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아드리아마이신 신증에서 신장 fibronectin 축적에 미치는 저염식이의 효과

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Increased Fibronectin Expression is Ameliorated by Dietary Salt Restriction In the Kidneys of Rats with Adriamycin Nephrosis

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Purpose : Adriamycin (ADR) induces severe nonselective glomerular proteinuria in rats, and proteinuria may have a role in tubulointerstitial fibrogenesis. Although high salt intake is believed to hasten progression of chronic kidney disease, whether low salt intake may relieve proteinuria-mediated tubulointerstitial injury is not clear. This study was undertaken to test the hypothesis that tubulointerstitial fibrogenesis may be modulated by dietary salt restriction in a rat model of adriamycin nephrosis.

Methods : Male Sprague-Dawley rats were randomly divided into normal-salt controls (n=4), normal-salt ADR (n=5), and low-salt ADR (n=5). ADR was intravenously given into the femoral vein as a single bolus (7.5 mg/kg). Five weeks later, kidneys were harvested for histopathologic studies, immunohistochemistry and semi-quantitative immunoblot analysis.

Results : At the end of the animal experiment, remarkable proteinuria was induced in both normal-salt ADR (234±37 mg/d/100 g BW), and low-salt ADR (210±27 mg/d/100 g BW) groups in contrast to controls (2±0 mg/d/100 g BW). Consistent with this, plasma albumin and total protein showed lower values in both ADR groups than in controls. However, no significant differences in proteinuria and serum proteins between normal-salt ADR and low-salt ADR rats. Renal tubulointerstitial injury was remarkable in both normal-salt ADR and low-salt ADR rats compared with controls although serum creatinine and daily urine volume were not significantly different between the 3 groups. Compared with controls, normal-salt ADR rat kidneys showed significant increases in fibronectin expression in both cortex (6.71±1.32 vs. 1.01±0.36) and medulla (2.52±0.23 vs. 1.01±0.10). When low-salt ADR rat kidneys were compared with normal-salt ADR, the increased expression of medullary fibronectin was significantly ameliorated (1.59±0.22, $p<0.05$). Notably, the degree of proteinuria was correlated with the expression level of fibronectin in both cortex ($r=0.87$, $p<0.0001$) and medulla ($r=0.79$, $p<0.001$).

Conclusions : In rats with adriamycin nephrosis, interstitial matrix molecules such as fibronectin may be produced in association with proteinuria. Dietary salt restriction may ameliorate fibronectin accumulation in kidney although it has no significant effect on proteinuria reduction.

Key Words : 독소루비신, 섬유증,콩팥증
Doxorubicin, Fibrosis, Nephrosis