The Role of Renal Tubular Cell Injury in the Early Period of Renal Crystal Formation: Identified from the Cell Injury-Inhibiting Effect of Green Tea

Introduction and Objective: Previously, we suggested the involvement of renal tubular epithelial cell (RTC) injury in the pathogenesis of renal stones, and reported the importance of RTC injury for renal crystal formation. We performed immunohistochemical staining and transmission electron microscopy (TEM) in the early period of renal crystal formation, and evaluated the difference with or without the cell injury-inhibiting effect of green tea (GT), and clarified the role of the RTC injury.
Materials and Methods: Daily intra-abdominal injection of glyoxylate (GOX) into mice treated with normal water or GT was performed for 6days. Kidneys were extracted before and at 6, 12, and 24hr and 3 and 6days after GOX administration. Crystal formation was detected using Pizzolato staining and polarized light optical microscopy. Immunohistochemical staining and Western blotting of superoxide dismutase (SOD), 4-hydroxynonenal (4-HNE) and malondialdehyde (MDA) were performed to observe oxidative stress, lipid peroxidation, and RTC injury, respectively. Immunohistochemical staining and Western blotting of osteopontin (OPN), part of the renal crystal matrix and inflammatory cytokines, were also performed. RTC microstructural damage and crystal nucleus formation were observed using TEM.
Results: In normal water-treated mice, we detected renal crystals after 3 days and detected more crystals after 6 days, but could not detect crystals after 6, 12, or 24 hours. After 6, 12, and 24 hours, we detected a decrease of SOD and increase of MDA and 4-HNE. OPN expression increased after GOX administration. In TEM, after GOX administration, mitochondria and microvilli of the RTC collapsed, aggregated in the renal tubular lumen, and crystal nuclei appeared. In GT-treated mice, we did not detect renal crystals after 3 days, but after 6 days. In the early period of renal crystal formation, the cell injury-inhibiting effect reduced the collapse of mitochondria of RTC, decreased cell debris, and delayed crystal formation. OPN was decreased in GT-treated mice compared with normal water-treatment.
Conclusion: Mitochondria are injured by GOX, and free radicals appearing from mitochondria cause inflammation through the OPN and injure the RTC. As a result, cell debris appears in the lumen of the renal tubule, and crystals are formed. This is our suggested mechanism of crystal formation, which was inhibited by GT.