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Original Article / Özgün Makale

The effect of renal dose dopamine use on renal tubular function in diabetic patients undergoing coronary artery bypass graft surgery

Koroner arter baypas greft cerrahisi yapılan diyabet hastalarında renal doz dopaminin renal tübüler fonksiyon üzerine etkisi

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Background: This study aims to evaluate clinical results of the prophylactic use of renal dose dopamine infusion in diabetic patients undergoing coronary artery bypass grafting (CABG).

Methods: In this prospective randomized study, 40 consecutive diabetic patients who were scheduled for elective CABG were randomized into two equal groups: group 1 received dopamine infusion at renal dose (2.5-4.0 mg/kg/min) starting from induction of anesthesia for 48 hours; group 2 consisted of untreated controls. Standard sternotomy technique using aortic and right atrial cannulation was performed for cardiopulmonary bypass.

Results: Daily urine output, fluid balance, serum creatinine, blood urea levels and creatinine clearance were measured at three and five days. In the control group, third and fifth postoperative day, creatinine clearance levels decreased about 24.8±12.3 mL/min and 18.1±10.1 mL/min, respectively. In the dopamine group, creatinine clearance levels in the third and fifth postoperative days increased by 7.7±10.8 mL/min (p=0.005) and 10.7±11.7 mL/min (p=0.001), respectively. Group 1 patients demonstrated less increase in serum creatinine level at three and five days than the controls (p<0.001).

Conclusion: Creatinine and creatinine clearance levels, suggestive of renal tubular function, were positively affected by renal dose dopamine infusion started at time of anesthesia induction. Our data may help us to re-normalize the renal functions in the postoperative period in diabetic patients, particularly.

Keywords: Coronary artery bypass grafting; diabetes mellitus; renal dose dopamine; renal dysfunction.

Amaç: Bu çalışmada koroner arter baypas greftleme (KABG) yapılan diyabet hastalarında renal doz dopamin infüzyonunun profilaktik kullanımının klinik sonuçları değerlendirildi.

Çalışma planı: Bu prospektif randomize çalışmada elektif KABG yapılması planlanan 40 ardışık diyabet hastası iki eşit gruba randomize edildi: grup 1'e anestezi indüksiyonundan itibaren 48 saat süreyle renal dozda (2.5-4.0 mg/kg/dk.) dopamin infüzyonu verildi; grup 2 ise tedavi edilmemiş kontrollerden oluşuyordu. Kardiyopulmoner baypas için aortik ve sağ atriyal kanülasyonu ile standart sternotomi tekniği uygulandı.

Bulgular: Günlük idrar çıkışı, sıvı dengesi, serum kreatinin, kan üre düzeyleri ve kreatinin klirensi üç ve beşinci günlerde ölçüldü. Kontrol grubunda ameliyat sonrası üçüncü ve beşinci günlerde kreatinin klirens düzeyleri sırasıyla 24.8±12.3 mL/dk ve 18.1±10.1 mL/dk azaldı. Dopamin grubunda ameliyat sonrası üçüncü ve beşinci günlerde kreatinin klirens düzeyleri sırasıyla, 7.7±10.8 mL/dk. (p=0.005) ve 10.7±11.7 mL/dk. (p=0.001) arttı. Kontrol grubuna kıyasla, grup 1'deki hastaların serum kreatinin düzeyinde üçüncü ve beşinci günlerde daha az artış görüldü (p<0.001).

Sonuç: Renal tübüler fonksiyonun göstergesi olan kreatinin ve kreatinin klirens düzeyleri, anestezi indüksiyonun başladığı zaman renal doz dopamin infüzyonu ile pozitif etkilendi. Verilerimiz, özellikle diyabet hastalarında ameliyat sonrası renal fonksiyonların yeniden normalleşmesine katkıda bulunabilir.

Anahtar sözcükler: Koroner arter baypas greftleme; diabetes mellitus; renal doz dopamin; renal fonksiyon bozukluğu.

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Renal dysfunction is a common complication in open heart surgery in which multiple etiological factors lead to renal hypoperfusion and ischemic injury to the kidney.[1] In addition, renal blood flow decreases by approximately 30% during cardiopulmonary bypass (CPB) and is accompanied by an increase in renal vascular resistance. The subsequent ischemia impairs both glomerular and tubular functions. In low doses, dopamine augments renal blood flow principally by inducing intrarenal vasodilatation, and increasing cardiac output.[2]

Various factors contribute to the development of postoperative renal failure, including postoperative low cardiac output, the need for an intraaortic balloon pump (IABP), emergency surgery, an extended CPB time, older age, diabetes mellitus (DM), and preoperative renal dysfunction.[3]

Keeping this in mind, a prospective randomized study was performed on diabetic patients who underwent coronary bypass surgery in order to evaluate the clinical results of the prophylactic use of renal-dose dopamine perfusion.

