RE000610

Prehypertensive treatment in spontaneously hypertensive rats: A comparison of losartan and amlodipine regarding blood pressure control and cardiovascular protection after drug withdrawal

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Objective: Compare the effectiveness of prehypertensive treatment with losartan and amlodipine in spontaneously hypertensive rats (SHR) on blood pressure control and cardiovascular protection after drug withdrawal. **Method:** 24 four-week-old male SHRs were divided into three groups at random:losartan (20 mg/kg per day, $n=8$), amlodipine (10 mg/kg per day, $n=8$) or placebo group (saline, $n=8$). 8 Wistar Kyoto rats (WKY) were served as normal control. Prehypertensive treatment were given by gavage for 6 weeks and animal were sacrificed four weeks after drug withdrawal, Systolic blood pressure (SBP) were measured before and after treatment and four weeks after drug withdrawal (i.e. at 4,10 and 14 weeks), cardiovascular structure and function was assessed at 14 weeks. **Result:** (1) At 10 and 14 weeks, both treated group had a significantly lower SBP than placebo group ($P<0.001$). (2) Compared with the placebo group, losartan significantly reduced the left ventricular index (LVI:2.29 ± 0.34 vs. 2.63 ± 0.34 mg/g, $P<0.05$), collagen volume fraction (CVF:2.62 ± 0.68 vs. 3.30 ± 0.56%, $P<0.05$) and perivascular circumferential area (PVCA:0.67 ± 0.27 vs. 2.05 ± 0.41, $P<0.001$), while amlodipine only decreased PVCA ($P=0.001$) and no effect on LVI and CVP ($P>0.05$). (3) The Wall to lumen area ratio (W/L) of third-order mesenteric artery was markedly reduced in the losartan groups compared to the placebo group (0.44 ± 0.03 vs.0.57 ± 0.05; $P<0.05$), and a significantly depressed vasoconstriction response to norepinephrine was observed ($P<0.05$), however, similar changes were not found in amlodipine group. **Conclusion:** prehypertensive treatment with losartan and amlodipine both delayed later blood pressure rise and meliorated cardiovascular structure and function, with better effect of losartan.

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Pressor and renal effects of angiotensin A

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Objective: Recently a new derivative of angiotensin (Ang) II called Ang A, was identified in human plasma, and was shown to be increased in end stage renal failure. The objectives of the study were to investigate the blood pressure and renal hemodynamic responses to Ang A as compared with Ang II in normal adult rats and the involvement of AT1 and/or AT2 receptors in these responses. Binding properties of Ang A and Ang II in CHO cells recombinantly expressing human AT1 receptors were also studied. **Method:** We measured mean artery pressure (MAP) and renal blood flow (RBF). Compounds were delivered as i.v. bolus injections or intrarenal (i.r.) infusion via jugular vein or renal artery catheters. **Results:** I.v. bolus injections of Ang A and Ang II (both, 0.01, 0.1, 1, 10 nmol/kg) dose-dependently increased MAP and decreased RBF. These effects were abolished by AT1 receptor blockade with candesartan (1 mg/kg), but were not altered by AT2 receptor blockade with PD 123315 (1 nmol/kg). I.r. infusion of Ang A and Ang II (1, 10, 100, 1000 pmol/20 µl/min) both dose-dependently reduced RBF and increased MAP; these effects were blocked by candesartan (5 µg/kg, i.r.) but were not affected by PD 123315 (0.5 mg/kg, i.r. bolus + 0.3 mg/h/kg, i.r. infusion). Ang A was about 10 times less potent than Ang II in both i.v. bolus and i.r. infusion studies. In vitro experiments indicated that Ang A has lower affinity for AT1 receptor compared to Ang II. **Conclusions:** Ang A increased MAP and induces renal vasoconstriction via stimulation of AT1 receptors but was less potent than Ang II. We could not detect any AT2 receptor-mediated effect of Ang A/II on blood pressure and RBF possibly due to the low expression of these receptors in normal adult rats.

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Renal vasoconstrictor and pressor responses to angiotensin IV in mice are AT1a-receptor mediated

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Objectives: Angiotensin (Ang) IV was reported to induce renal vasoconstriction or vasodilation in rats via AT1 or AT4 receptors, respectively, whereby the latter one has been identified to be the insulin-regulated aminopeptidase (IRAP). We investigated the effects of Ang IV on mean arterial pressure (MAP) and renal cortical blood flow (CBF) in AT1a, AT1b, AT2 receptor and IRAP knockout (−/−) mice and their corresponding wild type (WT) littermates. Ang II, known as a renal vasoconstrictor in mice, was used as a reference. **Design and methods:** MAP was recorded via a femoral catheter and CBF was measured using a laser Doppler probe; cortical vascular resistance (CVR) was calculated as MAP divided by CBF. Compounds were delivered to the mice as i.v. bolus injections via vascular catheters. **Results:** Baseline MAP, CBF and CVR in AT1a (−/−) mice were significantly lower than WT mice. AT2 (−/−) mice had a significantly higher baseline MAP, but similar CBF and CVR. In WT mice, Ang IV and Ang II induced dose-dependent pressor and renal vasoconstrictor responses which were antagonized by the AT1 receptor blocker candesartan. These responses were almost completely absent in AT1a (−/−) mice, but were enhanced in AT2 (−/−) mice; responses in AT1b (−/−) and IRAP (−/−) mice were comparable to those in corresponding WT mice. **Conclusions:** Ang IV mediates pressure and renal vasoconstrictor effects in mice via AT1a receptors, whereas IRAP/AT4 is not involved.

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Sleep apnea

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Higher levels of plasma TNF-α and neuropeptide Y in hypertensive patients with obstructive sleep apnea syndrome

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