Clinical Case Report

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Safety of potassium-bearing citrate in patients with renal transplantation

A case report

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Abstract

Rationale: Urinary lithiasis is one of severe postoperative complications in patients undergoing renal transplantation, possibly leading to anuria, urinary infection, or even acute renal failure. Potassium sodium hydrogen citrate (PSHC), a potassium-bearing citrate, is commonly prescribed to prevent stone formation.

Patient concerns: A 25-year-old man (patient 1) and a 31-year-old man (patient 2) receiving renal transplantation for end-stage renal disease (ESRD) were enrolled in this study. They were given 10 g/day of PSHC granules from the ninth day to the 17th day after surgery. Patient 1 presented chest tightness, nausea, muscle weakness, and ascending paralysis on the 10th day. Patient 2 presented weak waves on EGG on the 17th day. Moreover, their serum potassium concentrations (SPCs) were 7.67 and 6.05 mmol/L, respectively.

Diagnosis: Acute hyperkalemia.

Interventions: Hemo-filtration was performed for patient 1, while patient 2 received 10% calcium gluconate 10 mL, 5% $NaHCO_3$ 125 mL, and 10% glucose 500 mL with the addition of 10 units of insulin through intravenous drip.

Outcomes: Their SPCs dropped to the normal range.

Lessons: Physicians should pay close attentions to potential risks caused by PSHC, and monitor the SPCs to minimize the occurrence of hyperkalemia.

Abbreviations: BMI = Body mass index, BTCs = Blood tacrolimus concentrations, ECG = Electrocardiograms, ESRD = End-stage renal disease, PSHC = Potassium sodium hydrogen citrate, SCrCs = Serum creatinine concentrations, SPCs = Serum potassium concentrations.

Keywords: case report, hyperkalemia, potassium sodium hydrogen citrate, renal transplantation

1. Introduction

Allograft urolithiasis is a common postoperative complication among patients receiving renal transplantation, with a reported prevalence rate ranging from 0.2% to 10%.[1–4] The disease shows different manifestations such as oliguria, anuria, and acute renal failure, leading to serious consequences. Renal transplantation patients are at a high risk of allograft urolithiasis, especially early after transplantation due to unrecovered kidney function, hyperparathyroidism, chronic urinary tract infection, etc.[5,6] Currently, the application of alkaline citrate is the major therapeutic strategy for this disease, and this agent plays important roles in preventing stone formation via increasing urinary citrate.[7–9] Potassium sodium hydrogen citrate (PSHC), a potassium-bearing citrate, is widely used to prevent stone formation. Potassium citrate (PC) represents the first-line treatment for uric acid nephrolithiasis because it just causes mild gastrointestinal tract complications under acceptable doses, without adverse effects of calcium salt precipitation.[10]

The report presented 2 unusual patients suffering from acute hyperkalemia after renal transplantation caused by PSHC granules. The transplanted kidneys for these 2 patients were from cardiac death donors from the distribution of China's Organ Transplant Response System (COTRS) at the Second Affiliated Hospital of Zhengzhou City in June 2015. Data were obtained from the combination of COTRS, pharmacy records, and departmental transplantation database. The main causes of hyperkalemia and related prevention measures were discussed as follows. To our knowledge, acute hyperkalemia caused by PSHC, especially after renal transplantation, was rarely reported in published literature.

2. Case presentation

With normal BMI (body mass index, BMI), a 25-year-old man (patient 1, weight: 58 kg) and a 31-year-old man (patients 2, weight: 62 kg) receiving renal transplantation for end-stage

