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pad Refills

Your dose of drug information in between details

Drug information question: Can thiazides be continued in patients with chronic kidney disease when eGFR progresses below 30 mL/min/1.73m^2?

Conclusion: In the 2021 CLICK Trial, chlorthalidone lowered systolic blood pressure in people with an eGFR of 15 to 29 mL/min/1.73m^2 by 11 mmHg on average. Most of the blood pressure lowering effect occurred by week 4 at the 12.5 mg dose which can be achieved by quartering a 50 mg tablet. The occurrence of electrolyte abnormalities and acute kidney injury necessitates monitoring in clinical practice.

The BC Provincial Academic Detailing (PAD) Service's 2017 topic Hypertension in Primary Care: Blood Pressure Goals for Adults Aged 60 and Older reported from a 2009 Cochrane systematic review that thiazides improve cardiovascular morbidity and mortality when prescribed for hypertension.[1] A 2018 update to this systematic review re-confirms this conclusion.[2] In 2017 we stated that for patients with chronic kidney disease (CKD), limited evidence is available for or against the blood pressure lowering efficacy of thiazides in people with an eGFR < 30 mL/min/1.73m^2.[1]

What's changed since 2017?

Given the established role of thiazides in hypertension but uncertainty regarding their blood pressure lowering effect in CKD patients, the Chlorthalidone in Chronic Kidney Disease Trial CLICK 2021 randomized participants with stage 4 CKD to chlorthalidone or placebo.[3]

- Participants: 160 participants with eGFR 15-29 and blood pressure ≥ 130/80 mmHg who were already receiving at least one antihypertensive medication. Baseline demographics: mean eGFR 23, mean age 66, 23% women, 58% White, 40% Black, mean blood pressure 141/69 mmHg.
- Intervention: Chlorthalidone initiated at 12.5 mg once a day, which could be increased every 4 weeks up to 50 mg. The dose was not increased if a participant had symptomatic orthostatic hypotension, potassium < 3 mmol/L, acute gout or a recent hospitalization for diabetes-related hyperglycemia.
- Comparator: Placebo.
- Primary Outcome: At 12 weeks, systolic blood pressure decreased from baseline by approximately 11 mmHg with chlorthalidone compared to placebo as measured by 24-hour ambulatory blood pressure and confirmed with home blood pressure readings.
- Adverse events: Occurred in 91% of participants in the chlorthalidone group compared to 86% in the placebo group and lead to treatment discontinuation in 4 patients in the chlorthalidone group and 1 patient in the placebo group. Hypokalemia, hypomagnesemia, hyponatremia, hyperglycemia, hyperuricemia, acute kidney injury and dizziness occurred more often in the chlorthalidone group.
- Dose response: Most of the blood pressure lowering effect occurred by week 4 at the 12.5 mg dose. The CLICK authors state that "the lowest dose of chlorthalidone produced most of the blood-pressure-lowering effect, and this might be the safest dose to use." This dose can be achieved by quartering a 50 mg tablet. See our 2021 PAD Refill Hypertension Medication Table Update for formulations, cost and coverage.[4]

Important questions remain regarding the comparative efficacy and safety of chlorthalidone versus hydrochlorothiazide. A cardiovascular trial due in 2023, the Diuretic Comparison Project, comparing the two drugs in adults aged ≥ 65 will add evidence to this area.[5]

[1] BC PAD Service 2017 Hypertension in Primary Care: Blood Pressure Goals for Adults Aged 60 and Older; [2] WRIGHT Cochrane Database Syst Rev 2018 (PMID: 29667175); [3] CLICK 2021 N Engl J Med 2021 (PMID: 34739197); [4] BC PAD Service 2021 Hypertension Medication Table Update; [5] Clinicaltrials.gov Diuretic Comparison Project (NCT02185417)

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