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간 허혈 재관류 손상 후 발생하는 신장 손상의 발생 기전과 이에 미치는 S1P의 효과에 대한 연구

을지대학교 의과대학 신장내과학교실[1], 고려대학교 의과대학 신장내과학교실[2]

이소영[1] · 성수아[1] · 김명규[2] · 조원용[2] · 김형규[2] · 고윤숙[2] · 이희영[2] · 조상경[2]

The Mechanisms of Acute Kidney Injury after Hepatic Ischemia and Reperfusion Injury in Mice and the Effect of S1P on Kidney Dysfunction

So-Young Lee[1], Su-Ah Sung[1], Myung-Gyu Kim[2], Won-yong Cho[2]
Hyung-kuy Kim[2], Yun-sook Go[2], Hee-Young Lee[2], Sang-kyung Jo[2]

Eulji University Hospital Internal Medicine Nephrology[1] Department
Korea University hospital Internal Medicine Nephrology[2] Department

Background : Liver ischemia/reperfusion injury (IRI) potentially cause kidney dysfunction. Endothelial injury by hepatic IR could contribute to distant organ dysfunction but detailed mechanisms are unclear. The present study is designed to examine whether hepatic IR cause renal dysfunction and endothelial barrier enhancement by sphingosine-1-phosphate(S1P) could attenuate kidney injury following hepatic IR.

Methods : S1P and vehicle was given intravenously to C57BL/6 mice and animals were subjected to hepatic ischemia for 60 minutes followed by reperfusion for 6 hour and 24 hour. Plasma creatinine and ALT were measured. Expression of inflammatory cytokines of plasma and kidney tissue were measured by cytometric bead array (CBA). Renal histologic findings were determined. To study the role of S1P on endothelial progenitor cells, CD133 and CD34, as markers of hematopoietic stem cells and endothelial cells, were examined after S1p injection in animal models of kidney IRI.

Results : Hepatic IRI led to increase in plasma ALT, IL-6 and MCP-1. Increase in renal tubular cell apoptosis and neutrophil infiltration was observed following hepatic IRI. S1P significantly decreased plasma ALT, IL-6 and MCP-1. Analysis of kidneys by light microscopy revealed minimal histologic signs of neutrophil infiltration and apoptosis with S1P treatment compared with vehicle group. CD133 and CD34 positive cells increased by S1P treatment in kidney IRI spleen tissues.

Conclusion : We conclude that hepatic IRI induced kidney damage and endothelial dysfunction by hepatic IRI partially mediate the kidney damage. The machanisms of protection by S1P is not known but maybe related to endothelial protection by endothelial progenitor cell mobilization or anti-inflammatory actions.

Key Words : 급성 신손상, 간허혈, 내피세포 손상
Acute kidney injury, Hepatic ischemia-reperfusion, S1P