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## **Low GDP dialysate protects peritoneum from EMT by amelioration of decreased expression of anti-fibrotic factors in cultured human peritoneal mesothelial cells**

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**Introduction** : Epithelial-to-mesenchymal transition (EMT) is well known mechanism of tissue fibrosis including peritoneum in patients undergoing peritoneal dialysis which is continuously exposed to unphysiologic components of dialysate. Recent paper demonstrated that low GDP dialysate decreased EMT of peritoneum using cell morphology scoring of mesothelial cells from overnight effluent. To explore the mechanism of beneficial effect of low GDP dialysate on EMT, we performed an in-vitro study with primarily isolated human peritoneal mesothelial cell (HPMC) exposed to conventional or low GDP dialysate with investigating the expression of naturally occurring anti-fibrotic peptide, hepatocyte growth factor (HGF) and bone morphogenic protein-7 (BMP-7). We have also examined whether HGF and/or BMP-7 treatment prevent EMT of HPMC induced by conventional dialysate.

**Methods** : EMT was evaluated by comparing the expression of E-cadherin and  $\alpha$ -smooth muscle actin ( $\alpha$ -SMA) in HPMC exposed to a conventional, lactate-buffered dialysate (4.25% Perisis, Boryung, Korea) or a new, pH-neutral, lactate/ bicarbonate-buffered, low GDP dialysate (4.25% PeriPLUS, Boryung, Korea) with or without recombinant HGF (10 ng/ml) for 24 and 48 hours. Effect of BMP-7 on dialysate-induced EMT was evaluated in HPMCs transfected with adenoviral vector of human BMP-7. Expressions of HGF and BMP-7 were evaluated by RT-PCR and Western blotting.

**Results** : HPMC exposed to conventional dialysate decreased E-cadherin expression and increased  $\alpha$ -SMA from 24hours of stimulation. Compared to conventional dialysate, low GDP dialysate inhibited EMT of HPMC. Exposure of HPMC to conventional dialysate resulted in a significant decrease in expression of HGF and BMP-7 both at mRNA and protein levels, which was ameliorated by low GDP dialysate. However, neither rHGF treatment nor BMP-7 transfection prevented conventional dialysate-induced EMT. Treatment of rHGF in BMP-7 transfected HPMCs exposed to conventional or low GDP dialysate did not alter the expression of E-cadherin and  $\alpha$ -SMA.

**Conclusion** : Present study demonstrated that low GDP dialysate inhibited peritoneal EMT by preventing decreased expression of anti-fibrotic factor, HGF and BMP-7. Although conventional dialysate induced EMT of HPMC with decreased expression of HGF and BMP-7, HGF and/or BMP treatment may not be sufficient to prevent or reverse EMT in in-vitro condition. This finding suggests the possibility that beneficial effect of anti-fibrotic peptide in peritoneal fibrosis may be not a direct one on HPMC, rather activating other protecting systems inside of peritoneal cavity.