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Comparison of del Nido Cardioplegia and blood Cardioplegia in isolated CABG patients

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ABSTRACT

Introduction: Effective myocardial protection ensures safe operation during cardiac surgery. In this study, blood cardioplegia, which is the most preferred myocardial protection method in isolated coronary artery bypass grafting (CABG) operations, was compared with del Nido cardioplegia. *Material and Method*: Patients who underwent isolated CABG operation in our department between 04.01.2018- 06.30.2019 were analyzed retrospectively. The patients using blood cardioplegia constituted Group 1; whereas the patients using del Nido cardioplegia were in Group 2. *Result*: Isolated CABG was performed in 57 patients during the study period and all of the patients were over 35 (36-81 years). There were 32 patients (56%) in Group 1; and 25 patients (44%) in group 2. The duration of aortic cross-clamp and cardiopulmonary bypass were significantly higher in Group 1 (p= 0.009, p= 0.012). *Discussion*: Although the use of del Nido cardioplegia has shortened the duration of aortic cross-clamp and cardiopulmonary bypass, this positive effect was not reflected in postoperative variables. More comprehensive studies comparing myocardial protection methods are needed to fully evaluate this effect.

Keywords: coronary artery bypass, del Nido Cardioplegia, blood cardioplegia, myocardial protection

1. INTRODUCTION

In order to perform the open-heart surgery safely, effective myocardial protection is required during the intraoperative process. Optimal myocardial protection plays a key role in successful cardiac surgery by preserving the energy reserve and function of the heart (Eivind et al., 2010). Since the 1950's where the cardiopulmonary bypass device was invented, researches on myocardial protection method that will make a contribution to the functions of the heart continue today. Although many cardioplegia systems have been reported in this period, blood cardioplegia is the most preferred method today, yet there is no clear consensus in terms of the superiority of the application (Michel et al., 2012). Blood cardioplegia is frequently used as it is an easy to obtain and effective method. In addition to its advantages such as protecting the energy reserve of the heart and acting as a buffer; there are also

some disadvantages such as high volume solution administration, the need for multiple administration and difficulties in glucose regulation (Tomasz et al., 2016).

Del Nido cardioplegia solutions, which are reported to provide long-term reliable myocardial protection with a single administration, are widely used in pediatric cardiac surgery, minimally invasive surgery and aortic dissections (Arun et al., 2013). There are also studies indicating that it provides effective and reliable myocardial protection in coronary artery bypass surgery (Tomasz et al., 2016; Gustavo et al., 2016). In our study, we researched the effects to the operative process and postoperative period by comparing the blood cardioplegia which is the classical method of myocardial protection and del Nido cardioplegia which the frequency of use is increasing day by day.

2. MATERIAL AND METHOD

In this study, patients who underwent isolated CABG operation between April 01, 2018 and June 30, 2019 were evaluated retrospectively. Written informed consent was obtained from all patients prior to operation. Demographic data, preoperative and postoperative data of patients were obtained from the patient files. Patients who underwent isolated CABG along with cardiopulmonary bypass were included in the study. Patients who were operated on the beating heart, who underwent open-heart surgery for another reason or who had another concomitant surgery were not included in the study. Patients were divided into two groups according to the cardioplegia method applied during operation. The patients who were administered blood cardioplegia constituted Group 1; whereas the patients who were administered del Nido cardioplegia constituted Group 2. Del Nido cardioplegia solution (Boston Children's Hospital): was prepared by adding mannitol 20% 16.3 ml, lidocaine 1% 13 ml, magnesium sulfate 50% 4 ml, potassium chloride (2 mEq / ml) 13 ml and sodium bicarbonate 8.4% 13 ml, into 1 liter of plasma-lyte (140 mEq / L Sodium, 98 mEq / L Chloride, 27 mEq / L Acetate, 23 mEq / L Gluconate, 5 mEq / L Potassium, 3 mEq / L Magnesium). del Nido cardioplegia was given with 20% oxygenated blood.

Following standard median sternotomy, cardiopulmonary bypass was performed by arterial cannulation from the ascending aorta and by venous cannulation from the right atrium. Retrograde cannulation was performed by a cannula inserted to the coronary sinus through the purse-string suture placed in the right atrium. The location of the retrograde cannula was confirmed by palpation in each case. The cardioplegic solution was given by using the antegrade and retrograde route as myocardial protection method in both groups. Patients were cooled to an average of 30-32^{0}C. Cardioplegia was repeated at 20-minute intervals in Group 1. Half dose cardioplegia was repeated over 70 minute or electrical activity in the heart was started at in Group 2. Proximal anastomoses were performed using cross or side clamps according to the surgeon's preference.

