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CLINICAL STUDY

Effects of Normal Saline vs. Lactated Ringer's during Renal Transplantation

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Aim. We hypothesized that normal saline (NS) may have more deleterious effects compared with lactated ringer (LR) in kidney transplant recipients because of the higher risk of acidosis and higher levels of serum potassium. Thus, the aim of this study was to determine the safety of LR if used during a renal transplant. *Methods.* Adults undergoing kidney transplantations were enrolled in a double-blinded randomized prospective clinical trial. They were divided into two groups in order to receive NS and LR infusion as intraoperative IV fluid replacement therapy. *Results.* There was a significant difference in the serum potassium level (p = .000) and the PH (p = .007) between the two groups at the end of transplantations. Two patients in the LR group lost their kidneys due to vascular graft thrombosis. In other words, hyperkalemia and acidosis occurred more frequently in the NS group while thrombotic events may be of concern in the LR group. *Conclusion.* Compared with NS, LR infusion may lead to a lower serum potassium level and a lower risk of acidosis, while there is major concern of the hypercoagulable state in these patients.

Keywords normal saline, lactated ringer, renal transplant

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INTRODUCTION

The administration of large volumes of potassium-containing fluids such as lactated ringer (LR) is a known cause of hyperkalemia in patients undergoing surgery; this concern was the most frequently cited reason for the use of normal saline (NS) during renal transplants in the past decades.[1–4] Evidence suggests that balanced salt-based solutions such as LR may offer clinical benefits compared with NS or NS-based solutions; it is believed that this is because the administration of large volumes of NS is associated with hyperchloremic metabolic acidosis,[1,5,6] which may cause hyperkalemia through an extra cellular shift of potassium.[1,7] Hyperchloremia may cause vasoconstriction in afferent and efferent arteriolar beds of kidney and may result in a decrease in the urine output.[4,8] Furthermore, acidosis may have detrimental effects on the cardiovascular system in patients with chronic renal failure and

underlying acid-base derangements. The infusion of NS has also been recognized as the reason for complications such as mental changes and abdominal discomfort in healthy volunteers.[9]

While several studies have shown evidence indicating LR as a safe alternate for NS due to a lower risk of hyperkalemia, NS is still the most commonly used fluid in many centers. Thus, investigations in this area could result in meaningful practical changes. Many authors have carried out different studies addressing the question of whether LR offers advantages over NS if administered in different operations; for instance, O'Malley et al.[4] performed their study on patients undergoing renal transplants. This study is one of the most complete studies in this domain, though it was associated with various limitations and problems. The present study is a randomized double-blinded clinical trial designed in the same manner; however, it has tried to overcome the limitations and also to add necessary data. The aim of this study was to determine the safety of LR if used during renal transplants. The primary goal was to determine the serum potassium level and PH at the end of the surgery. Determining any need for dopamine or sodium bicarbonate, the incidence of possible thromboembolic events, and the amount of blood transfused and the urine volume in the first four hours after the operation as well as the creatinine level on the third postoperative day were the other purposes of the following study.

METHODS

The study was approved by the committee of Research Deputy of Tehran University of Medical Sciences. After obtaining a written informed consent, eligible patients awaiting a renal transplant were divided into two groups in a prospective double-blinded fashion; one group received NS, and the LR was administered in the other group as intraoperative fluid replacement. Randomization was achieved using sealed envelopes. Patients with serum potassium level of higher than 6 meq/L at admission were excluded. All of the transplant surgeries were performed by an expert team comprised of two urologists and a vascular surgeon in the urology operating room of Sina University Hospital. General anesthesia was induced via a combination of midazolam (2–4 mg), fentanyl (2–3 μg/kg), and sodium thiopental (2–4 mg/kg).

Anesthesia was maintained using isoflurane in an air/oxygen mix and the bolus injection of fentanyl; muscle relaxation was achieved using IV Atracurium (0.5 mg/kg). 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 CVP monitoring. The left kidney was procured from living donors via an open approach. The donor's kidney was flushed with ice cold LR before being transferred to the recipient and being implanted in the right retroperitoneal space. Ureteroneocystostomy was performed via Lich-Gregoir technique.[10]

Preoperative and postoperative immunosuppressive therapies were administered based on institutional protocols:

1. mycophenolate mofetil (cellcept): 1.5–2 gr;
2. cyclosporine (neoral): 6.5–7 mg/kg;
3. prednisolone: 2 mg/kg.

