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CASE REPORT

Management of hyperkalaemia in acute kidney injury in a heart failure patient with patiromer

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Abstract

Aims One prevalent comorbidity of chronic heart failure (CHF) is chronic kidney disease(CKD). Hyperkalemia is associated with both CHF and CKD, which often leads to withdrawal of heart failure medications in clinical praxis.
Methods and results A patient is presented who suffered from acute kidney injury with pre-existing CKD as heart failure comorbidity and a history of hyperkalemia.
Conclusions This case shows that potassium levels remained stable in acute kidney injury under ongoing heart failure medications, including an MRA, with the use of the potassium binder patiromer.

Keywords Chronic Heart Failure; Chronic Kidney Failure; Heart Failure Therapy; Hyperkalemia

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Introduction

In chronic heart failure (CHF), chronic kidney disease (CKD) is one of the most prevalent co-morbidities.[1] Patients with CHF and CKD show a worse prognosis than those without CKD.[2] The close interaction of the heart and the kidney was described by the term cardiorenal syndrome (CRS) depending on intra-renal haemodynamics, trans-renal perfusion pressures, and neurohormonal factors.[3] Associated with CRS is the problem of derailment of electrolytes especially a high incidence of hyperkalaemia. The risk of hyperkalaemia in HF is further increased by guideline-recommended drugs improving mortality and morbidity like mineralocorticoid antagonists or renin–angiotensin system inhibitors (RASi).[4] New potassium binders, like patiromer[5] or ZS9,[6] have been shown to be effective in the treatment of hyperkalaemia and will be assessed in HF to enable adequately dosed mineralocorticoid receptor antagonists (MRAs), RASi, and sacubitril/valsartan.[7]

Case report

A 69-year-old woman presented with shortness of breath, dizziness, and vomiting in the emergency room. The patient reported not to have drank and eaten for 48 h with limited sleep with consecutive socio-psychological stress owing to grief over the loss of a loved one. According her past medical history, the patient has been suffering from CHF disease due to ischaemic cardiomyopathy with a systolic ejection fraction of 28% at the last visit in the HF clinic. Because of a bradycardia–tachycardia syndrome in connection with atrial fibrillation, a pacemaker was implanted. Because of haemodynamically relevant ventricular tachycardia and reduced ejection fraction before, the pacemaker was upgraded to an implanted cardioverter defibrillator. She was recently discharged after an acute HF decompensation. Before admission, there was an interrogation of implantable cardioverter defibrillator. There was an atrial pacing of 76% with less than 0.1% ventricular pacing with no episodes of ventricular tachycardia or persisting atrial fibrillation detected. The medical treatment at discharge consisted of bisoprolol 5 mg/day, sacubitril/valsartan 24/26 mg, spironolactone 25 mg/day, and 80 mg of torasemide. In addition, peripheral arterial occlusive disease, coronary artery disease, and liver cirrhosis were other relevant co-morbidities. The patient was suffering from CKD with day-to-day variations of estimated glomerular filtration rates (eGFRs[8]; Chronic Kidney Disease Epidemiology Collaboration

