Article Title: Fludrocortisone for orthostatic hypotension
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Overview: This article is a Cochrane systemic review evaluating the effectiveness and safety of fludrocortisone in treating patients with orthostatic hypotension.

Background: Orthostatic hypotension is defined as a sustained reduction of systolic BP by at least 20 mmHg or diastolic BP by 10 mmHg within three minutes of standing. It is caused by decreased cardiac output or inadequate vasoconstriction and results in symptoms such as dizziness, lightheadedness, and fainting, which increase the risk of falls. Currently, the only FDA-approved medications for treatment of symptomatic orthostatic hypotension are Midodrine (alpha-1 adrenergic agonist) and Droxidopa (alpha/beta-adrenergic agonist → mimics epinephrine and norepinephrine). Fludrocortisone, a mineralocorticoid that promotes salt and water retention to expand intravascular volume, is frequently used off label. However, there has been no comprehensive review evaluating the efficacy and long-term safety of this medication for the management of orthostatic hypotension.

Method: A systemic search involving major medical databases (Cochrane, MEDLINE, Embase, and CINAHL) and trial registries up to November 11, 2019 was conducted to identify relevant studies evaluating fludrocortisone for the treatment of orthostatic hypotension. In total, 13 studies involving 513 patients – including both RCTs and observational studies – were identified, all focusing on chronic orthostatic hypotension secondary to autonomic failure.

Findings:
- Overall, the review concluded the evidence is very uncertain regarding fludrocortisone's effect on BP, its ability to improve orthostatic symptoms, and its long-term safety in patients w/ chronic orthostatic hypotension.

- There was a reduction in BP drop (-26 mmHg vs -39 mmHg systolic and -7 mmHg vs -11 mmHg diastolic) when fludrocortisone was compared w/ placebo for diabetic patients, but the evidence was very low certainty.
- In Parkison disease patients, fludrocortisone had less diastolic drop (-14 mmHg) than pyridostigmine (-22.1 mmHg; Ach inhibitor used off label for OH in Parkinson patients) but no clear symptom improvement.
- In patients w/ familial dysautonomia, fludrocortisone was associated w/ better survival time, with a median of 32.8 years compared to 22.2 years for those who never took it.

- No improvement in syncope recurrence; 38% of those w/ a history of fainting continued to experience it while on the medication.
- Adverse events were generally minimal. Documented risks include peripheral edema, hypokalemia, and supine hypertension.

Limitations:
- Small sample size – The included RCTs involved only a total of 28 participants.
- Short duration – Most of the studies lasted only two to three weeks, so long-term effectiveness and safety cannot be determined.
- High risk of bias – Many studies failed to report randomization procedures, and observational studies often lacked control for confounding factors. Many patients were also on antihypertensives, diuretics, or other drugs that may affect BP, which may skew results.
- No compare head-to-head to 1st line therapy like Midodrine or Droxidopa
- Side effects were often under-reported