Statistical analysis was performed with the IBM Statistical Package for the Social Sciences 24.0 (SPSS 24.0, SPSS Inc., Chicago, IL). N (%) was used for categorical variables and mean ± SD for continuous variables. For comparing Group 1 and Group 2, t-test and Wilcoxon tests were applied. In the comparisons, $p < 0.05$ was considered statistically significant.

3. RESULTS

Isolated CABG operation was performed in 57 patients in our department during the study period. Thirty-two of the patients (56%) were in Group 1; 25 (44%) were in Group 2. There was no statistically significant difference between the two groups in terms of preoperative data (Table 1).

Table 1 Evaluation of patient characteristics by groups before the operation.

Variable	Group 1 (n=32)	Group 2 (n=25)	p
Age (years)	60.3 ± 10.9	61.5 ± 11.2	1.000
Gender (female/male)	9 / 23	7 / 18	0.852
Euroscore	4.39 ± 1.57	4.76 ± 1.37	0.251
HT (n)	23 (71.8%)	18 (72%)	1.000
DM (n)	13 (40.6%)	11 (44%)	0.116
EF (%)	51.3 ± 9.2	50.4 ± 8.7	0.313

HT: Hypertension, DM: Diabetes Mellitus, EF: Ejection Fraction

There was no statistically significant difference between the groups in terms of hypothermia temperature, the number of grafts and inotropic requirement following cardiopulmonary bypassfor the operative data. However, the duration of aortic cross-clamping and cardiopulmonary bypass were significantly higher in Group 1 (Table 2).

Table 2 Evaluation of parameters by groups during operation

Variable	Group 1 (n=32)	Group 2 (n=25)	p
CPB (min)	79.54 ± 37.61	71.36 ± 31.54	0.012
ACC (min)	51.06 ± 28.47	46.55 ± 21.59	0.009
Hypothermia (^{0}C)	31.2 ± 1.3	30.5 ± 1.7	0.131
Grafts (n)	3.1 ± 1.6	3.3 ± 1.4	0.605
Inotropic support (n)	19 (%59.4)	15 (%60)	0.903

ACC: Aortic cross clamping, CPB: Cardiopulmonary bypass

When the postoperative data were examined, there was no statistically significant difference between the two groups and the patients were discharged on the 7th postoperative day (Table 3). There was no reoperation due to bleeding. Postoperative atrial fibrillation developed in 7 patients (21.9%) in Group 1 and 6 patients (24%) in Group 2 following the operation. Sinus rhythm was recovered in 12 patients with medical treatment and 1 patient with electrical cardioversion along with medical treatment. There was no mortality.

Table 3 Evaluation of parameters by groups after operation.

Variable	Group 1 (n=32)	Group 2 (n=25)	p
Intubation time (hours)	7.1 ± 2.5	6.7 ± 2.8	0.57
Intensive care time (days)	2.5 ± 1.2	2.3 ± 1.5	0.303
Drainage (ml)	540 ± 150	580 ± 190	0.150
Troponin level 1st day	56.23 ± 21.28	53.04 ± 24.96	0.290
Atrial Fibrillation (n)	7 (21.9%)	6 (24%)	0.107
Hospital stay (days)	7.1 ± 1.6	6.8 ± 1.9	0.605

4. DISCUSSION

Appropriate myocardial protection methods are crucial in the safe application of cardiac operations. Effective myocardial protection prevents ischemic damage while protecting the energy reserves of the heart. For this purpose, various cardioplegia methods have been developed since the day that cardiac surgery has started. In this study, we compared del Nido cardioplegia with blood cardioplegia in isolated CABG cases and found that the duration of aortic cross-clamp and cardiopulmonary bypass were significantly reduced with del Nido cardioplegia. In this study where fifty-seven patients were examined, the duration of ICU stay and hospital stay were high in Group 1, but this difference was not statistically significant. According to our results, del Nido cardioplegia is not less effective than blood cardioplegia in myocardial protection in isolated CABG cases.

