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Acute kidney injury increases gut permeability and provoke dysregulation of mucosal immunity : Effect of probiotics on AKI severity

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Objectives : Emerging evidence indicate the presence of kidney-gut crosstalk in diverse pathological conditions. In normal condition, healthy microbiome help maintain gut barrier and mucosal immune tolerance. In this study, we investigated kidney-gut crosstalk in AKI by assessing the effect of AKI on gut barrier integrity and immune tolerance mechanisms.

Methods : C57BL/6 mice underwent bilateral ischemia reperfusion injury (bilateral IRI) or sham operation. In probiotic treatment group, Bifidobacillus was administered via oral gavage once daily, started 3 weeks prior to injury. The gut barrier integrity was assessed by measuring orally administered fluorescein isothiocyanate-dextran (FITC-dextran) activity in blood. Western blot for tight junction protein claudin 1, occludin as well as heat shock protein 70 (Hsp 70) was performed. mRNA expression of Foxp3 in isolated colon immune cell population was also performed. The study was approved by Korea university laboratory animal research center institute of board review (KOREA-2016-0260).

Results : Following AKI, gut permeability increased significantly. Increased permeability was accompanied by decreased claudin-1, occludin as well as epithelial HSP 70 expression. Three week probiotic treatment resulted in preserved renal function and structure as well as decreased proteinuria. The renoprotective effect of probiotic treatment was associated with partial restoration of claudin-1, occludin and HSP 70 in colon epithelial cells. Probiotic supplementation also resulted in expansion of Foxp3 Tregs in colon as well as in kidney.

Conclusions : AKI induced gut barrier disruption might be one mechanism potentiating systemic inflammation and endotoxemia following AKI. Probiotic mediated renoprotective effect might be mediated by strengthening gut barrier and also mucosal immune tolerance mechanisms. Probiotics might be one promising strategy aiming for reducing AKI associated systemic inflammation and remote organ injury.

Keywords : AKI, kidney gut cross talk, probiotics