Evaluation of the effects of phosphorylcholine coated membrane oxygenators on renal functions in cardiac surgery patients

Arda Ozyuksel1, Ahmet Baris Durukan2, Hasan Alper Gurbuz2, Mustafa Yilmaz3, Riza Dogan3, Metin Demircin3, Ilhan Pasaoglu1

1Department of Cardiovascular Surgery, Medipol University, Istanbul, Turkey
2Department of Cardiovascular Surgery, Medicana International Ankara Hospital, Ankara, Turkey
3Department of Cardiovascular Surgery, Hacettepe University, Ankara, Turkey
*Corresponding Author: Medipol Üniversitesi Kalp ve Damar Cerrahisi Bölümü, TEM Otoyolu Göztepe Çokuşu No:1, Bağcılar, İstanbul Tel: +902124607777
e-mail: ozyukselarda@yahoo.com

Key words: Cardiopulmonary bypass; coronary artery bypass; oxygenators membrane; renal insufficiency; albuminuria

Received: 16.08.2013 Accepted: 27.08.2013 e-published: 30.08.2013

Abstract

Objectives: Acute and chronic renal injury has an important effect on the surgical outcome of cardiovascular diseases in terms of morbidity and mortality. The coating techniques which have been significantly improved in the recent years aim to decrease the contact of blood with foreign surfaces in the cardiopulmonary bypass. The aim of this study is to research the effects of phosphorylcholine coating in the membrane oxygenators of cardiopulmonary bypass on renal functions in patients undergoing cardiac surgery.

Materials and Methods: Thirty patients undergoing cardiac surgery were included to the study. Phosphorylcholine coated membrane oxygenator was used in one group (group 1) (n=15) and membrane oxygenator without coating with phosphorylcholine (group 2) (n=15) was used in the other group of patients. Preoperative and postoperative blood and urine analysis were obtained and data between the two groups were compared in order to evaluate the alterations in renal function.

Results: Although plasma sodium and potassium as well as urine creatinine and microalbumin levels showed statistically significant difference within the groups, these values were not statistically different between the study groups. In both groups, creatinine clearance levels did not differ significantly. When the data within the groups are evaluated, creatinine clearance had a decrease in the early postoperative period whereas it increased over the preoperative levels in the third day after the operation. This situation did not show any statistical significance in the group 2 but the group 1. In our study groups, urine microalbumin analysis showed an increase in the early postoperative period, but then a steep decline was observed in the postoperative third day, which still has a value more than the preoperative one.

Conclusions: Postoperative renal dysfunction is a multi-factorial entity with a wide spectrum of clinical presentations. The applied cardiac surgical procedure has a definitive role on the fate of renal failure. Although blood urea nitrogen and serum creatinine levels did not show statistically different variation, creatinine clearance was even increased in the study group.

Introduction

Acute and chronic renal insufficiency still has an important role on morbidity and mortality of cardiac surgery today. Although development of clinically significant renal insufficiency is relatively rare, in the worst scenario, postoperative renal failure necessitating hemodialysis increases the mortality by tenfold (1).

Cardiopulmonary bypass (CPB) is related with a high degree of inflammation due to the effects of laminar blood flow, contact with foreign surface, cold cardiac ischemia and hypothermia. Postoperative complications in relation with renal, pulmonary, cardiac and renal dysfunction are clinically named as ‘post perfusion syndrome’. Following the contact of blood with foreign surface, complement system and leukocyte activation plays additive role in the development of this syndrome (2). At least five plasma proteolytic systems (coagulation, fibrinolysis, complement cascade, kallikrein-kinin pathway and contact cascades) and three cellular systems (leukocytes,
thrombocytes and endothelial cells) are known to be activated following the initial contact of blood with the foreign surface of CPB(3).

The pathophysiology of the renal damage development is multi factorial. Preoperative renal diseases, diabetes mellitus (DM), impaired left ventricle functions and advanced age at operation may have adverse effects on renal functions of patients at whom cardiac surgery procedures are performed. CPB leads to some adverse effects on renal functions (RF) especially related with renal blood flow and distribution. Non pulsatile flow, hypothermia and hemodilution may also affect the RF. In the last decade, some other parameters like high plasma homocysteine levels are blamed for glomerular cellular damage and fibrosis which may have additive effects on the development of postoperative renal failure(4).

