P052 Vinegar via altering the acetic acid/AR/miR-147a/SLC26A1 signals to suppress liver oxalate biosynthesis/excretion to inhibit the hyperoxaluria-induced intrarenal CaOx crystals deposition

EUR Urol Suppl 2019;18(7):e2793

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Introduction & Objectives: The results from epidemiological study in China revealed a potential linkage between the vinegar intake and the prevalence of kidney stone formers. The incidence of male stones is much higher than that of women, and previous report observed the linkage of kidney stones to the testosterone level in clinical samples. However, none of these reports further linked their clinical observations to the detailed mechanisms. The underlying mechanisms by which androgen and its receptor, the androgen receptor (AR), play roles in kidney stone formation remains unclear.

Materials & Methods: Real-time polymerase chain reaction and Western blot assay were used to analyze the changes in the expression of the relevant signaling pathway molecules. Chromosome co-immunoprecipitation and dual luciferase reporter gene systems were used to study the mechanism of molecular expression regulation. Immunohistochemical staining of human hepatocellular carcinoma tissue samples was performed to analyze the expression levels of AR and Sat-1 in hepatocellular carcinoma tissues. Pizzolato staining was used to detect the renal calcium oxalate (CaOx) crystals formation. An animal model of renal CaOx crystal was used to study the effect of vinegar on AR and its downstream on oxalate transport in the liver in vivo

Results: Mechanism studies revealed that vinegar or acetic acid (AC), the major component of vinegar, could decrease the intrarenal CaOx crystal deposition on the parenchyma via decreasing the urinary oxalate through altering the androgen receptor AR/SLC26A1 signaling-mediated oxalate excretion from liver to the blood. Mechanism dissection further revealed that AR might function via transcriptional regulating the miRNA-147a expression to increase the SLC26A1 protein expression (Sat-1) that involved the direct binding to its mRNA 3'UTR. In vitro data from multiple liver cell lines showed that manipulated AR could affect oxalate level in culture medium via regulating SLC26A1 protein expression. Results from two in vivo rat models with 5% hydroxyl-L-proline (HP)- or ethylene glycol (EG)-induced intrarenal CaOx crystal deposition on the renal parenchyma all proved that rat received vinegar or AC via gavage developed less intrarenal CaOx crystal deposition on the renal parenchyma with less urinary oxalate that involved the altering the AR/SLC26A1 signals.

Conclusions: Vinegar may decrease renal CaOx crystals formation via altering the AR-miR-147a-SLC26A1 signaling axis. A potential therapy to target vinegar/AC/AR/SLC26A1 signaling with AC or AR degradation enhancer ASC-J9 all led to suppress the hyperoxaluria-induced intrarenal CaOx crystal deposition on the renal parenchyma, a key phenotype seen in some selective kidney stone formers with primary hyperoxaluria or intestinal bypass.