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Retrospective Research of Clinical and Hematological Changes Occurred by del Nido Cardioplegia in the Perioperative Period of Patients who Underwent Open-Heart Surgery

Açık Kalp Cerrahisi Geçiren Hastalarda del Nido Kardiyoplejisinin Perioperatif Dönemde Neden Olduğu Klinik ve Hematolojik Değişikliklerin Retrospektif İncelenmesi

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ABSTRACT

Objective: Aortic cross-clamping and postischemic myocardial dysfunction are fundamentally related to myocardial protection during open-heart surgery. Various cardioplegia solutions have been developed because of this issue. del Nido cardioplegia (DNC) solution is one of these solutions and has a vital impact on metabolic markers and cardiac protection in individuals of all ages. This study aimed to examine the effects of DNC on the perioperative follow-up period after cardiac surgery.

Methods: Preoperative and postoperative variations in selected biochemical and hematological variables of 71 patients who underwent open-heart surgery in our medical faculty between 2018 and 2020 were retrospectively examined and compared with normal values. SPSS 20.0 statistical software was used, and a statistically significant difference was defined as $p<0.05$.

Results: Hemoglobin, platelet, albumin, and uric acid levels were significantly lower at the end of cardiopulmonary bypass and the postoperative 24th hour than in the preoperative period. At the end of the cardiopulmonary bypass and the postoperative 24th hour, aspartate aminotransferase and lactate dehydrogenase levels were significantly greater than those in the preoperative period. Remarkable increases in hemoglobin, albumin, urea, and platelets in the postoperative 24th hour compared with the end of cardiopulmonary bypass were noted. We also reported substantial differences in glucose, lactate, creatine kinase-MB, and troponin levels.

Conclusion: We found significant changes in different parameters critical for the perioperative period of open-heart surgery. Although

ÖZ

Amaç: Aortik kross klemp uygulaması ve postiskemik miyokardiyal disfonkiyon, açık kalp cerrahisinde miyokard korunması ile ilişkili temel konulardandır. Bunun bir sonucu olarak değişik kardiyolpleji solüsyonları geliştirilmiştir. Bu solüsyonlardan birisi olan del Nido kardiyoplejisi (DNC), her yaştan bireyde kardiyak koruma ve metabolik değerler üzerinde önemli bir etkiye sahiptir. Çalışmamız DNC'nin kardiyak cerrahi geçiren hastalarda perioperatif periyottaki etkilerini incelemeyi amaçlamaktadır.

Yöntemler: 2018 ile 2020 yılları arasında merkemizde açık kalp cerrahisi operasyonu geçiren 71 hastaya ait, seçili biyokimyasal ve hematolojik parametrelerin preoperatif ve postoperatif dönemdeki değişiklikleri retrospektif olarak incelendi, normal laboratuvar değerleri ile karşılaştırıldı. İstatistiksel inceleme için SPSS 20.0 yazılımı kullanıldı ve $p<0,05$ değeri anlamlı kabul edildi.

Bulgular: Hemoglobin, platelet, albümin ve ürik asit değerleri, pompa çıkışında ve postoperatif 24. saatte yapılan ölçümlerde preoperatif döneme göre anlamlı olarak düşük çıktı. Aspartat aminotransferaz ve laktat dehidrojenaz da ise pompa çıkışı ve postoperatif 24. saatte, preoparatif döneme oranla anlamlı yükseklik tespit edildi. Hemoglobin, platelet, albümin, üre değerlerinin postoperatif 24. saatte, pompa çıkışına göre önemli yüksekliği görüldü. Ayrıca glukoz, laktat, kreatin kinaz-MB ve troponin değerlerinde de anlamlı farklılıklar tespit edildi.

Sonuç: Açık kalp cerrahisinde perioperatif dönemde kritik olan farklı parametrelerde anlamlı farklılıklar tespit ettik. Çalışmamız neticesinde DNC'nin güvenilir bir seçenek olduğunu göstermemize rağmen yeni klinik çalışmalara ihtiyaç vardır.

