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**Research Article** 

# Clinical Outcomes and Electrolyte Balance Factors in Complex Cardiac Operations in Adults; Del Nido<sup>®</sup> Versus Custodiol<sup>®</sup> Cardioplegia Solutions: A Randomized Controlled Clinical Trial

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## Abstract

**Background:** Cardioplegia is used for protection of myocardium during cardiac operations. Del Nido<sup>®</sup> (DN) and Custodiol<sup>®</sup> cardioplegia (CC) solutions are used for prolonged protection of the myocardium during cardiopulmonary bypass (CPB). Custodiol<sup>®</sup> cardioplegia solution is gaining popularity for myocardial protection during cardiopulmonary bypass.

**Objectives:** This study aimed to compare the effects of Custodiol<sup>®</sup> with another cardioplegia solution, Del Nido<sup>®</sup>, on myocardial protection during cardiopulmonary bypass.

**Methods:** In a randomized controlled clinical trial, forty patients were randomly allocated to Del Nido<sup>®</sup> and Custodiol<sup>®</sup> (CC) groups. Patients in both groups received a standard anesthesia protocol. For cardioplegia, in the DN group, the Del Nido<sup>®</sup> solution was administered every 90 minutes by the antegrade route. In the CC, group, the Custodiol<sup>®</sup> solution was administered in the same way at the beginning of the cardioplegia. Demographic information, blood chemistry parameters and other related perioperative and postoperative clinical indices were recorded.

**Results:** Frequency of female patients was 14/21 (66.66%) in the DN and 12/19 (63.15%) in the CC group (P = 0.816), age was 57.14 ± 12.48 years versus 59.47 ± 11.96 years (P = 0.551), weight was 70.95 ± 9.56 kilograms versus 69.63 ± 7.64 kilograms (P = 0.635), CPB time was 103.19 ± 23.43 minutes versus 97.36 ± 16.7 minutes (P = 0.376), and cross-clamp time was 73.76 ± 19.66 minutes versus 83.95 ± 16.14 minutes (P = 0.083). Blood chemistry and blood gas analysis revealed a similar trend between the two groups in these parameters (P > 0.05) except for higher sodium levels after cardioplegia (P = 0.016) and end of CPB (P = 0.002), potassium levels after cardioplegia (P = 0.029), and bicarbonate anions at the end of bypass (P = 0.03) in the Custodiol<sup>®</sup> group.

**Conclusions:** In conclusion, CC and DN offer effective myocardial protection during cardiopulmonary bypass. It is recommended to restrict the use of CC in patients susceptible to electrolyte disturbances.

Keywords: Anesthesia, By Pass, Cardiac, Cardioplegia, Cardiopulmonary, Castodiol®, Del Nido®, Outcome, Solutions

# 1. Background

Cardiovascular diseases are amongst the most important causes of mortality and morbidity worldwide. Atherosclerosis, lifestyle, and congenital disorders may cause cardiovascular diseases, which are complex in nature (1-4). These complications require surgical treatment. In complex cardiac disorders, duration of the operation is more than normal and prolonged protection of the myocardial tissue against the post-cardiopulmonary bypass (CPB) ischemia/reperfusion injury (IRI) is required (1). Cardioplegia provides a still and blood-free work field for the surgeon (5). Inactivity of the muscles along with hypothermia during cardioplegia causes decline in cell's metabolic demand. Although cellular inactivity decreases the metabolic demand and reduces ischemic damage, basal metabolism is active inside the cells and causes cells to enter anaerobic metabolism in the absence of oxygen. The anaerobic metabolism and collection of its byproducts causes elevation of free radicals in the tissue (5). Af-

