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경구흡착제 (AST-120)의 만성 싸이클로스포린신증 진행에 미치는 예방효과

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Oral Adsorbent AST-120 Prevents the Progression of Chronic Cyclosporin Nephrotoxicity

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Background : The most common cause of kidney-transplant failure is chronic allograft nephropathy (CAN), which caused by multifactorial etiologies and there is no effective treatment option. Recently, AST-120 (Kremezin®) is effective in inhibiting progression of established chronic kidney diseases by reducing uremic toxins and oxidative stresses. Our aim is to evaluate the effects of AST-120 on late stage of cyclosporine nephropathy, which is one of CAN model.

Materials and Methods : Adult Sprague-Dawley rats kept on a salt-depleted diet (0.05% sodium). Animals were divided into 4 groups: Control rats were treated with vehicle (VH group, olive oil 1 mL/kg per day) and chronic CsA nephropathy was induced by administering CsA (CsA group, 15mg/kg subcutaneously) for 6 weeks. To evaluate late effect of AST-120 on established CsA-induced nephrotoxicity, AST-120 was added to the rats for 3 weeks after 3 weeks treatment of VH or CsA (CsA/AST group and VH/AST group). The effect of AST-120 on CsA-induced renal injury was evaluated with renal function, tubulointerstitial fibrosis, the expression of ED-1 and osteopontin and measuring oxidative stress with 8-OHdG urinary excretion. We also measured serum indoxyl sulfate (IS) levels, a marker of uremic toxins by HPLC.

Results : The CsA/AST group showed significantly higher creatinine clearance (0.36±0.02 vs 0.24±0.01 ml/min/100 g, $p<0.001$), and less interstitial fibrosis score, number of infiltrated macrophage and apoptotic cell death than the CsA group. Moreover, increased expression of osteopontin in the CsA group was attenuated in the CsA/AST group. Increased urinary 8-OHdG concentrations in the CsA group were significantly decreased in the CsA/AST group (163±84 vs. 37±22 ng/day, $p<0.05$). Serum concentration of IS was significantly increased in the CsA group compared to VH group (0.097±0.036 vs. 0.172±0.02 mg/dL, $p<0.001$) but addition of AST-120 markedly decreased the serum IS levels (0.052±0.023 mg/dL, $p<0.001$) compared with the CsA group. AST-120 treatment did not affect on serum CsA concentrations.

Conclusion : AST-120 is effective in inhibiting progression of established cyclosporine nephrotoxicity without affecting drug level. AST-120 is recommended in patients with chronic allograft dysfunction as well as chronic kidney disease.

Key Words : AST-120, 만성싸이클로스포린신증, 산소성스트레스
AST-120, chronic cyclosporine nephropathy, oxidative stress