F-D5

MCP-1/CCR2계가 인간 복막중피세포의 상피-중간엽 이행 (epitherial-mesenchymal transition)에 미치는 영향

BK 21 의과학 사업단 연세대학교 의과대학 내과학교실[1]
서울대학교 의과대학 내과학교실[2], 이화여자대학교 의과대학 내과학교실[3]

이순하[1] · 강혜영[1] · 남보영[1] · 김도희[1] · 곽승재[1] · 김승혜[1]
김동기[2] · 한승혁[1] · 류동열[3] · 유태현[1] · 강신욱[1]

MCP-1/CCR2 System is Involved in Epithelial-mesenchymal Transition of Peritoneal Mesothelial Cells

Sun Ha Lee[1], Hye Young Kang[1], Bo Young Nam[1], Do Hee Kim[1], Seung-Jae Kwak[1]
Seung Hye Kim[1], Dong Ki Kim[2], Seung Hyeok Han[1], Dong-Ryeol Ryu[3], Tae-Hyun Yoo[1], Shin-Wook Kang[1]

Brain Korea 21 Department of Internal Medicine[1] Yonsei University College of Medicine
Department of Internal Medicine[2] Seoul National University
Department of Internal Medicine[3] College of Medicine Ewha Womans University

Background : Monocyte chemoattractant protein-1 (MCP-1) is a potent chemokine that plays a critical role in the recruitment of macrophages. However, recent studies have shown that monocyte chemoattractant protein-1 (MCP-1)/C-C chemokine receptor2 (CCR2) system is directly involved in extracellular matrix accumulation (ECM) under diabetic conditions. Since human peritoneal mesothelial cells (HPMCs) also synthesize MCP-1 and its expression is increased under high glucose conditions, there is a possibility that MCP-1/CCR2 system plays an important role in peritoneal fibrosis (PF), a serious long-term complication of continuous ambulatory peritoneal dialysis.

Purpose : This study was undertaken to investigate the functional role of MCP-1/CCR2 system in epithelial-mesenchymal transition (EMT) of HPMCs, which has been considered to play a role in the pathogenesis of fibrosis in various conditions including PF.

Methods : HPMCs were isolated from a piece of human omentum and were incubated with M199 media containing 5.6 mM glucose (NG), NG+94.4 mM mannitol (NG+M), NG+recombinant human MCP-1 (10 ng/mL) (NG+MCP-1), or 100 mM glucose (HG) with or without a specific inhibitor of CCR2 (1 □M RS102895) for 72 hours. Levels of secreted MCP-1 in culture media were determined by ELISA. Western blot was performed to determine E-cadherin, α-smooth muscle actin (α-SMA), and fibronectin protein expression.

Results : MCP-1 levels were significantly increased in HG-conditioned media compared to NG media. CCR2 protein expression was demonstrated in HPMCs, but there was no difference in CCR2 expression between NG- and HG-stimulated cells. α-SMA protein expression in HG and NG+MCP-1 groups were 2.7- and 1.9-folds higher relative to NG cells, respectively, while E-cadherin protein expression were decreased in HG and NG+MCP-1 groups by 58% and 43% compared to NG cells, respectively ($p<0.05$). In addition, there was significant increase in fibronectin protein expression in HG- and MCP-1-stimulated HPMCs ($p<0.05$). These HG- and MCP-1-induced changes were significantly abrogated by RS102895 pretreatment.

Conclusion : HG and MCP-1 directly induced EMT and enhanced fibronectin expression in HPMCs, and these HG-induced changes were ameliorated by the inhibition of MCP-1/CCR2 system, suggesting that increased MCP-1 levels by HG may contribute to the development of PF.

Key Words : 단백구 화학주성 단백-1/CCR2계, 상피-중간엽 이행
MCP-1/CCR2 system, Epithelial-mesenchymal transition