RESEARCH ARTICLE

Effects of Ringer Lactate Normal Saline Combination versus Normal Saline during Renal Transplantation Surgery on Early Postoperative Outcome

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Background: Traditionally normal saline is the most common crystalloid solution that is used in transplant surgery. Normal saline (NS) because of the higher risk of acidosis and higher levels of serum chloride may have more deleterious effects in kidney transplant recipients Thus; the aim of this study was to determine the safety of ringer lactate normal saline combination if used during a renal transplant.

Methods: One Hundred adults undergoing kidney transplantations were enrolled in a double-blinded randomized prospective clinical trial. They were divided into two groups in order to receive RL& NS and NS infusion as intraoperative IV fluid replacement therapy. All patients received 40 ml/kg fluid during surgery. Serum chloride, sodium, Cr and BUN were checked before operation and 6hour after surgery. Urine output BUN and Cr was also checked in 1, 3 and 7 day after surgery. At the end of surgery, we corrected the acid base status with bicarbonate according to base excess< -15 or PH<7.15 if needed in both groups.

Results: There was a significant difference in the serum chloride level (p= 0.001) and urine output (p= 0.003) between the two groups at the 6 hours after transplantations. Postoperative BUN and Cr level at 2,3 and 7 days in RL&NS group was significantly lower than group of NS (P= 0.011). Also, urine output during this study time was significantly higher in RL&NS group (p=0.001).

Conclusion: Combination of Ringer lactate &normal saline crystalloid solutions are associated with higher urinary output and most favorited out come in the early post-operative days after renal transplantation surgeries.

Keywords: Normal saline; Ringer lactate; Renal transplant; Graft function

Kidney transplantation is a choice method and the most cost-effective treatment modality used for the patients with End-stage kidney disease (ESRD) [1].

During a kidney transplant surgery, maintaining good hydration helps the transplanted kidney to work after the operation. The choice of fluids that are given during and after the operation may have an effect on how the transplant kidney works after surgery and on the patient's acid-base measures in the blood [2].

Many crystalloid solutions have been examined during renal translantation. Normal saline which is the commonly preferred IV fluid for administration during kidney transplant surgery [3]. The high chloride content of normal saline is associated with an increased risk of hyperchloraemic metabolic acidosis, which may in turn increase the risk of hyperchloremia, hyperkalemia and delayed graft function. Lactated Ringer's solution which contains lactate anion, and can be transformed into bicarbonate in the liver; its infusion prevents aggravation of metabolic acidosis and so, produces less hyperkalemia in comparison with normal saline solution [4].

Plasmalyte solution contains acetate and gluconate which can be converted to bicarbonate in the liver [5]. Half saline in combination with bicarbonate is another option that was used in previous our study [6].

Delayed graft function has been variably defined as a failure of the Serum creatinine to fall by 20%within the first 72 hours post-transplantation, or a requirement for dialysis within seven days posttransplant [7].

Delayed graft function is dependent on multiple factors, including donor type, comorbidities, and ischemic time. In addition, the peri-operative fluid status of the recipient and the regimen of fluid therapy are a possible consideration [8].

While it is well accepted that maintaining adequate peri-operative fluid volume facilitates early graft function, the type of fluid that is administered varies substantially between transplant units [9]. To find out a good fluid solution with low chloride contents we designed this clinical trial in hope to determine the safety and efficacy of Ringer lactate and Normal saline combination (R&N) if used during a deceased renal transplant on early graft function.

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Methods

This study was approved by the committee of Research Deputy of Tehran University of Medical Sciences (IR.TUMS.MEDICINE.REC.1396.2027).

After obtaining a written informed consent, eligible patients awaiting a cadaveric renal transplant in operating room were divided into two groups in a prospective double-blinded fashion; one group received RL&NS, and the NS was administered in the other group as intraoperative fluid maintenance. Randomization was achieved using sealed envelopes.

The exclusion criteria were patients with serum potassium level of higher than 5.5 meq/L at admission, patients with chronic liver disease, COPD (chronic obstractive pulmonary disease), chronic heart failure (Ejection fraction <30%), acid base abnormality: BE≤ 15meq, HCO3≤ 10meq, pH≤ 7.15 and if patients needed blood or colloid fluid during surgery.

General anesthesia was induced with a combination of IV midazolam (0.05 mg/kg), fentanyl (2-3 µg /kg), sodium thiopental (4 mg/kg) and atracurium (0.5mg/kg). Anesthesia was maintained using isoflurane in an air/oxygen mixture and the bolus injection of fentanyl (2 µg/kg) every hour; muscle relaxation was achieved by use of IV injection of atracurium (0.2 mg/kg every 50 min). The standard monitoring was used according to ASA recommendations. After the anesthetic induction, a radial arterial cannula was inserted in order to monitor the blood pressure and to obtain blood samples. The central vein catheter was used for IV fluid therapy. All patients received 40 ml/kg fluid RL&NS or NS during surgery.

Serum chloride and sodium, was checked before operation and 6hour after surgery. Urine output BUN and Cr were also checked in 1, 2, 3 and 7 day after surgery. Acid base status was checked near arterial declamping and acid base abnormality corrected with bicarbonate according to base excess< -10 or PH< 7.25 in both groups.

Our primary endpoint was to evaluate the effects of RL&NS on the postoperative early renal function.

Statistical analysis

Data are presented as means ± SD for continuous variables and as percentages for categorical variables. A sample size of 100 in each group was calculated to have at least 80% power to detect the expected difference between treatment protocols with respect to the primary goal. All data were checked for a normal distribution using the Kolmogorov-Smirnov test.

