Urine Chloride levels are Associated with Chronic Kidney Disease Progression in Chronic Kidney Disease Patients

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Objectives: Tubuloglomerular feedback is the physiologic mechanism responsible for autoregulation of GFR and renal blood flow. This response is mainly driven by chloride level in the distal tubules, thus prevents glomerular hypertension. Here, we studied the relationship between urinary chloride level and CKD progression.

Methods: Data were retrieved from the KoreaN Cohort Study for Outcome in Patients With Chronic Kidney Disease cohort. Among 2,238 participants, a total of 2,019 patients were eligible for the analysis after excluding patients with missing data. Patients were categorized into 3 groups according to baseline tertiles of random urinary chloride excretion: < 76, 76-115, and ≥ 116 mEq/L. The study endpoint was a composite of >50% decrease in eGFR, or ESRD.

Results: The mean age was 53.7 ± 12.1 years, and 1234 (61.2%) patients were male. During a median follow-up of 2.8 years, 436 (21.6%) participants reached the renal endpoint. CKD progression occurred in 236 (34.8%), 159 (24.1%), and 41 (6.0%) patients in the lowest, middle, and highest tertile groups (P < 0.001), respectively. Compared to the lowest tertile, the middle (HR, 0.811; 95% CI, 0.660-0.997; P=0.047) and highest (HR, 0.619; 95% CI, 0.434-0.882; P=0.008) tertiles were significantly associated with decreased risk of adverse renal outcome in multivariable models after adjustment of confounding factors. This association was consistently observed in adjusted multivariable model where urinary chloride was entered as a continuous variable (HR per 10 mEq/L increase, 0.961; 95% CI, 0.931-0.993; P=0.016). There was a significant interaction between urinary chloride level and eGFR (P=0.009) and the significant association between urinary chloride level and CKD progression was evident particularly in patients with eGFR < 60mL/min/1.73m²; HR in the highest tertile was 0.444 compared to the lowest tertile (95% CI, 0.287-0.686; P < 0.001).

Conclusions: This hypothesis generating study showed that higher urinary chloride level is associated with the progression of CKD.