

Concomitant inhibition of Renin Angiotensin System and Endothelin-1 attenuates Renal fibrosis induced by Unilateral Ureteral Obstruction in Mice

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Introduction: Both Endothelin-1 (ET-1) and Renin angiotensin system (RAS) may play an important role in renal fibrosis in obstructed kidney. However, there was few study for the relationship between RAS and renal ET-1 activation in experimental unilateral ureteral obstruction (UUO). We investigated the role and relationship of renal RAS and ET-1 in UUO.

Methods: 8 weeks old male C57BL/6 mice were divided into the 6 groups; 1) Sham, 2) bosentan+Sham, 3) valsartan+Sham, 4) vehicle+UUO, 5) bosentan+UUO 6) valsartan+UUO, and 7) Valsartan+bosentan+UUO. Valsartan and bosentan were administrated via oral using NG tube (valsartan 10 mg/kg/day, bosentan 100 mg/kg/day for 8 days). We performed realtime RT PCR and immunohistochemistry for molecular study and H&E stain and Masson trichrome (MT) stain for histologic examination of kidneys.

Results: Although angiotensinogen and angiotensin II receptor are increased in bosentan+UUO kidney compared to vehicle+UUO kidney, bosentan treatment reduced significantly renal expression of TGF- β in UUO kidney. Also, it reduced renal tubular injury in H&E stain and blue stained area in MT stain of UUO kidney. Valsartan treatment in UUO mice showed similar results to Valsartan treated UUO mice. Valsartan treatment did not affect the expression of ET-1 in UUO kidney. Concomitant treatment of valsartan and bosentan decrease significantly renal expression of TGF- β compared to both valsartan+UUO and bosentan+UUO respectively. Also, they reduced significantly renal tubular injury in H&E stain and blue stained area in MT stain of UUO kidney compared to both valsartan+UUO and bosentan+UUO respectively.

Conclusions: Concomitant inhibition of RAS and ET-1 attenuates renal fibrosis induced by UUO in mice. It may have additive effects compare to single inhibition of RAS or ED-1.

Key Words: 섬유화, 일측요관폐쇄, ED-1, RAS
Renin anigtensin system, Endothelin-1, Ureteral obstruction