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Individual Salt Sensitivity Index in Daytime or Nighttime Predicts Intrarenal Renin-Angiotensin System Activity, Renal Damage and Nocturnal Hypertension

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Summary

(Background) We have clarified that intrarenal renin-angiotensin system (RAS) activation is associated with renal damage independent of circulating RAS, and that urinary angiotensinogen (AGT) is a useful biomarker that reflects intrarenal RAS activity. Salt sensitive hypertension is often associated with renal damage in chronic kidney disease (CKD) patients, and blood pressure (BP) becomes salt sensitive as renal damage makes progress. In addition, salt sensitivity is associated with urinary AGT excretion levels. Recently, we have clarified that the oscillation of intrarenal RAS activation leads to renal damage, hypertension, and diurnal BP variation. However, because the amount of salt intake was not equal, it was impossible to clarify whether the vicious cycle due to intrarenal RAS activation, nocturnal hypertension and renal damage is affected by salt loading. Moreover, it has not been clear whether salt sensitivity influences the circadian BP rhythm, intrarenal RAS activity and renal damage. Especially, there are no reports to investigate the levels of salt sensitivity in daytime or nighttime, respectively.

(Methods) We recruited 20 IgA nephropathy patients (7 men and 13 women and age: 45.4±15.1 years). CKD patients consumed a standard diet (10 g/day of salt), and after data collection, low salt diet (6 g/day of salt) was fed. Daytime (6:00 am to 9:00 pm) and nighttime (9:00 pm to 6:00 am) urine collection were conducted, respectively. We divided the daytime and nighttime for 24-h ambulatory BP monitoring using sleep and waking times. Salt sensitivity index (SSI) was calculated as follows: the difference between averaged systolic BPs of standard and low salt diets was divided by the difference between the urinary sodium excretion per hour of standard and low salt diets. SSI was calculated in daytime or nighttime, respectively, and “salt non-sensitive group (group A)”, “salt sensitive group during daytime (group B)” and “salt sensitive group during all day long (group C)” were created.

(Results) Urinary protein excretion levels during a standard diet were significantly increased compared with those during a low salt diet in daytime. Although significant differences were not found, systolic BP and urinary albumin and AGT excretion levels during a standard diet tended to be increased compared with those during a low salt diet in daytime. In addition, urinary AGT levels were significantly and positively correlated with the degree of hypertension and the levels of urinary albumin and protein excretion. The experiments of SSI indicated that although urinary albumin excretion during standard and low salt diets were lowest in group A and urinary albumin excretion during a standard and low salt diets were the same levels between group B and group C in daytime, the parameter in nighttime for group B were lower than those for group C.

(Conclusions) Salt loading may cause BP elevation by intrarenal RAS activation in daytime, and lead to

increase of urinary protein excretion. Moreover, it is possible that salt sensitivity index is a surrogate marker to estimate the renal damage.

(Perspectives) Because statistical significance has not been found until now, it has not been confirmed that intrarenal RAS activation due to salt loading causes renal damage, and that salt sensitivity index reflects intrarenal RAS activity and renal damage. We will continue this research to clarify these issues.