Postoperative renal dysfunction is encountered in a wide spectrum such as subclinical signs to end stage renal failure necessitating hemodialysis. Acute renal damage is experienced in up to 30% of patients following cardiac surgery (5). This condition significantly increases the morbidity and mortality of cardiac operations as well as the intensive care unit stay and costs (6).

The coating techniques which have been significantly improved in the recent years aim to decrease the contact of blood with foreign surfaces in the CPB. Modifications of the CPB surfaces can be performed with various techniques such as chemical coating, addition of macro molecules or mixing the hydrophilic and hydrophobic surfaces (7). Phosphorylcholine is one of the main components of the cell membrane. The blood of the patient contacts with a surface mimicking the surface of the vessels following the coating of CPB. Recent studies indicate that the thrombogenic, toxic and allergic reactions are minimized by this method of coating which also does not lead to any immunologic or carcinogenic effect (8, 9).

The aim of this study is to research the effects of phosphorylcholine coating in the membrane oxygenators of CPB on renal functions in patients undergoing cardiac surgery

Materials and Methods

The study was approved by Instutional Ethics Committee (HEK 08/118) and informed consent was obtained from the patients. The study applies the guidelines of the Declaration of Helsinki. Thirty patients undergoing cardiac surgery were included to the study. Phosphorylcholine coated membrane oxygenator (Phosphorylcholine Inert Surface-Phisio, D-903 Avant®, Dideco, Mirandola, Italy) was used in one group (group 1) (n=15) and membrane oxygenator without coating with phosphorylcholine (Dideco EVO CompactFlo®, Dideco, Mirandola, Italy) (group 2) (n=15) was used in the other group of patients.

Cardiac surgery procedures such as coronary artery bypass grafting (CABG), valvular replacements, ascending aorta replacements and atrial septal defects were included in the group 1. In order to obtain a more homogenous patient profile in the group 2, only on pump CABG patients were included.

The preoperative exclusion criteria were determined as low left ventricle ejection fraction (below 30%), hepatic failure, hemorrhagic diathesis and/or diseases with tendency for hemorrhage, acute/chronic renal insufficiency, reoperative cardiac surgery and operations performed under emergency conditions.

Anesthesia Protocol

The patients were administered 10 mg (p.o.) diazepam the night before the surgery and 10 mg (p.o.) on the day of surgery. The induction of anesthesia was performed with ethomidate 0.3 mg/kg (i.v.) and fentanyl 1µgr/kg (i.v.). In order to provide muscle relaxation, vecuronium bromide 0.1 mg/kg (i.v.) was administered before endotracheal intubation. The maintenance of anesthesia was provided with sevoflurane (2% inspiration concentration) that was applied with nitrogen oxide and oxygen mixture (1:1). Heparin sulphate (3mg/kg) was administered into the right atrium by the surgeon prior to aortic cannulation. The activated clotting time (ACT) was maintained above 480 seconds during the CPB. Following the termination of the CPB, circulating heparin was neutralized with protamine sulphate (1 to 1.3 fold dosage of heparin).

Extracorporeal Circulation Protocol

The roller pump (Jostra HL 20 Classical, Maquet Cardio-pulmonary AG, Hirrlingen, Germany) was used in CPB in all patients. CPB circuits were primed with 1600-1800mlt ringer lactate solution. 1ml/kg mannitol and 25mgr heparin were added to the prime solution. Following the aortic cannulation, non-pulsatile CPB was initiated with a mean perfusion pressure of 50-70 mmHg and a flow rate of 2.0-2.4 L/min/m2. Moderate hypothermia (nasopharyngeal measurement 28-32°C) was employed. The hematocrit level was maintained above 24% with addition of erythrocyte suspensions to the CPB below this level.

Cannulation and Cardioplegia Protocol

Ascending aorta was cannulated in all cases but two operations for ascending aortic aneurysm, in which right femoral artery access was used. The venous cannulation was provided with two stage or bicaval venous cannulas. In order to administer the cardioplegia, the ‘Y’ cannulas were inserted.
into the aorta distal to the sinotubular junction. Selective coronary ostial administration was used in cases with severe aortic insufficiency or aortic aneurysm. 10-15 ml/kg cold blood cardioplegia was administered with addition of 20mmol/L potassium. The dosage was repeated every 20 minutes during the CPB. Retrograde cardioplegia was not used.

