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Angiotensin II AT1A Receptor Blockade Decreases Vasopressin-induced Urine Concentration in NaCl-restricted Rats

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The vasopressin and angiotensin II (AngII) are mainly coupled to the cAMP/PKA and phosphoinositide pathways, respectively. Therefore, vasopressin induces an increase in intracellular cAMP levels and AngII a rise in intracellular calcium. Recently in vitro studies have demonstrated that AngII potentiates the vasopressin-dependent cAMP accumulation (Klingler et al., 1998) as well as forskolin potentiates the AngII-induced increase of [Ca2+]i (Hus-Citharel et al., 2002), suggesting a cross-talk between the signaling pathways of vasopressin and AngII. It is therefore hypothesized that AngII AT1A receptor blockade may decrease the vasopressin-induced urine concentration and AQP2 expression in rats with high plasma AngII level. We performed renal tubule profiling studies in vasopressin-treated rats (V-group, n=8) and vasopressin and candesartan co-treated rats (VC-group, n=8) both of which were maintained with NaCl-deficient diet (0.1meq Na+/200 g bw/d) for 7d. Candesartan (1 mg/kg/day for 7 d, sc) and/or dDAVP (20 ng/h for 7 d, sc) were infused via osmotic minipumps. The urine output was significantly decreased in V-group (3.1±0.2 vs. 9.8±1.0 ml in VC-group, $p<0.05$), whereas the urine output in VC-group was similar to vehicle-infused control rats (Con, n=8) which were maintained with NaCl-deficient diet. Fractional excretion of sodium (FENa) was higher in VC-group, compared with V group or control rats, consistent with the decreased plasma aldosterone level. Consistent with the functional changes, medullary expression of AQP2 and inner medullary p-AQP2 (phosphorylated at the PKA-phosphorylation consensus site Ser-256) was significantly reduced in VC group, compared with V-group. In addition, cortical and medullary AQP1 expression was downregulated in VC-group. In contrast, medullary BSC-1 expression was unchanged but its molecular mass was ~20 kDa higher in VC-group compared with V group. Moreover, cortical NHE3, TSC and Na,K-ATPase expression was decreased. Taken together, AngII AT1A receptor blockade in dDAVP-treated rats was associated with increased urine output, decreased urine concentration and decreased AQP2 expression compared with dDAVP-treated rats, suggesting that activation/inactivation of AngII AT1A receptor may play a role in the vasopressin V2 receptor-mediated AQP2 expression and urine concentration in vivo. This work was supported by Korea Research Foundation Grant (KRF-2003-015-E00026).