

Electrolyte disturbance with diuretics and ACEIs

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Clinical question

What is the risk of electrolyte disturbances with diuretics and angiotensin-converting enzyme inhibitors (ACEIs) and when should we check levels?

Bottom line

Moderate hyponatremia (sodium [Na] <130 mmol/L) and hypokalemia (potassium [K] <3.2 mmol/L) occur in about 4% of thiazide users; hyperkalemia (K >5.4 mmol/L) occurs in 4% of ACEI (and angiotensin receptor blocker) users. Limited evidence suggests checking electrolyte levels 2 to 4 weeks after starting or increasing doses of these agents, and at least annually thereafter.

Evidence

- The ALLHAT substudy¹ (n=19731 with normal baseline K levels) found the following results at 1 year.
 - Overall, 3.5% of those taking chlorthalidone (12.5 to 25 mg), 0.2% of those taking lisinopril (10 to 40 mg), and 0.3% of those taking amlodipine (2.5 to 10 mg) had K levels less than 3.2 mmol/L; 1.2% of those taking chlorthalidone, 3.6% of those taking lisinopril, and 1.9% of those taking amlodipine had K levels greater than 5.4 mmol/L. Further, 8% of those taking chlorthalidone were taking K supplements at 5 years.²
- The SHEP study³ of 4736 patients taking chlorthalidone (12.5 to 25 mg) or placebo found, within 4.5 years, 3.9% and 4.1% of those taking chlorthalidone had K levels below 3.2 mmol/L and Na levels below 130 mmol/L, respectively (vs 0.8% and 1.3% for placebo, respectively).
- The HYVET trial⁴ (indapamide vs placebo) excluded patients with abnormal K levels; compared with placebo, K levels were 0.05 mmol/L lower with indapamide at 2 years (Na levels were not reported).
- Chlorthalidone (12.5 to 25 mg) decreases K levels an average of 0.2 to 0.4 mmol/L^{5,6} (about 0.1 to 0.2 mmol/L more than the same dose of hydrochlorothiazide).⁶
- Angiotensin receptor blockers have rates of hyperkalemia similar to those for ACEIs.⁷

Context

- Diuretics are inexpensive first-line agents for patients with uncomplicated hypertension.⁸
- Limited evidence suggests that thiazide-induced hypokalemia or hyponatremia occur within the first days to weeks of therapy^{9,10} but can also develop years later.¹¹
- Hypokalemia and hyponatremia risk factors include being female^{1,12} and increasing age¹² or diuretic dose.¹²

- Mild hypokalemia is often asymptomatic, but symptoms can include weakness, myalgia, and cardiac arrhythmia.¹³
- Moderate to severe hyponatremia (Na <130 mmol/L) can cause lethargy, dizziness, nausea, and confusion.¹⁴

Implementation

Common nondrug causes of hypokalemia include vomiting, diarrhea, renal losses, congestive heart failure, or systemic alkalosis. If patients have hypokalemia from diuretics, adding ACEIs¹⁵ or using K-sparing diuretics (like amiloride)¹⁶ can help maintain normokalemia. Consider primary aldosteronism and Cushing syndrome in patients with hypertension who have hypokalemia before medical therapy. 🌿

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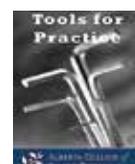
Competing interests

None declared

The opinions expressed in Tools for Practice articles are those of the authors and do not necessarily mirror the perspective and policy of the Alberta College of Family Physicians.

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