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ACE INHIBITORS IMPROVE ENDOTHELIAL VASODILATOR FUNCTION IN RATS WITH CHRONIC NITRIC OXIDE DEFICIENCY

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Endothelial dysfunction was investigated in male rats given N^{ω}-nitro-L-arginine methyl ester (L-NAME), an inhibitor of nitric oxide (NO) synthesis, in drinking water for 8 weeks.
L-NAME-treated rats showed: 1) a clear-cut increase in systolic blood pressure (BP); 2) a consistent decrease of endothelial-cell NO synthase (eNOS) gene expression in aortic and cardiac tissue; 3) a reduction of the relaxant activity of acetylcholine (ACh) (Ach, from 10^{-10} to 10^{-4} M) on norepinephrine (NE)-precontracted aortic rings (reduction by 52 $\pm$ 5%); 4) a marked decrease (-50%) of the basal release of 6-keto-prostaglandin $F_{1\alpha}$ (6-keto-$PGF_{1\alpha}$) from aortic rings. In L-NAME-treated rats administration in the last 2 weeks of either the ACE-inhibitor enalapril (1 mg/kg/die) or the cognate drug quinapril (1 mg/kg/day) decreased systolic BP levels, completely restored eNOS mRNA levels in aortic and cardiac tissue and allowed a consistent recovery of both the relaxant activity of ACh and the generation of 6-keto-$PGF_{1\alpha}$. No differences was present in the ability of the two ACE-inhibitors to reverse NAME-induced endothelial dysfunction. These findings indicate that L-NAME-induced hypertension in the rats relies on the marked impairment of the endothelial vasodilator function, with an ensuing contribution by a decreased production of prostacyclin by the endothelial cells. ACE inhibition by enalapril or quinapril was equally effective in improving endothelial vasodilator function, prostacyclin endothelial production and restoring eNOS mRNA.