KSN 2021
FULLY VIRTUAL MEETING
September 02 (Thu) - 05 (Sun)

Abstract Submission No. : 2328

The impact of CCL8 on peritoneal fibrosis and inflammatory activity

Yeonhee Lee[1], Seung Hee Yang[3], Jangwook Lee[4], Yong Chul Kim[3], Dong Ki Kim[2], Yon Su Kim[2], Kwon Wook Joo[2]
[1]Department of Internal Medicine-Nephrology, Uijeongbu Eulji Medical Center, Eulji University, Korea, Republic of
[2]Department of Internal Medicine, Seoul National University College of Medicine, Korea, Republic of
[3]Department of Kidney Research Institute, Seoul National University College of Medicine, Korea, Republic of
[4]Department of Internal Medicine, Dongguk University Ilsan Hospital, Korea, Republic of

Objectives: Peritoneal fibrosis (PF) is an intractable complication of peritoneal dialysis (PD) that leads to peritoneal membrane failure. The present study aimed to investigate the association between PD effluent levels of chemokine (C-C motif) ligand 8 (CCL8) and PD failure and the mechanism of action of CCL8 in PF using cell-based models.

Methods: A total of 80 end-stage renal disease (ESRD) patients with PD were enrolled. CCL8 levels were measured with an Enzyme-linked immunosorbent assay (ELISA) in PD effluents and serum and were analyzed with peritoneal transport parameters. Peritoneal mesothelial cells (PMCs) from 20 PD patients were obtained from PD effluent. PF was induced in primary cultured PMCs with recombinant TGF-β. To evaluate the role of CCL8 in fibrosis, TGF-β–stimulated PMCs were pretreated with CCL8 blocking antibody. To confirm that CCL8 is expressed during PF in PMCs, the cells were treated with TGF-β, and CCL8 protein expression was evaluated by western blotting.

Results: Correlations of peritoneal transport parameters with CCL8 levels were presented. There were positive associations between CCL8 levels and peritoneal Kt/V, D/P creatinine, and D/P60 Na, and a negative association between CCL8 level and D/D0 glucose (All $P < 0.05$). CCL8 was upregulated by TGF-β treatment; this was accompanied by increases in fibronectin, collagen 1, and fibroblast growth factor-2 (FGF-2) expression. These results indicate that TGF-β induces fibrosis in PMCs, with up-regulation of CCL8. CCL8 blockade suppressed the TGF-β–induced increase in CCL8 expression, with a concomitant decrease in fibronectin, collagen 1, and FGF-2 expression.

Conclusions: High CCL8 levels in PD effluent may be associated with increased risk of PD failure and that CCL8 blockade can ameliorate PF. Thus, PD effluent CCL8 level could be a promising biomarker for peritoneal fibrosis and inflammation, and therapeutic strategies that inhibit CCL8 function may effectively prevent PF development and progression.