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패혈증에 동반되는 급성 신 손상의 발병 기전 및 줄기 세포 투여의 효과에 대한 연구

을지병원 신장내과[1], 고려대학교병원 신장내과[2]

이소영[1] · 성수아[1] · 김명규[2] · 최혜민[2] · 조원용[2] · 김형규[2] · 조상경[2]

The Mechanism of Septic Acute Kidney Injury and the Effect of Mesenchymal Stem Cells on Septic AKI

So-Young Lee[1], Su-Ah Sung[1], Myung-Gyu Kim[2], Hae-Min Choi[2]
Won-Yong Cho[2], Hyung-Kyu Kim[2], Sang-Kyung Jo[2]

Department of Nephrology[1], Eulji University Hospital
Department of Nephrology[2], Korea University Hospital

Although mechanism of septic acute kidney injury (AKI) has been known to be associated with intense renal vasoconstriction with tissue inflammation, precise pathophysiologic mechanisms leading to AKI is largely unknown. Recent reports suggested that excessive immune suppressive status (compensatory antiinflammatory response syndrome, CARS) following systemic inflammatory response syndrome (SIRS) in sepsis might be responsible for transient organ dysfunction. The purpose of this study was to examine mechanisms of septic AKI by providing on site quantitative comparison of systemic and kidney injury, inflammation in ischemia/reperfusion (I/R) and septic AKI animal models.

C57/BL6 mice underwent 30 min ischemia followed by reperfusion or cecal ligation and puncture. At 24 hrs, biochemical, histologic kidney injury, inflammation as well as systemic inflammation were compared and effect of mesenchymal stem cells (MSCs) pretreatment on these parameters were compared.

Despite comparable level of functional impairment in both groups, degree of systemic inflammation, kidney inflammation and histologic kidney injury showed marked differences. Tubular cell necrosis or apoptosis, predominant in I/R kidneysI was hardly observed in septic kidneys. Systemic inflammation assessed by plasma cytokine level in septic AKI was characterized by marked increase in both pro- and anti-inflammatory cytokines, compared to that in I/R induced AKI that showed minimal increase of proinflammatory cytokine only. Tissue and plasma cytokine profile also showed the marked decrease in ratio of proinflammatory vs anti-inflammatory cytokines in septic kidneys compared to I/R kidneys, suggesting the possible transition from proinflammatory to antiinflammatory milieu in septic kidneys. Tissue inflammation measured by flow cytometry also showed minimal tissue inflammation in septic kidneys that is characterized by minimal infiltration of F4/80+ macrophages, Gr-1+ neutrophils, and CD4+, CD8+ T cells compared to that from I/R kidneys. Administration of MSCs that has known to have immune-modulatory effect protected kidney dysfunction in both I/R or septic AKI. However, while MSCs pretreatment resulted in marked decrease in kidney inflammation in I/R kidneys, beneficial effect of MSCs in septic AKI was associated with paradoxical increase in kidney inflammation. These results showed a distinct pathophysiologic mechanism of septic AKI and suggest that excessive immune suppressive status induced by sepsis might be responsible for transient functional impairment in septic AKI.

Key Words : 급성 신손상, 패혈증, 줄기 세포
Acute kidney injury, Sepsis, Mesenchymal stem cells