PATIENTS AND METHODS

This was a prospective, double-blind, randomized trial. After obtaining the approval of the local ethics committee at our university clinic and the written informed consent of the patients, 40 consecutive diabetic patients who planned to undergo elective surgery were prospectively randomized into two equal groups. Group 1 included those who received a renal-dose dopamine infusion (2.5-4.0 mg/kg/min) for 48 hours beginning from the induction of anesthesia, whereas group 2 was made up of patients who served as untreated controls. The measured data included daily urine output (ml/kg), fluid balance (input/output), and serum creatinine and blood urea nitrogen levels as well as creatinine clearance levels at the third and fifth days.

Coronary bypass surgery with CPB was performed on all patients, all of whom were diabetic and had no known preoperative renal dysfunction. Patients undergoing off-pump coronary artery bypass graft (CABG) surgery associated with heart valve replacement or repair and those who had previously undergone a resection of a ventricular aneurysm or an extracardiac surgical procedure were excluded from the study. Other exclusion criteria included patients with preoperative serum creatinine levels of >1.5 mg/dl, an ejection fraction (EF) of <30%, and bleeding of more than 1000 ml in the first 24 hours after the operation In addition, patients over the age of 70, those with myocardial infarction (MI) within the last month, and those using an IABP were also not included.

Fentanyl-based general anesthesia in combination with vecuronium as a muscle relaxant were used for all of the patients, and they were ventilated with 10 ml/kg tidal volume and 4 cm H_2O of positive end-expiratory pressure (PEEP). The renal-dose dopamine perfusion was initiated with the induction of anesthesia in group 1. None of the inotropic agents were used for the patients in group 2.

The standard sternotomy technique involving aortic and right atrial cannulation was performed for the CPB under moderate (32 °C) hypothermia, and intermittent antegrade cold blood cardioplegia (10 °C) was employed every 20 minutes.

Once the surgery was completed, each patient's hemodynamic condition was monitored by measuring the systemic arterial and right atrial pressure, and central venous pressure was maintained between 8 and 12 mmHg with the use of Gelofusine® (B. Braun Medical Ltd., Melsungen, Germany). Donor blood transfusion was only indicated when the hematocrit levels fell below 28%.

Statistical comparisons were made using the Mann-Whitney U test and an independent t-test. In addition, the changes in creatinine and creatinine clearance levels in the third and fifth postoperative days were evaluated via a paired t-test. Values of $p<0.05$ were accepted as being statistically significant with a 95% confidence interval (CI).

RESULTS

The demographic and operative data are shown in Table 1. No differences were detected between the preoperative and operative variables of the two groups regarding age, blood glucose, urea, creatinine, body surface area (BSA), CPB time, cross-clamp time, or number of bypass vessels ($p>0.05$ for all).

The blood urea nitrogen, creatinine, and creatinine clearance levels were evaluated at the postoperative third and fifth days, and the results are shown in Table 2. In group 2, the postoperative third and fifth day creatinine clearance levels decreased by approximately 24.8±12.3 mL/min and 18.1±10.1 mL/min, respectively, both of which were statistically significant ($p<0.001$).

In contrast, the creatinine clearance levels in the postoperative third and fifth days for group 1 increased by 7.7±10.8 mL/min ($p=0.005$) and 10.7±11.7 mL/min ($p=0.001$), respectively, and these amounts were also statistically significant.

Table 1. Preoperative and operative variables of the patients

	Group 1	Group 2	
	Mean±SD	Mean±SD	*p*
Age (years)	61.3±6.2	63.1±5.8	0.3**
Blood glucose (mg/dL)	163.1±13.6	171.9±4.9	0.1**
Urea (mg/dL)	38.8±4.2	41.5±11.5	0.5**
Creatinine (mg/dL)	1.1±0.1	1.01±0.2	0.1*
Creatinine clearance (mL/min)	81.5±9.6	86±9.8	0.1*
Body surface area (m^2)	1.8±0.05	1.83±0.09	0.5**
Cardiopulmonary bypass time (min)	98±12	103±15	0.6**
Cross clamp time (min)	59±8.7	61.7±13	0.43*
Number of bypasses	3.1±0.8	3.1±0.9	0.8**

SD: Standard deviation; * Independent t-test; ** Mann-Whitney U test.

Furthermore, the patients in group 1 demonstrated less of an increase in the serum creatinine levels on the third and fifth days than group 2 ($p<0.001$).

DISCUSSION

The incidence of renal dysfunction following open heart surgery varies between 0.1 and 39%, depending on the criteria that is used,[4] and the extent of the dysfunction can range from subclinical to full-blown acute renal failure that requires replacement therapy. Hashimoto et al.[5] reviewed the pertinent literature and suggested that acute renal dysfunction secondary to cardiac surgery may have both glomerular and tubular components.[5] The traditional tests for measuring renal function in clinical practice focus on the serum creatinine and creatinine clearance levels, which are primarily related to glomerular filtration.

