

Abstract Type : Oral

Abstract Submission No. : OR-1679

Safety Assessment of Thiazide As a First-line Antihypertensive Drug in the Elderly

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Objectives: Thiazide-induced hyponatremia is one of the major causes of decreased sodium levels in the elderly population. Despite this adverse event, thiazide diuretics have been used as first-line drugs in the management of hypertension for over the past several decades.

Methods: This is a retrospective, nationwide, longitudinal population-based study using the National Health Insurance Service-National Sample Cohort Database. Among the 1,125,691 participants, we excluded subjects who were younger than 19 years, had a previous diagnosis of hyponatremia or medical conditions which could cause hyponatremia before the index year (2004) and had taken antihypertensive drugs for less than 90 days. The primary outcome is incidence of severe hyponatremia defined using the combination criteria: (1) At least one claim for emergency care under International Classification of Diseases 10th (ICD-10) codes E87.1 or (2) at least one claim for the prescription of hypertonic saline in emergency department patients.

Results: 113,201 participants were included in this study and tracked from the index year to 2013. The subjects were assigned to two groups according to thiazide based or non-thiazide based antihypertensive drugs. During the follow-up period, 808 participants developed severe hyponatremia. We observed that the thiazide based antihypertensive group had a greater risk for severe hyponatremia development (HR 1.467, 95% C.I. 1.272-1.692, $p < 0.001$), even after being adjusted for age, gender and several comorbidities (HR 1.425, 95% C.I. 1.233-1.647, $p < 0.001$). We found that subjects who were female, older (≥ 60 years), or non-CKD were more susceptible for severe hyponatremia.

Conclusions: We demonstrated that thiazide based antihypertensive drugs significantly increased the risk of severe hyponatremia development. Therefore, careful review of the safety of thiazide diuretics as first-line antihypertensive drugs is needed.