

How can Oral Alkalizing Agents Prevent Renal Damage in Chronic Kidney Disease?

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To the Editor

The increased incidence of end-stage kidney disease (ESRD) is one of the biggest problems worldwide, and chronic kidney disease (CKD) results in the high risk of cardiovascular events and renal death. Eating habits and lifestyle affect the prognosis of some kinds of CKD [1]. Treatment with sodium bicarbonate or fruit and vegetable intake has been known to ameliorate renal damage in patients with CKD [2]. Physiologically, renal tubule acidification is observed because of reabsorption of bicarbonate and excretion of ammonia and considered not harmful. Metabolic acidosis and aciduria due to urinary excretion of acidic metabolic wastes produced in daily life are known to be augmented in patients with CKD. A stronger acid condition in renal tubules was previously reported to result in increased production of reactive oxidative stress (ROS), which could be aggravated by albuminuria. In an animal model, an oral alkalinizing agent improved aciduria and prevented renal-tubular injury [3]. Oral alkalinizing agents are suggested to be useful in delaying the development of ESKD due to some unknown mechanisms. Here, we aimed to verify the renal protective effects of oral alkalinizing agents by neutralizing the aciduria in patients with mild and moderate CKD stages. A single-center, randomly allocated cohort trial, open-label study, entitled as "Estimating the efficacy of the Oral Alkalinizing Agents in CKD (CKOALA) study" was started [4]. Sodium bicarbonate and sodium potassium citrate were used as oral alkalinizing agents. A total of 104 patients with CKD stages G2, G3a, and G3b were finally registered and allocated by four valuable stratifications of age, sex, presence of diabetes mellitus, and renal function into the following three cohort groups: sodium bicarbonate, sodium potassium citrate, and standard therapy groups without any alkalinizing agents. They were followed up for 6 months (short-term) and those with re-agreement were followed up for 1 or 2 years (long-term study). Primary end-points are renal dysfunction progression or cardiovascular disease occurrence, and secondary end-points include a search for any renal protective surrogate markers affected by oral alkalinizing agents. Metabolic acidosis is a result of renal dysfunction; however, the

possibility of metabolic acidic wastes to cause renal dysfunction has been controversial. The kinds of acidic metabolic compounds, known as uremic toxins (UTs), are substances primarily considered to cause metabolic acidosis and aciduria. The UT accumulation is more common in patients with CKD than that in healthy individuals. Some UTs are reported to stimulate ROS production, which may result in further renal tubule-interstitial dysfunction [5]. In the CKOALA study, the plasma and serum samples and early morning urine samples at every visit were analyzed by metabolomics to investigate the renoprotective mechanisms and find new renal surrogate biomarkers. This study found the importance of taking oral alkalinizing agents for the treatment of patients with early and moderate CKD stages.

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