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Can anti-hypertensive thiazide diuretics also reduce fragility fracture risk?

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Topic(s):
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Introduction: A great deal of fractures are related to osteoporosis. Thiazide diuretics have been associated with reduced age-related bone loss, by decreasing urinary calcium excretion. On the other hand, they can also induce hyponatraemia, which is a risk factor for fracture occurrence, potentially jeopardizing hypocalciuric protective effects. Recently, a secondary analysis of the ALLHAT trial found that chlorthalidone may reduce hip and pelvic fractures, when compared to lisinopril.

Purpose: To compare fracture outcomes of hypertensive thiazide users with those of hypertensive patients not treated with thiazides.

Methods: MEDLINE, EMBASE, Cochrane and SCOPUS databases were comprehensively searched, from inception to the first of February of 2019, for cohort studies mentioning thiazide diuretic usage and fracture rates. Literature search, study eligibility, including methodological quality assessment, and data extraction were independently conducted by two investigators. Meta-analysis was performed using generic inverse variance outcome and, due to heterogeneity of the original studies, a random effects model. Confounder-adjusted relative risk (RR) was pooled. Primary outcome was total fracture rate, whereas hip and women-specific fracture risk were regarded as secondary endpoints.

Results: Fourteen eligible studies were identified. Overall, 3,601,779 patients were included and 290,885 incidental fractures were recorded. Prototype patient was middle-aged to old and three studies only enrolled females. Clinical follow-up was documented at a median of five years. Thiazide diuretic users, as compared with non-users, had a significant 11% reduction in total fractures (RR=0.86, 95% confidence interval [CI]=0.82–0.97, p=0.008, i²=77%). Seven studies, encompassing 553,614 patients and 5,005 cases, allowed for estimation of hip fracture risk, with thiazides demonstrating an even larger effect (RR=0.78, 95% CI=0.68–0.89, p=0.0004, i²=45%). Likewise, four studies, incorporating 149,024 patients and 150,998 cases, were able to provide insight into women fracture risk, in whom thiazides seem to exert no significant protective effect (RR=1.00, 95% CI=0.78–1.27, p=0.98, i²=77%).

Conclusion: Thiazide diuretics may convey a decreased risk of fracture, particularly in the potentially lethal hip location. This protective secondary effect of thiazides should be considered in hypertension clinic, with osteoporotic men seeming the best candidates for this therapy.
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