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ABSTRACT

our study found DNC to be a safer option, additional research into clinical usage is required.

Keywords: del Nido cardioplegia solution, cardiopulmonary bypass, perioperative period

ÖZ

Anahtar Sözcükler: del Nido kardiyopleji solüsyonu, kardiyopulmoner bypass, perioperatif dönem

INTRODUCTION

All types of cardiac surgery keep their frequency related to cardiovascular disease as a fundamental cause of death worldwide. Although coronary bypass graft surgery (CABG) is one of the most common operations in the world (1), it still has high morbidity and mortality levels (2) correlated with myocardial protection and injury (3-5). Cardiopulmonary bypass (CPB) and aortic cross-clamping provide surgical teams with a bloodless and non-beating heart (6) but interrupt myocardial perfusion during CABG, valve, or congenital heart surgery. Inadequate or no blood supply to myocardial tissue means cessation of oxygen and loss of ATP production. At the end of this process, the Na^{+}/Ca^{++} exchanger's dysfunction causes Ca^{++} accumulation in the intracellular area (5). Different cardioplegia solutions, which have been used to prevent myocardial dysfunction as a result of myocardial ischemia and reperfusion, have been investigated by many researchers. One of these solutions is del Nido cardioplegia (DNC), named by Dr. Pedro del Nido (5). This solution has been developed for tolerating the vulnerability of immature myocyte after increasing intracellular calcium (7). It has long been used in the pediatric population. Today, there are many studies about DNC's reliability not only for pediatric patients but also; for adult patients. DNC, which mostly comprises potassium chloride, lidocaine, mannitol, magnesium sulfate, and sodium bicarbonate, is more dilute with a 4:1 ratio (crystalloid to blood) (2,8,9). Several studies have also shown that DNC outperforms other treatments in terms of cardiac protection lasting longer than 90 min with a single dosage application (5-7). This manuscript aimed to compare the perioperative changes in clinical and hematological parameters of patients who underwent open-heart surgery with DNC.

MATERIALS AND METHODS

Study Design and Patients

We retrospectively reviewed preoperative and postoperative changes in selected biochemical and hematological values of 71 patients who underwent open-heart surgery at our center between 2018 and 2020. Patients with active infection, older than 80 years, and those unable to cooperate were excluded from the study. The procedures in the experiment were carried out according to the permission of the Gazi University Institutional Local Animal Care and Use Ethics Committee (approval number: 585, date: 28.06.2021).

Demographic Data

The following variables were examined: age, gender, weight, height, ejection fraction (EF), presence of diabetes mellitus, ASA risk, EuroSCORE, and type of operation.

Perioperative Data

We looked to see if there were any significant differences in the time of CPB, aortic cross-clamp, intensive care unit (ICU) stay, extubation, and the amount of drainage and urine output within 24 h of admission to the ICU, all of which are critical clinical parameters for the postoperative period of open-heart surgery. We also discovered the need for defibrillation, a pacemaker, an intraortic balloon pump (IABP), inotropic agent support intraoperatively, and the presence of a cerebrovascular stroke, mortality, and atrial fibrillation within 24 h after surgery in the postoperative period.

Glucose and lactate levels were measured at four scheduled time points and compared with baseline laboratory values: before CPB, before and after the aortic cross-clamp was released, and after CPB was terminated.

Selected hematological and biochemical values, including hemoglobin, platelet count, albumin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), blood urea nitrogen (BUN), creatinine, lactate dehydrogenase (LDH), and uric acid, were measured at baseline, after the termination of CPB, and 24 h after surgery, were noted additionally. These parameters were also compared with normal laboratory values.

The occurrence of atrial fibrillation, cerebrovascular stroke, mortality, drainage, and urine output within 24 h of ICU admission, duration to extubation, and length of ICU stay were all documented. Creatine kinase-MB (CK-MB) and troponin levels were also retrieved at three time points: preoperative, 1 h after surgery, and 24 h after surgery.

