Risk of heart failure associated with thiazide diuretics compared with calcium channel blockers in patients with type 2 diabetes: a nationwide nested case-control study

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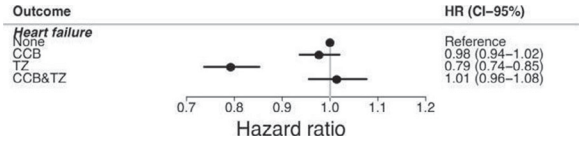
Background: Thiazide diuretics and calcium channel blockers (CCB's) are two important and widely used antihypertensive drugs classes among patients with type 2 diabetes (T2D). The risk of developing heart failure (HF) is increased in patients with T2D but whether use of these two drugs are associated with changes in HF risk is unknown.

Purpose: To examine and compare the association of two different classes of antihypertensive drugs, thiazide diuretics and CCB's, with the development of new onset HF in patients with T2D.

Methods: The study cohort comprised T2D patients >40 years on metformin and renin-angiotensin system inhibitor (RAS-i) without a history of HF or use of loop diuretics identified in Danish health care registers (period 1995 to 2015). A nested case-control study was conducted by matching all HF cases on sex, age and duration of T2D with 10 controls from the T2D population. Exposure was defined as three redeemed prescriptions of either a thiazide diuretic or a CCB up to 365 days before index, which corresponds to one year of antihypertensive therapy. Conditional logistic regression adjusted for comorbidities (atrial fibrillation, chronic obstructive pulmonary disease and anemia) was used to estimate and compare the treatment effect of thiazide diuretics and CCB's, with patients receiving neither of the two drugs as reference.

Results: The study population consisted of 170,514 T2D patients using metformin and RAS-i, comprising 13,814 HF cases each matched on sex, age and duration of T2D with 10 controls. The median age was 62 years and 55% were men. T2D patients, who had received antihypertensive treatment with only thiazide diuretics one year prior to index had a significantly lower risk of HF compared to the reference group who did not receive treatment with neither thiazide diuretics or CCB's: Hazard ratio (HR) 0.79 [95% confidence interval (CI) 0.74–0.85]. Patients who had received treatment with only CCB's had a comparable risk of HF: HR 0.98 [95% CI 0.94–1.02]. Patients who had received treatment with both thiazide diuretics and CCB's were not associated with a lower risk of HF: HR 1.01 [95% CI 0.96–1.08].

Conclusion: Patients with T2D who received antihypertensive therapy with thiazide diuretics for at least one year had a significantly lower risk of HF compared to those who were not treated with either thiazide diuretics or CCB's. No association between use of CCB's and HF was observed. Use of thiazide diuretics may prevent development of HF in T2D and a randomized clinical trial evaluating diuretics is patients with T2D is warranted.



Risk of new onset heart failure