Quantitative variables were compared between groups using the Student's t-test or Mann-Whitney U-test, depending on whether normal or non-normally distributed variables were used, respectively. Data were analyzed using SPSS 24 software (SPSS, Chicago, IL, USA). A P-value less than 0.05 was considered statistically significant.

Results

One hundred renal recipient patients were enrolled in this study with an age range of 20 to 57 years and a mean age of 37.8 ± 8.45 years. Demographic characteristics of the recipients are shown in (Table 1). Median cold ischemic time of all transplanted kidneys was 4 hours, 35 minutes (range, 2 h, 15 min to 6 h, 25 min).

The duration of the transplant procedure was on average 143 minutes (range, 125-162 min) from skin incision to skin closure.

According to blood gas calculation at near to arterial declamping, serum of patients in normal saline group were more acidotic and they needed more bicarbonate compared to RL&NS group (89.2±5.5 ml versus 56.5±6.4 ml) p=0.0012.

The concentration of chlorine ion in the blood of patients in the group RL&NS after surgery was lower than that of the group NS and the urinary output during the 24 hours after surgery was clearly higher in this group in compare to group NS (Table 2).

The concentration of urea and creatinine in the group RL&NS on the third day after the operation was less than that of group NS but on the seventh day there was no significant difference.

Table 1- Baseline Preoperative Characteristics of Study Patients

Variable	RL&NS (50)	NS (50)	P value
Age (yr)	49.6±8.6	48.7±10.5	0.42
Male/female	35/15	32/18	0.51
MAP (mmgh)	86.12±12.24	83.82±12.09	0.35
Cr	6.49±2.39	6.16±1.79	0.44
BUN	90.64±11.2	95.40±12.1	0.32
Weight (kg)	68.11±5.2	70.12±4.3	0.45
Hemoglobin, g/dL	11.2±1.5	11.6±1.2	0.12

Table 2- Postoperative Variables

Variable	RL&NS (50)	NS (50)	P value
Na1	136.68±4.16	137.25±3.12	
Na2	137.96±2.806	141.40±4.845	
Cl1	103.56±8.51	102.34±23	0.2
Cl2	100.26±5.59	106.2±5.48	0.001
Urine output6	580.60±79.77	462.20±30.355	0.001
Urine output24	1351.4±17.163	961.60±80.507	0.001
Urine output48	2392.0±71.706	1666.0±91.287	0.03
BUN1	80.64±12.2	85.40±14.1	0.04
BUN3	65.2±11.1	71.4±5.7	0.001
BUN7	52.8±8.5	61.5±21	0.01
Cr1	5.36±1.4	5.45±1.8	0.01
Cr3	2.69±1.49	3.2±18	0.001
Cr7	2.1±00	2.3±0.4	0.01

Discussion

Clinical outcomes of renal graft function are likely to be affected by the choice of intra-operative and post-operative administration of fluids.

This prospective clinical trial, was designed to assess the safety of Ringer lactate and Normal saline (RL&NS) combination if used during a renal transplant surgery.

At the end of this clinical trial, we found that intra-operative RL&NS solutions was associated with a lower chloride concentration at the end of surgery compared to normal saline in patients undergoing kidney transplantation. The recipient patients in RL&NS group have higher urine output and low Cr level in three days after surgery.

The hyperchloremic acidosis caused by infusion of moderate-to-large quantities of 0.9% saline can last for several hours after the end of the infusion in healthy volunteers, sluggish urinary response, Time to first micturition was slower, and urine volumes and sodium excretion were smaller compared to Hartmann's solution [10].

In a meta-analysis, Krajewski et al. assessed the relationship between the chloride content of intravenous resuscitation fluids and patient outcomes in the perioperative or intensive care setting. They concluded that high-chloride fluids did not affect mortality but were associated with a significantly higher risk of acute kidney injury and hyperchloraemia/metabolic acidosis [11].

The kidney in recipient patients lack the capacity to rapidly compensate for electrolyte and acid-base derangements to a variable degree. Therefore this makes slight effects due to the infusion solution in early days after surgery. In a study by Etezadi et al. closed acid-base monitoring and intra-operative tight control of metabolic acidosis by infusion of Sodium Bicarbonate in renal transplant recipients may improve early post-operative renal function [12].

In a systematic review by Wan et al, balanced electrolyte solutions infusion during renal transplantation are associated with less hyperchloraemic metabolic acidosis compared to normal saline, however it remains uncertain whether lower-chloride solutions lead to improved graft outcomes compared to normal saline [13].

A similar trial of this group in which two liter of normal saline or a low chloride balanced crystalloid was administered to healthy volunteers showed that administration of normal saline even resulted in a decline in renal blood flow velocity and renal cortical tissue perfusion [14].

Weinberg et al, evaluated intraoperative and early postoperative normal saline or Plasma-Lyte 148 in deceased donor renal transplantation. The results show that, participants receiving NS were more acidaemic [pH 7.32 (0.06) vs 7.39 (0.05), P= 0.001] and had higher serum chloride concentrations (107 vs 101 mmol litre−1, P<0.001) at the end of surgery. No differences in the rate of delayed graft function were observed. Subjects receiving PL who did not require dialysis had a greater reduction in creatinine on day 2 [5]. Given this evidence together, it is plausible that hyperchloremia induced by infusion of chloride-rich solutions, has unfavorable effects in recipient kidney function as seen in our study.

Conclusion

Intra-operative administration of low chloride solution such as half saline compared to normal saline is associated with less hyperchloraemic metabolic acidosis and improved early graft outcomes compared to normal saline after deceased renal transplantation.

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