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**DUAL BLOCKADE OF RAAS & ET SYSTEM IN BLOOD PRESSURE REGULATION**

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**Objectives** To compare the level of expression of the renin-angiotensin-aldosterone system (RAAS) in mice with or without the endothelin-1 receptor antagonist bosentan and to examine the potential value in blood pressure regulation.

**Methods** Bosentan (10 mg/kg/d) and placebo were given to two groups of male C57BL/6 mice (n=5) from ages 6–12 weeks. The mRNAs of liver, kidney and lung were isolated for Northern blot analysis. A further 15 male C57BL/6 mice were divided into three groups (n=5): mice in group A were given the angiotensin II type 1 receptor blocker valsartan (10 mg/kg/d); mice in group B were given bosentan (10 mg/kg/d); and mice in group C were given both valsartan and bosentan (10 mg/kg/d for each drug). All mice were administered the drugs from 6 to 12 weeks of age and had their systolic blood pressure (SBP) measured at the end of the drug treatments.

**Results** Northern blot analysis demonstrated that the expression levels of angiotensinogen in liver (p=0.0126), renin in kidney (p=0.002), and angiotensin-converting enzyme in lung (p=0.0041) were upregulated in mice treated with bosentan. No difference in SBP was found among the groups before drug administration. Six-weeks after monotherapy with valsartan, SBP was slightly lowered (126±2 vs 122±3 mm Hg, p=0.0381). Monotherapy with bosentan also had a small effect on SBP (126±2 vs 122±3 mm Hg, p=0.0381), whereas dual blockade with valsartan and bosentan significantly lowered SBP (127±3 vs 103±3 mm Hg, p<0.001).

**Conclusions** We conclude that RAAS components are upregulated under endothelin blockade. Dual blockade of the RAAS and endothelin system is beneficial for blood pressure control. Currently Bosentan was only used for the treatment of pulmonary artery hypertension. This study create a new approach for the therapy of hypertension with endothelin receptor antagonist.