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ter blood flow reestablishment after clamp removal, reperfusion injury starts with the recruitment of the immune cells to the ischemic tissue. The inflammatory response, including cellular immune response and inflammatory mediators, damages the cardiomyocytes and may impair its function. Furthermore, IRI causes a series of events in the affected tissue, which results in cell death and impaired organ function (6-9). Furthermore, the systemic inflammatory response is induced in response to this local IR injury. The release of cytokines and other inflammatory mediators may result in critical organ damage in sites distant to the myocardium (10). To prevent this cascade of adverse events, management of myocardial ischemia and reperfusion injury is very important to 1, prevent damage to myocardium itself and 2, to stall systemic inflammatory response and distant critical organ damage. Many methods, including premedication and post-medication strategies, ultrafiltration, and cytokine filters have been studied in the management of the inflammatory response and reperfusion injury (5-9, 11-13). However, cardioplegia solutions as the first agent achieving the cardiomyocytes, exactly upon ischemia, are of profound importance. Various formulations of cardioplegia solutions have been developed to go further beyond just stopping the heartbeat and offer superior protection against ischemia by multitude of actions like free radical scavenging activity, blocking the calcium influx and diastolic stiffness, and resisting pH changes through high buffering capacity (1, 10, 14-16).

Classical cardioplegia solutions are administered in a multi-dose manner, which requires renewing the cardioplegia shots in definite intervals. Cardiac surgeons are interested in single-dose cardioplegia solutions because of their durable tissue protection during cardiopulmonary bypass (CPB). Two cardioplegia solutions are introduced for more durable myocardial protection during complex procedures: histidine-tryptophan-ketoglutarate (HTK), Bretschneider's, or Custodiol<sup>®</sup> (CC), and Del Nido<sup>®</sup> (DN) cardioplegia solution. Durable protection by these cardioplegia solutions enables uninterrupted performance of complex procedures (15-21). Due to low sodium and calcium content of the CC, sodium depletion of the extracellular space occurs after hyperpolarization of the myocyte plasma membrane by administration of this solution and results in diastolic cardiac arrest (5, 21, 22). Like CC, DN solution is also intended for one-shot administration. Formulation, properties, and methods of use of Custodiol® and DN solutions have been described elsewhere (10, 23). However, their cardioprotective properties has not been compared in the context of complex cardiac operations, including coronary artery bypass grafting (CABG), aortic valve replacement (AVR), and mitral valve replacement (MVR). The current study aimed at comparing the cardioprotective properties and perioperative and post-surgical clinical and biochemical outcomes between patients receiving DN and Custodiol<sup>®</sup> cardioplegia solutions.

## 2. Methods

## 2.1. Study Design

A randomized, double-blinded, no use of placebo, single-center controlled clinical trial study was performed to compare the effects of two cardioplegia solutions, DN and Custodiol<sup>®</sup>, on perioperative outcomes, including the following criteria duration of operation, duration of CPB and pump-time, blood chemistry parameters, blood and blood products transfusion, intensive care unit (ICU) stay duration, use of defibrillator, hemodynamics, cardiac muscle damage, and blood gas analysis. All ethical concerns regarding medical research, including human subjects, according to the Helsinki declaration was followed. The study protocol was confirmed by the research ethics committee of Tehran University of the Medical Sciences (TUMS) (registration code: IR.TUMS.MEDICINE.REC.1396.3509). All patients gave their informed consent for participation in the study. Study protocol was registered at the Iranian registry of clinical trials (http://irct.ir/) with registration number IRCT2016042627617N1. Blinding was done on patients and outcome assessors (nurses registering the clinical outcomes and laboratory personnel measuring the biochemical parameters). Patients were unaware of the type of cardioplegia solution. The anesthesiologist and the anesthesia team performed the allocation of the patients to two groups and administered the cardioplegia solution. Since both cardioplegia solutions were single-dose, surgeons and other surgery team members were also unaware of the allocation sequence. Also ICU nurses and laboratory technicians were blind to the patients and their samples being analyzed in the laboratory. Patients were included in the study, if they were a candidate for at least two of the conditions of coronary artery bypass grafting, mitral valve graft surgery, and aortic valve graft surgery. Patients were excluded if they were diagnosed with inflammatory diseases before surgery, acute myocardial infarction, and patient dissatisfaction in any part of the study, dialysisrequiring renal failure, ejection fraction less than 15%, second surgery, emergency patients, predictive pulmonary disease patients, and cardiomyopathy patients. Since there was no estimate of differences in parameters between the groups of patients treated with these two cardioplegia solutions, the researchers used convenience sampling and conducted this pilot study to find an estimate of the differences between two cardioplegia solutions. The researchers

