INTRODUCTION

Perioperative fluid management in patients undergoing kidney transplantation is crucial to maintaining adequate intravascular volume, as well as acid-base and electrolyte balance, and may also affect graft tissue perfusion and function.\(^1\) Crystalloids, such as normal saline (NS) or balanced low-chloride solutions, are the most common and widely used fluids for intraoperative management to maintain optimal intravascular volume.\(^4,5\) Potassium-containing fluids may theoretically cause hyperkalemia in patients during kidney transplantation; therefore, NS, which lacks potassium, is typically used during the perioperative period of kidney transplantation. However, rapid administration of a large volume of NS may lead to hyperchloremic metabolic acidosis and subsequent hyperkalemia.\(^6 - 9\) Hyperchloremia itself has also been reported as a risk factor associated with acute kidney injury.\(^10 - 13\)

Effects of the Type of Intraoperative Fluid in Living Donor Kidney Transplantation: A Single-Center Retrospective Cohort Study

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Purpose: Perioperative fluid management in kidney transplant recipients is crucial to supporting the fluid, acid-base, and electrolyte balance required for graft perfusion. However, the choice of intraoperative crystalloids in kidney transplantation remains controversial. We conducted a single-center retrospective cohort study to evaluate the impact of intraoperative fluids on acid-base and electrolyte balance and graft outcomes.

Materials and Methods: We included 282 living donor kidney transplant recipients from January 2010 to December 2017. Patients were classified into two groups based on the type of intraoperative crystalloids used (157 patients in the half saline group and 125 patients in the balanced crystalloid solutions group, Plasma-lyte).

Results: Compared with the half saline group, the Plasma-lyte group showed less metabolic acidosis and hyponatremia during surgery. Hyperkalemia incidence was not significantly different between the two groups. Changes in postoperative graft function assessed by blood urea nitrogen and creatinine were significantly different between the two groups. Patients in the Plasma-lyte group exhibited consistently higher glomerular filtration rates than those in the half saline group at 1 month and 1 year after transplantation after adjusting for demographic differences.

Conclusion: Intraoperative Plasma-lyte can lead to more favorable results in terms of acid-base balance during kidney transplantation. Patients who received Plasma-lyte showed superior postoperative graft function at 1 month and 1 year after transplantation. Further studies are needed to evaluate the superiority of intraoperative Plasma-lyte over other types of crystalloids in relation to graft outcomes.

Key Words: Kidney transplantation, fluid therapy, Plasma-lyte, acid-base balance, glomerular filtration rate
anced crystalloid solutions as both resuscitation and maintenance crystalloids in critical care and perioperative fluid management.14-16 Half saline has been used as an intraoperative fluid during kidney transplantation instead of NS to prevent sodium retention and hyperchloremic metabolic acidosis in our hospital. Half saline may theoretically reduce the risk of hyperchloremic metabolic acidosis but may cause dilutional hyponatremia. Plasma-lyte, one of several balanced crystalloids, is an isotonic, buffered solution with an electrolyte composition similar to that of human plasma.14 Plasma-lyte has a pH of 7.4 and has a lower chloride concentration than NS. In our hospital, a change in the intraoperative fluid from 0.45% half saline to Plasma-lyte.

Previous studies have compared clinical effects between NS and balanced crystalloids in kidney transplantation.4,9,17-19 Balanced crystalloids showed a better metabolic profile. The effect of the type of intraoperative fluid type on postoperative graft function, however, remains uncertain. Meanwhile, tight control of intraoperative metabolic acidosis was reported to improve early kidney graft function.20 This study aimed to compare the effects of half saline and Plasma-lyte on acid-base and electrolyte balance and postoperative kidney graft function after living donor kidney transplantation.

MATERIALS AND METHODS

Ethical considerations
This study was approved by the Institutional Review Board (IRB) of Severance Hospital (IRB No. 4-2020-0850). The requirement for informed consent was waived by the IRB due to the retrospective nature of this study.

Study design and patients
This was a single-center, retrospective cohort study. Data were obtained from electronic medical records. Patients who underwent living donor kidney transplantation between January 2010 and December 2017 were enrolled, while those who underwent multi-organ transplantation were excluded. Patients were classified into two groups based on intraoperative fluid (half saline vs. Plasma-lyte).

