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허혈/재관류 급성 신손상에서 파리칼시톨의 염증 억제 효과

고려대학교 안암병원 신장내과

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Paricalcitol Suppresses the Renal Inflammation During Ischemia/reperfusion-induced Acute Kidney Injury

Jae-Won Lee, Eunjung Cho, Myung-Gyu Kim, Sang-Kyung Jo, Won Yong Cho, Hyung Kyu Kim

Korea University Anam Hospital Department of Internal Medicine Division of Nephrology

Introductions and Aims: The pathophysiologic mechanisms of ischemic acute kidney injury (AKI) are thought to include a complex interplay among vascular endothelial cell dysfunction, inflammation and tubular cell damage. Several lines of evidence suggest a potential anti-inflammatory effect of vitamin D in various kidney injury models. In this study, we investigated the effect of the synthetic vitamin D analogue paricalcitol on renal inflammation in a mouse model of ischemia/reperfusion (I/R)-induced AKI.

Methods: Paricalcitol or vehicle was administered via intraperitoneal injection 24 hour before ischemia, and then mice underwent ischemia through bilateral clamping of renal pedicles. Biochemical, histologic kidney injury and tissue inflammation were assessed. Quantitation of various cytokines and chemokines in kidney tissue was done by using cytometric bead array. Western blot analysis of protein in kidney was performed using primary antibodies for nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB), inhibitor of κB (IκB) and Bcl-2-associated X protein (Bax). Effect of paricalcitol on NF-κB pathway in HK2 cell line was also examined.

Results: Pretreatment with paricalcitol attenuated I/R injury and reduced kidney neutrophil and macrophage infiltration. It also reduced pro-inflammatory cytokine, interleukin-6, in kidney tissue. Paricalcitol pretreatment suppressed I/R-induced depletion of cytosolic IκB and nuclear translocation of P65, suggesting that it blocked the activation of NF-κB mediated inflammatory pathway following I/R. In in vitro experiment, paricalcitol pretreatment also suppressed the depletion of cytosolic IκB induced by TNF-α in HK-2 cells. Tubular cell apotosis, determined by the number of terminal deoxynucleotidyl transferase-mediated dUTP nick-end labeling (TUNEL)-positive nuclei, was decreased by paricalcitol pretreatment. Bax in kidney tissue was also decreased by paricalcitol.

Conclusion: These results suggest that beneficial effect of paricalcitol might be mediated by its effect on blocking NF-κB mediated inflammation and also on preventing apoptosis.

Key Words: 급성 신손상, 파리칼시톨, 염증반응
Acute kidney injury, Paricalcitol, Inflammation