set a target sample size for this study as 40 patients. Data extraction center was a central state-owned independently operating specialty hospital in cardiac care. Patients were randomly allocated to two groups as described earlier. One group received DN and the other received Custodiol<sup>®</sup> cardioplegia (CC) solution.

## 2.2. Anesthesia Induction and Cardioplegia

Anesthesia induction was performed with the same procedure and similar medications for all patients. Patients were then ventilated with an anesthesia machine with a respiratory flow volume of 10 mL/kg of body weight adjusted to respiratory rate, according to the age and maintenance of  $CO_2$  pressure (PaCO<sub>2</sub>) between 30 and 35 mmHg. Cardioplegia solutions were administered with a standard procedure in an antegrade manner as previously described for DN (10, 23) and CC (24) solutions. Briefly, DN was administered in the antegrade delivery through aortic root as a single-shot (20 mL/kg; 1000 mL maximum) and further doses delivered after 90 minutes if required. Custodiol<sup>®</sup> cardioplegia was administered in antegrade manner as a single dose of 25 mL/kg over five to seven minutes. Further doses were administered after three hours.

#### 2.3. Data Collection

Patients' demographic information including age, weight, height, body surface area (BSA), and gender were recorded. Cardiac troponin I were measured in all patients before anesthesia induction, after CPB and 24 hours after ICU. Other parameters of cross-clamp time, CPB time, mechanical ventilation, hemodynamic parameters, blood chemistry, transfusion of blood and blood products, and the use of inotropes were recorded according to the medical records of the hospital. Laboratory measurements were performed by the clinical diagnostic laboratory of the hospital as part of a routine practice of in vitro diagnostics in the center. The devices were checked and calibrated as a part of everyday practice in the diagnostics laboratory of the center. Laboratory staff were unaware of the groups to which every patient was assigned.

### 2.4. Statistical Analysis

Data were analyzed using IBM SPSS Statistics for Windows, Version 20 (IBM Corp., Armork, N,Y., USA). Data for continuous variables were presented as mean  $\pm$  standard deviation (SD) if they followed normal distribution. In case of violation from normal distribution, data were presented as median (interquartile range, IQR). Categorical data were presented as relative frequency and frequency percentage. Mixed analysis of variance (ANOVA) was used for analysis of changes in measurements of continuous

Table 1. Demographic Information of the Patients Receiving Two Cardioplegia Solutions Del Nido® and Custodiol $^{\circledast a}$ 

| Variables                                     | Del Nido®         | Custodiol®        | P Value |
|---|-------------------|-------------------|---------|
| Age, y  | $57.14 \pm 12.48$ | $59.47 \pm 11.96$ | 0.551   |
| Weight, kg                                    | $70.95 \pm 9.56$  | $69.63 \pm 7.64$  | 0.635   |
| Body surface area, m <sup>2</sup>             | $1.79\pm0.14$     | $1.75\pm0.12$     | 0.291   |
| Frequency, referent: female,<br>Frequency (%) | 14/21 (66.66)     | 12/19 (63.15)     | 0.816   |

<sup>a</sup>Continuous data are presented as mean  $\pm$  standard deviation (SD). Patients' gender distribution of each group is presented as relative frequency and frequency percent of female patients to male and female patients in each group.

variables over time wherever required. To control the postintervention measures of variables for differences in preintervention measures, these values were set as covariates in mixed ANOVA models. Mann-Whitney U test was used for comparison of continuous variables between groups if the data distribution violated the normal distribution assumption. Chi-square test was used for comparison of the frequency of categorical variables between the two groups. The level of significance and power of the analysis were set to 0.05 and 0.8, respectively.

