

FPIN's Help Desk Answers

Hydrochlorothiazide vs. Chlorthalidone for the Treatment of Hypertension

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Clinical Question

Is hydrochlorothiazide more effective than chlorthalidone for the treatment of hypertension?

Evidence-Based Answer

Chlorthalidone reduces systolic blood pressure (SBP) by 10 mm Hg more than hydrochlorothiazide at equal dosages (12.5 to 25 mg daily) in patients using monotherapy. (Strength of Recommendation [SOR]: B, meta-analysis of randomized controlled trials [RCTs].) Low-dose chlorthalidone (6.25 mg daily) and controlled-release hydrochlorothiazide (12.5 mg daily; not currently available in the United States) reduce 24-hour ambulatory SBP and diastolic blood pressure (DBP), whereas immediate-release hydrochlorothiazide (12.5 mg daily) may only reduce daytime SBP. (SOR: B, single RCT.)

Evidence Summary

A 2010 meta-analysis (137 RCTs; N = 10,443) evaluated the effect of hydrochlorothiazide and chlorthalidone on SBP and serum potassium.¹ Adult patients were on hydrochlorothiazide or chlorthalidone monotherapy. Further patient demographics were not defined. Chlorthalidone dosing ranged from 12.5 to 200 mg daily (mean dosage = 31.6 mg daily) with an average baseline SBP of 166 mm Hg (29 RCTs; n = 4,380). Hydrochlorothiazide dosing ranged from 3 to 450 mg daily (mean dosage =

42.7 mg daily) with an average baseline SBP of 163 mm Hg (108 RCTs; n = 6,063). Studies lasted four to 52 weeks. Pooled results showed that chlorthalidone (12.5 to 25 mg daily) reduced SBP more than hydrochlorothiazide at the same dosage (137 RCTs; N = 10,443; -24 mm Hg vs. -14 mm Hg, respectively; $P < .05$). However, chlorthalidone also caused larger decreases in serum potassium levels (-0.4 mEq per L [-0.4 mmol per L] vs. -0.2 mEq per L [-0.2 mmol per L], respectively; $P < .05$). Heterogeneity was not reported. The analysis was limited to patients with hypertension who were on monotherapy.

A 2016 RCT (N = 54) evaluated the effect of low-dose chlorthalidone and hydrochlorothiazide on mean 24-hour ambulatory blood pressure.² Patients were 18 to 65 years of age (mean = 45 years of age) with essential hypertension (SBP of 140 to 159 mm Hg, DBP of 90 to 99 mm Hg) and an average blood pressure of 148/93 mm Hg. Patients were excluded if they had secondary hypertension, diabetes mellitus, hyperuricemia, gout, chronic kidney disease, parathyroid disease, or recent cardiovascular disease. Patients were randomized to receive chlorthalidone, 6.25 mg (n = 16), hydrochlorothiazide, 12.5 mg (n = 18), or controlled-release hydrochlorothiazide, 12.5 mg (n = 20). Ambulatory (24-hour) blood pressure monitoring was done at baseline and after four and 12 weeks of therapy. Chlorthalidone and controlled-release hydrochlorothiazide reduced SBP and DBP during the day and at night at four and 12 weeks. Hydrochlorothiazide showed a significant improvement in SBP only during the day at four weeks. The study was limited by excluding many disease processes often present as comorbid conditions in patients with hypertension.

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2. Pareek AK, Messerli FH, Chandurkar NB, et al. Efficacy of low-dose chlorthalidone and hydrochlorothiazide as assessed by 24-h ambulatory blood pressure monitoring. *J Am Coll Cardiol*. 2016;67(4):379-389. ■

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Author disclosure: No relevant financial affiliations.