The effect of losartan and carvedilol on vasopressor responses to adrenergic agonists and angiotensin II in the systemic circulation of Sprague Dawley rats.

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Abstract
1. Interaction between renin-angiotensin (RAS) and sympathetic nervous systems (SNS) was investigated by examining the effect of cumulative blockade of angiotensin II (Ang II) and adrenergic receptors in normal Sprague Dawley rats. 2. Rats were treated with losartan (10 mg/kg), carvedilol (5 mg/kg), or losartan plus carvedilol (10+5 mg/kg) orally for 7 days. On day 8, the animals were anaesthetized with pentobarbitone and prepared for systemic haemodynamic study. Dose-response relationships for the elevation of mean arterial pressure or change in heart rate (HR) in response to intravenous injections of noradrenaline (NA), phenylephrine (PE), methoxamine (ME) and Ang II were determined. 3. Losartan or the combination of losartan with carvedilol blunted vasopressor responses to ME and Ang II. Dose-response relationships for agonist action on HR were significantly inhibited by all treatments except for the combination of losartan and carvedilol on the decrease in HR induced by PE. Carvedilol decreased vasopressor responses to NA, PE and Ang II, and HR responses to NA, ME and Ang II. Combination treatment produced similar effects to losartan on the vasopressor and HR responses but had a greater effect on vasopressor responses to ME and Ang II, and on HR responses to NA and Ang II than carvedilol alone. 4. It is concluded that peripheral vasoconstriction induced by Ang II is partly mediated by adrenergic action and that the vasopressor responses to adrenergic agonists depend on an intact RAS. These observations suggest an interactive relationship between RAS and SNS in determining systemic haemodynamic responses in 'normal' rats.

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