Biochemical Analysis and Evaluation of the Patient Data

The preoperative demographic data and the medical history of the patients were recorded. Serum sodium, potassium, chloride, urea, creatinine, calcium and phosphorus as well as urine protein, sodium, potassium, chloride and creatinine levels were analyzed (urine analysis-UA). Renal function tests (RFT) were analyzed preoperatively (preoperative RFT), postoperatively in the first (postoperative RFT-1), twenty fourth (postoperative RFT-2) and seventy second (postoperative RFT-3) hours. The urine samples were evaluated and creatinine clearances were calculated in the preoperative period (preoperative UA) as well as in the twenty fourth (postoperative UA-1) and seventy second hours (postoperative UA-2). The operative and postoperative data of the patients were recorded and evaluated.

Statistical Analyses

Statistical analysis was performed with SPSS software for Windows (version 17.0) (Statistical Package for the Social Sciences - SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as ‘mean values ± standard deviation (SD)’ and median values. The categorical variables were expressed as number and percentages. The demographic characteristics and outcomes of the groups were compared using ‘Mann Whitney U Test’ for continuous variables and ‘chi-square test’ and ‘Fisher’s exact test’ for categorical variables. The variables within the groups were compared by means of variance analysis (Friedman Test). Statistical significance was set as p<0.05.

Results

The average age of the patients in group 1 and 2 were 53.6 ± 17.5 and 59.8 ± 8.6 respectively. The average body mass index values were 26.5 ± 5.6 and 29.0 ± 5.3 respectively. The preoperative demographic properties of the patients in both groups are shown in table 1. The average left ventricle ejection fraction in group 1 and 2 was 63.2 ± 7.1 % and 58.1 ± 7.7 % respectively (p>0.05).

The operative and postoperative descriptive properties of the patients are summarized in table 2. Low cardiac output or requisite for intraaortic counter pulsation (IABP) was not encountered in any patient in both groups. Moderate doses of dopamine (<7.5 µgr/kg/min) was administered in 20% and &.7 of the patients in group1 and 2 respectively (p>0.05).

The averages and standard deviations of the operative and postoperative properties of the patients are shown in the table 3. Any statistical difference was not encountered between the study groups when the CPB time, cross clamping time, postoperative drainage, extubation time and intensive care unit stay are considered.

When the tests about renal functions are considered serum and urine analysis are summarized in table 4 and 5 respectively. Although plasma sodium and potassium as well as Urine creatinine and microalbumin levels showed statistically significant difference within the groups, these values were not statistically different between the study groups. Creatinine clearance distribution in the study groups are shown in Table 6.

Discussion

Postoperative renal dysfunction is a multi-factorial entity with a wide spectrum of clinical presentations. Although many studies have evaluated the postoperative data in order to determine RF disorders, any consensus on the definition has still not been determined. Some authors compare the serum creatinine levels of the patients in the preoperative and postoperative periods, whereas others consider RF disorder when the elevation of the creatinine levels above a basal value is encountered. Glomerular filtration rate and urine output seems to be a more accurate determinant for RF alterations (10).

The applied cardiac surgical procedure has a definitive role on the fate of RF. When CABG is considered, the incidence of acute renal injury and necessity of hemodialysis is as low as 2.5% and 1% respectively, whereas these incidences rise up to 2.8% and 1% for valvular surgery; 4.6% and 3.3% for combined valvular and coronary bypass surgery (1,11).

We aimed to setup two homogenous study groups when the preoperative properties are concerned. Although group 1 was including patients with different cardiac surgical interventions, group 2 was including only the CABG patients. There was not any statistical difference when the preoperative and intraoperative properties are evaluated.

In both groups, creatinine clearance levels did not differ significantly. When the data within the groups are evaluated, creatinine clearance had a decrease in the early postoperative period whereas it increased over the preoperative levels in the third day after the operation. This situation did not show any statistical significance in the group 2 but the group 1. This condition may be related to the low number of the patients in both groups.

Microalbuminuria is a valuable marker for the determination of acute renal injury.
of renal damage. In our study groups, urine microalbumin analysis showed an increase in the early postoperative period, but then a steep decline was observed in the postoperative third day, which still has a value more than the preoperative one. In our both groups, microalbuminuria shows a statistically significant increase, which may be related to the increased capillary permeability as a result of CPB usage.

In conclusion, we aimed to research the phosphorylcholine coated oxygenator effect on the renal functions in patients undergoing cardiac surgery. Although blood urea nitrogen and serum creatinine levels did not show statistically different variation, creatinine clearance was even increased in the study group. These findings should be confirmed on larger study groups.

Acknowledgements

None

Conflicts of Interest

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

References