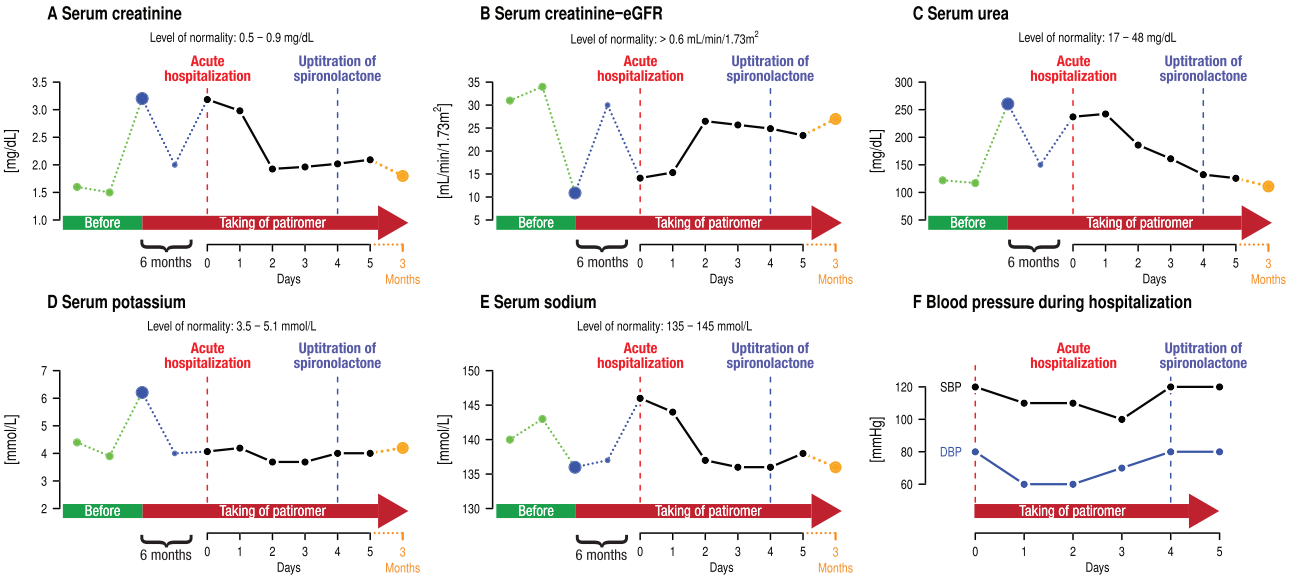
equation) between 25 and 40 mL/min/1.73 m^2. Also according her past medical history, she has been hospitalized recurrently owing to acute-on-chronic kidney failure with consecutive hyperkalaemia. Because even small reductions of renal function in this patient were accompanied by hyperkalaemia episodes with serum potassium up to 6.2 mmol/L previously, therapy with patiromer 8.4 g/day was established after discharge from the previous hospital stay 6 months ago.

Physical examination on admission revealed dry mucosa and standing skin folds. The patient presented with impaired orientation. At hospitalization (Day 1 in *Figure 1A–D*), lab values showed high creatinine of 3.2 mg/dL, eGFR of 14.1 mL/min/1.73 m^2, and urea of 242 mg/dL but still normal potassium of 4.0 mmol/L on patiromer. Creatinine and urea concentrations were higher and eGFR significantly lower than the average outpatient values after the previous HF hospitalization, which were also accompanied by impaired renal function. Other electrolytes showed normal values. Electrocardiogram showed sinus rhythm with atrial pacing with intrinsic atrioventricular transition that persisted throughout the hospitalization. The patient was not suffering from palpitations at admission or during hospitalization.

Therapy

Upon physical examination, elevated creatinine and urea led to the diagnosis of acute kidney failure due to exsiccosis. Physical examination and medical history were suggestive of volume depletion, but interestingly, potassium concentrations were in the normal range. Therefore, volume was substituted with electrolyte solutions with 2 L in the first 24 h and another 3 L in the subsequent 2 days. Under fluid therapy, creatinine value decreased to 3.0 mg/dL at Day 1 (*Figure 1A*). Continuing fluid therapy lowered creatinine levels to 1.96 mg/dL corresponding to her former creatinine levels. In parallel, urea levels decreased from 242 to 126 mg/dL (*Figure 1C*), and creatinine–eGFR levels increased from 15.4 to 35.8 mL/min/1.73 m^2 (*Figure 1B*). Serum sodium concentrations decreased from 147 to 136 mmol/L during fluid therapy (*Figure 1E*). Initially, potassium was at 4.2 mmol/L at a patiromer dose of 8.4 mg twice a day. At the following days, potassium level was kept stable between 3.7 and 4.0 mmol/L (*Figure 1D*). On Day 5, we were able to up-titrate spironolactone to 50 mg/day (*Figure 1D*) to intensify HF treatment without rise of potassium. Blood pressure was kept stable between systolic 120 mmHg and

Figure 1 A 69-year old female patient presented with acute kidney failure with increased serum creatinine and serum urea and decreased serum creatinine–eGFR. Under ongoing heart failure medication and patiromer, serum potassium values could be kept stable. At acute hospitalization, serum creatinine (A) was at 3.2 mg/dL, serum creatinine–eGFR (B) at 14 mL/min/1.73 m^2, elevated serum urea (C) at 237 mg/dL, and serum sodium at 146 mmol/L (E). Under fluid therapy in the next 3 days, these values improved and reached output value. Potassium value (D) could be kept stable at output value throughout the acute kidney failure accompanied with stable blood pressure values during acute hospitalization (F). At Day 5, even up-titration of spironolactone was possible. Big blue circles indicate value at index event when patiromer was started; small blue circles, average value under patiromer before acute hospitalization; green circles, values before taking of patiromer; yellow circles, value after 3 months' control. DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; SBP, systolic blood pressure.



diastolic 60 mmHg (*Figure 1F*). All parameters were stable in 3 months' control under ongoing HF and patiromer therapy (*Figure 1A–E*).