# 3. Results

Seventy-one patients were initially screened according to the inclusion and exclusion criteria. Thirty-one were not included because twenty-two did not meet the inclusion criteria and nine patients refused to participate. Forty patients were included in the current study, 21 of which received DN and 19 underwent deep cardioplegia with CC. All patients finished the study, and their data were included in the analysis (Figure 1). Mean age of the subjects in two groups was 57.14  $\pm$  12.48 and 59.47  $\pm$  11.96 years in DN and CC groups, respectively (P = 0.551). No significant difference was observed between the subjects of the two groups in terms of their demographic variables (P > 0.05; Table 1). Also, the kind of operations between the two groups were similar (P = 0.594; Table 3).

 
 Table 2. Type of Operations in the Two Groups of Patients Receiving Different Kinds of Cardioplegia Solutions

|          | Del Nido <sup>®</sup> Group | Custodiol <sup>®</sup><br>Group | P Value |
|----------|-----------------------------|---------------------------------|---------|
| CABG.AVR | 3                           | 3                               |         |
| MVR.AVR  | 7                           | 9                               | 0.594   |
| MVR.CABG | 11                          | 7                               |         |

Abbreviations: CABG.AVR, Coronary Artery Bypass Grafting and Aortic Valve Replacement; MVR.AVR, Mitral Valve Replacement and Aortic Valve Replacement; MVR.CABG, Mitral Valve Replacement and Coronary Artery Bypass Grafting.





The findings of the study on the relationship between kind of cardioplegia solution and the perioperative outcomes demonstrated no significant differences between the two groups in case of CPB time, cross-clamp duration, urine output, chest tube drainage, duration of mechanical ventilation, and ICU stay (P > 0.05; Table 3).

No significant differences were observed in mean arterial pressure (MAP) and ejection fraction (EF) between the two groups (Table 3).

Blood chemistry parameters and blood gas analysis revealed a similar trend between the two groups in these parameters (P > 0.05) except for sodium levels after cardioplegia (P = 0.016) and end of CPB (P = 0.002), potassium levels after cardioplegia (P = 0.029), and bicarbonate anions at the end of bypass (P = 0.03). These amounts were lower in the CC group as compared with the DN group (Table 4). Two groups were also identical in the use of blood products, such as pack cell, platelet, fresh-frozen plasma, and plasma

cryoprecipitate. Also, use of dopamine, epinephrine, norepinephrine, and Milrinone during operation and in the ICU was similar between the two groups (Table 5).

# 4. Discussion

In the current trial, the researchers demonstrated that Custodiol<sup>®</sup> and DN cardioplegia solutions had similar cardioprotective properties. Patients undergoing cardioplegia using one of these solutions demonstrated similar outcomes in terms of perioperative and postoperative parameters. They did not show any significant differences in CPB time, cross-clamp duration, urine output, chest tube drainage, and duration of mechanical ventilation.

The convenience offered by single dose cardioplegia solutions encouraged the development of various cardioplegia solutions for the myocardial protection during CPB. Because they enabled durable cardioplegia without the need

