

ORIGINAL ARTICLE

Effects of different methods of diuresis on renal function of patients receiving kidney transplantation: A randomized, controlled, double-blind trial

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ABSTRACT

Objectives: A number of pharmacological methods are being used for preserving the function of the transplanted kidney; however, their effects on the future performance of these kidneys remain controversial. We aimed to compare the effects of different methods of induced diuresis on the function of transplanted kidneys.

Methods: This randomized, controlled, double-blind trial was conducted among 140 candidates of renal transplantation. They were randomly assigned into four equal groups of 35 patients each: control group (receiving furosemide and mannitol), group receiving dopamine, group receiving aminophylline, and group receiving a hyperosmolar solution containing dextrose and sodium bicarbonate (forced diuresis group). To assess renal function, urine volume, creatinine clearance, urinary sodium excretion, and serum creatinine were measured. Data were analyzed using SPSS software. Pearson correlation and analysis of variance (ANOVA) tests were used as appropriate.

Results: Age and gender distribution of kidney graft recipients and donors of transplanted kidneys had no statistically significant difference among the four studied groups. During the first postoperative day, creatinine clearance was significantly higher in the groups receiving either dopamine or forced diuresis compared with other groups. Likewise, in the first 2 hours after surgery the mean urinary output and creatinine clearance were significantly higher in the groups receiving either dopamine or forced diuresis.

Conclusion: The stimulation of transplanted kidneys by dopamine and using forced diuresis were the best methods in increasing the surrogate markers of renal function, i.e. urinary output, and creatinine clearance. They may be suggested as methods of choice for supporting the function of transplanted kidneys.

Key words: Kidney transplantation; Renal function; Diuresis; Mannitol; Dopamine; Aminophylline

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INTRODUCTION

Kidney transplantation is considered as the best and cost-effective method for the treatment of chronic

renal failure. In addition to providing a better quality of life for the patients, it can reduce the mortality rate by 40-60%.¹ The survival of the kidney tissue is a major concern for the anesthesiologists, the surgeons and the

nephrologists, and much effort is required to protect the transplanted kidney and to increase its survival.^{2,3} Most of the strategies adopted to protect the kidneys have largely been based upon previous studies on the subject. In this regard, some animal studies and clinical trials have been performed. Large clinical trials for the evaluation of the predictors of renal lesions in patients undergoing surgery did not yield favorable results.

The common methods for protecting the transplanted kidney include intravenous hydration, using mannitol, dopamine, loop diuretics, and/or a combination of these methods.^{4,6} By influencing the dopamine receptors in renal arteries, dopamine increases the production of cyclic adenosine monophosphate, and results in vasodilatation.^{7,8} However, the benefits of dopamine in renal transplantation still need to be determined.^{9,10}

Mannitol is another medication with confirmed protective effects during surgical procedures using aortic cross-clamping.^{11,12} Most studies suggest that in addition to using such medications, preserving intravascular volume at the optimal level is of crucial importance.^{4,13}

Considering the growing success rates in kidney transplantation, maintaining its performance becomes more and more important. In this regard, anesthesiologists have a pivotal role in protecting the transplanted kidney by suitable diuresis during and after the surgical procedure. Given the existing controversies in this field, we aimed to compare the effects of different medications on diuretic capabilities of transplanted kidneys.

METHODOLOGY

This randomized, controlled, double-blind trial was conducted during 2006-2007 among 140 patients, suffering from end-stage renal disease, who were candidates for kidney transplantation in Nemazee Teaching Hospital affiliated to Shiraz University of Medical Sciences, Shiraz, Southern Iran. This study was approved by the Ethics Committee of the mentioned university.

Patients below 15 or above 60 years of age, those with symptomatic congestive heart failure, pericarditis, and myocardial dysfunction on echocardiography before surgery, and/or a history of current treatment for ischemic heart disease were not included in the trial. Those patients with hypernatremia, hyperglycemia and/or a history of diabetes mellitus were not included in the group receiving forced diuresis. Patients who developed surgical or non-surgical problems in diuresis

immediately after the surgery were also excluded from the trial.

The patients' demographic data, including age, sex, weight on the morning of surgery, the underlying renal disease, and the time of hemodialysis were recorded. The patients were randomly assigned to four groups of equal number using software of random allocation.

Anesthesia induction was similar in all the four studied groups. First, the following premedication was administered: 0.03 mg/kg of midazolam and 3 μ /kg of fentanyl. Then anesthesia was induced by thiopental sodium (4 mg/kg) and cisatracurium (0.15 mg/kg) as the muscle relaxant dose. The patients were intubated and anesthetized with isoflurane 1% in 50% each of oxygen and nitrous oxide. For maintaining adequate perfusion pressure, we kept the patients' systolic blood pressure and heart rate at 100-140 mmHg and about 80-100 beats per minute, respectively, and monitored pulse pressure.