The etiology of renal dysfunction can be categorized according to preoperative, perioperative, and postoperative factors, with elevated preoperative creatinine levels being crucial for the development of renal functional impairment following open heart surgery. Other factors which may be involved are impaired ventricular functions, emergency surgery, diabetes mellitus (DM), and advanced age. Furthermore, the total length of time spent on CPB is also known to adversely affect renal functions because of the presence of free plasma hemoglobin, elastase, endothelin, and free oxygen radicals.[6] In addition, Kron et al.[7] reported that non-pulsatile flow, renal hypoperfusion, and hypothermia can also adversely affect renal functions.

The use of prophylactic renal-dose dopamine is somewhat controversial. For years it was thought to be effective for preventing renal functions during CPB, but Keller and Decker[8] determined that dopamine has diuretic effects but no renoprotective action.

Moreover, Tang et al.[9] evaluated the levels of retinol binding protein (RBP), a marker of early renal tubular necrosis, and reported that renal-dose dopamine offered no renal protection for patients with normal heart and kidney functions who undergo elective coronary surgery. In the study by Woo et al.,[10] they found that renal-dose dopamine infusion provided no benefits for patients who were at risk for renal dysfunction following cardiac surgery, and Gatot et al.[3] showed that prophylactic dopamine administration after CABG surgery improved

Table 2. Blood urea, creatinine and creatinine clearance values in the early postoperative follow-up

	Group 1	Group 2	
	Mean±SD	Mean±SD	*p*
Blood urea (3rd day) (mg/dL)	53±4.5	57±7	0.003*
Blood urea (5th day) (mg/dL)	44.7±3.6	53.7±4.6	<0.001*
Creatinine (3rd day) (mg/dL)	1.08±0.07	1.36±0.2	<0.001*
Creatinine (5th day) (mg/dL)	0.9±0.08	1.25±0.17	<0.001*
Creatinine clearance (3rd day) (mL/min)	87.2±5.6	61.2±10.6	<0.001*
Creatinine clearance (5th day) (mL/min)	90.2±5.8	67.8±9.9	<0.001*

SD: Standard deviation; * Mann Whitney U test.

patients' hemodynamic and renal status and reduced the need for additional medical support, thereby providing a stable postoperative course. The dopamine dose regimen was 2-4 μg/kg/min for all of the aforementioned studies, and the patient groups were homogenously created. In the Woo et al.[10] study, they particularly selected patients who were at risk for renal dysfunction (older patients and those with a pre-existing renal disease, elevated preoperative serum creatinine levels, poor ventricular function, hypertension, and unstable angina requiring intravenous therapy. However, none of these studies clearly identified how the risk factors were directly related to the dopamine infusion.

Coronary artery disease (CAD) is the leading cause of death among adult patients with DM and accounts for an approximately three-fold increase in the risk of death versus those patients without DM.[11] Diabetes mellitus is commonly seen in a majority of CABG patients, and several preoperative risk factors for postoperative renal dysfunction have been identified, such as advanced age, a history of moderate-to-severe congestive heart failure, prior CABG surgery, type 1 DM, and preexisting renal disease.[12] When evaluating the diabetic patients in this study, we thought that it would be more valuable to investigate whether or not renal-dose dopamine infusion had any effect on them, so we designed our study with this in mind and performed a statistical search to determine whether the renal functions of diabetic patients who underwent CABG surgery demonstrated any correlation with renal-dose dopamine infusion. We made a conscious decision to enroll patients with no renal impairment in our study because the possible correlation that we were looking for would have been impaired in patients with more severe renal dysfunction. Since renal functions are severely affected during the cardiac operation process and because we were searching for the prophylactic renal protective effect of dopamine, we decided to give the infusion starting as the time of anesthesia induction. Our findings indicated that there were statistically significant changes between the two groups in our study regarding both the preoperative and postoperative creatinine and creatinine clearance levels, which suggests that the renal-dose dopamine infusion might help to renormalize renal functions in the postoperative period, especially in diabetic patients who are at high risk.

Conclusion

The complication of renal dysfunction after open heart surgery is not uncommon, but diabetic patients fall into a special category since they have an increased risk for renal impairment in the postoperative period. In our study, the creatinine and creatinine clearance levels were positively affected by renal-dose dopamine infusion started at the time of anesthesia induction. We believe that this data could help reestablish normal renal functions in the postoperative period, especially in diabetic patients. Hence, our results suggest that dopamine infusion might be clinically beneficial, especially in patients with impaired or slightly impaired renal functions.

Declaration of conflicting interests

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