Statistical Analysis

Data were analyzed using SPSS. $P<0.05$ was the threshold for a statistically significant difference. The findings are presented as mean ± standard deviation and the median of the biochemical variables.

RESULTS

The mean age of the patients included was 60.12±9.10. There were 76.1% male patients and 17.23% female patients. When we checked the ASA Score of patients. ASA 3 was the most common, accounting for 80.3% of the patients. The mean EuroScore was 3.91±2.40. Table 1 displays the patients' demographic information.

There was a significant increase in CK-MB's postoperative first-hour level compared with the preoperative level ($p<0.0001$). On the other hand, we found a remarkable decrease in CK-MB's postoperative 24 h level compared with the postoperative first-hour level ($p<0.0001$). Increased troponin in the postoperative first hour and postoperative 24^{th} hour compared with the preoperative value was significant. In Table 2, Figure 1, troponin and CK-MB levels are shown.

As compared with before CPB, there was a significant increase in all planned time points of glucose and lactate levels (p<0.0001, p<0.0001, p<0.0001, respectively). Similarly, we found considerable

Table 1. Patients' demographic data [mean ± SD, n (%)]

Parameter	Mean ± SD
Age	60.12±9.10
Sex	
Male, n (%)	54 (76.1)
Female, n (%)	17 (23.9)
Weight (kg)	166.20±12.76
Diabetes mellitus	
Yes, n (%)	41 (57.7)
No, n (%)	30 (42.3)
Height (cm)	78.37±17.09
Ejection fraction (%)	54.56±8.94
Operation type	
CABG, n (%)	50 (70.4)
Other, n (%)	21 (29.6)
Euro score	3.91±2.40
ASA score	
ASA II, n (%)	5 (7)
ASA III, n (%)	57 (80.3)
ASA IV, n (%)	9 (12.7)

SD: Standard deviation, CABG: Coronary bypass graft surgery, ASA: American Society of Anesthesiologists.

Table 2. CK-MB and troponin data [median (minimum-maxium)]

Marker	Preoperative	Postoperative first hour	Postoperative first day
Troponin	20 (0.6-26,358)	2,807 (91-26,358)*	1,486 (50-26,358)*
CK-MB	16 (6.5-135)	48 (21-245)*	24.5 (7.7-122)&

*P<0.05: Compared to preoperative, &p<0.05: Compared to postoperative first hour, CK: Creatine kinase.

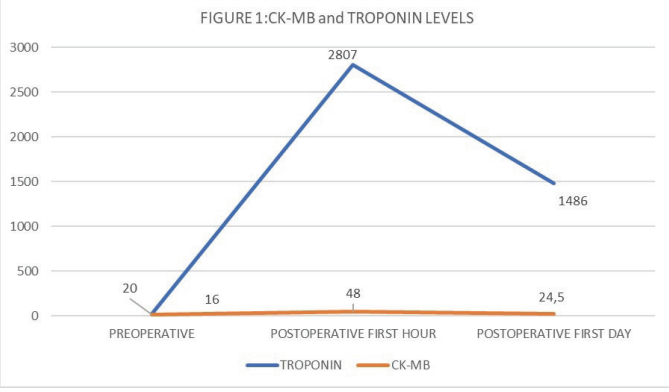

Figure 1. CK-MB and troponin levels.

CK: Creatine kinase.

Table 3. Glucose and lactate levels [median (minimum-maxium)]

	Glucose	Lactate
Before the CPB	135 (90-260)	1 (0.2-2.70)
Before releasing the aortic cross clamp	159 (103-258)*	1.6 (0.6-4)*
After releasing the aortic cross clamp	185 (109-260)*,&	2.1 (0.6-4.6)*,&
After the termination of CPB	186 (114-278)*,&	2.1 (0.5-4.6)*,&

CPB: Cardiopulmonary bypass, *p<0.05: Compared to preoperative, &p<0.05: Compared to before releasing the aortic cross clamp. CPB: Cardiopulmonary bypass.