The responsible clinician determined the precise combination and dose of the medications. All the patients received heparin 5,000 units IV (three minutes before the clamp was performed).

The patients were all ventilated on a CMV mode with the following setting: RR = 12, TV = 10 CC/Kg, I/E ratio = 1/2. The responsible clinician was told to maintain PCO2 at 35–40 mmHg according to the patient's ABG in different stages in order to exclude the resulting confounding factors. An algorithm was imposed for the amount of fluid administered. According to this algorithm, every patient received 60mL/kg of the fluid titrated continuously during the operation, while CVP was kept between 10–15 mm Hg. Blood products were administered based on ASA recommendations, if clinically indicated. The fluid bags were covered with tape so that the personnel and clinicians do not have any idea of the type of the fluid administered. Post operative IV fluid therapy was the same in all of the patients. Blood samples were obtained three times: at the beginning of the operation (after the insertion of the arterial cannula), in an hour, and at the end of the surgery. The responsible clinician could take blood samples for measuring serum potassium, sodium, and ABG any time during the operation. The treatment of any derangement was performed at the discretion of the clinician.

All data were tested for normality using the method of Kolmogorov–Simironov. T-Tests and Fisher's exact test were used to analyze the resultant data. p value ≤ 0.05 (two-tailed) was considered to be significant. A sample size of 26 in each group was calculated to have at least 80% power to detect the expected differences between fluids with respect to the primary goal. A 0.45 meq/L difference in the mean serum potassium level and 0.05 units for PH were noted to be significant. All the laboratory measurements were analyzed at the central laboratory of Sina University Hospital.

RESULTS

Fifty-two patients enrolled in this study were randomly divided into two equal groups, age- and sex-matched.

Table 1 outlines the demographic data of the patients participated in this study. Both groups received similar volumes of the fluid during the surgery. Two units of packed cells were transfused to a patient in the LR group, while none of the patients in the other group required any blood ($p = 1.00$). Patients in the NS group had a lower mean PH level during the transplantation compared with those who received LR ($p < 0.001$). Mean serum potassium levels in the NS and LR groups were 4.88 ± 0.7 and 4.03 ± 0.8 meq/L, respectively ($p < 0.001$; see Figure 1). Mean changes of the serum potassium were $+0.5 \pm 0.6$ meq/L in the NS group and -0.5 ± 0.9 meq/L in the LR group ($p < 0.001$). Mean changes of PH were -0.06 ± 0.05 in the NS group and -0.005 ± 0.07 in the LR group ($p < 0.001$; see Figure 2).

Two patients in the NS group received sodium bicarbonate infusion in order to correct the resulted metabolic acidosis, while such a treatment was not needed in either of the LR cases ($p = 0.496$). Dopamine was administered in one patient in each group ($p = 1.00$). The mean urine volumes in the first four hours following the operations in the NS and the LR groups were 3710.77 ± 1868.2 and 3035.00 ± 1797.87 cc, respectively ($p = 0.190$). Mean creatinine level on the third postoperative day in the NS group was $1.9 \pm .7$ mg/dL, but in the LR group, it was 2.2 ± 2.2 mg/dL ($p = .425$). The difference in the mean creatinine level on the third postoperative day and the mean first-four-hour postoperative urine volume were not statistically significant. Two cases in the LR group had no urine output during the first four postoperative hours; this was associated with a high creatinine level on the third day following the surgery (9.1 mg/dL, 7.4 mg/dL); further work-up revealed renal artery thrombosis in these cases. As a result, two patients in the LR group lost their kidneys secondary to vascular graft thrombosis, while such a complication was absent in the NS group ($p = 0.496$).

