Overcoming the Causes (and Consequences) of Chronic Hyperkalemia

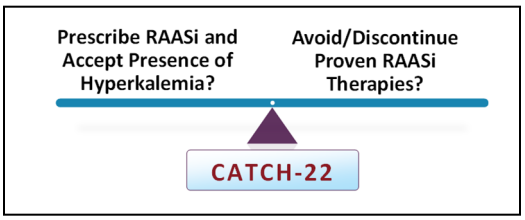
Clinical Insight

INTRODUCTION

Hyperkalemia is common in patients who have chronic kidney disease (CKD), particularly those with underlying conditions that disrupt the renin-angiotensin-aldosterone system (RAAS).[1] Chronic hyperkalemia is a long-term concern, given the epidemiologic data to show that hyperkalemia is associated with worse outcomes, including an annual mortality rate of 25%.[2] Hyperkalemia is associated with several clinical consequences, including cardiac toxicity and muscle weakness. Unfortunately, the electrocardiogram has poor sensitivity and specificity for hyperkalemia.[3, 4] Hyperkalemia often coexists with a normal gap acidosis that may be related to suppression of ammoniagenesis, thereby secondarily impairing kidney acidification.

RENIN-ANGIOTENSIN-ALDOSTERONE INHIBITOR THERAPY

Although excess potassium intake is not a typical cause of chronic hyperkalemia, dietary potassium restriction can be considered a treatment strategy for chronic hyperkalemia. An important consideration, however, is that many fruits and vegetables high in potassium content are associated with lower all-cause mortality and are considered heart healthy.[5] Another strategy is to reduce the dose or discontinue RAAS inhibitor therapy in patients with CKD or chronic heart failure. This strategy is also a catch-22 since RAAS inhibitor therapy is a recommended treatment option due to its proven cardiovascular benefit in these patients.[6, 7] In fact, lowering the dose or discontinuing RAAS inhibitor therapy in patients with CKD or chronic heart failure has been shown to increase the risk of death.[8] Concerns about hyperkalemia is a major reason for not starting RAAS inhibitor therapy in these patients.[9]



Patients hospitalized due to chronic hyperkalemia should receive multifaceted care, once stabilized, with the goal to facilitate patient self-management in the outpatient setting. Ideally, RAAS inhibitor therapy should be continued, if indicated.[10] Patient education about adherence to diet and treatment, as well as symptom recognition, with a written action plan, is of paramount importance. Care provided by a multidisciplinary team is recommended.

POTASSIUM-BINDING MEDICATIONS

Sodium polystyrene sulfonate has been used for decades for the treatment of patients with hyperkalemia. There is, however, no evidence to support its use for treating patients with chronic hyperkalemia. Moreover, gastrointestinal (GI) safety is a concern. Patiromer and sodium zirconium cyclosilicate have been approved for use in patients with chronic hyperkalemia due to their affinity to bind potassium in the GI tract, resulting in lowering the serum potassium level. In patients concomitantly treated with RAAS inhibitor therapy, both agents provide significantly greater reduction in the serum potassium level, within hours, compared with

placebo.[11-14] The serum potassium level generally remains in the normal range while treatment is continued. Both patiromer and sodium zirconium cyclosilicate provide durable normalization of the serum potassium level over 52 weeks of treatment. Both medications are well tolerated. A small percentage of patients experience constipation, diarrhea, or nausea, with patiromer, or peripheral edema with sodium zirconium cyclosilicate. Clinical trials clearly show that a key benefit of patiromer and sodium zirconium cyclosilicate is that the serum potassium level can be normalized in most patients while RAAS inhibitor therapy is continued.

	Patiromer[11, 12]	Sodium zirconium cyclosilicate[13, 14]
% Patients who achieve normokalemia	76% at 4 weeks	98% at 48 hours[2]
Durable potassium lowering	✓	✓
Common AEs	Constipation, diarrhea, nausea	Peripheral edema
Enables continuation of RAAS inhibitor therapy	✓	✓

[1]Dosing was 4.2 g or 8.4 g twice daily for 4 weeks
[2]Dosing was 10 g 3 times daily for 48 hours

OTHER TREATMENT CONSIDERATIONS

Another strategy to minimize the risk of chronic hyperkalemia in patients treated with RAAS inhibitor therapy has led to the development of finerenone, a nonsteroidal mineralocorticoid receptor antagonist. The addition of finerenone to other RAAS inhibitor therapy, ie, angiotensin converting enzyme inhibitor or angiotensin receptor blocker, in patients with CKD and diabetes mellitus, results in significantly greater reduction than placebo over 48 months in the composite primary outcome of kidney failure, sustained >40% decrease in eGFR, or renal death, as well as composite secondary outcome of cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for heart failure.[15] Hyperkalemia is observed in a small percentage of patients.

For optimal patient care, good communication among the multidisciplinary care team, including the patient, is critical. Communication between the hospital team and outpatient team is particularly important upon patient discharge from the hospital. Patients should be provided ongoing education and support so that they are able to successfully self-manage and adhere to the treatment plan over time.

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