Demographics, perioperative fluid intake, and acid-base and electrolyte balance were compared between the two groups. Acid-base and electrolyte balance during surgery were recorded after induction of anesthesia (T0), reperfusion (T1), and during the immediate postoperative period (T2). Postoperative electrolyte concentrations were recorded on postoperative days (PODs) 1, 2, and 7. Daily urine volume and fluid balance were recorded until POD 2. Postoperative kidney graft function on PODs 1, 2, and 7 was assessed using serum blood urea nitrogen (BUN), creatinine, and estimated glomerular filtration rate (eGFR). eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation.21 The eGFR values were calculated until 1-year post-transplantation to monitor graft outcomes. Delayed graft function was defined as the need for dialysis during the first week after transplantation. Renal biopsies were performed in cases of acute allograft dysfunction (>30% increase in serum creatinine levels, compared with the baseline value or proteinuria of >500 mg/day). Allograft biopsy samples were processed using light, immunofluorescent, and electron microscopy. All biopsy-proven acute rejections within the first 3 months post-transplantation were taken into account in the statistical analyses.

Intraoperative care
Intraoperative anesthetic management was performed according to the standard protocols of the center. General anesthesia was induced with 1.5–2.5 mg/kg propofol and 0.6 mg/kg of rocuronium and was maintained with sevoflurane or desflurane (0.85–1.2 minimum alveolar concentration). Remifentanil was continuously infused at a rate of 0.1–0.3 μg/kg/min during surgery. The radial artery was catheterized for continuous blood pressure monitoring and arterial blood gas analysis. Either 0.45% half saline or Plasma-lyte was used as an intraoperative maintenance fluid. The half saline solution included sodium (77 mEq/L) and chloride (77 mEq/L). Plasma-lyte (Plasma solution A, CJ Pharmaceutical, Seoul, Republic of Korea) contained sodium (140 mEq/L), potassium (5 mEq/L), magnesium (3 mEq/L), chloride (98 mEq/L), acetate (27 mEq/L), and gluconate (23 mEq/L). The intraoperative fluid choice was determined by our institute’s protocol, which was changed from 0.45% half saline to Plasma-lyte after a discussion with surgeons and anesthesiologists. Fluid administration was guided by central venous pressure and adjusted by urine output after reperfusion of kidney graft.

Postoperative care
Postoperative care was performed according to the standard protocols of our institute. Until discharge, 0.45% half saline and 0.9% NS with sodium bicarbonate (6 mEq/L) were used alternately during the postoperative period in both groups, depending on serum sodium levels. The immunosuppressive regimens used in our hospital are presented in the Supplementary Table 1 (only online).

Statistical analyses
Continuous variables are presented as means±standard deviations or medians (interquartile ranges). Categorical variables are presented as frequencies and proportions. Intergroup comparisons were performed using an independent t-test or a Mann-Whitney U test for continuous variables and Fisher’s exact test or a chi-square test for categorical variables. Linear mixed models were used adjusting the first measured values between the two groups to analyze changes in perioperative acid-base balance, electrolytes, and parameters associated with kidney graft function. The first values of each parameter were taken as co-
RESULTS

Of the 282 patients included in this study, 157 received half saline and 125 received Plasma-lyte during kidney transplantation. Significant demographic differences were observed between the groups, including recipient age, donor eGFR, ABO-incompatible donors, graft kidney weight to recipient body weight ratio, and amount of fluid administration during surgery (Table 1). There were no significant differences in delayed graft function and acute rejection between the groups.

Table 1. Patient Characteristics

| Characteristics                  | Half saline (n=157) | Plasma-lyte (n=125) | p value |
|----------------------------------|--------------------|---------------------|---------|
| Age (yr)                         | 45 (33–51)         | 47 (37–57)          | 0.006   |
| BMI (kg/m²)                      | 22.1 (20.1–24.2)   | 22.3 (20.0–24.7)    | 0.919   |
| Male sex                         | 89 (56.7)          | 67 (53.6)           | 0.604   |
| Hypertension                     | 126 (80.3)         | 103 (82.4)          | 0.647   |
| Diabetes mellitus                | 35 (22.3)          | 29 (23.2)           | 0.857   |
| Preemptive kidney transplant     | 44 (28.0)          | 47 (37.6)           | 0.088   |
| Re-transplant                    | 5 (3.2)            | 10 (8.0)            | 0.074   |
| Donor age (yr)                   | 42 (29–49)         | 43 (34–51)          | 0.083   |
| Donor eGFR                       | 101 (90–111)       | 107 (100–116)       | <0.001  |
| ABO incompatible donor           | 13 (8.3)           | 30 (24.0)           | <0.001  |
| Number of HLA mismatches         | 3 (2–4)            | 3 (2–4)             | 0.090   |
| Kidney weight (g)/body weight (kg) | 2.89 (2.42–3.57)   | 3.18 (2.63–3.91)    | 0.013   |
| Warm ischemic time (min)         | 35 (30–40)         | 35 (29–40)          | 0.805   |
| Intraoperative fluid input (mL/kg/h) | 9.0 (7.6–11.9)    | 7.0 (6.0–9.3)       | <0.001  |
| Intraoperative furosemide use (mg) | 30 (20–40)         | 20 (20–40)          | 0.059   |
| Delayed graft function           | 7 (4.5)            | 2 (1.6)             | 0.307   |
| Acute rejection                  | 14 (8.9)           | 11 (8.8)            | >0.999  |

