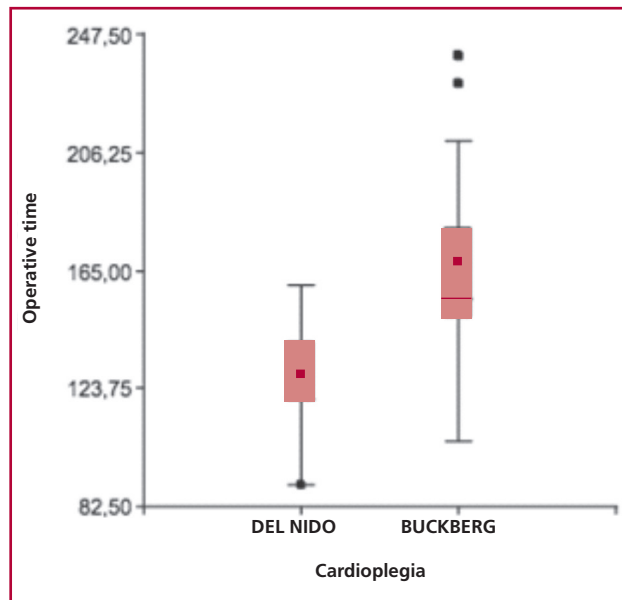


Fig. 1. Relationship between total operative time and type of cardioplegia

was 8.8 days in the DN group and 8.2 days in the BK group. Mortality in both groups was 2%, with only one dead patient per group, indicating no statistically significant differences.

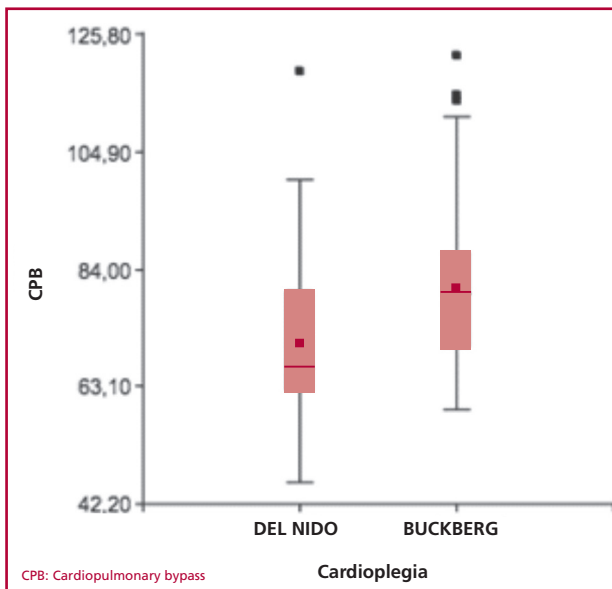


Fig. 2. Relationship between cardiopulmonary bypass time and type of cardioplegia

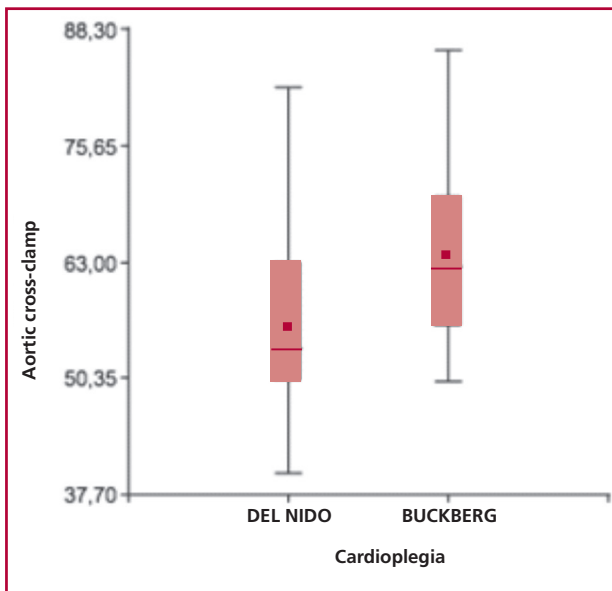


Fig. 3. Relationship between cross-clamp time and type of cardioplegia

DISCUSSION

Although both cardioplegic solutions achieve diastolic cardiac arrest due to their composition with potassium chloride, Del Nido cardioplegia, contains magnesium sulphate, which blocks calcium channels, not only prolonging and protecting cardiac ischemic time but also decreasing intracellular calcium concentration, thus resulting in less cardiomyocyte injury from ischemia-reperfusion. (2) Another advantage of Del Nido cardioplegia is having the antiarrhythmic agent lidocaine among its components, which blocks sodium channels, increasing the refractory period of cardiac myocytes.

Chalmers et al demonstrated that the prolongation of surgical times (comprising not only the duration of surgery but also the length of time the patient spends in the operating room) increases morbidity and mortality risks. (3) In our work, the total operative, aortic cross-clamp and CPB times were markedly reduced, i.e. using Del Nido cardioplegia significantly shortened these times, reducing morbidity and mortality and also the times the patient stays in the operating room.

