KSN 2018
Seoul, Korea · May 17 - 20

Abstract Type : Oral
Presentation No. : OR 06 CK-05

Intestinal barrier disruption and dysregulated mucosal immunity contribute to kidney fibrosis in CKD

Jihyun Yang, Hyunseo Kim, Ki Joon Lim, Jun Yong Lee, Se Won Oh, Myung-gyu Kim, Won-Yong Cho, Sang-Kyung Jo
Department of Internal Medicine-Nephrology, Korea University Anam Hospital, Korea, Republic of

Objectives: Intestinal dysbiosis is known to play a pivotal role in progression of chronic kidney disease (CKD). It is associated with gut barrier disruption, uremic toxin increment and provocating systemic inflammation. diverse pathological processes, including diabetes, obesity, and inflammatory bowel disease. In this study, we demonstrated intestinal barrier disruption and aberrant mucosal immunity in 5/6 nephrectomized mice and the effect of probiotics on these parameters, systemic inflammation, and the progression of CKD.

Methods: CKD was induced in 6 week old C56BL/6 mouse by 5/6 nephrectomy. *Lactobacillus Rhamnosus R0011* and *Lactobacillus Acidophilus R0052* mixture were given via oral gavage for 8 weeks. All animal protocols were approved by the Korea University Institutional animal care and use committee (KUIACUC-2015-180).

Results: In CKD mice, the expression of colon HSP 70, a key protein in intestinal barrier integrity, and tight junction protein claudin-1 was significantly decreased; however, pore-forming claudin-2 expression and the incidence of apoptosis in colon epithelial cells was increased. These changes were accompanied by increased permeability. Although the percentage of CD4+ Foxp3+ Tregs, essential for immune tolerance, was not different than that in control mice, the ratio of CX3CR1intermediate/CX3CR1high proinflammatory/resident macrophages was increased in the colon of CKD mice with higher cytokine expression. Orally administered Lactobacilli mixture partially mitigated CKD-induced “leaky gut,” restored colon epithelial HSP 70, claudin-1, and claudin-2 expression, and decreased apoptosis. Probiotic treatment restored the ratio of CX3CR1intermediate/CX3CR1high macrophages and increased the percentage of CD103+ CD11c+ regulatory dendritic cells, Tregs, in the colon. These changes suppressed systemic inflammation and kidney fibrosis.

Conclusions: Our data showed that intestinal dysbiosis-associated gut barrier disruption and aberrant mucosal immunity may be important in the systemic inflammation and progressive fibrosis of CKD. Intestinal targeting may provide novel opportunities for CKD therapy.