Group 1 (control group) received an average of 3 lit/70kg normal saline solution plus 2 mg/kg furosemide and 500 mg/kg mannitol.

Group 2 received dopamine as infusion (3 μ g/kg/min) plus the drugs to the control group.

Group 3 received 3 mg/kg aminophylline, 10 minutes before arterial anastomosis, plus the drugs to the control group.

Group 4 (the forced diuresis group), instead of 500 ml normal saline, received 300 ml of dextrose 5%, plus 100 ml sodium bicarbonate and 100 ml mannitol 10%, and the rest of the needed liquid was provided by normal saline.

The same protocol was continued until the recovery time and resolution of anesthesia. The indices of renal function were studied from drug administration to 24 hours after the surgery. These indices were as follows:

- 1 - The volume of urine output in the operating room after the ureteral anastomosis until recovery
- 2 - The volume of urine output in the recovery room up to transfer to the ward
- 3 - The urine volume was measured in the ward for 24 hours.
- 4 - A homogeneous sample of 24-hour-urine was sent to the laboratory to assess the sodium and creatinine concentrations.

Moreover, serum creatinine was measured twice and

the mean value was used for calculating the creatinine clearance. All the patients were hemodialyzed the day before the transplantation in order to resolve the possible water retention and electrolyte imbalances.

Statistical analysis: Data were analyzed using SPSS software, version 11 (SPSS Inc., Chicago, IL, USA). Data are expressed as mean \pm standard error of mean (SEM). Independent *t* test was used to compare the mean values between two groups, and analysis of variance (ANOVA) for multiple group comparisons as well as Tukey post hoc test as appropriated. The intragroup and intergroup association of each two variables was assessed by the Pearson Correlation test. We also used Analysis of Curve Estimation by Regression where appropriated.

RESULTS

The demographic data of the patients are shown in Table 1. The mean \pm SEM age of the recipients was 36.18 ± 1.13 years. The sex distribution of patients receiving kidney transplants was similar with female preponderance in the three interventional groups without significant difference between groups. In the control group 60% of the recipients were men. The mean weight (60.75 ± 0.92) and the duration of hemodialysis before the transplantation was not significantly different among the groups studied ($P=0.98$ and 0.06 respectively). The duration of dialysis in of the patients before operations is shown in Table 2.

At the time of discharge from the ward and after successful kidney transplantation, the mean serum creatinine of the four groups studied was not significantly different. Table 3 presents the mean values of renal function markers in different groups before and after the kidney transplantation. In the first 2 hours after arterial and ureteral anastomosis, the mean urine output was significantly higher in the groups receiving dopamine and forced diuresis than the other two groups ($P < 0.05$). The urine output was significantly higher in the group receiving forced diuresis than in

the group receiving dopamine ($P < 0.05$). Likewise, the urine flow, i.e. urine volume/minute, was significantly higher in the groups receiving forced diuresis and dopamine than in the two other groups ($P < 0.05$). The increased urine output continued in the next day. We also found that the higher the amount of urine in the first two hours, the higher was the creatinine clearance in the first 24 hours after kidney transplantation ($P < 0.01$).

Table 2: Duration of dialysis of patients before operations

Groups	Time of dialysis before surgery (yrs)
Group 1 (Control)	1.92 \pm 0.38
Group 2	1.53 \pm 0.24
Group 3	1.61 \pm 0.21
Group 4	0.96\pm0.11
All groups	1.51 \pm 0.12

In the first day after kidney transplantation, the creatinine clearance was higher in the groups receiving forced diuresis and dopamine than in the other two groups ($P < 0.01$). The sodium excretion in the first 24 hours after surgery was higher in the group receiving dopamine than in other groups ($P < 0.01$). While the baseline serum creatinine level was not significantly different between the four groups studied, after the surgery it was significantly lower in the group receiving dopamine than in the other groups ($P < 0.05$).

DISCUSSION

In our study the urinary sodium excretion, the urine output, and creatinine clearance were higher in patients receiving either dopamine or forced diuresis than in the other groups. During surgery and in situations of hemodynamic instability, anesthesiologists rely on surrogate markers of renal function rather than on direct calculation of renal perfusion, which is not feasible in clinical settings. There is a large body of evidence on the necessity of optimization the hemodynamic status and

Table 1: Demographic data of the patients in all groups presented as Mean \pm SEM and percentage

Parameter		Group 1 (Control)	Group 2	Group 3	Group 4	P value
Age (years)*	Recipient	38.17 \pm 2.42	31.61 \pm 2.11	37.68 \pm 2.30	37.19 \pm 2.11	0.14
	Donor	34.48 \pm 2.34	33.17 \pm 1.71	37.15 \pm 2.61	31.19 \pm 1.71	0.24
Gender (%)	Men	60	34.5	38.2	19.4	<0.05
	Women	40	65.5	61.8	80.6	
Weight (kg)*		56.83 \pm 1.84	62.61 \pm 2.22	60.82 \pm 1.53	62.58 \pm 1.64	0.98