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renal disease (ESRD) were enrolled in the current study. The 2 patients, following normal operation processes, received the kidneys of cardiac death donors from the Second Affiliated Hospital of Zhengzhou City. General systemic examinations for these 2 patients before surgery showed normal statuses: hematocrit, 0.26 and 0.24; hemoglobin, 87 and 82 g/L; serum albumin, 43 and 40 g/L; total serum proteins, 75.8 and 70.5 mg/L; aspartate aminotransferase, 18 and 20 units/L; alkaline phosphatase, 75.7 units and 78.4 units; and alanine aminotransferase, 24 and 29 units/L. HIV and HbsAg were nonreactive. Preoperative hemodialysis was conducted for more than 6 months for both cases. The electrolyte levels and electrocardiograms (ECGs) of the patients before renal transplantation were normal. During the operation, the first patient lost 1000 mL blood, and received blood transfusion of 400 mL. The second patient needed no blood transfusion. After operations, both of them received immunosuppressive therapy with tacrolimus, mycophenolate mofetil, and prednisolone. The following described the immunosuppressive therapy in detail. Tacrolimus was given at a dose of 0.1 mg/kg/day and then adjusted to maintain target trough level of 7 to 12 ng/mL in the first month, 6 to 10 ng/mL during the second and third months, and 3 to 8 ng/mL for the following time. Mycophenolate mofetil was supplied at a daily dose of 500 mg for 3 days followed by 1 g/day. Prednisolone was provided 250 mg directly after transplantation, followed by 100 mg/day for 3 days, and then reduced to 20 x0200A;mg per day for the rest of the first month following the operation. Afterwards, it was continued to be given at 10 mg/day for the next 5 months, and reduced to 5 mg/day 6 months after transplantation. Postoperative ECG detection and blood component analyses were performed to monitor the electrolyte levels of the 2 patients. At the fourth day after renal transplantation, both of the patients exhibited normal renal function, with normal blood pressure and serum potassium concentration (SPC). According to doctor's advice and the pH values of their urine, the patients were given recommended doses (10 g/day) of PSHC granules (trade name: Uralyt-U, made in Germany Madausag) from the ninth day to the 17th day after surgery. The daily dose was 4 standard measuring spoon (2.5 g/standard measuring spoon), and supposed to be taken orally 3 times a day after meal. The patients took 1 spoon of Uralyt-U in the morning and at noon, respectively, and 2 spoons in the evening. Both of them showed different symptoms after taking the drug. The first patient presented chest tightness, nausea, muscle weakness, and ascending paralysis at the second day after taking the drug with a cumulative dose of 12.5 g. This patient's blood pressure, heart rate, respiratory rate, and SPCs were 106/51 mm Hg, 46 beats/min, 16 times/min, and 7.67 mmol/L, respectively. The ECG with peaked T waves for patient 1 is shown in Fig. 1. Bedsides, hemo-filtration was performed immediately for patient 1, showing stably improved status, with SPCs dropping to 5.30 mmol/L and discomfort disappearing gradually. On the 17th day with a cumulative dose of 62.5 g, patient 2 had stable vital signs but slightly weakened waves on ECG. SPCs of patient 2 was 6.05 mmol/L. Patient 2 was then given 10% calcium gluconate 10 mL, 5% $NaHCO_3$ 125 mL, and 10% glucose 500 mL with the addition of 10 units of insulin through intravenous drip. One hour later, patient 2 recovered well and SPCs dropped to 5.48 mmol/L. The information on SPCs (mmol/L), serum creatinine concentrations (SCrCs, $\times 10^{-2}$ μmol/L), and blood tacrolimus concentrations (BTCs, μg/L) of the 2 cases were recorded along with the process of the treatments after renal transplantation (Fig. 2A, B).

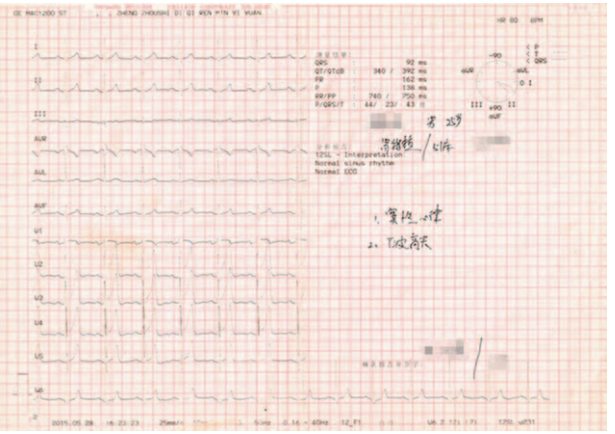

Figure 1. ECG at presentation for the first patient. ECG at presentation shows dramatically peaked T waves. ECG = electrocardiogram.

3. Discussion

Stone formation, which is caused by metabolic anomalies and side effects of relevant medical treatments, is frequently observed after renal transplantation.[11] Immunosoppressive agents, such as calcineurin inhibitor glucocorticoid, may cause calculi after transplantation, thus leading to hyperuricemia, hyperoxaluria, and hypocitraturia.[12–15] Therefore, to reduce the risk of calculi formation, alkaline citrate is given to the patients to increase urinary citrate excretion and urinary solubility index.[16–19] Currently, several types of potassium-bearing citrates (PC, sodium PC, potassium magnistium citrate, and PSHC) are available. With its alkalinizing effect, PSHC can reduce urinary

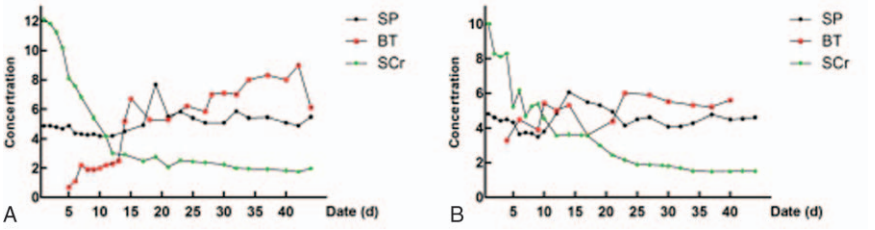

Figure 2. The changes in the concentrations of SP (mmol/L), BT (mmol/L), and SCr ($\times 10^{-2}$ μmol/L) in the 2 patients along with the passage of time after renal transplantation. (A) It shows that hyperkalemia happens on the 18th day for the first patient 1 day after taking the drug with a SP concentration of 7.67 mmol/L; (B) It shows that hyperkalemia happens on the 14th day for the second patient 5 days after taking the drug with a SP concentration of 6.05 mmol/L. BT = blood tacrolimus, SCr = serum creatinine, SP = serum potassium.

saturation of calcium, and then decrease ionic calcium concentration, thus preventing stone formation.[20–23] Therefore, this agent is commonly used for the prevention of stone formation among patients undergoing renal transplantation.