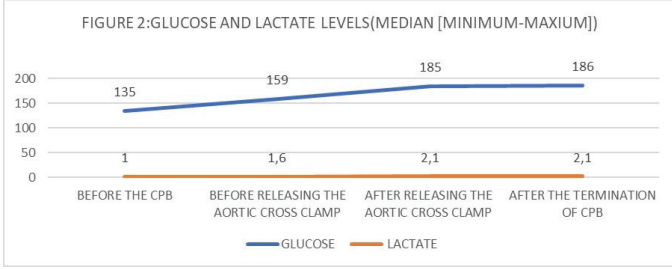

Figure 2. Glucose and lactate levels [median (minimum-maximum)].

CPB: Cardiopulmonary bypass.

Table 4. Cross-clamp time, CPB time, defibrillation, pacemaker, intra-aortic balloon pump, and inotropic agent usage [median (minimum-maximum), n (%)]

Variable	Mean ± SD
CPB time (minute)	115 (50-1451)
Cross-clamp (minute)	78 (37-821)
Defibrillation	
Yes, n (%)	13 (18.3)
No, n (%)	58 (81.7)
Pacemaker	
Yes, n (%)	17 (23.9)
No, n (%)	54 (76.1)
IABP	
Yes, n (%)	4 (5.6)
No, n (%)	67 (94.4)
Inotropic agent	
Yes, n (%)	54 (76.1)
No, n (%)	17 (23.9)

SD: Standard derivation, CPB: Cardiopulmonary bypass, IABP: Intraortic balloon pump.

Table 5. Extubation, ICU stay, amount of drainage, and urine [median (minimum-maximum)]

Data	
Extubation	*186 (114-278)*
ICU stay (hour)	48 (12-120)
Drainage (mililiter)	500 (50-2,900)
Urine (mililiter)	3,000 (640-6,000)

ICU: Intensive care unit.

Table 6. Biochemical and hematological data [mean ± SD, median (min.-max.)]

	Preoperative	End of CPB	Postoperative 24th h
Hemoglobin	12.81±1.99	8.37±1.03*	9.35±0.77*,&
Platelet	248507.04±75395.13	136126.76±50713.74*	168507.04±56629.84*,&
Albumin	3.96±0.49	2.20±0.36*	3.24±0.30*,&
AST	24 (13-878)	39 (11-128)*	45 (10-234)*
ALT	21 (9-1525)	25 (6-85)	29 (13-101)
BUN	17 (9-69)	16 (7-55)	20 (7.1-61)&
Creatinin	0.80 (0.4-7.7)	80 (0.3-6.1)	0.9 (0.3-4.9)
LDH	230 (113-1125)	323 (149-705)*	355 (204-908)*
Uric acid	5.80 (2.9-11)	5.25 (2.6-0.8)*	5.4 (2.1-10)*

*P<0.05: Compared to preoperative, &p< compared to end of CPB, SD: Standard deviation, min.: Minimum, max.: Maximum, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, BUN: Blood urea nitrogen, LDH: Lactate dehydrogenase, CPB: Cardiopulmonary bypass.

increases in glucose and lactate levels at two time points, which were after releasing the cross-clamp and after the termination of CPB, compared with before releasing the aortic cross-clamp (p<0.0001, p<0.0001, respectively) (Table 3, Figure 2).

During the intraoperative period, 18.3% of patients required defibrillation, and 76.1% of patients needed inotropic agent assistance. In 4 patients, an intra-aortic balloon pump was used, and 17 patients required a pacemaker. Table 4 shows that the mean aortic cross-clamp time was 78 (37-821) minutes and the mean CPB time were 115 (50-1451) minutes.