| Varietals                               | Del Nido <sup>®</sup> | Custodiol®          | P Value |
|---|-----------------------|---------------------|---------|
| CPB time, min                           | $103.19\pm23.42$      | $97.36 \pm 16.7$    | 0.376   |
| Cross clamp time, min                   | $73.76\pm19.66$       | $83.95 \pm 16.14$   | 0.083   |
| Urine output during operation, mL       | $507.14 \pm 215.22$   | $555.26 \pm 228.46$ | 0.497   |
| Chest tube drainage after operation, mL | $319.0 \pm 125.65$    | $316.11 \pm 102.73$ | 0.939   |
| Duration of mechanical ventilation, h   | $10.91 \pm 4.0$       | $10.79 \pm 3.59$    | 0.934   |
| ICU stay, days                          | $2.22\pm0.45$         | $2.53\pm0.68$       | 0.101   |
| MAP before bypass, mmHg                 | $75.95 \pm 11.83$     | $70.94 \pm 5.73$    | 0.109   |
| MAP bypass beginning, mmHg              | $64.81\pm6.16$        | $67.9\pm6.72$       | 0.138   |
| MAP post-bypass, mmHg                   | $65.96 \pm 15.11$     | 71.26.9.63          | 0.199   |
| MAP ICU entrance, mmHg                  | $72.5\pm10.09$        | $72.75\pm8.7$       | 0.937   |
| MAP 24 hours post-ICU, mmHg             | 72.1±9.64             | $76.06 \pm 12.04$   | 0.267   |
| MAP 48 hours post-ICU, mmHg             | $66.33 \pm 8.6$       | $67.63 \pm 7.34$    | 0.612   |
| EF before surgery, %                    | $42.14\pm8.79$        | $43.84\pm8.12$      | 0.531   |
| EF post-bypass, %                       | $40.52\pm7.17$        | $42.32\pm7.75$      | 0.452   |
| EF on discharge, %                      | $41.67 \pm 12.32$     | $41.79\pm7.15$      | 0.97    |
| BUN pre-operation, mg/dL                | $23.38 \pm 16.24$     | $19.32\pm5.94$      | 0.31    |
| BUN post-operation, mg/dL               | <b>21.33</b> ± 12.12  | $23.26 \pm 11.03$   | 0.603   |
| BUN 24 hours post-operation, mg/dL      | $22.19\pm7.14$        | $22.26\pm 6.6$      | 0.974   |
| Cr pre-operation, mg/dL                 | $0.9\pm0.21$          | $0.92\pm0.21$       | 0.713   |
| Cr post-operation, mg/dL                | 0.86 ± 0.3            | $1.03\pm0.28$       | 0.07    |
| Cr 24 hours post-operation, mg/dL       | $0.86\pm0.3$          | $1.03\pm0.28$       | 0.982   |
| CK pre-operation, U/L                   | $13.76\pm6.33$        | $5.74\pm9.93$       | 0.464   |
| CK 24 hours post-operation, U/L         | $65.72 \pm 31.38$     | $54.66 \pm 29.16$   | 0.255   |
| CInI pre-operation, ng/mL               | $0.59\pm2.61$         | $0.49\pm2.06$       | 0.893   |
| CTnI 24 hours post-operation, ng/mL     | $3.71 \pm 2.39$       | $3.06 \pm 2.75$     | 0.431   |

Table 3. Perioperative Parameters, Hemodynamics and Blood Chemistry Parameters of Two Groups of Patients Receiving Two Cardioplegia Solutions Del Nido<sup>®</sup> and Custodiol<sup>®a</sup>

Abbreviations: BUN, blood urea nitrogen; CK, creatine kinase; CPB, cardiopulmonary bypass; Cr, creatinine; cTnI, cardiac troponin I; EF, ejection fraction, ICU, intensive care unit; MAP, mean arterial pressure. <sup>a</sup>Values are expressed as mean ± standard deviation (SD).

to stop the flow of surgical operation, one of the advantages of the use of single-dose cardioplegia solutions was the decrease of cross-clamp time. Since both cardioplegia solutions used in the current study were cardioplegia solutions for single-dose administration, similar cross-clamp time between the two groups appeared sensible. The decrease in the cross-clamp time is usually associated with other outcomes, such as CPB time, mechanical ventilation duration, and intensive care unit stay (23, 25), although further evidence supports the notion that even multi-dose cardioplegia does not influence the CPB time and crossclamp duration (1, 17). It is no surprise that these items are also similar in the groups of patients receiving two different single-doses of cardioplegia solution. Also, no differences in hemodynamic parameters, including mean arterial pressure and EF, were observed between the two groups, which is consistent with the data available from other studies (1, 10).

