Influence of Hypernatremia and Polyuria of Brain-Dead Donors Before Organ Procurement on Kidney Allograft Function

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Introduction: Polyuria and hypernatremia are common problems during the pretransplant care of brain-dead donors. They have not only important role in hemodynamic stability, but also may influence organ transplantation outcomes. The influence of donor hypernatremia in liver transplantation was reported. This study aimed to determine these effects on kidney allograft.

Materials and Methods: We retrospectively studied on 57 transplanted kidney allografts from cadaveric donors. The effects of the urine output volume and serum level of sodium of the donors were on the recipients' serum creatinine levels 1 week after transplantation and at the last follow-up visit were assessed.

Results: Of the donors, 58% had polyuria and 45% had hypernatremia. The median pretransplant urine output of the donors was 130 mL/h (range, 35 mL/h to 450 mL/h), and their mean serum sodium level was 152.0 ± 13.0 mEq/L. Serum creatinine concentrations in the recipients at the 1st posttransplant week correlated significantly with the recipients' age ($r = 0.355$, $P = .02$) and the donors' urine output volume ($r = 0.329$, $P = .04$). The serum creatinine measured in the last follow-up visit significantly correlated only with the donors' serum sodium levels ($r = 0.316$, $P = .02$) and the donors' age ($r = 0.306$, $P = .02$). Multivariate regression analysis showed that the donors' serum levels of sodium and potassium were the predictors of the last measured serum creatinine level.

Conclusion: Polyuria and hypernatremia in brain-dead donors are frequent. Elevated serum level of sodium and polyuria in the donor can have adverse effects on kidney allograft function.

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INTRODUCTION

During the period before organ retrieval for cadaveric transplantation, polyuria and hypernatremia are two common findings that can compromise hemodynamic stability of the organs. These may be due to diabetes insipidus; central diabetes insipidus is present in 30% to 90% of the brain-dead donors,[1,2] resulting from insufficient blood levels of antidiurethic hormone from the posterior pituitary gland. Other causes of polyuria are hyperglycemia and administration of mannitol and diuretic drugs. Polyuria may lead to severe metabolic and hemodynamic disturbances during procurement. In this situation, substitution with common electrolyte solutions

will induce disturbances of water and electrolyte balance (edema, hyperosmolarity, hypernatremia, and hypokalemia) with deterioration of cell membrane and organ function.[2,3]

The influence of elevated serum sodium levels of the donor on early postoperative graft function has been reported in human liver transplantation.[4-6] However, there is a lack of knowledge on these effects on kidney transplant outcome. In the present study, we assessed the effect of elevated urine volume and hypernatremia on kidney transplantation outcomes.

MATERIALS AND METHODS

We reviewed our records of the kidney allograft recipients from the brain-dead donors. The allografts were retrieved between June 2005 and December 2007 in the organ procurement unit of Shariati Hospital in Tehran, Iran. During this period, a total of 141 organs were harvested from 46 brain-dead donors. Eighty-four of these organs were kidneys, half of which were transplanted at the same hospital and another half were transferred to other centers of transplantation sharing in the *Iranian Network for Transplant Organ Procurement*. We could collect the complete data of 69 kidney allograft recipients and analyzed 55 of those with functioning kidneys after transplantation in this retrospective study. All of the kidney allograft recipients were on prednisolone, cyclosporine, and mycophenolate mofetil for immunosuppressive therapy.

According to our protocol, management and maintenance of the donor was started since the initial brain death identification and continued for at least 24 hours. This time is necessary for re-evaluation of brain death and reconfirmation of the diagnosis by a group of specialists with legal authorization. During this period, if polyuria or diabetes insipidus was evident, volume substitution was preferably done with hypotonic solutions, ie, 2.5% glucose with 0.45% sodium chloride. Fluid substitution was controlled by continuous measurement of arterial blood pressure, central venous pressure, and hourly determination of urine output. Once urine output exceeded 300 mL/h or 4 mL/kg/h,

desmopressin (1 μg to 4 μg, every 8 to 12 hours) was administered.[3,7,8]

Data on polyuria (urine output of 125 mL/h or greater during the average 3 hours before organ retrieval) and hypernatremia (serum sodium level higher than 155 mEq/L) were collected and the donors were grouped accordingly (normal serum sodium level versus hypernatremia). Serum creatinine levels of the recipients and other characteristics of the donors and the recipients were compared between these groups. Serum creatinine levels at the end of the first posttransplant week and the latest follow-up visit were considered in this study.

