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# 복막중피세포에서 알도스테론이 상피-중간엽 세포이행에 미치는 영향

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# Effect of Aldosterone on Epithelial-to-Mesenchymal Transition of Human Peritoneal Mesothelial Cell

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Although the exact mechanisms of peritoneal damage during PD still remain unclear, epithelial-to-mesenchymal transion (EMT) of peritoneum has been emerged as an early and reversible mechanism of peritoneal fibrosis. Recent data revealed a pro-fibrotic role of aldosterone in various organ fibrosis. Human peritoneal mesothelial cell (HPMC) is known to have its own renin-angiotensin-aldosterone system (RAAS), but it has not been investigated whether aldosterone induces EMT in HPMC and which mechanisms are responsible for aldosterone-induced EMT. The presence of mineralocorticoid receptor (MR) in HPMC was identified by RT-PCR. EMT of HPMCs was evaluated by comparing the expression of epithelial cell marker, E-cadherin and mesenchymal cell marker, $\alpha$-smooth muscle actin ($\alpha$-SMA) after the stimulation with aldosterone (1-100 nM) and/or spironolactone, MR antagonist. Aldosterone-induced phosphorylation of ERK and p38 MAPKinases and generation of reactive oxygen species (ROS) were assessed by Western blotting and DCF-DA staining of cells. Effect of MAPKinase inhibitors (SB20358, PD98059) or anti-oxidants [N-acetyl cystein (NAC), rotenone and apocynin] on aldosterone-induced EMT was evaluated as a mechanism of phenotypic transformation of HPMCs induced by aldosterone. HPMC expressed human mineralocorticoid receptor. Aldosterone induced EMT in cultured HPMC, expressed as a decrease in the expression of E-cadherin and an increase in the expression of $\alpha$-SMA in dose- and time-dependent manner from a concentration of 10 nM and 48 hours of stimulation. Spironolactone (1 □M) completely blocked aldosterone-induced EMT. Aldosterone induced an activation of both ERK and p38 MAPKinase from 5 minutes of stimulation. PD98059, an inhibitor of ERK MAPK, attenuated aldosterone-induced EMT, however SB20358, an inhibitor of p38 MAPK, did not alter the expression of E-cadherin and $\alpha$-SMA induced by aldosterone. Aldosterone induced oxidative stress in HPMCs, and pre-treatment of cells with NAC or rotenone ameliorated the aldosterone-induced EMT. NAC also blocked aldosterone-induced activation of ERK. Aldosterone induced EMT in HPMC by MR-dependent mechanism. Aldosterone-induced generation of ROS followed by an activation of ERK played a key role in aldosterone-induced EMT of cells. Further studies will be necessary to understand the pathogenetic mechanism of aldosterone-induced EMT and to verify the clinical implication of inhibition of RAAS.

**Key Words :** 알도스테론, 상피중배엽세포이행, 복막투석
Aldosterone, EMT, Peritoneal Dialysis