Blood cardioplegia applications are easy to obtain, effective and nowadays widely used in cardiac surgery. Long-term reliable myocardial protection might be provided with del Nido cardioplegia which is used with increasing frequency in especially congenital heart surgery (Stacy et al., 2011; Baburhan et al., 2018). Although blood cardioplegia applications require multiple administrations performed every twenty minutes in high volumes, del Nido cardioplegia has been reported to provide effective

myocardial protection with a single dose for 90 minutes (Kevin et al., 2012). In our study, as a result of repeated cardioplegia applications, the duration of aortic cross-clamp and total CPB were found to be high in the blood cardioplegia group.

It was reported by Tomasz et al., (2016) in 100 adult CABG operations; and by Robert et al., (2014) in 113 aortic valve surgery that del Nido cardioplegia provided reliable myocardial protection for 90 minutes and prevented ischemic damage. We repeated del Nido cardioplegia at a half-dose when the aortic cross-clamp time exceeded 70 minutes or when the electrical activity of heart started. We revealed that del Nido cardioplegia provides effective myocardial protection in isolated CABG cases as indicated by Tomasz and Robert series.

It was reported that lidocaine, which is not present in the classical blood cardioplegia solution but present in del Nido cardioplegia solution, has a positive effect on tissue vasoactivity and increases nitric oxide release. In addition, it has been reported that it plays an important role in long-term reliable myocardial protection with its effect on maintaining intracellular pH and limiting calcium ion (Darcy et al., 2009). Besides, mannitol present in del Nido cardioplegia solution also helps to remove free radicals by reducing intracellular and extracellular edema. In the study of Maroun et al., (2015) where they compare the lidocaine-containing del Nido cardioplegia with blood cardioplegia, 24-hour postoperative creatine kinase-MB values were significantly higher in the del Nido cardioplegia received group, but this situation did not make a significant difference in terms of mortality during the operation and first postoperative year (Carettal et al., 1995).

In the study of Niv et al., (2017) where blood and del Nido cardioplegia in adult cardiac surgery were compared, no significant difference was found between groups in terms of cardiac troponin levels during surgery. In our study where we compared the retrospectively obtained results, the first postoperative day troponin values were compared and no significant difference has been found between the groups. In cardioplegia applications, the administration methods of the solution may lead to a number of disadvantages. Antegrade administration method alone may be insufficient for effective myocardial protection in severe proximal coronary artery lesions and aortic insufficiency (Carettal et al., 1995). Retrograde administration alone may also cause problems in the distribution of homogeneous myocardial cardioplegia, especially due to the presence of canals in the right part of the heart (Terrence et al., 1993). In our study, the patients who were administered cardioplegic solution using the antegrade and retrograde route were examined in order to eliminate these disadvantages and effectively compare the applied cardioplegic solution.

The hypothermia applied during cardiac surgery is also important in myocardial protection. There are reports that moderate hypothermia (29-32°C) provides more effective cardiac protection (Nobuhiko et al., 1994). We routinely use moderate hypothermia method in CABG operations and we performed the operation with 30-32°C hypothermia in our patients. As well as del Nido cardioplegia solution, the Custodiol solution, which is commonly used in transplant and minimally invasive cardiac surgeries, is also included in cardioplegia strategies containing single-dose crystalloid. It has been reported that reliable myocardial protection is also provided with this solution which is ready and practical to use but has a higher cost compared to blood and del Nido cardioplegia (George et al., 2015; Brian et al., 2016). Due to its cost, the Custodiol solution has limited use except for selected cases in clinical practice. The del Nido solution, which provides myocardial protection similar to blood cardioplegia in isolated CABG operations, establishes a good alternative to Custodiol solution with its cost advantage. To evaluate the effectiveness of these 3 cardioplegia strategies, studies with wide series are needed where blood, del Nido and Custodiol cardioplegia solutions are used and different myocardial protection methods are compared.

5. CONCLUSION

In isolated CABG operations, the del Nido solution can be safely used without interrupting the operation with avoiding multiple cardioplegia applications and with the advantage of myocardial protection similar to blood cardioplegia. The del Nido solution, which has a lower cost compared to other long-term cardioplegic solutions that provide myocardial protection, may be preferred more widely in cardiac surgery after studies with large series.

Author Contributions

Concept/Design - BO, MCA; Analysis/Interpretation - MCA; Data Collection – BO, MCA; Writing - BO; Critical Revision - BO; Final Approval - BO; Statistical Analysis - MCA; Overall Responsibility - BO, MCA.

Financial Disclosure

This study has not received any external funding.

Conflict of Interest

The authors declare that there are no conflicts of interests.

Informed Consent

Written and oral informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this manuscript.

Ethıcal Statement

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Data and materials availability

All data associated with this study are present in the paper.

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