Statistical analyses were performed using the SPSS software (Statistical Package for the Social Sciences, version 15.0, SPSS Inc, Chicago, Ill, USA). Data distribution was tested with the 1-sample Kolmogorov-Smirnov test. The recipients' serum creatinine levels, donors' urine volume, and donors' age were nonparametric variables. Correlations of quantitative variables were analyzed by Spearman rho correlation or Pearson correlation tests, where appropriate. Differences between the groups were assessed by the Mann-Whitney U test and t test. A P value less than .05 was considered significant.

RESULTS

A total of 55 kidney allograft recipients from 44 brain-dead donors were evaluated in this study. The median age of the donors was 25 years (range, 10 to 60 years). Two-thirds of them were men. The main causes of brain death were head trauma (70.5%), cardiac arrest, and intracranial hemorrhage. The time interval from the initial diagnosis of brain death to the retrieval of the organs was approximately 24 hours, and almost all transplantations were performed within 6 hours thereafter. Of the donors, 58% had polyuria and 45% had hypernatremia. The median pretransplant urine output of the donors was 130 mL/h (range, 35 mL/h to 450 mL/h). At the terminal phase, the donors had a mean serum creatinine of 1.25 $\pm$ 0.4 mg/dL, serum sodium of 152.0 $\pm$ 13.0 mEq/L, and serum potassium of 3.7 $\pm$ 0.7 mEq/L.

The mean age of the 55 recipients was 41.0 ± 14.0 years. Their median serum creatinine after 1 week of transplantation was 1.8 mg/dL (range, 0.8 mg/dL to 9.0 mg/dL). They were followed up for a median of 20 months (range, 2 to 36 months), and the median value of the last measured serum creatinine level was 1.4 mg/dL (range, 0.9 mg/dL to 5.0 mg/dL). These early and last serum creatinine values significantly correlated with each other (r = 0.311, P = .04). Of note, all except 3 patients had a follow-up period of at least 6 months, and excluding the 3 patients with shorter follow-ups did not alter the results of analyses.

Serum level of creatinine after 1 week significantly correlated with the recipients' age (r = 0.355, P = .02) and the donors' urine output volume (r = 0.329, P = .04). The linear correlation between the donors' urine output volume and the recipients' serum creatinine level after 1week of transplantation was more prominent in the group of recipients who had a donor with polyuria (r = 0.486, P = .02; Figure 1). Comparison of this finding with that in the group with normal urine output was difficult, because the high and low urine outputs could influence kidney function and make categorizations impractical.

Polyuria was not associated with the last measured serum creatinine level of the recipients. The last measured serum creatinine significantly correlated only with the donors' serum sodium levels (r = 0.316, P = .02; Figure 2) and the donors' age (r = 0.306, P = .02). Multivariate regression analysis showed that the donors' serum levels of sodium and potassium were the predictors of the last measured serum creatinine level (P = .03). The Table outlines the differences between the two groups of kidney allograft recipients with and without hypernatremia.
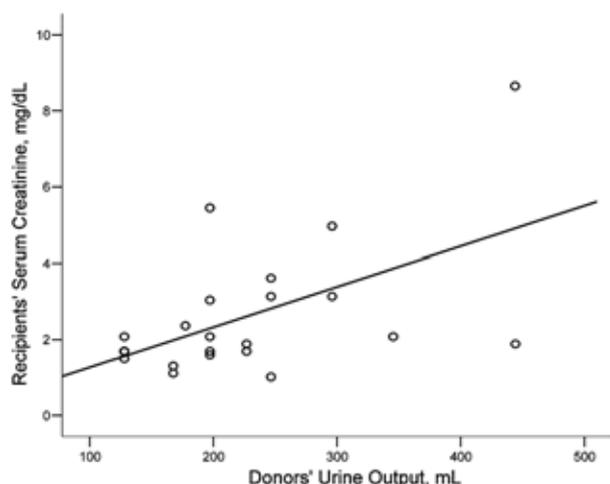

Figure 1. Correlation of the urine output volume of brain-dead donors with serum creatinine levels of their recipients 1 week after transplantation.
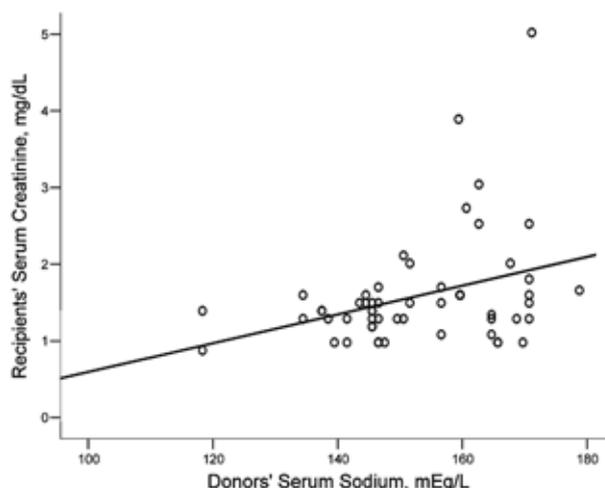

Figure 2. Correlation of the serum sodium level of brain-dead donors with the last measured serum creatinine of the recipients during the follow-up period.