First, in the present study, we found that in both cases, SPCs increased gradually and hyperkalemia only occurred 1 and 6 days after the treatment with PSHC granules for patient 1 and patient 2, respectively (Fig. 2A, B). The degrees of hyperkalemia in the 2 patients were observed to be directly influenced by PSHC. According to previous studies, single oral potassium at a dose of 0.5 mmol/kg produced a minimal increase in serum potassium, while total doses of approximately 1 mmol/kg increased serum potassium by as much as 1 mmol/L in a healthy man.[24,25] The molecular formula of PSHC is $K_6Na_6H_3(C_6H_5O_7)_5$, with the molecular weight of 1321.06. According to the instructions of PSHC granules, each gram of PSHC contains 4.4 mmol potassium. Patient 1 (weight: 58 kg) presented hyperkalemia after orally taking a cumulative dose of 12.5 g PSHC, equal to 0.95 mmol/kg potassium, while patient 2 (weight: 62 kg) developed hyperkalemia after being given a cumulative dose of 62.5 g PSHC, equal to about 1 mmol/kg. For the patients undergoing renal transplantation, the cumulative doses they taking might be a "heavy" load, increasing the risk of hyperkalemia. In addition to PSHC, some other factors might also contribute to the occurrence of hyperkalemia in the 2 patients, such as the application of calcineurin inhibitors, glucocorticoids, and diuretics.[26–28] In this report, both of the cases received tacrolimus (calcineurin inhibitor) and prednisolone (a type of glucocorticoid) in immunosuppressive treatment that might increase the risk of hyperkalemia. Furthermore, blood transfusion might also stand for a potential risk factor for hyperkalemia. It was reported that supernatant potassium concentration of stored blood was frequently higher than potassium levels in normal human plasma, and that rapid intravenous infusion might allow a mass of potassium into receiver's body in a short time, thus swiftly increasing blood potassium concentration.[29,30] However, the specific mechanisms of blood transfusion inducing hyperkalemia remain unclear. Besides, surgical procedure represented another potential risk factor for hyperkalemia. Hirata et al[31] reported that anesthesia contributed to a sharp potassium increase after kidney transplantation. In a word, the application of PSHC together with the uses of calcineurin inhibitors and glucocorticoids, as well as blood transfusion and invasive surgical procedures might contribute to hyperkalemia in the 2 cases.

Second, there was a clear correlation between the application of PSHC and the occurrence of hyperkalemia, the situation also applying to other potassium-bearing citrates.[23] The correlation between PC and hyperkalemia-related complications has been investigated in previous studies.[17–19] Hyperkalemic ventricular fibrillation was even observed in patients with fine renal function after ingesting small amounts of PC (40–60 mmol/L).[23,24] It might be not harmless for patients with normal renal function even at an acceptable dosage, although there is 28 mmol potassium in 10-mL PC mixture. The recommended daily dose is up to 40 mL, more than twice the daily intake of PSHC, which means more dangers of hyperkalemia. Therefore, we suggest that more attentions should be given when potassium-bearing citrate is prescribed, especially for the elderly and those with impaired renal functions.

Third, these cases highlighted potentially serious consequences of PSHC application in patients receiving renal transplantation. We would like to emphasize side effects of potassium alkaline citrate, despite its significant advantage in preventing urinary lithiasis.[24] Physicians should evaluate the role of potassium-bearing citrates besides PSHC in patients after renal transplantation, particularly in those with renal insufficiency or combination medication. It has been suggested that when coprescribing medicine, it would be better to avoid using potassium-bearing citrate that may interfere with potassium homeostasis among patients with renal dysfunction.[26,32] If not, oral dose should be reduced according to the severity of renal dysfunction. In a previous study, sodium bicarbonate did not allow additional potassium into blood, and showed an effect equivalent to potassium-bearing citrate in the treatment of urinary stone, suggesting that sodium bicarbonate might be a better choice for patients who could not tolerate PC.[33] At the moment, people can purchase all types of potassium-bearing citrates from counters in any retail pharmacies in communities, while many patients and even physicians pay little attention on this issue.

Considering the analysis results about the 2 unusual patients in our study, it was not safe to use PSHC or other potassium-bearing citrates (PC, sodium PC, and potassium magnistium citrate) for patients undergoing renal transplantation. Both frequencies and timing of potassium evaluation should be regimented to control the level of serum potassium during the therapy. Besides, the therapy should be better performed in centers with advanced equipment and more experts who make appropriate treatment plans.

4. Conclusion

The application of PSHC may increase the risk of hyperkalemia in patients undergoing renal transplantation. Physicians should keep a watchful eye on potential risks caused by potassium-bearing citrates, and monitor SPCs to minimize the rate of drug-induced hyperkalemia.

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