P12

The Effect of Antisense Oligodeoxynucleotides for CTGF in Unilateral Ureteral Obstruction in Rats

Kidney Institue, Departments of Internal Medicine[1],
Keimyung Unversity School of Medicine, Daegu, Korea

Sang Mi Han, Kwan Kyu Park, Jin Gu Lee, Hey Jeong Noh, Sung Bae Park[1], Hyunl Chul Kim[1]

Objects: Connective tissue growth factor (CTGF) is a profibrotic growth factor, which is upregulated in renal fibrosis. The kinetics of CTGF mRNA expression in unilateral ureteral obstruction (UUO) suggested that CTGF regulation might contribute to glomerular response to injury downstream of transforming growth factor (TGF)-β1. The present UUO model, study addresses the possible role of CTGF in renal fibrosis, and circular type antisense oligodeoxynucleotides (ODN) for CTGF which is to reduce TGF-β1 and tublointerstitial fibrosis.

Methods: We introduced circular type antisense ODN for CTGF in rats with UUO model to block interstitial fibrosis by tail vein injection. A combination of two antisense sequences for CTGF was adopted to construct a large antisense molecule with a loop and stem. Artifical viral envelope (AVE)-type hemagglutinating virus of Japan (HVJ)-liposomes were used as a vector system for delivery antisense ODN.

Results: After UUO, CTGF mRNA expression expression in the obstructed kidney was significantly upregulated subsequent to TGF-β1 mRNA. *In situ* hybridization, CTGF mRNA was detected mainly in the interstitial fibrotic areas and tubular epithelial cells as well as in parietal glomerular epithelial cells in the obstructed kidney. The obstructed kidneys treated CTGF antisense ODN significantly reduced TGF-β1 mRNA and protein compared with untreated rat, together with inhibited synthesis of tcollagen. The fibrosis of the obstructed kidneys treated CTGF antisense ODN was dramatically less than that of the untreated rats.

Conclusion: These results demonstrate the introduction of antisense ODN for CTGF may be a potential therapeutic maneuver for preventing interstitial fibrosis