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복막투석에서 복막의 염증과 섬유화에 미치는 TLR-4 의 역할

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최순연, 류혜명, 안지선, 오은주, 오세현, 김유진, 최지영, 조장희, 김찬덕, 김용림, 박선희

The Role of TLR-4 in Peritoneal Inflammation and Fibrosis During Peritoneal Dialysis

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Background: Toll-like receptors, a family of signaling pattern-recognition receptors also have been implicated in the pathogenesis of acute and chronic kidney diseases. However, there were few reports on the role of TLR-4 in high glucose-induced inflammation and fibrosis in peritoneal dialysis (PD). This study aims to evaluate the effect of high glucose on peritoneal TLR-4 expression and its impact on peritoneal inflammation and fibrosis in PD.

Methods: Using cultured HPMCs, TLR-4 and its downstream signaling molecules were measured after high glucose (50mmol) exposure by real-time PCR and/or western blot. The effect of TLR-4 on inflammation and fibrosis were evaluated after inhibition of TLR-4 by siRNA for TLR-4.

Results: High glucose induced TLR-4 mRNA and protein expression in HPMCs. In addition, MyD88 mRNA and NF-kB p65 protein were increased after high glucose exposure for 24 h. MCP-1 mRNA, TGF-b mRNA and protein expression were also significantly increased after high glucose exposure. siRNA for TLR-4 reduced high glucose-induced increase of MyD88 and NF-kB p65, MCP-1 and TGF-b mRNA expression.

Conclusions: Exposure to glucose induced innate immune responses and subsequently increased MCP-1 and TGF-b expression in HPMCs. It was mediated by TLR-4-MyD88-NF-kB pathway. This inflammatory-fibrosis cascade to high glucose was partly blocked by TLR4 inhibition, but further investigation in vivo system is clearly warranted for its clinical relevance in PD.

Key Words: 복막투석, 복막섬유화, TLRs
Peritoneal dialysis, Peritoneal fibrosis, TLRs