Hyperkalaemia represents an important clinical problem, because the frequent CRS is associated with impaired potassium excretion[9] and with high mortalitiy.[10] Mortality and morbidity are reduced by guideline-directed MRAs and RASi, although these drugs can lead to or augment life-threatening hyperkalaemias.[11] In clinical praxis, physicians often continuously stop or do not up-titrate potassium-retaining drugs like spironolactone despite their benefits on outcomes.[12] A recent study showed that only 54% of hyperkalaemia episodes were directly associated with MRA therapy, while on placebo, hyperkalaemia occurred also in 46%.[13] In consequence, 46% were related to other reasons,[13] but hyperkalaemia workup is often dismissed.[14] The Guidelines of the European Society of Cardiology recommend not only to continuously withdraw but also to intermittently pause renin–angiotensin–aldosterone system (RAAS) inhibitor therapy until the workup of hyperkalaemia is finished. Even though RAAS blockers can frequently cause a decrease in eGFR, the treatment benefit in these patients is maintained.[15]

Pathophysiology of hyperkalaemia involves either extracellular potassium shifts or decreased renal excretion.[15] Approximately 73% of patients with advanced CKD and 40% of HF patients may be at risk of elevating potassium levels.[16] Equivalent to reasons, treatment of hyperkalaemia consists either of shifting potassium into cells via insulin/glucose, with beta-agonists activating the Na^+-K^-ATPase or sodium bicarbonate. The other approach consists of elimination of potassium from the body by diuretic therapy o haemodialysis.[15] A new approach for suppressing hyperkalaemia in CKD and HF is the potassium binder patiromer.[17–19] The active moiety of patiromer is a non-absorbable oral K^+-binding polymer that primarily acts in the distal colon to increase faecal K^+ excretion.[20] In the OPAL-HK study, 2015 patients with CKD on RAAS inhibitor medication were randomized to patiromer or placebo. Patiromer lowered mean serum K^+ compared with placebo and also reduced the number of patients with recurrent hyperkalaemia, allowing significantly more patients to remain on RAAS inhibitor therapy.[21] In the case presented here, there was an impressive dissociation of creatinine and urea concentrations and potassium levels on patiromer in acute kidney injury, even though this patient had regular episodes of hyperkalaemia before as reason to treat her with patiromer and include her in an observational patiromer study (CONTINUE-HF NIS, DRKS-ID: DRKS00014825).

Effective treatment of arterial hypertension is essential to prevent patients from developing CHF and CKD.[22,23] According to European Society of Cardiology (ESC) Guidelines for the treatment of hypertension, spironolactone is recommended for patients with uncontrolled, resistant hypertension.[24] The AMBER trial evaluated whether the use of patiromer allows persistent use of spironolactone in patients with CKD and resistant hypertension. More patients (86% vs. 66%) on patiromer therapy were able to continue treatment with spironolactone with less hyperkalaemia as compared with those on placebo.[25]

One might ask why this patient suffered from acute kidney injury. The patient was discharged after an acute decompensation from the hospital. On admission, the patient presented with generalized oedema and was recompensated with diuretics, and sacubitril/valsartan was added to the discharge medication together with diuretics. Sacubitril/valsartan reduces diuretic demand in the PARADIGM trial[26] and in real-life conditions, when patients are being treated by their family physicians[27] owing to haemodynamic intrarenal and natriuretic effects of the drug.[28,29] Therefore, the reduced fluid intake due to psychosocial stress as well the reduced diuretic demand under sacubitril/valsartan at high diuretic discharge doses probably might have caused acute kidney injury in this patient.

Taken together, this case study shows that potassium levels can be kept stable even in acute kidney failure and ongoing HF medications and even in a patient with previous hyperkalaemia with the use of potassium binder patiromer.

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Conflict of interest

J. S., I. K., and J. D. have nothing to declare. M. B. received consulting honoraria from Vifor and is the chairman of CONTINUE-HF.

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