BMI, body mass index; HLA, human leukocyte antigen; eGFR, estimated glomerular filtration rate. Values are expressed as medians (interquartile ranges) or n (%).

Perioperative acid-base balance showed significant differences between the two groups after adjusting the first measured values by the linear mixed model (Table 2). Preoperative total CO₂ levels were significantly higher in the half saline group (p=0.003). However, total CO₂ levels during surgery were significantly higher in the Plasma-lyte group. The mean serum bicarbonate concentration (reference range, 21–28 mmol/L) was significantly higher in the Plasma-lyte group than in the half saline group, even under physiologic ranges during the reperfusion (19.29±2.46 mmol/L vs. 22.93±3.48 mmol/L, p<0.001) and immediate postoperative periods (18.68±2.53 mmol/L vs. 21.85±2.64 mmol/L, p<0.001). Base excess in the extracellular fluid was also significantly higher in the Plasma-lyte group than in the half saline group during surgery. Sodium bicarbonate was administered in one patient in the half saline group and no patients in the Plasma-lyte group (data not shown).

Hyponatremia (sodium <130 mmol/L) occurred more frequently in the half saline group during the reperfusion period (p<0.001), immediate postoperative period (p<0.001) and POD 1 (p=0.032) (Table 3). Hyperchloremia (chloride >110 mmol/L) occurred more frequently in the half saline group on POD 2 and 7, although there were no significant differences between the groups (p=0.163 and 0.067, respectively). Hyperkalemia (potassium >5.5 mmol/L) at the reperfusion period occurred in five
In this retrospective study, we demonstrated that Plasma-lyte administration during surgery reduces the occurrence of metabolic acidosis during the intraoperative and early postoperative periods, compared with the administration of 0.45% half saline. Postoperative kidney graft function measured using eGFR showed favorable results in the Plasma-lyte group.

Various factors may affect acid-base and electrolyte balance in patients undergoing kidney transplantation, such as the type of intravascular solution used during surgery.\textsuperscript{4,8,9,19,22,23} Crystalloid fluids comprise different components based on their composition of electrolytes and the presence of buffers. Comparisons of clinical outcomes associated with different types of intravenous crystalloids used in kidney transplantation have been reported,\textsuperscript{4,8,17,19,24-26} with each fluid demonstrating its own pros and cons. Recently, a balanced crystalloid solution has shown a better metabolic profile and is preferred in kidney transplantation.\textsuperscript{27}

Metabolic acidosis after using a large volume of NS is a risk factor for subsequent hyperkalemia that is mediated by an extracellular shift of potassium ions.\textsuperscript{49} Solutions with lower chloride content, such as balanced crystalloids, have been administered to minimize the risk of hyperchloremic metabolic acidosis.\textsuperscript{4,30}

Compared with NS, Hartman’s solution contains potassium (4 mEq/L) and has a lower chloride concentration (109 mEq/L). O’Malley reported that the use of Hartman’s solution reduced hyperkalemia and acidosis during kidney transplantation when compared with the use of NS.\textsuperscript{29}

Unlike Hartman’s solution, half saline does not contain potassium ions. Based on the same reasons outlined for NS, the lack of potassium ions may reduce the risk of hyperkalemia. Patients with end-stage renal disease may also have co-morbid salt-sensitive hypertension and coronary artery disease.\textsuperscript{30} These
conditions may adversely affect left ventricular function. Consequently, administration of a large volume of a salt solution may cause sodium retention and volume overload, which can worsen cardiac and renal function in these patients. The lower sodium concentration in half saline may reduce the risk of such events. The risk of hyperchloremic metabolic acidosis may also be reduced with the administration of half saline compared with NS administration. This rationale supported the use of half saline during preoperative and intraoperative periods in kidney transplant patients treated at our hospital. However, the administration of a large volume of hypotonic fluid, such as half saline, may cause dilutional hyponatremia due to its lower sodium concentration. Hyponatremia may contribute to serious brain injury, and efforts to correct hyponatremia may even cause osmotic demyelinating syndrome in patients. However, no experience of brain injury has been recorded over several de-

