Renin-Angiotensin System in HPMC : Implication for Peritoneal Fibrosis and Hyperpermeability

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Background : Angiotensin (Ang) II plays an important role in renal fibrosis in diabetes and may similarly promote peritoneal fibrosis during long-term peritoneal dialysis (PD) using glucose-based PD solutions. It is not known, however, if human peritoneal mesothelial cells (HPMC) express renin-angiotensin system (RAS).

Methods : In cultured HPMC, the expression of mRNAs for angiotensinogen, angiotensin-converting enzyme (ACE), Ang II receptor type 1 (AT1), and transforming growth factor (TGF)-β1 was evaluated by real-time PCR, ACE, AT1, and vascular endothelial growth factor (VEGF) proteins by Western blot analysis, and Ang I, Ang II, and TGF-β1 proteins by ELISA. We also measured Ang II, TGF-β1, and VEGF proteins in overnight PD effluent from 22 PD patients with or without ultrafiltration failure (UFF).

Results : HPMC constitutively expressed all the components of RAS. 50 mM D-glucose (high glucose : HG) significantly increased expression of angiotensinogen, ACE, and AT1 mRNAs. HG upregulated ACE, AT1, and Ang II proteins. Ang II increased TGF-β1 and VEGF expression. Losartan prevented HG-induced upregulation of TGF-β1. Effluent Ang II and TGF-β1 protein concentrations were significantly higher in patients with UFF and significant correlations were found among effluent Ang II, TGF-β1, and VEGF and between dialysate to plasma creatinine ratio and concentrations of Ang II, TGF-β1, or VEGF in PD effluent.

Conclusion : These data demonstrate that HPMC constitutively express all components of RAS and suggest that locally produced Ang II by HPMC may be a potential therapeutic target in peritoneal fibrosis and hyperpermeability during long-term PD.