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Chlorthalidone for Poorly Controlled Hypertension in Chronic Kidney Disease: An Interventional Pilot Study

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Commentary

By Professor Richard Glassock

Thiazide type diuretics are frequently recommended for control of elevated blood pressure, but their effectiveness can be impaired in patients with chronic kidney disease (CKD) and reduced renal function. In a particularly well-done pilot observational study, Agarwal and colleagues examined the blood pressure and volume depleting effects of escalating once a day doses of chlorthalidone (a long-acting thiazide-like diuretic) over 12 weeks in 14 subjects with poorly controlled blood pressure and eGFR values between 30 and 45 ml/min/1.73 m^2. The average prescribed dose of chlorthalidone at 4, 8 and 12 weeks was 34, 55 and 51 mg/day. Systolic blood pressure measured at home fell from 152 mm Hg to 139 mm Hg at 8 weeks (–13 mm Hg), and plasma rennin and plasma aldosterone levels rose. Body volume declined by about 1.8 l, and serum creatinine levels increased by about 0.25 mg/dl (from 2.87 to 3.12 mg/dl – indicating a fall in eGFR of about 10%). Adverse events were common (50% of the subjects had at least one event) and included hypokalemia, elevated uric acid, mild hyponatremia, orthostatic dizziness, and hyperglycemia. Interestingly, central aortic systolic pressure did not decline, but albuminuria did fall modestly. Sodium intake did not change during the study.

This pilot study provides valuable data for the design of a subsequent randomized controlled trial of the safety and efficacy of chlorthalidone in CKD with modest reduction of eGFR. Hopefully this drug will be compared to dietary salt restriction and the effects on left ventricular anatomy and function as well as progression of CKD will be incorporated into the study design. For the moment at least, thiazide-type diuretics can be effective in lowering systemic arterial pressure (most probably via their effects on extracellular volume) in patients with moderately advanced CKD and difficult to control elevated blood pressure, but side effects are frequent and careful monitoring for adverse events is mandatory.

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