CONCEPTS IN HYPERTENSION

A Journal Article Based Approach to Understanding the Clinical Aspects of Hypertension

Volume 1 Issue 12 June 2016

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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. Tweeddale et al sought to establish the dose-response relationship of chlorthalidone among hypertensives with an emphasis on dose related anti-hypertensive efficacy and side effects.

Design, Setting, and Participants

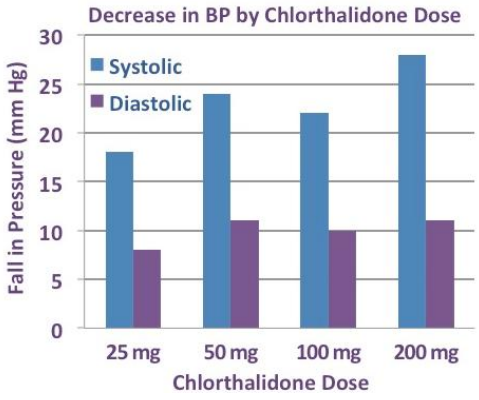
In a double blind fashion, treatment naive hypertensive individuals received 25, 50, 100 or 200mg of chlorthalidone in a random fashion for 8 weeks with a minimum 4 week washout period between dose adjustments. Individuals with a creatinine > 2.0 mg/dL were excluded. A "no salt added diet" was encouraged.

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 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.

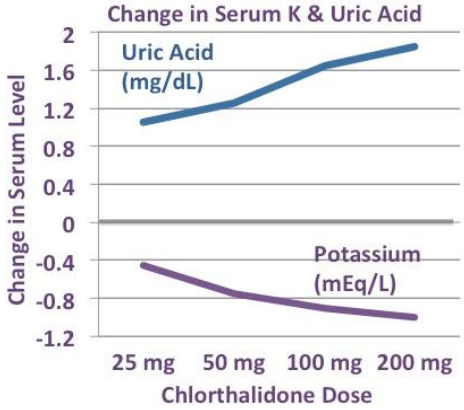


-Symptom questionnaires failed to reveal a difference in the frequency of gout, cramping, or fatigue.

Clinical Perspective

-Senior physicians often recall a time when furosemide was administered as 500mg IV boluses while current housestaff rarely prescribe more than 25 mg 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. An earlier e-newsletter (click here) explored the merits of low dose therapy.



-Shortcomings of the study include a lack of standardization of salt intake and virtually no African Americans. Given the small sample size, the study was underpowered to detect smaller differences in the dose-anti-hypertensive response with some additional anti-hypertensive effects at higher doses. Nonetheless, the results are consistent with the larger literature.

Creator & Author: Hillel Sternlicht, M.D.