DISCUSSION

During an optimum renal transplantation surgery in an adult patient (70 kg weight), approximately 16 meq of potassium is administered (60 cc/kg). This potassium is distributed through the total body water, and as a result, a 0.3 meq/L increase in the serum potassium level is unsurprising. On the other hand, lactate is a strong anion; the absorption of lactate by liver may lead to an increased strong ion difference (SID) and lower acidosis. Subsequently, the conversion of lactate to bicarbonate can increase the buffering capacity of plasma, and as a result, it can increase the capability to prevent changes in PH. Any decrease, as much as 0.1 units, in plasma PH increases the serum potassium to as high as 0.7 meq/L based on transcellular shifts.[7] Two cases of renal artery graft thrombosis were reported in the LR group just after the renal transplant. No renal artery thrombosis was seen in the NS group. G. Martin et al. had also stated the exhibition of a hypercoagulable state, which persisted during the postoperative period in those treated with LR.[11]

Table 1
Demographic and perioperative variables

	NS (I) Mean ± SD	LR (II) Mean ± SD	*p* value
Age, yrs	40 ± 14	37 ± 13	0.37
Change of k during surgery, meq/L	+0.5 ± 0.6	−0.5 ± 0.9	0.000
Change of Na during surgery, meq/L	+0.5 ± 0.4	−0.5 ± 0.04	0.000
Change of PH during surgery, unit	−0.06 ± 0.05	−0.005 ± 0.07	.001
Warm ischemia time, min	4.5 ± 0.9	3.9 ± 101	0.04
End of surgery PH, unit	7.29 ± 0.08	7.34 ± 0.05	0.007
End of surgery K, meq/L	4.8 ± 0.7	4 ± 0.8	0.000
End of surgery Na, meq/L	140 ± 3.2	136 ± 4.5	0.000
Blood loss, ml	457 ± 135	488 ± 177	0.48
End of surgery serum osmolality, mOsm/kg	299 ± 19	292 ± 11	0.12
Baseline serum K, meq/L	4.3 ± 0.6	4.6 ± 0.8	0.16
Baseline serum Na, meq/L	140 ± 4.7	141 ± 4.2	.017
Baseline serum PH, meq/L	7.35 ± 0.7	7.34 ± 0.8	0.71
Postoperative day three creatinine level, mg/dL	1.9 ± 0.7	2.2 ± 2.2	0.42
First four hour's urine output, ml	3710 ± 1868	3035 ± 1797	0.19
Patients transfused, No (%)	1 (3.8)	0	1
Patients treated with dopamine, No (%)	1 (3.8)	1 (3.8)	1
Patients treated with sodium bicarbonate, No (%)	2 (7.7)	0	0.49
Patients who had vascular thrombosis, No (%)	0	2 (7.7)	0.49

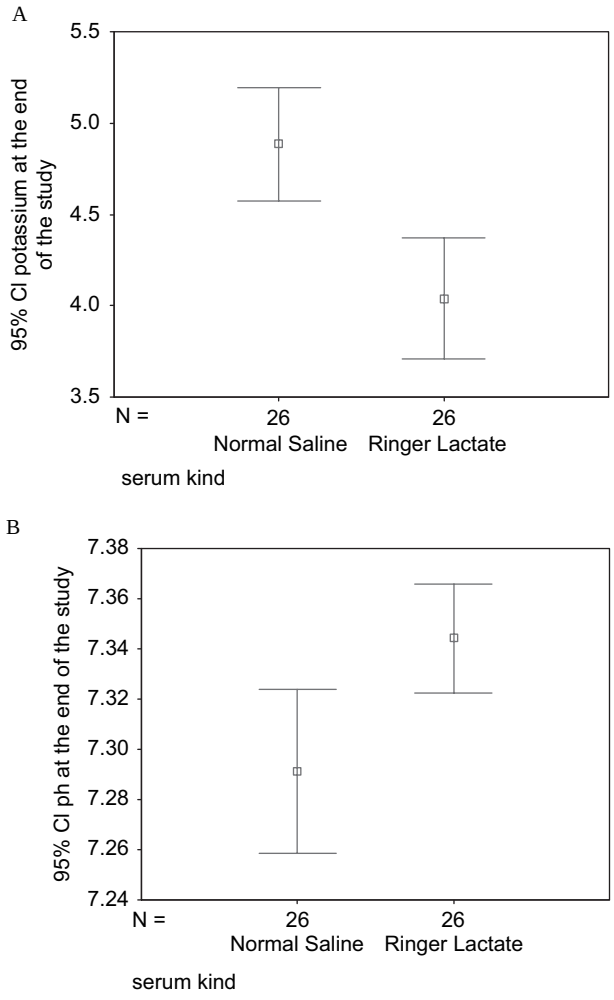

Figure 1. Comparison of (A) mean serum potassium and (B) mean serum PH between the two groups at the end of renal transplantation.

