How low can the potassium and sodium go with commonly prescribed blood pressure medications?

Clinical Question: What is the risk of electrolyte disturbances with diuretics and ACE Inhibitors and when should we check?

Bottom-line: Moderate hyponatremia (Na <130 mmol/L) and hypokalemia (K <3.2 mmol/L) each occur in ~4% of thiazide users, and hyperkalemia (K >5.4 mmol/L) occurs in 4% of ACE inhibitor (and angiotensin receptor blocker) users. Limited evidence suggests checking electrolytes in the first 2-4 weeks after starting, and again after increasing doses of these agents, and at least annually thereafter.

Evidence:

- Large hypertension Randomized Controlled Trials (RCTs) reporting sodium (Na) and Potassium (K).
  - ALLHAT sub-study\(^1\) of 19,731 patients with normal baseline potassium: Results for chlorthalidone (12.5-25 mg) or lisinopril (10-40mg) or amlodipine (2.5-10 mg). At one year:
    - K <3.2 mmol/L: Chlorthalidone 3.5%, lisinopril 0.2%, amlodipine 0.3%.
    - K >5.4mmol/L: Chlorthalidone 1.2%, lisinopril 3.6%, amlodipine 1.9%.
    - 8% of ALLHAT chlorthalidone users were on potassium supplements at five years.\(^2\)
  - SHEP:\(^3\) 4,736 patients on chlorthalidone (12.5-25mg) or placebo. At any time in 4.5 years:
    - K <3.2 mmol/L: Chlorthalidone 3.9%, placebo 0.8%.
    - Na < 130 mmol/L: Chlorthalidone 4.1%, placebo 1.3%.
  - Other large diuretic RCTs:
    - HYVET\(^4\) (indapamide vs placebo): Excluded patients with abnormal potassium.
      - Compared to placebo, K was 0.05 mmol/L lower with indapamide at two years.
      - Na not reported.
    - ANBP2\(^5\) (enalapril vs hydrochlorothiazide): Electrolyte results not reported.
Chlorthalidone 12.5-25 mg decreases potassium on average by ~0.2-0.4 mmol/L\textsuperscript{6-8} about 0.1-0.2 mmol/L more than the same dose of hydrochlorothiazide.\textsuperscript{7}

Angiotensin receptor blockers (ARBs) have similar hyperkalemia rates as ACE inhibitors.\textsuperscript{9}

**Context:**
- Diuretics are first line agents for uncomplicated hypertensive patients\textsuperscript{10} with additional advantage of low cost.\textsuperscript{11}
- Limited evidence suggests that thiazide induced hypokalemia or hyponatremia may occur within the first days to weeks of therapy,\textsuperscript{12,13} but can also develop years later.\textsuperscript{14}
- Hypokalemia and hyponatremia risk factors: Women>men,\textsuperscript{1,15} increasing age,\textsuperscript{15,16} and diuretic dose.\textsuperscript{15,16}
  - Most patients with mild hypokalemia are asymptomatic, but symptoms can include weakness, myalgias, and cardiac arrhythmias.\textsuperscript{17}
  - Moderate-to-severe hyponatremia (Na <130) may produce lethargy, dizziness, nausea, and confusion.\textsuperscript{18}
- Combining diuretics with ACE\textsuperscript{19} or using potassium-sparing diuretics (like amiloride)\textsuperscript{20} may help maintain normokalemia.

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**References:**
physicians who are joined occasionally by a health professional from another medical specialty or health discipline. Each article is peer-reviewed, ensuring it maintains a high standard of quality, accuracy, and academic integrity.

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