Del Nido cardioplegia is infused at low temperatures (4° C), generating a cardiac temperature of approximately 15° C measured at the level of the inter-ventricular septum, as demonstrated by Kim et al. of the Cleveland Clinic (4). The heart decreases oxygen consumption by 50%, per 10° C of myocardial temperature drop, (5, 6) a situation that further favors the use of Del Nido cardioplegia.

Use of Del Nido cardioplegia not only involves shorter surgical times. Mick et al. (5), conducted a study at the Cleveland Clinic analyzing among other results, the economic aspect. Transferring this consideration to our national reality, we concluded that the cost of Del Nido cardioplegic solution is \$ 1,653 pesos (U\$S 29) per surgery, while that with Buckberg solution is \$ 14,535 pesos (U\$S 255). The cost difference between both cardioplegic solutions is \$12,882 per surgery in favor of Del Nido cardioplegia. If we calculate an average of 20 interventions with CPB per month, this difference would be \$257,640 pesos, generating an annual difference of \$3,091,680 pesos, which would increase even more taking into account the use of the operating room and surgical costs.

Although the behavior of glycemia during surgery was not evaluated in this study, numerous scientific works demonstrate that intraoperative and postoperative glycemic control is better with Del Nido cardioplegia, as this solution has lower glucose concentration, requiring less insulin for its correction. (2, 7, 8)

The resistance to use Del Nido cardioplegia in coronary heart disease patients with myocardial revascularization surgery using CPB, has been based until now on two main reasons: the first is myocardial hypertrophy found in the hearts of adult patients, which may not be well protected during very prolonged ischemia, and the second is coronary heart disease affecting in a greater or lesser extent all adult hearts, also altering myocardial protection in times of prolonged ischemia. Both arguments are slowly being counteracted, since there are reports such as that of Tomasz Timek, (8) among others, (9, 10) in which Del Nido cardioplegia is performed in coronary artery bypass surgery.

CONCLUSION

Del Nido cardioplegia is a solution with proven efficacy in pediatric cardiac surgery that is being more frequently used in adult patients. In our experience, and as evidenced by different scientific works, it significantly shortens operative, aortic cross-clamp and CPB times, generating not only advantages for the patient in terms of morbidity and mortality, but also economic benefits, allowing to work without reinfusion for longer periods (> 90 minutes). Although few works document the use of this cardioplegia, they provide very favorable results encouraging its use, and opening a new scenario for combined surgeries, as well as myocardial revascularization surgeries with CPB. Undoubtedly, the development of randomized, prospective studies and with a larger number of patients will generate greater use of Del Nido cardioplegia in adult cardiac surgery with CPB.

Conflicts of interest

None declared.

(See authors' conflicts of interest forms on the website/ Supplementary material).

REFERENCES

1. Matte GS, del Nido PJ. History and use of del Nido cardioplegia solution at Boston Children's Hospital. *J Extra Corpor Technol* 2012;44:98-103. <http://doi.org/f53vh9>
2. Niv Ad. del Nido cardioplegia: Ready for prime time in adult cardiac surgery? *J Thorac Cardiovasc Surg* 2015;149:637-8. <http://doi.org/c97q>
3. Mick SL, Robich MP, Houghtaling PL, Gillinov AM, Soltesz EG, Johnston DR, et al. del Nido versus Buckberg cardioplegia in adult isolated valve surgery. *J Thorac Cardiovasc Surg* 2015;149:626-36. <http://doi.org/f64nqc>
4. Timek T, Willekes C, Hulme O, Himelhoch B, Nadeau D, Borgman A, et al. Propensity Matched Analysis of del Nido Cardioplegia in Adult Coronary Artery Bypass Grafting: Initial Experience With 100 Consecutive Patients. *Ann Thorac Surg* 2016;101:2237-4. <http://doi.org/f8pzzr9>
5. Chalmers J, Pullan M, Mediratta N, Poullis M. A need for speed? Bypass time and outcomes after isolated aortic valve replacement surgery. *Interact Cardiovasc Thorac Surg* 2014;19:21-26. <http://doi.org/f6cmqc>
6. Kim K, Ball C, Grady P, Mick S. Use of del Nido Cardioplegia for Adult Cardiac Surgery at the Cleveland Clinic: Perfusion Implications. *J Extra Corpor Technol* 2014;46:317-23.
7. Gravlee GP, Davis RF, Stammers AH, Ungerleider RM, eds. *Cardio-pulmonary Bypass: Principles and Practice*, 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2008. p.172-9
8. Hensley FA, Martin DE, Gravlee GP. *A Practical Approach to Cardiac Anesthesia*, 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2013. p.649-50.
9. Govindapillai A, Hancock Friesen C, O'Blens SB. Protecting the aged heart during cardiac surgery: Use of del Nido cardioplegia provides superior functional recovery in isolated hearts. *Perfusion* 2016;31:135-42. <http://doi.org/f8b5q4>
10. O'Blens SB, Friesen CH, Ali A, Howlett S. Protecting the aged heart during cardiac surgery: the potential benefits of del Nido cardioplegia. *J Thorac Cardiovasc Surg* 2011;141:762-70. <http://doi.org/dns5cc>