Table 4. Postoperative Kidney Graft Function Changes

|                      | Half saline (n=157) | Plasma-lyte (n=125) | p value |
|----------------------|---------------------|----------------------|---------|
| **BUN (mg/dL)**      |                     |                      |         |
| Preoperative period  | 47.14±19.83         | 48.52±16.18          |         |
| Immediate postoperative period | 49.86±16.78 | 40.98±13.34 | <0.001 |
| POD 1                | 35.94±15.39         | 31.60±12.99          | 0.600   |
| POD 2                | 28.92±18.85         | 26.41±12.51          | >0.999  |
| POD 7                | 24.02±17.41         | 23.78±13.09          | >0.999  |
| **Creatinine (mg/dL)** |                     |                      |         |
| Preoperative period  | 8.14±3.78           | 7.51±3.04            |         |
| Immediate postoperative period | 6.06±2.84 | 4.61±2.25 | <0.001 |
| POD 1                | 3.64±1.93           | 2.91±1.84            | 0.024   |
| POD 2                | 1.82±1.24           | 1.52±1.15            | >0.999  |
| POD 7                | 1.48±1.09           | 1.19±0.72            | >0.999  |
| **eGFR (mL/min/1.73 m²)** |                     |                      |         |
| Preoperative period  | 8.46±4.00           | 8.40±3.69            |         |
| Immediate postoperative period | 12.50±7.88 | 15.23±7.94 | 0.029   |
| POD 1                | 24.28±15.38         | 31.31±18.75          | 0.008   |
| POD 2                | 52.40±24.56         | 58.75±23.72          | >0.999  |
| POD 7                | 65.10±25.41         | 69.28±21.75          | >0.999  |
| **Urine volume (mL/day)** |                     |                      |         |
| Intraoperative period | 540 (300–1000)      | 1045 (625–1655)      |         |
| Immediate postoperative period | 7460 (5650–10110) | 7900 (5250–10070) | >0.999  |
| POD 1                | 6850 (5180–8740)    | 8185 (6500–10070)    | <0.001  |
| POD 2                | 5750 (4430–7260)    | 6750 (5565–8330)     | <0.001  |
| **Fluid balance (mL)** |                     |                      |         |
| Immediate postoperative period | 2685 (1920–3310)  | 1995 (1110–2610)     |         |
| POD 1                | -25 (-405–300)      | -150 (-510–180)      | 0.729   |
| POD 2                | -75 (-488–267)      | -125 (-690–270)      | >0.999  |

BUN, blood urea nitrogen; POD, postoperative day; eGFR, estimated glomerular filtration rate. Values are expressed as means±standard deviations or medians (interquartile ranges). The first measured values of each parameter were taken as fixed covariates in the linear mixed model. p values were adjusted using Bonferroni’s method.

Fig. 1. Changes in BUN and creatinine during the perioperative period. Data shown as mean±standard deviation. p value from a linear mixed model to compare changes in BUN and creatinine over time between groups. BUN, blood urea nitrogen; POD, postoperative day; HS, half saline.
Table 5. Factors Associated with eGFR at 1 Month after Transplantation in Univariable and Multivariable Linear Regression

