

## Risk of Gout with the Use of Thiazide Diuretics

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### Clinical Question

Does the use of thiazide diuretics increase the risk of gout?

### Evidence-Based Answer

Thiazide diuretics may be used in most patients with hypertension who have only minimally increased risk of gout. (Strength of Recommendation [SOR]: B, based on a single randomized controlled trial [RCT].) There is no increased risk in patients older than 60 years or in women, but there is a slightly increased risk (about 1%) in men younger than 60 years (SOR: B, based on a single RCT.) Usual doses of thiazides (less than 25 mg) are not associated with an increased risk of gout, although doses of 25 mg or greater are. The risk of gout with hydrochlorothiazide and chlorthalidone is similar. Thiazides may be used in patients with asymptomatic hyperuricemia because they are not associated with an increased risk of gout in these patients. (SOR: C, based on retrospective cohort studies.)

### Evidence Summary

A double-blinded RCT of patients 60 years and older ( $n = 822$ ) found no difference in the incidence of gouty arthritis attacks in patients who received 25 mg of hydrochlorothiazide plus 50 mg of triamterene (Dyrenium) compared with those who received placebo.<sup>1</sup> Most of the eight patients who developed gouty arthritis were men, seven received the thiazide combination, and all had higher pretreatment uric acid levels.

A single-blinded placebo-controlled RCT (23,582 patient-years) found that treatment with bendrofluzide (a thiazide available

in Europe) was associated with a slight increase in medication discontinuation due to gout in younger men, but not in women.<sup>2</sup> Weaknesses of this study included lack of blinding for clinicians and trial evaluators, and lack of comparison of treatment groups.

A retrospective cohort study of patients 65 years and older ( $n = 9,249$ ) found no associated risk of anti-gout therapy initiation in patients who received lower doses of thiazides (relative risk [RR] = 1.78; 95% confidence interval [CI], 0.66 to 4.78 for doses less than 25 mg).<sup>3</sup> However, higher doses were associated with gout symptoms (RR = 2.39; 95% CI, 1.29 to 4.43 for doses of 25 to 49 mg; RR = 2.41; 95% CI, 1.39 to 4.19 for doses of 50 mg or more). Another retrospective cohort study ( $n = 3,033$ ) found no increased risk of first-time gout attacks in patients receiving hydrochlorothiazide vs. chlorthalidone.<sup>4</sup> A third retrospective cohort study ( $n = 5,234$ ) found no associated risk of gout in patients with elevated uric acid levels who received thiazides.<sup>5</sup>

### Recommendations from Others

The 2012 American College of Rheumatology guidelines for the management of gout list thiazide diuretics as a prime example of urate-elevating medications.<sup>6</sup> The task force panel recognized the benefits of thiazides for blood pressure control and improved mortality in patients with hypertension.

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## Clinical Inquiries

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