

Angiotensin-(1-7) Attenuates Kidney Injury by Obstructive Nephropathy in Rats

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Background: Angiotensin-(1-7) [Ang-(1-7)] counteracts many actions of the rennin-angiotensin-aldosterone system. Despite its renoprotective effects, little is known about the role of Ang-(1-7) on obstructive nephropathy, a model that is characterized by tubulointerstitial fibrosis and apoptosis in kidney.

Methods: Male Spargue-Dawley rat were divided into three groups; control, unilateral ureteral obstructed (UUO) rats and Ang-(1-7) treated UUO rats. Ang-(1-7) (24 µg/kg/hr) was continuously infused using osmotic mini pump for 10 days. The protein expression of angiotensin II (Ang II), cleaved caspase-3, pro-apoptotic Bax, anti-apoptotic Bcl-2, α-SMA, tumor growth factor (TGF)-β and Smad pathway was determined by western blot. Apoptosis was examined by TUNEL staining. Using an in vitro model, we treated NRK-52E cell with 1µM Ang II and pretreated with Ang-(1-7) (1 µM).

Results: Ang II and angiotensin type 1 receptor (AT1R) was significantly increased in UUO injured kidneys compared with control. Ang-(1-7) decreased renal protein expression of Bax and cleaved caspase-3, but significantly increased Bcl-2 in UUO rats. Ang-(1-7) also significantly ameliorated TUNEL positive cells in UUO rats. In addition, Ang-(1-7) reduced pro-fibrotic proteins and also blunted the increased TGF-β/Smad signaling in UUO rats. In NRK-52E cells, Ang II induced the expression of TGF-β/Smad signaling protein, pro-apoptotic marker and fibrotic proteins, such as α-SMA and connective tissue growth factor, which were attenuated by Ang-(1-7) pretreatment. However, A-779, an inhibitor of Ang-(1-7), again worsen Ang II induced apoptosis and fibrosis.

Conclusion: Ang-(1-7) prevents the obstructive nephropathy by suppressing renal apoptosis and fibrosis, possibly mediated by the modulation of TGF-β/Smad signaling pathway through the suppression of AT1R.

Key Words: Angiotensin 1-7, UUO, Fibrosis