|                        | Univariable model | Multivariable model |
|------------------------|-------------------|---------------------|
|                        | β coefficient (95% CI) | p value | β coefficient (95% CI) | p value |
| Male sex               | -6.283 (-11.514 to -1.053) | 0.019 | 4.389 (-0.735 to 9.514) | 0.093 |
| Intraoperative Plasma-lyte use | 10.941 (5.813 to 16.068) | <0.001 | 9.156 (4.276 to 14.038) | <0.001 |
| Recipient age (yr)     | -0.266 (-0.471 to -0.062) | 0.011 | -0.330 (-0.503 to -0.157) | <0.001 |
| Donor age (yr)         | -0.475 (-0.693 to -0.257) | <0.001 | -0.419 (-0.677 to -0.161) | 0.002 |
| Preemptive kidney transplant | -1.504 (-7.119 to 4.110) | 0.598 | -1.913 (-6.481 to 2.655) | 0.410 |
| ABO incompatible donor | 6.002 (-1.270 to 13.273) | 0.105 | 4.868 (-1.321 to 11.058) | 0.123 |
| Number of HLA mismatches | -1.433 (-3.204 to 0.337) | 0.112 | -0.771 (-2.249 to 0.707) | 0.305 |
| Kidney weight (g)/body weight (kg) | 8.680 (5.832 to 11.529) | <0.001 | 9.881 (6.879 to 12.883) | <0.001 |
| Acute rejection         | -18.919 (-27.886 to -9.951) | 0.001 | -15.255 (-22.813 to -7.697) | <0.001 |
| Warm ischemic time (min) | -0.126 (-0.396 to 0.145) | 0.361 | -0.131 (-0.350 to 0.088) | 0.241 |
| Donor eGFR             | 0.555 (0.376 to 0.734) | <0.001 | 0.322 (0.106 to 0.539) | 0.004 |
| Intraoperative vasopressor use | -1.580 (-7.403 to 4.243) | 0.598 | 0.086 (-4.728 to 4.900) | 0.972 |

CI, confidence interval; HLA, human leukocyte antigen; eGFR, estimated glomerular filtration rate.

Table 6. Factors Associated with eGFR at 1 Year after Transplantation in Univariable and Multivariable Linear Regression

|                        | Univariable model | Multivariable model |
|------------------------|-------------------|---------------------|
|                        | β coefficient (95% CI) | p value | β coefficient (95% CI) | p value |
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CI, confidence interval; HLA, human leukocyte antigen; eGFR, estimated glomerular filtration rate.

Fig. 2. Change in eGFR at 1 year after surgery. Data shown as mean±standard deviation. p value from a linear mixed model to compare changes in eGFR over time between groups. eGFR, estimated glomerular filtration rate; POD, postoperative day; HS, half saline.
cades in our institute.

Several studies have reported that the use of Plasma-lyte in kidney transplantation is associated with a lower prevalence of hyperchloremic metabolic acidosis and hyperkalemia events than NS. In our study, no significant differences were observed in the incidence of hyperkalemia events between both groups during surgery. This is consistent with previous reports that have compared the use of NS-based crystalloids and balanced crystalloids containing potassium during kidney transplantation. Metabolic acidosis was more severe in the half saline group than in the Plasma-lyte group. The buffer components in the Plasma-lyte solution may have contributed to a more favorable acid-base balance.

Early diuresis is a good marker of successful transplantation because it reflects the recovery status of kidney graft function. In this study, administration of Plasma-lyte in the intraoperative period was associated with more urine output on PODs 1 and 2 (\(p<0.001\), both). Similarly, serum creatinine reduction over time was more rapid in the Plasma-lyte group than in the half saline group (\(p<0.001\)). Plasma-lyte use was also associated with better postoperative kidney graft function as measured by eGFR in a multivariable linear analysis at both 1 month and 1 year after transplantation (\(p<0.001\) and \(p=0.043\), respectively). The influence of the type of crystalloid solution used only during the intraoperative period on long-term kidney graft recovery may be limited, as reported previously. Kidney graft function may be affected by several factors in addition to intraoperative fluid type. As metabolic acidosis may negatively affect kidney function, intraoperative fluid management employing improved acid-base balance may be associated with postoperative kidney graft function.

In conclusion, intraoperative Plasma-lyte use was associated with more favorable results in terms of acid-base balance during kidney transplantation. Compared to the administration of half saline, Plasma-lyte administration did not lead to an increase in the occurrence of hyperkalemia. Patients receiving Plasma-lyte showed superior postoperative graft function at 1 month and 1 year after transplantation. Further studies are needed to evaluate the superiority of intraoperative Plasma-lyte over other types of crystalloids with regards to graft outcomes.

AUTHOR CONTRIBUTIONS

Conceptualization: Bon-Nyeo Koo. Data curation: Juhan Lee, Su Youn Choi, and Hye Ji Joo. Formal analysis: Seungho Jung and Su Youn Choi. Investigation: Hye Ji Joo. Methodology: Seungho Jung and Juhan Lee. Project administration: Jeongmin Kim and Bon-Nyeo Koo. Resources: Jeongmin Kim. Software: Su Youn Choi. Supervision: Bon-Nyeo Koo. Validation: Su Youn Choi. Visualization: Jeongmin Kim. Writing—original draft: Seungho Jung. Writing—review & editing: Jeongmin Kim, Juhan Lee, and Bon-Nyeo Koo. Approval of final manuscript: all authors.

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