S-D19

MCP-1이 인간 복막중피세포의 상피-중간엽 이행 (epithelial-mesenchymal transition)에 미치는 영향

이화여자대학교 의학전문대학원 내과학교실[1], 연세대학교 의과대학 내과학교실[2]

류동열[1] · 이금희[2] · 유태현[2] · 한승혁[2] · 김승정[1] · 강덕희[1] · 최규복[1] · 윤견일[1] · 강신욱[2]

Monocyte Chemoattractant Protein-1 (MCP-1) Directly Induces Epithelial-Mesenchymal Transition in Human Peritoneal Mesothelial Cells

Dong-Ryeol Ryu[1], Jinji Lee[2], Tae-Hyun Yoo[2], Seung-Hyeok Han[2], Seung-Jung Kim[1]
Duk-Hee Kang[1], Kyu Bok Choi[1], Kyun Il Yoon[1] and Shin-Wook Kang[2]

Department of Internal Medicine[1] School of Medicine Ewha Womans University,
Department of Internal Medicine[2] College of Medicine Yonsei University

Background : After long- term treatment with continuous ambulatory peritoneal dialysis (CAPD), peritoneal fibrosis (PF) has been observed in some patients, resulting in membrane failure. Recently, epithelial- mesenchymal transition has been considered to play an important role in the pathogenesis of fibrosis in various conditions, including PF. MCP- 1 is known to be involved in the pathogenesis of PF via recruiting inflammatory cells into the peritoneum and its expression is increased in human peritoneal mesothelial cells (HPMCs) exposed to high glucose.

Purpose : This study was undertaken to elucidate whether C- C chemokine receptor 2 (CCR2) existed in HPMCs and whether MCP- 1 had direct effects on EMT and fibronectin expression in HPMCs.

Methods : HPMCs were isolated from a piece of human omentum and were incubated with M199 media containing 5.6 mM glucose (LG), 5.6 mM glucose+94.4 mM mannitol (LG+M), LG+10 ng/mL recombinant human MCP- 1 (LG+MCP- 1), or 100 mM glucose (HG) with or without a specific inhibitor of CCR2, 1 uM RS102895, for 4 days. Levels of secreted MCP- 1 in culture media were determined by ELISA. Western blot was performed to determine fibronectin, E- cadherin, α - smooth muscle actin (α - SMA) and CCR2 protein expression.

Results : MCP- 1 protein levels was significantly increased in HG- conditioned media compared to LG media (1600.6±9.4 vs. 956.1±19.1 pg/mL, $p<0.05$). CCR2 protein expression was detected in HPMCs, but there was no difference between LG- and HG- stimulated cells. α - SMA protein expression in HG and LG+MCP- 1 groups were 2.7- fold and 1.9- fold higher relative to LG cells, respectively, while E- cadherin protein expression were decreased in HG and LG+MCP- 1 groups by 48% and 37% compared to LG cells, respectively ($p<0.05$). In addition, fibronectin protein expression in HG and LG+MCP- 1 groups were 2.1- fold and 1.8- fold higher compared to LG cells, respectively ($p<0.05$). These HG- induced changes were significantly abrogated upon pre- treatment with RS102895.

Conclusion : HG and MCP- 1 directly induce EMT and enhance fibronectin expression in HPMCs, and these HG- induced changes were attenuated 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 : 단핵구 화학주성 단백- 1, 상피- 중간엽 이행, 복막중피세포
MCP- 1, Epithelial- mesenchymal transition, Mesothelial cell