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REGULATION OF RENAL PROXIMAL FLUID UPTAKE BY LUMINAL AND PERITUBULAR ANGIOTENSIN II

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Angiotensin II (AngII) when was added to either luminal or peritubular capillary exerts a dose-dependent biphasic action on proximal fluid reabsorption. Low dose (10^{-12}-10^{-10}M) stimulates fluid transport while higher dose (>10^{-9}M) inhibits (1-2). The concentration of AngII in proximal lumen is reported to be in the nanomolar range, 100-1,000 times higher than in peritubular blood (3-4) and it has been suggested that the proximal tubule secretes AngII into the tubular lumen. The physiological significance of the effects of luminal AngII on proximal tubular fluid transport is unclear but it is likely that it stimulates fluid uptake via angiotensin receptor type I (AT_1)(5). We investigated the regulation of renal proximal fluid transport by luminal (predominantly locally produced) and peritubular capillary (circulatory) AngII using a selective angiotensin receptor type I (AT_1) antagonist (candesartan).

Male Wistar Kyoto rats (BW 185-440g) were anaesthetised with Inactin (110 mg/kg; ip) Saline (0.9% NaCl) was infused (1.6 ml/hr per 100 g BW; iv) and carotid pressure monitored throughout the experiment. The left kidney was exposed and after 1-2 hour equilibration, shrinking-split droplet microperfusion was performed in proximal tubules by injecting Sudan Black stained castor oil from a double barrelled micropipette. The oil column was then split by injection of an artificial tubular fluid solution (in mM: NaCl 145; $NaHCO_3$ 5; KCl 5 and $CaCl_2$ 1.5) as vehicle control or with similar solution containing 10^{-6}M candesartan. Peritubular capillary perfusion was performed simultaneously with a single barrelled micropipette containing a solution with plasma-like electrolyte composition (in mM: NaCl 98.3; $NaHCO_3$ 35; Na_2HPO4 1.6; NaH_2PO_4 0.2; $CaCl_2$ 1.5; KCl 5; $MgCl_2$ 0.8 and CH_3COONa 10) or similar solution containing 10^{-6}M candesartan. Measurement of proximal fluid reabsorption rate (Jv_s) was performed using computerized video-based method for digital image capture and analysis of shrinking split-droplet micropuncture (6). Experiments were divided in to 4 groups. In each animal, mean control or initial Jv_s values were obtained from 2-7 tubules. Average Jv_s values were then obtained when luminal and peritubular capillaries were perfused with or without AT_1 antagonist.

RESULTS	Jv_s ($\times10^{-4}mm^3mm^{-2}s^{-1}$)	Jv_s ($\times10^{-4}mm^3mm^{-2}s^{-1}$)		
	Initial	Luminal perfusion	Peritubular capillary perfusion	% decrease
Group 1 (n = 15)	2.94 ± 0.17	no AT_1 antagonist	no AT_1 antagonist (2.10 ± 0.12)	27.3*
Group 2 (n = 8)	3.02 ± 0.18	10^{-6}M candesartan	no AT_1 antagonist (2.14 ± 0.11)	27.8*
Group 3 (n = 6)	3.26 ± 0.19	no AT_1 antagonist	10^{-6}M candesartan (2.22 ± 0.30)	32.8*
Group 4 (n = 6)	3.51 ± 0.16	10^{-6}M candesartan	10^{-6}M candesartan (1.99 ± 0.12)	43.1*#

Data are means ± S.E.M. *$p < 0.05$ compared with initial Jv_s values, #$p < 0.05$ compared with group 2 (Student's paired and unpaired t-test, respectively).

Fluid uptake rates decreased by between 27 and 43% during perfusion when compared with the corresponding initial values and this could be interpreted as removal of a stimulatory action of AngII. Perfusion of the lumen or capillaries with either artificial tubular solution or with the antagonist was effective in reducing fluid uptake. The magnitude of this decrease was similar in Groups 1-3 but significantly greater in Group 4 compared with Group 2, consistent with an effect of AT_1 receptor blockade in addition to the removal of AngII from these compartments by perfusion. These results suggest that the presence of endogenous AngII in both peritubular blood and luminal fluid is important for maximal expression of the stimulatory influence of this peptide on fluid absorption.

References:

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