Thiazide Diuretics Are Associated with Lower Risk of Hip Fractures


Study Overview

Objective. To describe the association between dose and duration of thiazide use and risk for hip fracture.

Design. Prospective population-based cohort study.

Setting and participants. Investigators enrolled 7983 residents of a suburb of Rotterdam in the Netherlands who were at least 55 years old and had lived in the region for at least 1 year.

Main outcome measures. Thiazide diuretic use was determined from local pharmacy records and divided into 7 mutually exclusive categories: non-use, current use for more than 365 consecutive days, current use for 43–365 days, current use for 1–42 days, discontinuation of use since 1–60 days, discontinuation of use since 61–120 days, and discontinuation of use since greater than 120 days. Participants were followed from June 1991 until one of the following 3 major endpoints: incident hip fracture, death, or the end of the study in December 1999. The day the endpoint occurred was defined as the index day.

Main results. 281 hip fractures were reported. Use of thiazides more than 365 consecutive days prior to the index day was associated with a lower risk of hip fractures (hazard ratio, 0.46 [95% confidence interval, 0.21–0.96]) as compared with non-use. No significant dose-dependent relationship between thiazide use and hip fractures was found. 4 months after patients discontinued thiazides, the risk of hip fracture returned to that for nonusers.

Conclusion. Thiazide use is protective against hip fractures, but the protective effect is lost 4 months after use is discontinued.

Commentary

Several epidemiologic reports have suggested that thiazide diuretics protect against hip fractures [1]. One proposed mechanism is that thiazides reduce urinary calcium excretion and subsequently increase bone density. However, changes to bone density during thiazide use are modest, and uncertainties remain about both the mechanism and magnitude of the thiazide effect. Few previous investigations have characterized the duration and dose of thiazide needed to obtain a protective effect nor have they examined the persistence of the effect following discontinuation.

The strength of this large cohort study lies in the careful measurement of thiazide exposure using actual prescription fill data from pharmacies exclusively patronized by the observed population. The precise data on thiazide use allows the authors to estimate fracture risk for 7 different categories of patients, separating long-term users from short-term and past users. Only the longest duration of current use (> 1 year) was significantly protective. There was a trend towards lower risk of hip fractures with shorter duration of thiazide use but not dose. Despite the large size of the cohort, there was likely insufficient power to show a clear dose-response effect since only 26 fractures occurred among current users of thiazides.

The results of this well-designed cohort investigation confirm the protective benefits of thiazides but would be insufficient to recommend thiazide treatment strictly for treatment of osteoporosis or infrequent fallers. It is unclear if the effect persists in the absence of hypertension. Do thiazides reduce falls and associated hip fractures by treating vascular disease and disequilibrium? Do they provide benefits above and beyond bisphosphonates and calcium therapy? With the strong evidence favoring the protective effect of thiazides, the time is ripe for a clinical trial in osteoporotic and high-risk elderly populations.

Applications for Clinical Practice

Thiazide diuretics are excellent choices for elderly hypertensive patients who may benefit from the protection against hip fractures due to osteoporosis.
(continued from page 578)

hip fracture. However, there is insufficient data to support the use of thiazides to treat osteoporosis or frequent falling in the absence of hypertension.

—Review by Josh F. Peterson, MD, MPH

References