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Thiazide-Related Hyponatremia: A Nationwide Population-Based Cohort Study

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Objectives: After thiazides were recommended as the first-line drug for adult hypertension in the JNC 7 guideline, hospitalization for thiazide-related hyponatremia (TRH) has often been experienced in clinical settings, but the exact incidence and risk of TRH have not been documented in Korea.

Methods: For risk evaluation of thiazide and other drug-associated hyponatremia, we used the big data provided by the National Health Insurance Sharing Service. A total of 1,943,345 adult patients who were confirmed to have been treated for hypertension from January 2014 to December 2016 were included for analysis set. The patients were divided into two groups depending on the use of thiazides.

Results: Hospitalization for hyponatremia was significantly higher in the thiazide group than control group (2.19 vs. 1.45%), and the risks further increased when two or more thiazides were concurrently prescribed (2.8 times), or combination therapy with other diuretics or desmopressin (4 times), and thiazide+spironolactone+desmopressin were used at the same time (6.9 times). When thiazide and desmopressin were used together, the risk of multiple hospitalization was 11 times higher. In multivariate analysis, the occurrence of hyponatremia increased with age (HR 1.069, per 1-year increase), DM (HR 1.453), depression (HR 1.53), and the use of thiazides (HR 1.436, all $P < 0.001$). The thiazide group showed a better 6-year overall survival than the control group ($P < 0.001$), but had more fractures, and hyponatremia (all $P < 0.001$). Among all patients, patients with hyponatremia showed significantly higher mortality rates, hospitalizations for fractures, and pneumonia compared to those without hyponatremia (all $P < 0.001$).

Conclusions: There is an increased risk of hyponatremia and related complications in those who were prescribed thiazides. However, the survival rate decreased in those who received thiazides, suggesting that thiazide itself is not harmful, but that it will be more helpful in reducing complications and improving the prognosis if properly used with caution in high-risk groups.