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

Oral Communication Abstract
Presentation No. OC3-06 (Abstract Submission No. 2359)

Oral Communications 3 Sep. 2 (Thu), 15:40-16:40

Paricalcitol attenuated cyst growth and renal fibrosis via modulation of phenotype transition of renal tubular cells in polycystic kidney

Jung Won Lee[1], Hyun-Soo Shin[2], Mina Yu[2], Duk-Hee Kang[2]
[1]Department of Pediatrics-Nephrology, Ewha Womans University College of Medicine, Korea, Republic of
[2]Department of Internal Medicine-Nephrology, Ewha Womans University College of Medicine, Korea, Republic of

Objectives: Recent data demonstrated the reno-protective effect of vitamin D analogs via anti-inflammatory, immunomodulatory and anti-fibrotic effects. Polycystic kidney disease (PKD) is the most common inherited disease characterized by multiple cysts formation accompanied by renal fibrosis. However, there have been no studies investigating whether vitamin D imposes any effect on cyst formation, growth & renal fibrosis in PKD.

Methods: The effects of intraperitoneal administration of paricalcitol (50 ng/kg/day, for 3 weeks) in juvenile cystic kidney (jck) mice (N=14) on renal function, pathology and phenotype transition of renal tubular cells were examined. 3D culture system of forskolin-treated Madin-Darby canine kidney (MDCK) cells was used to examine the effect of paricalcitol (20 nM) on cyst formation and growth. Effect of paricalcitol on TGF-β (10 ng/ml)-induced phenotype transition and apoptosis of human PKD cyst-lining epithelial cells (WT9-12 cell) was also evaluated with an assessment of phosphorylation of p38 and ERK1/2 MAPK, GSK-3β and nuclear translocation of β-catenin.

Results: Intraperitoneal paricalcitol injection in 3-week-old jck mice for 3 weeks significantly decreased kidney weight/body weight, cyst size, serum creatinine and interstitial fibrosis score compared to vehicle-treated mice. Altered expression of E-cadherin and α-smooth muscle actin in *jck* mice was also alleviated with paricalcitol treatment. Paricalcitol inhibited forskolin-induced in-vitro cyst formation and growth with an attenuation of B-Raf, ERK1/2 MAPK activation. Paricalcitol also inhibited TGF-β-induced epithelial-to-mesenchymal transition of WT9-12 cells with an amelioration of p38- and ERK1/2 MAPK activation, GSK-3β phosphorylation and nuclear translocation of β-catenin.

Conclusions: Paricalcitol ameliorated cyst formation and pro-fibrotic phenotype transition of renal tubular cells in renal tubular cells and animal model of PKD, which can be one of the therapeutic options targeting early and late mechanisms of renal disease progression in PKD.