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쥐의 급성 심근경색 모델에서 심장-신장 증후군의 병태생리기전에 관한 연구

고대안암병원 신장내과

조은정, 김명규, 조원용, 김형규, 조상경

Role of Inflammation in the Pathogenesis of Cardiorenal Syndrome in a Rat Myocardial Infarction Model

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Background: Cardiorenal syndrome is now frequently recognized and the combined dysfunction of heart and kidney increases morbidity and mortality. This study aimed to investigate possible mechanisms that underlie renal damage following heart dysfunction using a rat myocardial infarction model, focusing on the inflammatory pathway.

Methods: Rats were randomized into four groups: normal, volume depletion, sham operation and myocardial infarction (MI). MI was induced by left coronary artery ligation and a volume depletion model was produced by low salt diet and furosemide injection. Biochemical, histological and flow cytometric analyses were performed at 3 days, 4 and 8 weeks after MI.

Results: On day 3 following MI, the development of subclinical acute kidney injury was identified through significantly increased serum and urine neutrophil gelatinase-associated lipocalin level. We detected the increase of activated monocytes (CCR2+, ED-1+) in peripheral blood, along with the infiltration of ED-1+ macrophages and the increment of nuclear p65 in the kidney of MI rats, suggesting the contribution of NF-κB-mediated inflammation in the development of type 1 cardiorenal syndrome. The inflammatory cytokines interleukin-6 and TNF-α mRNA expression, as well as microvascular endothelial permeability and tubular cell apoptosis significantly increased in the kidneys of MI rats. At 4 and 8 weeks after MI, tubular cell apoptosis, ED-1+ macrophage infiltration, and interstitial fibrosis increased in MI rats and these chronic changes were significantly mitigated by systemic monocyte/macrophage depletion using liposome clodronate.

Conclusion: This study identifies the possible important role of inflammatory response as a mediator of heart-kidney crosstalk in cardiorenal syndrome.

Key Words: 심근경색, 신장, 염증
Myocardial infarction, Kidney, Inflammation