Best Practices in Managing

HYPERKALEMIA

in Chronic Kidney Disease

- Hyperkalemia in Chronic Kidney Disease (CKD)
- Treatment with RAAS Inhibitors (RAASi) in CKD
- Diagnosis and Evaluation of Hyperkalemia
- Treatment of Hyperkalemia in CKD

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HYPERKALEMIA
IN CKD

The definition of hyperkalemia varies and limits such as >5.5, >6.0, or >7.0 mEq/L are used to indicate severity.[1] Repetitive consecutive measures of serum potassium are needed to determine if hyperkalemia is sustained or a transient event. Many factors affect potassium homeostasis.[2]

Table 1. **Acute Versus Chronic Hyperkalemia** [3, 4]

Acute Hyperkalemia	Chronic Hyperkalemia
Caused by abnormal net release of potassium from cells, often due to trauma, metabolic acidosis (depends on etiology), hemolytic states	Caused by impairment of potassium excretory process and/or increased potassium load
Requires immediate attention, ie, cardiac monitoring, acute medical interventions, possibly dialysis	Requires ongoing management to correct the underlying disturbances in potassium balance, ie, nonpharmacological and pharmacological interventions
Management goals: induce potassium redistribution and excretion, restore normal electrophysiology of the cell membrane, prevent cardiac arrhythmia	Management goals: induce potassium redistribution and excretion to prevent the development or recurrence of hyperkalemia; monitor potassium intake through diet

Table 2. Chronic Risk Factors for Hyperkalemia in CKD [5, 6, 7, 8]

Risk Factor	Due To
Potassium intake	Increased dietary potassium intake from salt substitute, potassium-rich heart-healthy diets, and herbal supplements
Metabolic acidosis	Potassium shift from the intracellular to the extracellular space
RAASi	Treatment with ACEIs and ARBs block the renin-angiotensin system and cause lower serum aldosterone
Diabetes	Insulin deficiency and hypertonicity caused by hyperglycemia contribute to an inability to disperse high acute potassium load into the intracellular space
Heart failure	Reduction in renal perfusion, use of RAASi or MRA
Coronary artery and peripheral vascular disease	Use of RAASi, oxidative stress, atherosclerosis
Advanced age	Decreases in plasma renin activity and plasma aldosterone levels with age, as well as frequent use of NSAIDS in this population.

Abbreviations: ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; MRA, mineralocorticoid receptor antagonist; NSAIDS, nonsteroidal anti-inflammatory drugs; RAASi, renin-angiotensin-aldosterone system inhibitors.

TREATMENT WITH RAASi
IN CKD

Studies show that use of ACEIs or ARBs in people with CKD reduces the risk for kidney failure and cardiovascular events, but their use contributes to hyperkalemia.[9] The clinical practice guidelines for the use of RAASi in CKD are as follows:[10, 11]

- KDIGO Guidelines suggest that an ARB or ACEI be used in diabetic adults with CKD and urine albumin excretion 30-300 mg/24 hours (or equivalent). (2D)
- KDIGO Guidelines recommend that an ARB or ACEI be used in both diabetic and nondiabetic adults with CKD and urine albumin excretion >300 mg/24 hours (or equivalent). (1B)
- There is insufficient evidence to recommend combining an ACEI with ARBs to prevent progression of CKD. (Not Graded)
  - Subsequent research shows that dual RAAS inhibition with ACEI plus ARB not only fails to improve cardiovascular or renal outcomes, but predisposes patients to serious adverse events.[12]

Considerations for using an ACEI or ARB in patients with CKD:

- Hyperkalemia and worsening kidney function can develop.
- It is important to monitor serum potassium and estimated glomerular filtration rate (eGFR) within several weeks of starting or escalating a RAASi.[13]
- Discontinuing these drugs is helpful in controlling or treating hyperkalemia, but the disadvantage is that it increases the risk for kidney disease progression and cardiovascular events.[6]

DIAGNOSIS AND EVALUATION
OF HYPERKALEMIA

Hyperkalemia is often asymptomatic, but patients may complain of nonspecific symptoms such as palpitations, nausea, muscle pain, weakness, or paresthesia. Moderate and especially severe hyperkalemia can lead to cardiotoxicity, which can be fatal. The cause of hyperkalemia has to be determined to prevent future episodes. [14]

Emergency diagnostic workup:[14]	Elective/etiologic workup:[14]
1. Assessment of cardiac function, kidneys, and urinary tract	1. Comprehensive laboratory workup
2. Assessment of hydration status	2. Review of medication used
3. Electrocardiogram	

TREATMENT OF HYPERKALEMIA IN CKD

The steps to address hyperkalemia include stabilization redistribution, and excretion/removal of potassium.