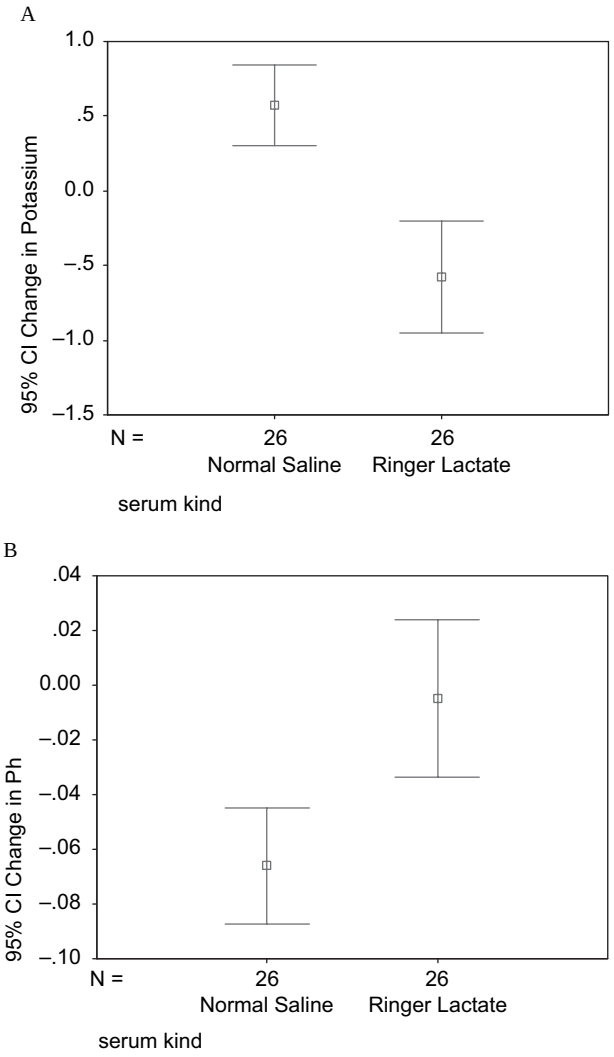

Figure 2. Comparison of (a) mean potassium change and (B) PH change during renal transplantations between the two groups under study.

O'Malley et al. compared the outcome of LR and NS infusions in their study and concluded LR to be a safer choice for IV fluid therapy during renal transplantations.[12]

It should be noted that the results of the present study showed that while patients had a better condition regarding pH and potassium levels in the LR group, the creatinine levels on the third postoperative day was lower in the NS patients. Moreover, the patients in the latter group had higher urinary amounts on the first four postoperative hours. It is noteworthy that statistical analysis did not reveal these differences to be significant, but according to the fact that the power of the study appropriately calculated for the primary objectives was not proper enough for the secondary ones, a larger study is needed to focus on these points. However, as the renal artery thrombosis reported in two of the studied cases is a rare finding, but can lead to dreadful outcome; it could be concluded that LR is not as safe as approved in O'Malley's study.

The mean serum changes of the PH and the potassium levels at the beginning and the end of the surgery were, respectively, –0.005 units and –0.576 meq/L in the LR group. The decline reported in the serum potassium could not be explained by alkalosis-induced intracellular shift of potassium. Other mechanisms responsible for such changes are not yet recognized. In the NS group, the mean serum PH and the potassium changes were –0.066 unit and 0.576 meq/L, respectively. Any increase in the serum potassium in this group is secondary to extra cellular shift of potassium because of the decreased serum PH.

CONCLUSION

Compared with NS, LR infusion may lead to a lower serum potassium level and a lower risk of acidosis, while lower urinary amount in the first four postoperative hours, higher mean creatinine levels on the third post-transplant day, and higher risk of renal artery thrombosis in these patients brings up concerns on the safety of the solution during renal transplantation. As a result, further studies are needed to evaluate its safety.

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