KSN 2021
FULLY VIRTUAL MEETING
September 02 (Thu) - 05 (Sun)

Abstract Submission No. : 2197

Fisetin protects against renal fibrosis in murine unilateral ureteral obstruction

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Objectives: Renal fibrosis characterized by accumulation of extracellular matrix (ECM), infiltration of inflammatory cells, and kidney dysfunction is a major pathway of the progression of chronic kidney disease (CKD). Accumulating evidence indicates that oxidative stress caused by reactive oxygen species plays a critical role in the initiation and progression of CKD via proinflammatory and profibrotic signal pathways. Fisetin (3,3′,4′,7 - tetrahydroxyflavone), a flavonol molecule found in a variety of fruits and vegetables, has biological activities including anti-oxidant, anti-inflammatory, anti-cancer, anti-aging. Based on the biological effect of fisetin, we evaluated the anti-oxidative and anti-fibrotic effects of fisetin on unilateral ureteral obstruction (UUO)-induced kidney in mice.

Methods: C57BL/6 female mice were subjected to right unilateral ureteral obstruction. Some mice were intraperitoneally injected every other day with fisetin (25 mg/kg/day) or vehicle from 1 day before surgery to 7 days after surgery. Kidney samples were analyzed for renal fibrosis (α-smooth muscle actin expression, Masson trichrome staining, TGF-β/p-SMAD3 pathway), inflammation (pro-inflammatory cytokine and chemokine synthesis as well as neutrophil and macrophage infiltrations), and apoptosis (TUNEL positive renal tubular cells).

Results: In this study, we found that fisetin treatment protected against renal fibrosis by inhibiting profibrotic and proinflammatory signal pathways and apoptotic/necrotic cell death in the obstructed kidneys.

Conclusions: These data suggest that fisetin alleviates kidney fibrosis to protect against UUO-induced CKD progression and fisetin can be a novel therapeutic drug for CKD treatment.