S-C19

일측요로폐쇄 동물모델에서 tempol의 PI3K/Akt/FoxO 조절을 통한 신장보호효과

가톨릭대학교 의과대학 내과학교실

윤혜은, 정현화, 정성진, 박철휘, 양철우, 김용수, 신석준

Tempol Attenuates Renal Injury Via PI3K/Akt/FoxO Modulation in Mice with Unilateral Ureteral Obstruction

Hye Eun Yoon, Hyun Wha Chung, Sungjin Chung, Cheol Whee Park
Chul Woo Yang, Yong-Soo Kim, Seok Joon Shin

The Catholic University of Korea, College of Medicine, Department of Internal Medicine

Purpose: Forkhead box O (FoxO) transcription factors are downstream targets of the phosphatidylinositol 3-kinase (PI3K) and serine/threonine protein kinase B/Akt. Phosphorylation of FoxOs by activation of PI3K-Akt inhibits transcriptional functions of FoxOs and controls cell growth, cell survival and oxidative stress. Renal fibrosis is a pathologic hallmark of chronic kidney disease and oxidative stress contributes to the pathogenesis of renal fibrosis. This study investigated the effect of tempol, an antioxidant, on renal injury via modulation of PI3K/Akt/FoxO signaling pathway, using mice with unilateral ureteral obstruction (UUO).

Methods: C57BL/6 mice received either sham or UUO surgery, with or without administration of tempol. We evaluated the change in renal fibrosis and apoptosis, and the renal expressions of PI3K, Akt, FoxO3a and their target molecules, superoxide dismutase (SOD2), Bax and Bcl-2.

Results: The amount of total kidney collagen was significantly lower in the obstructed kidneys of tempol-treated mice compared with that in control mice on day 7 and day 14 ($p<0.05$). The number of interstitial F4/80+ macrophages significantly decreased in tempol-treated mice compared with control mice on day 3, day 7 and day 14 ($p<0.05$). Tempol significantly decreased the expressions of PI3K and phosphorylated Akt on day 3 and day 7, and those of phosphorylated FoxO3a on day 3, day 7 and day 14 ($p<0.05$). The expression of SOD2, an antioxidant protein, was significantly higher in tempol-treated mice than that in control mice on day 3 and day 7 ($p<0.05$). In addition, the ratio of Bax (proapoptotic protein) to Bcl-2 (antiapoptotic protein) and the number of TUNEL-positive cells significantly decreased in tempol-treated mice compared with those in control mice on day 3, day 7 and day 14 ($p<0.05$).

Conclusion: The results demonstrated that tempol attenuates renal inflammation, fibrosis and oxidative stress via modulation of PI3K/Akt/FoxO3a pathway in mice with UUO.

Key Words: 신섬유화, 일측요로폐쇄, FoxO
Renal fibrosis, Unilateral ureteral obstruction, FoxO