Blood chemistry parameters were similar between the two groups. Exceptions were sodium ions after cardioplegia and after bypass, potassium ions after cardioplegia and bicarbonate ions, which were significantly lower in the CC group compared to the DN group. Hyponatremia is reported as a common outcome when using intracellular cardioplegic solutions (17, 26, 27). The same was observed in the current study. Moreover, potassium level in patients in the CC group was slightly lower, which makes sense as Custodiol® cardioplegia solution is a non-potassium based

| Variables                  | Del Nido®          | Custadiol         | P Value |
|----------------------------|--------------------|-------------------|---------|
| Na pre-CPB, mEq/L          | $142.8\pm4.59$     | $142.52\pm6.22$   | 0.87    |
| Na early CPB, mEq/L        | $134.91 \pm 3.25$  | $132.37\pm3.1$    | 0.016   |
| Na end CPB, mEq/L          | $133.86\pm3.58$    | $129.58\pm4.43$   | 0.002   |
| Na ICU entrance, mEq/L     | 139.76 $\pm$ 4.25  | $137.26\pm5.27$   | 0.106   |
| Na 6 hours post-ICU, mEq/L | $140.67\pm4.16$    | $139.52\pm4.72$   | 0.422   |
| K pre-CPB, mEq/L           | $3.54\pm0.47$      | $3.63\pm0.66$     | 0.602   |
| K early CPB, mEq/L         | $4.72\pm0.74$      | $4.25\pm0.54$     | 0.029   |
| K end CPB, mEq/L           | $4.6\pm0.8$        | $4.33\pm0.56$     | 0.238   |
| K ICU entrance, mEq/L      | $4.14\pm0.62$      | $4.05\pm0.61$     | 0.623   |
| K 6 hours post-ICU, mEq/L  | $4.48\pm0.5$       | $4.37\pm0.44$     | 0.456   |
| BS pre-CPB, mg/dL          | $95.52\pm29.73$    | $94.84 \pm 24.63$ | 0.938   |
| BS early CPB, mg/dL        | $130.95\pm35.37$   | $126.16\pm30.05$  | 0.649   |
| BS end CPB, mg/dL          | $161.91 \pm 46.09$ | $146.42\pm33.08$  | 0.234   |
| BS ICU entrance, mg/dL     | $176.95\pm60.74$   | $168.39\pm56.55$  | 0.657   |
| 3S 6 hours post-ICU, mg/dL | $163.05\pm56.18$   | $154.24\pm49.4$   | 0.622   |
| Hgb pre-CPB, g/dL          | $12.58 \pm 1.32$   | $12.75\pm1.12$    | 0.672   |
| Hgb early CPB, g/dL        | $8.63 \pm 1.54$    | $7.95\pm1.09$     | 0.115   |
| Hgb end CPB, g/dL          | $8.9\pm1.21$       | $8.46 \pm 1.08$   | 0.248   |
| Hgb ICU entrance, g/dL     | $10.34 \pm 1.0$    | $10.23 \pm 1.28$  | 0.755   |
| Hgb 6 hours post-ICU, g/dL | $10.41\pm1.15$     | $10.0\pm1.33$     | 0.313   |
| pH pre-CPB                 | $7.47\pm0.07$      | $7.43\pm0.07$     | 0.132   |
| pH early CPB               | $7.38\pm0.08$      | $7.37\pm0.08$     | 0.652   |
| pH end CPB                 | $7.41 \pm 0.04$    | $7.39\pm0.05$     | 0.106   |
| HCO3 pre-CPB, mEq/L        | $20.95\pm2.59$     | $22.21\pm2.64$    | 0.137   |
| HCO3 early CPB, mEq/L      | $20.0 \pm 2.1$     | $19.37 \pm 1.77$  | 0.313   |
| HCO3 end, CPB mEq/L        | $21.24\pm2.17$     | $19.95 \pm 1.39$  | 0.03    |

Abbreviations: BS, blood sugar; K, blood potassium.

<sup>a</sup>Na, blood sodium.

 $^{\rm b}$  Values are expressed as mean  $\pm$  standard deviation (SD).

cardioplegic solution and lacks potassium ions (22, 26).