Table 3. **Summary of interventions used for acute or chronic treatment of hyperkalemia[6]**

Treatment	Route of administration	Onset/ duration	Mechanism	Comments
6.8 mmol of calcium, corresponding to 10 ml CaCl (10%)* or 30 ml calcium gluconate (10%) solutions	Intravenous (acute)	1-3 min 30-60 min	Membrane potential stabilization	■ Does not affect serum potassium level ■ Effect measured by normalization of electrocardiographic changes ■ Dose can be repeated if no effects noted ■ Caution advised in patients receiving digoxin
50-250 ml hypertonic saline (3-5%)**	Intravenous (acute)	5-10 min ~2 h	Membrane potential stabilization	■ Efficacy only in hyponatremic patients
50-100 mmol sodium bicarbonate	Intravenous (acute) or oral (chronic)	5-10 min ~2 h	Redistribution	■ Sodium may worsen pre-existing hypertension and heart failure ■ Efficacy questioned for acute treatment of patients on dialysis
10 units of regular insulin	Intravenous (acute)	30 min 4-6 h	Redistribution	■ Administer with 50 g of glucose intravenously to prevent hypoglycemia
$ß_2$-receptor agonists: 10-20 mg aerosol (nebulized) or 0.5mg in 100ml of 5% dextrose in water (intravenous)	Intravenous or nebulized (both acute)	30 min 2-4 h	Redistribution	■ Effect independent of insulin and aldosterone ■ Caution in patients with known coronary artery disease
40 mg furosemide or equivalent dose of other loop diuretic. Higher doses may be needed in patients with advanced CKD	Intravenous (acute) or oral (chronic)	Varies Until diuresis present or longer	Excretion	■ Loop diuretics for acute intervention ■ Loop or thiazide diuretics for chronic management; loop diuretic for GFR <40 ml/min/1.73 m^2 [15] ■ May not be effective in patients with reduced GFR
Fludrocortisone acetate ≥0.1 mg (up to 0.4-1.0 mg daily)	Oral (chronic)	NA	Excretion	■ In patients with aldosterone deficiency, large doses might be needed to effectively lower potassium levels ■ Sodium retention, edema, and hypertension might occur, and acceleration of kidney and cardiovascular disease
Cation exchange resins Sodium polystyrene sulfonate 25-50 g	Oral or rectal (either acute or chronic), with or without sorbitol	1-2 h ≥4-6 h	Excretion	■ Cases of intestinal necrosis, which may be fatal, and other serious GI adverse events have been reported[16] ■ May cause hypokalemia and electrolyte disturbances[16] ■ Cannot be used in medical emergencies[16] ■ Caution in patients with heart failure due to sodium load[16]
Cation exchange polymer Patiromer 8.4, 16.8, or 25.2 g	Oral (either acute or chronic)	7 h ~48 h	Excretion	■ Should not be used as an emergency treatment for life-threatening hyperkalemia because of its delayed onset of action[17] ■ There are no restrictions regarding concomitant use of patiromer with immediate-acting emergency treatments for hyperkalemia ■ Risks include worsening of gastrointestinal motility and hypomagnesemia[17] ■ The most common Adverse Reactions in clinical trials were constipation, hypomagnesemia, diarrhea, nausea, abdominal discomfort and flatulence[17]
Dialysis	Hemodialysis (acute or chronic); Peritoneal dialysis (chronic)	Within minutes until end of dialysis or longer***	Removal	■ Effects of dialysis on serum sodium, bicarbonate, calcium and/or magnesium levels can affect results ■ For chronic hemodialysis, missed treatments and 2-day interdialytic interval may have a negative impact on outcomes.

*CaCl is caustic and could damage peripheral veins. **Limited data available from clinical studies. ***Effects can last for an unspecified length of time, depending on ongoing potassium intake or cellular redistribution. Abbreviations: CKD, chronic kidney disease; GFR, glomerular filtration rate; GI, gastrointestinal; NA, not applicable. | Adapted with permission from Kovesdy CP. Management of hyperkalaemia in chronic kidney disease. *Nat Rev Nephrol*, 2014;10:659-662.

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