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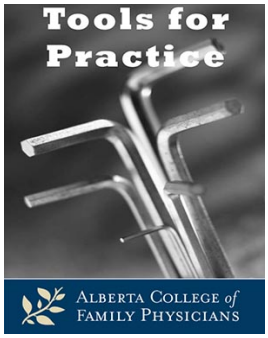
May 24, 2016



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[6-8] about 0.1-0.2 mmol/L more than the same dose of hydrochlorothiazide.[7]
- Angiotensin receptor blockers (ARBs) have similar hyperkalemia rates as ACE inhibitors.[9]

Context:

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

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Disclosure:
Authors do not have any conflicts to disclose.

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