Another significant outcome was lower bicarbonate ions at the end of CPB in the CC group compared with the DN group. This decrease in blood ions may also be due to excess fluid infusion in the CC group compared with the DN group, which may have caused the decline in the blood plasma electrolytes. Although bicarbonate level was lower in the blood of the CC group, the amount of this metabolite was in the normal range in most of the patients in both groups and was not associated with considerable blood pH deviations from the normal range. These are consistent with previous findings (14, 22, 26).

Cardiac troponin I (cTnI) levels were elevated in 24 hours post-operation. However, the amount of this marker

was not significantly different between the two groups as measured in before and 24 hours post-operation. The cTnI is a marker of cardiac muscle damage, which is elevated in response to the death of cardiac myocytes and the release of its contents to the circulation (1, 5, 14, 17, 22, 27). The similarity of the cTnI levels between the two groups demonstrated that two cardioplegia solutions offered similar protection against the acute damage of the cardiomyocytes.

The two groups had a similar profile regarding the use of inotropes, blood cells, transfusion of blood products, hemoglobin, and hematocrit levels. This indicates that these cardioplegia solutions affect the parameters in the same way. Other studies have demonstrated that these parameters are not significantly affected by single dose

| Variables     | Del Nido® | Custodiol® | P Value |
|---------------|-----------|------------|---------|
| PC OR         | 23.8      | 15.8       | 0.408   |
| PC ICU        | 38.1      | 42.1       | 0.525   |
| PLT OR        | 4.8       | 15.8       | 0.265   |
| PLT ICU       | 4.8       | 0.0        | 0.525   |
| FFP OR        | 4.8       | 15.8       | 0.265   |
| FFP ICU       | 4.8       | 15.8       | 0.265   |
| CRYO OR       | 0.0       | 5.3        | 0.475   |
| CRYO ICU      | 0.0       | 0.0        | 1.0     |
| DOPAMIN OR    | 0.0       | 5.3        | 0.475   |
| DOPAMIN ICU   | 0.0       | 5.3        | 0.475   |
| EPI OR        | 28.6      | 42.1       | 0.51    |
| EPI ICU       | 28.6      | 26.3       | 0.578   |
| NOREPI OR     | 0.0       | 5.3        | 0.475   |
| NOREPI ICU    | 4.8       | 0.0        | 0.525   |
| Milrinone OR  | 19        | 10.5       | 0.381   |
| Milrinone ICU | 19        | 21.1       | 1.0     |

 
 Table 5. Blood Products Transfusion of Two Groups of Patients Receiving Two Cardioplegia Solutions Del Nido<sup>®</sup> and Custodiol<sup>® a</sup>

Abbreviations: CRYO, plasma cryoprecipitate, EPI, epinephrine; FFP, fresh frozen plasma; ICU, intensive care unit; NOREPI, norepinephrine, OR, operating room; PC, pack cell, PLT, platelet.

<sup>a</sup>Data are presented as relative frequency percent of the patients receiving the specific item of the blood and blood components during operation or in the intensive care unit (ICU) to all patients in that group.

cardioplegia solutions in comparison with conventional multi-dose cardioplegia solutions (1, 10, 14, 20). Therefore, it appears that this finding can also be justified by the results of previous studies.

In summary, it appears that the cardioprotective properties of the DN and Custodiol<sup>®</sup> cardioplegia solutions during CPB are comparable. Therefore, the choice of one of these single-dose cardioplegia solutions is very dependent on its availability, pricing, and the choice of the surgeon, perfusionist and the anesthesia team. However, a major concern exists over its use in patients susceptible to severe electrolyte disturbances. Since electrolytes imbalance raise due to various reasons, such as hormonal imbalance, renal dysfunction or use of specific medications (e.g. diuretics) (28, 29) may cause serious damage to multiple organs including the brain, kidneys, and other critical organs (30, 31), special care should be taken in case of patients susceptible to electrolytes imbalance. It is recommended to restrict the use of Custodiol<sup>®</sup> in these patients to prevent the adverse outcomes linked to electrolyte imbalance during and after CPB.

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