*(Mean \pm SEM)

Table 3: Markers of renal function in patients before and after kidney transplantation (Mean±SEM)

Markers	Group 1 Control	Group 2	Group 3	Group 4 (Forced diuresis)	P Value
Pre-operative serum creatinine	8.91±0.45	8.92±0.59	8.92±0.54	10.41±0.72	NS
Post-operative serum creatinine	4.22±0.45	*2.97±0.34	5.28±0.54	4.14±0.41	P<0.05
Urine volume after the first 2 hrs from the surgery	946.66±75.39	**1234.19±64.54	845.29±77.49	**1719.04±130.20	P<0.05
Urine volume after the first 24 hours from the surgery	9227±1321.31	**14140.97±1335.99	10125.29±1020.03	**14712.26±1411.37	P<0.05
Creatinine clearance	33.80±4.98	*67.47±4.95	36.73±4.30	*60.99±6.16	P<0.05
Urine sodium concentration	80.37±3.24	*98.45±1.51	82.06±2.36	77.94±1.43	P<0.01

the intravascular volume to protect renal function, and it is considered as the most effective method for preventing the risk of postoperative renal dysfunction^{12,14,15}.

Olsen found that a renal dose of dopamine increased the renal blood flow and the glomerular filtration rate, and was effective in increasing the urine output and the urinary salt excretion¹⁶. In Carmellini and Grundman’s study, dopamine reduced the incidence of renal dysfunction after kidney transplantation. This effect may have resulted from stimulation of dopamine receptors and in turn by renal artery vasodilatation, and improving the blood flow of the kidney cortex^{17,18}. In our study, patients receiving forced diuresis and dopamine had higher urine output than the other groups. Perdue suggested that although dopamine had beneficial effects and might increase the blood flow in the kidney cortex, the glomerular filtration rate, sodium excretion, and urine production, it could also have harmful effects on the kidney function. He proposed that producing large volumes of urine after dopamine administration might not be a sign of improvement in renal function¹⁹. It is reported that urinary sodium is not a specific ratio to assess renal function, and this function is associated with the amount of sodium intake, diuretic therapy, and sympathetic tone²⁰.

In our study, the urine output in the first two hours, the urinary volume in the first 24 hours, and the first day creatinine clearance of the patients who received aminophylline were not better than the other groups. In Shin and Rosenberg’s studies on treatment with different diuretics, they did not document any relationship between creatinine clearance and urine production. They concluded that increase in urinary

output was not necessarily associated with higher creatinine clearance^{21,22}. This finding is confirmatory evidence that urine excretion cannot be used as an appropriate predictor for future kidney damage²³. Shinn and Sladen also showed that creatinine clearance was the best available test for evaluating the glomerular filtration rate, and can be used in the evaluation of renal reserve^{21,23}.

In our trial, creatinine clearance was associated with urine output, and was higher in groups receiving dopamine and forced diuresis than in other groups. Moreover, urinary sodium was not associated with creatinine clearance and urine volume excretion. It can be assumed that in addition to sodium excretion (natriuresis), some other factors may influence the urinary output.

CONCLUSION

In our study, increased urinary output was associated with higher creatinine clearance in patients receiving dopamine and forced diuresis. The stimulation of transplanted kidneys by dopamine and using forced diuresis were the best methods in increasing the surrogate markers of renal function, i.e. urinary output, and creatinine clearance. They may be suggested as methods of choice for supporting the function of transplanted kidneys. Studies with long-term follow-ups are necessary to determine the effects of various medications on renal function after kidney transplantation.

Conflict of interest: None to declare

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Quotations

"No one know, till he tries, how easily a habit of walking is acquired. A person who never walked three miles will in the course of a month become able to walk 15 or 20 without fatigue...Should you be disposed to try it, as your health has been feeble, it will be necessary for you to begin with a little and to increase it by degrees."

"It is your future happiness that interests me, and nothing can contribute more to it than the contracting a habit of industry and activity."

"Interesting occupations are essential to happiness."

Thomas Jefferson in 'Thomas Jefferson: Lessons from a Secret Buddha', by Suneel Dhand

Needless words

"Vigorous writing is concise. A sentence should contain no unnecessary words...for the same reason that a drawing should have no unnecessary lines and a machine no unnecessary parts. This requires not that the writer make all his sentences short, or that he avoid all detail and treat his subjects only in outline, but that every word tell." (Strunk & White, 1979, p.23). This advice is true about writing in general, but lean writing is particularly important in scientific writing, because of its emphasis on conveying quantitative information efficiently.

Use superlatives sparingly or not at all. If a word expresses an absolute quality or condition, the comparative has no place. You can almost always delete "very", "quite", "rather", "somewhat", and similar words.

Style Points for Scientific Writing

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