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당뇨병성 신증의 진행을 지연시키는 항산화제 효과의 기전에 대한 연구

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Mechanisms of Antioxidant Effects Delaying Progression of Diabetic Kidney Damages

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Introduction : Hyperglycemia causes a marked production of free radicals that stimulate the inflammatory process via reactive oxygen species (ROS) system and triggers diabetic changes in the kidney. Pyruvate, an effective scavenger of ROS, is known to have potent anti-inflammatory and anti-oxidant effects. N-acetyl cystein (NAC), another anti-oxidant, may also counteract the glycation cascade in the diabetes. In this study, protective effects of pyruvate and NAC in the development and progression of diabetic nephropathy was investigated.

Method : 24 Sprague-Dawley rats were induced diabetic by intravenous streptozotocin (STZ) injection. Eight control rats were injected with citrate vehicle only (group C). STZ injected diabetic rats were subdivided into three-untreated diabetes group (group UD), diabetes with intra-peritoneal ethyl pyruvate injection (group P), diabetes with NAC oral ingestion (group N). We measured the body weight, blood pressure, serum glucose, blood urea nitrogen (BUN), serum creatinine, urine volume and proteinuria at baseline and every three weeks, thereafter. At 12 weeks, rats were sacrificed and the kidneys were harvested for PAS and type IV collagen immunohistochemical stain. Glomerular collagen deposition was scored semi-quantitatively (from 1 to 4) by three blinded observers.

Result : At baseline, there were no differences in the body weight, blood pressure, serum glucose level among the four groups. Over 12-week period, no differences were observed in the above parameters among the three diabetic groups (group UD, P, and N). At 12 weeks, proteinuria (1.51±0.70 vs 5.51±4.11 mg/day, p=0.010), glomerular type IV collagen deposition (2.45±0.47 vs 1.91±0.30, p=0.010) and serum creatinine(0.88±0.21 vs 1.46±038, p=0.001) were significantly increased in group UD, compared with group C. Compared to the untreated diabetic rats (UD), pyruvate-treated rats had reduced proteinuria (2.17±1.70 vs 5.51±4.11 mg/day, p=0.039), glomerular collagen deposition (1.71±0.28 vs 2.45±0.47, p=0.026) and lower serum creatinine concentration (0.88±0.21 vs 1.46±0.38 mg/dL, p=0.001). NAC treatment did not show a protective effect in our study.

Conclusion : Pyruvate treatment ameliorated proteinuria in diabetic rats. This protective effect was associated with decreased glomerular deposition of type IV collagen. NAC failed to show a protective effect in our animal model. Further research will follow to clarify protective effects of pyruvate in diabetic nephropathy.

Key Words : 당뇨병성 신증, 피루베이트, 엔아세틸시스테인
Diabetic nephropathy, Pyruvate, N-acetyl cystein