The mean extubation time was 186 min (114-278) and 48 h (12-120) were the average length of ICU stay. The total amount of tube drainage in the postoperative 24 h was 500 milliliters (50-2900) and urine was 3000 milliliters (640-6000) as shown in Table 5.

In the first 24 h following surgery, 7% of patients were noted with atrial fibrillation, whereas no cerebrovascular attack or death occurred. Table 6 summarizes the biochemical and hematological data of the patients, including hemoglobin, platelet count, albumin, AST, ALT, BUN, creatinine, LDH, and uric acid. There were significant decreases in hemoglobin, platelet, albumin, and uric acid levels at the end of CPB compared with preoperative values. Similarly, hemoglobin, platelet, albumin, and uric acid levels were remarkably lower at the postoperative 24 h compared to preoperative values. When compared with the end of CPB, BUN, albumin, platelet, and hemoglobin levels were higher in the postoperative 24 h. Another notable difference was in LDH levels greater in the postoperative 24 h and at the end of CPB compared with preoperative levels. At the end of CPB, AST was the only parameter to be significantly higher than its preoperative value. Likewise, AST was increased in postoperative 24 h compared to the preoperative value.

DISCUSSION

In this retrospective and single-center study, we presumed that DNC was a safe solution. The considerable decrease in troponin and CK-MB levels 24 h after surgery and the reduced use of defibrillation, IABP, and pacemakers corroborated our theory.

We did not collect the postoperative EF records. Therefore, the probable cause of increased inotropic drug administration could not be evaluated. On the other hand, we believe it can be associated with DNC's ingredients and their potential vasodilatation effects.

In several studies, the incidence of postoperative atrial fibrillation (POAF) varies. However, to the best of our knowledge, the incidence of POAF in the first 24 h following surgery has not been adequately documented. According to our data, atrial fibrillation was observed in 7% of patients in the 24 h following surgery; however, a lot of studies on POAF limit our comparison.

Cerebrovascular attack is one of the most serious consequences of open-heart surgery. Based on our findings, we believe that DNC has a protective effect against neurological problems; nevertheless, long-term results may be more definite to consider.

Only a few studies have shown a significant change in creatinine levels following open-heart surgery. We found no significant difference in creatinine levels in the current trial. In addition, we noted 3000 mL of total urine and a statistically meaningful increase in BUN at 24 h following surgery. Based on these findings, we conclude that DNC has no harmful effect on renal function. Another problem with our theory is the inability to precisely characterize postoperative renal insufficiency. Not only do patients need hemodialysis after surgery but also long-term outcomes for urine output might be parameters to consider.

Study Limitations

Our study has limitations on a few topics. Firstly, there were no patients under 18 or older than 80. On the other hand, all the patients had undergone elective surgeries, and we excluded patients with active infections.

CONCLUSION

DNC is a highly safe option for protecting the myocardium and organs. Future research is necessary.

Ethics

Ethics Committee Approval: The procedures in the experiment were carried out according to the permission of the Gazi University Institutional Local Animal Care and Use Ethics Committee (approval number: 585, date: 28.06.2021).

Informed Consent: Patient approval has not been obtained as it is performed on animals.

Author Contributions

Concept: A.Ö., B.K., M.A., E.Ş., A.Ö., Y.Ü., E.İ., H.Z., L.O., Design: A.Ö., B.K., M.A., E.Ş., A.Ö., Y.Ü., E.İ., H.Z., L.O., Data Collection or Processing: A.Ö., B.K., M.A., E.Ş., A.Ö., Y.Ü., E.İ., H.Z., L.O., Analysis or Interpretation: A.Ö., B.K., M.A., E.Ş., A.Ö., Y.Ü., E.İ., H.Z., L.O., Literature Search: A.Ö., B.K., M.A., E.Ş., A.Ö., Y.Ü., E.İ., H.Z., L.O., Writing: A.Ö., B.K., M.A., E.Ş., A.Ö., Y.Ü., E.İ., H.Z., L.O.

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