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Weight loss has an additive effect on the anti-proteinuric effects of angiotensin II receptor blockers in hypertensive patients with chronic kidney disease

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Objectives : Because weight gain and obesity contribute to the development of chronic kidney disease (CKD) and end stage renal disease (ESRD), weight reduction is a lifestyle intervention that has been introduced for the prevention and management of CKD. However, CKD patients with obesity sometimes exhibit a slow progression of renal deterioration. We investigate the additive anti-proteinuric effect of weight reduction on the usage of an angiotensin II receptor blocker and the potential mechanisms of the beneficial effect in hypertensive CKD patients.

Methods : This study is a subanalysis of data from an open-label, randomized, controlled clinical trial (NCT01552954). Among the 235 participants, the body weight of 227 participants was measured and 24h urine samples were collected at baseline and after 16 weeks. The participants were assigned to subgroup according to changes in their body weight. Urinary cytokines as well as urine creatinine, sodium, urea nitrogen, and albumin excretion were measured over the 16-week study period.

Results : Fifty-eight participants (25.7%) were assigned to group 1 (a ≥ 1.5% decrease in body weight after 16 weeks), 32 participants (14.1%) were assigned to group 2 (a 1.5% ~ 0.1% decrease in body weight after 16 weeks), and 136 participants (60.2%) were assigned to group 3 (a ≥ 0.0% increase in body weight after 16 weeks). Over the study period, unintentional weight loss independently increased the probability of reduced albuminuria (Group 1, RR 6.234, 95% CI 1.913 – 20.315, p=0.002). The relationship between weight loss

and a decrease in albuminuria was even more significant in several subgroups, including participants who were female, younger (< 65 years), non-obese and obese (BMI ≥ 18.5 kg/m2), as well as those who had a CKD stage ≥ 3a (≥ 45 ml/min/1.73m2), consumed a low salt diet (urinary sodium excretion < 200 mEq/day), consumed a low protein diet (< 1.2 g/kg/day), and had a low baseline level of albuminuria (< 2000 mg/day). Among the urinary cytokines, only podocalyxin levels decreased significantly in participants who lost weight (p=0.013).

Conclusions : We observed that unintentional weight loss has additive effect on the anti-proteinuric effects of treatment with ARBs in hypertensive CKD patients, which is possibly related to the reduced damage of podocytes. Therefore, physicians recommend weight reduction to hypertensive CKD patients even if they are not obese.

Keywords : weight loss, proteinuria, angiotensin II receptor blocker, chronic kidney disease, hypertension