

Role of Glucose Degradation Products in Human Peritoneal Mesothelial Cell Activation

*Hyonam Kidney Laboratory, Soon Chun Hyang University,
College of Pharmacy*, Ewha Womans University*

Jae Sook Song · Hunjoo Ha* · Hi Bahl Lee

Background : Both high glucose (HG) and glucose degradation products (GDP) have been implicated in alterations of peritoneal membrane structure and function during long-term peritoneal dialysis (PD). However, the relative importance of GDP in human peritoneal mesothelial cell (HPMC) activation has not been elucidated. The present study examined the role of GDP in HPMC activation using PD solutions containing 1.5% or 4.25% glucose and 40 mM lactate with high GDP (H1.5 and H4.25, respectively) and low GDP (L1.5 and L4.25, respectively). The effect of individual GDP including methylglyoxal (MGO), acetaldehyde, and 3,4-dioxyglucosone (3,4-DGE) was also examined.

Method : Using M199 culture medium as a control, growth-arrested and synchronized HPMC were continuously stimulated by PD solutions diluted twofold with M199, MGO, acetaldehyde, or 3,4-DGE for 48 hours. VEGF, TGF-1, ig-h3, fibronectin, plasminogen activator inhibitor-1 (PAI-1) secreted into the media were analyzed by ELISA, procollagen I C-terminal peptide (PICP) and procollagen III N-terminal peptide (PIIICP) by radioimmunoassay and heat shock protein 47 (hsp47) expression by Western blot analysis.

Results : All PD solutions tested increased the secretion of VEGF, TGF-1, ig-h3, PICP, and PIIINP, but not fibronectin or PAI-1. H4.25- and L4.25-induced VEGF, TGF-1, and PIIINP secretion was significantly higher than those by H1.5 and L1.5, respectively. No difference was observed between H1.5 and L1.5 and between H4.25 and L4.25. MGO at 310 M significantly increased hsp47 expression and secretion of VEGF and fibronectin, but not TGF-1 or PIIINP, compared with control M199. Acetaldehyde stimulated but 3,4-DGE inhibited VEGF secretion. Fibronectin and hsp47 expression in HPMC was not affected by acetaldehyde or 3,4-DGE.

Conclusion : HG rather than GDP appears to be the major component of lactate-buffered PD solution responsible for activation of cultured HPMC. Since MGO in high concentration up-regulated VEGF, fibronectin, and hsp47 by HPMC, it is possible that low concentration of GDP contained in PD solution may adversely affect the peritoneum over a long-term.