Characteristics of Donors and Recipients in Two Groups With Different Pretransplant Serum Sodium Levels of Donors*

Characteristics	Serum Sodium of Donor		P
	≤ 155 mEq/L	> 155 mEq/L	
Donors			
Mean age, y	28.1 ± 11.8	28.2 ± 14.0	.71
Median urine volume, mL	130 (40 to 350)	170 (35 to 450)	.43
Mean serum creatinine, mg/dL	1.20 ± 0.40	1.27 ± 0.38	.45
Mean serum potassium, mEq/L	4.04 ± 0.54	3.45 ± 0.67	.002
Recipients			
Median serum creatinine after 1 week, mg/dL	1.8 (0.8 to 6.0)	1.9 (0.9 to 9.0)	.59
Median latest serum creatinine, mg/dL	1.3 (0.9 to 2.1)	1.6 (0.8 to 5.0)	.02

*Values are presented as mean ± standard deviation or median (range).

DISCUSSION

The most important goal of the care of brain dead potential organ donors is to stabilize their hemodynamic status. The management period of brain-dead donors takes at least 24 hours in our center to confirm brain death and prepare for organ retrieval. To control the hemodynamic status, serum sodium level and urine output should be monitored. Almost half of the donors in our series had polyuria (urine output greater than 125 mL/h) and hypernatremia. These findings are consistent with the results of other studies.[1,2] Polyuria and hypernatremia could be induced by central diabetic insipidus resulting from insufficient blood levels of antidiurethic hormone from the posterior pituitary gland of brain-dead patients.[2] Polyuria causes hypovolemia and impairment of the balance in electrolytes that contributes to decrease blood pressure and result in cardiovascular problem.[9] Therefore, it is necessary to evaluate urine output and serum electrolytes every 2 to 4 hours.[1] These parameters are not only important for donor maintenance and preventing cardiac arrest, but also are necessary for adequate tissue perfusion and preservation of organ viability. As we found in this study, hypernatremia and polyuria may influence kidney allograft function. Hypernatremia correlated to the serum creatinine levels of the recipients recorded in their last follow-up visits. We categorized the recipients with donors who had serum sodium levels lower and upper than 155 mEq/L and found that the serum creatinine levels of those with lower sodium concentrations in their donors were significantly lower ($P = .02$). Although we could not consider all the factors that might have impacted the recipients' kidney function, the influence of donors' serum levels of sodium was a noticeable finding that should be further studied.

Similar results have been reported only in liver transplant recipients.[4-6] Figueras and colleagues reported that hypernatremia in the donors led to a higher frequency of liver allograft loss.[6] It was explained that high serum sodium concentrations in the donor might promote the accumulation of idiogenic osmoles within the liver allograft cells.

The subsequent transplantation of these livers into recipients with relatively normal sodium levels may promote intracellular water accumulation, cell lysis, and death during recirculation.[4,5]

In this study, polyuria also correlated with increased recipient's serum creatinine level early after transplantation. However, polyuria did not have such an effect in the long term. Of course, this may depend on other factors such as hypovolemia or hypernatremia in the donor. The urine output categorization and analysis of the complications of polyuria is not easy, since both oliguria and polyuria in the brain-dead donor may influence the kidney transplantation outcome, and there is no definite cutoff point for urine output in the brain-dead subjects. Some guidelines for donor management recommended keeping urine output around 100 mL/h.[3] They suggest that treatment of diabetic insipidus be started if urine output exceeds 300 mL/h.[3] Larger randomized studies are necessary to define the potentially harmful range of urine output in brain-dead donors in the context of kidney transplantation.

CONCLUSION

The rate of polyuria and hypernatremia in brain-dead donors are high and the elevated serum sodium level and polyuria might be risk factors of kidney allograft dysfunction. As the results of this study showed, donor hypernatremia may influence the recipient's serum creatinine in the long term.

ACKNOWLEDGMENT

CONFLICT OF INTEREST

None declared.

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