Adiponectin Ameliorates Kidney Stone Formation in Metabolic Syndrome Model Mice

Introduction and Objective: Kidney stone formation has been recognized as a metabolic syndrome (MetS)-related disease. The aims of the present study were to elucidate a possible mechanism of kidney stone formation under MetS conditions by using MetS mouse model and to assess the effectiveness of adiponectin (APN) treatment for the prevention of kidney stone. Further, we performed genome-wide expression analyses to detect genes related to kidney stone.
Materials and Methods: Wild-type (+/+) and ob/ob mice (having a disorder in which to produce leptin) were administered daily doses of 50 mg/kg glyoxylate (GOx) for 6 days. To prevent kidney stone formation, exogenous APN treatment (2.5 μg/ml, 0.1 ml) was administered daily. At day 0 and 6, their kidneys were extracted. A genome-wide microarray analysis was performed to extract genes related to the MetS-related kidney stone formation and genes associated with the prevention of APN-related kidney stone. The genes with significant expression values were sorted by the Venn diagram function of the microarray software GeneSpring® GX11.0. Gene ontology (GO) analyses were performed on the extracted genes to hypothesize the mechanisms of MetS-derived kidney stone formation and APN treatment.
Results: The only ob/ob mice showed crystal depositions in their renal tubules. Expression analysis of genes associated with MetS-related kidney stone formation identified 259 genes that were >2.0× up-regulated and 243 genes that were <0.5× down-regulated. GO analyses revealed that the up-regulated genes belonged to the categories of immunoreaction, inflammation, and adhesion molecules. The down-regulated genes belonged to the categories of oxidative stress and lipid metabolism. Expression analysis of APN-induced genes related to stone prevention revealed that the numbers of up- and down-regulated genes were 154 and 190, respectively. GO analyses indicated that the up-regulated genes belonged to the categories of cellular and mitochondrial repair, whereas the down-regulated genes belonged to the categories of immune and inflammatory reactions and apoptosis.
Conclusion: Collectively, kidney stone formation in the MetS environment involves the progression of an inflammatory and immunoresponse, including oxidative stress and adhesion reaction in renal tissue. Further, this study showed that APN treatment prevented kidney stone formation by inhibition of inflammation and apoptosis.