Gambro 연구비

실험적 피막성 복막경화증에서 DNA 탈메칠화에 의한 섬유화 감소 효과

경북대학교 의학전문대학원 내과학교실

박선희, 안지선, 오은주, 류혜명, 오세현, 최순연, 김유진, 최지영, 조장희, 김찬덕, 김용림

Effect of DNA Demethylation in Experimental Encapsulating Peritoneal Sclerosis

Sun-Hee Park, Ji-Sun Ahn, Eun-Joo Oh, Hye-Myung Ryu, Se-Hyun Oh, Soon-Youn Choi
You-Jin Kim, Ji-Young Choi, Jang-Hee Cho, Chan-Duck Kim, Yong-Lim Kim

Division of Nephrology and Department of Internal Medicine,
Kyungpook National University School of Medicine

Background: Encapsulating peritoneal sclerosis (EPS) is characterized by a progressive, intra-abdominal inflammation and fibrosis of peritoneum in patients on peritoneal dialysis and eventually leads to intestinal obstruction and malnutrition in the later stages. This study aims to evaluate the therapeutic effect of DNA demethylation in experimental EPS.

Methods: Experimental EPS was induced by intraperitoneal injection of 0.1% chlorhexidine gluconate (CG) and 15% ethanol to non-uremic male SD rats (n= 19) which were divided into 3 groups: control group (C, n=5) with normal saline injection, EPS group (CG, n=7) with CG injection for 4 weeks and treatment group (CGA, n=7) with 5'-azacytidine injection for 2 weeks during CG injection. Morphometric analysis of peritoneum was performed with immunohistochemical staining for type 1 collagen and α-SMA. The expression of TGF-β, fibroblast-specific protein (FSP)-1 and DNA methyltransferase (DNMT)-1 were analyzed by western blot. Methylation specific PCR for RAS protein activator like-1 (RASAL1) was performed with measurement of RASAL1 protein expression.

Results: The thickness of parietal peritoneum and the number of vessels in omental tissue were significantly increased in CG group compared to CGA group. The expression of type 1 collagen, α-SMA, TGF-β and FSP-1 were significantly increased in CG group compared to CGA group. DNMT1 was significantly increased in CG group, whereas it was reduced in CGA group. Hypermethylation of RASAL1 was associated with decreased expression of RASAL1 protein in CG group, whereas it was reversed in CGA group.

Conclusions: DNA demethylation by 5'-azacytidine treatment improved pathologic changes of peritoneum in experimental EPS and it was associated with increased expression of DNMT1 and hypermethylation of RASAL1.

Key Words: 복막투석, 피막성 복막경화증, 탈메칠화
Peritoneal dialysis, EPS, Demethylation