

Article of Interest

Tweeddale, M et al. Antihypertensive and biochemical effects of chlorthalidone. Clinical Pharmacology and Therapeutics. 1977. (Click to Access)

Context and Study Objective

By historical standards, current diuretic doses are quite low; however, this wasn't always the case. This paper sought to establish the dose-response curve of chlorthalidone among hypertensives with an emphasis on dose related anti-hypertensive efficacy and side effects.

Design, Setting, and Participants

In a double blind fashion, treatment naive hypertensive individuals received 25, 50, 100 or 200mg of chlorthalidone in a random fashion for 8 weeks with a minimum 4 week washout period between dose adjustments. Individuals with a creatinine > 2.0 mg/dL were excluded. A "no salt added diet" was encouraged.

Results

-37 patients completed the study, 50% of which were women. 1 patient was African American. Mean arterial pressure (MAP) was 132 mm Hg (120/ 80 mm Hg equals MAP of approximately 93 mm Hg). No other relevant characteristics were provided.

-Top Figure: There was no statistically significant increase in anti-hypertensive effect with escalating chlorthalidone doses.

-Bottom Figure: In a dose dependent fashion, serum potassium declined between 0.4-1.0 mEq/L and serum uric acid rose from 1.2-1.8 mEq/dL.

-Blood urea nitrogen and creatinine did not vary by dose. Episodes of acute kidney injury, changes in fasting blood glucose, and lipid parameters were not reported.

-Symptom questionnaires failed to reveal a difference in the frequency of gout, cramping, or fatigue.

Clinical Perspective

-Senior physicians often recall a time when furosemide was administered as 500mg IV boluses; current housestaff rarely prescribe more than 25mg of hydrochlorothiazide. This transition in dosing practices was only made possible by early dose finding studies such as this one.

-While perhaps self-evident to younger physicians, using low dose therapy was an innovation allowing patients to capture nearly the entire anti-hypertensive benefit of a medication with only a fraction of the adverse effects experienced at higher doses. A later newsletter will explore the merits of low dose therapy.

-Shortcomings of the study include a lack of standardization of salt intake and virtually no African Americans. However, the results are consistent with the larger literature.

