SHORT COMMUNICATION

Effect of propranolol on blood pressure and renin in renal hypertension in the rat

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Summary

1. Propranolol was administered to groups of mature rats before and during the development of renal hypertension induced by ligation of the aorta between the renal arteries.

2. At a dose of 10 μmol (3 mg) of propranolol/kg, administered by intraperitoneal injection, the onset and severity of hypertension were not affected, although plasma renin concentration was significantly lower than in the untreated hypertensive rats in the first 5 days after the operation.

3. With 200 μmol (60 mg) of propranolol/kg, administered in the drinking water, peak blood pressure 5 days after aortic ligation was lower than in the untreated control rats, but plasma renin concentration was no lower than with the smaller dose.

4. The development of severe hypertension despite reduction in plasma renin concentration on the low dose of propranolol suggests the participation of renal vasopressor factors other than renin in this model.

5. A higher dose of propranolol reduced the rise in plasma concentration to an equal extent but the rise of blood pressure at 5 days was also reduced, which supports this concept.

Key words: hypertension, propranolol, renin.

Introduction

Although the anti-hypertensive effect of β-adrenoreceptor-blocking agents in man has been demonstrated (Conway, 1975), their precise mechanism of action has not yet been elucidated. Suggested mechanisms include a reduction in cardiac output with subsequent adaptation of the peripheral circulation (Tarazi & Dustan, 1972), a decrease in peripheral plasma renin activity (Bühler, Laragh, Baer, Vaughan & Brunner, 1972) and a cardiovascular effect mediated by the central nervous system (Reid, Lewis, Myers & Dollery, 1974).

The purpose of this study was to evaluate the effect of administration of propranolol on the blood pressure and plasma renin concentration during the development of severe renal hypertension in the rat.

Methods

Male Sprague-Dawley rats weighing 300–350 g were used. Hypertension was induced by ligation of the aorta between renal arteries just below the origin of the superior mesenteric artery (Fernandes, Onesti, Weder, Dykyj, Gould, Kim & Swartz, 1976). Arterial pressure was measured in conscious rats through an indwelling Teflon/Tygon catheter in the left common carotid artery (Popovic & Popovic, 1960) at the time-intervals specified in Table 1, after which 1 ml of blood was withdrawn. Plasma renin concentration was determined by the method of Gould & Goodman (1970). Groups of rats were killed at 3, 5, 12, 20 and 30 days after aortic ligation. Carotid cannulation was performed 24 h before measurement of blood pressure and blood collection. One group remained untreated and served as control rats. Drug
administration was initiated 15 days before aortic ligation and continued thereafter for the duration of the experimental observations. Propranolol was administered to one group in a low dose [1.7 μmol (0.5 mg)] by intraperitoneal injections every 12 h, i.e. 10 μmol day⁻¹ kg⁻¹ and to another group at a higher dose (about 200 μmol day⁻¹ kg⁻¹ in the drinking water).

Results
The administration of propranolol was associated with an increase in blood pressure despite plasma renin suppression before aortic ligation.

The low dose of propranolol did not affect the onset and severity of hypertension. Plasma renin concentration was significantly lower than in the untreated control rats on days 3 and 5 only.

The high dose of propranolol did not produce further reduction in plasma renin concentration. This was an unexpected finding, and hence additional rats were studied on days 5, 12 and 20. The peak elevation of blood pressure on day 5 was lower, but no significant effect on blood pressure was detectable after this (Table 1).

Discussion
A pressor response after administration of propranolol has previously been noted in acute administration (Yamamoto & Sekiya, 1972) and after 2 weeks of treatment at a dose of 62 μmol (18 mg) day⁻¹ kg⁻¹ in spontaneously hypertensive rats (Forman & Mulrow, 1974). The mechanism for this response is not clear, and has been attributed to blockade of β-adrenergic tone in the peripheral blood vessels (Yamamoto & Sekiya, 1972), or an increased a-adrenergic activity in response to a fall in cardiac output (Forman & Mulrow, 1974).

With a low dose of propranolol, equally severe hypertension developed despite a significant decrease in plasma renin concentration, compared with the control group. Failure of propranolol to decrease the blood pressure in established renal hypertension in the rat has been previously noted (Lundgren, 1974; Conway, Darwin, Hilditch, Loveday & Reeves, 1975). The dissociation between effects on renin and blood pressure on the fifth day suggests the possibility that hypertension in this model is sustained, in part, by factors other than the renin–angiotensin system. Similar conclusions were reached with studies conducted with the angiotensin II-blocking agent, Sar¹-Ala⁸-angiotensin II, in two-kidney renal artery clip hypertension in the rat (MacDonald, Boyd &
Peart, 1975), although this antagonist is usually much more effective in lowering blood pressures.

High doses of propranolol resulted in a lower blood pressure 5 days after aortic constriction. Renin concentration, however, was affected similarly by the high and low doses of propranolol at all phases. Thus the blood pressure effect observed 5 days after aortic ligation does not appear to be related to renin suppression. These results are in keeping with the report of Leonetti, Mayer, Morganti, Terzoli, Zanchetti, Bianchetti, Di Salle, Morselli & Chidsey (1975).

In addition to peripheral β-adrenoreceptors in the heart and kidney, there are similar receptors elsewhere less accessible to low doses of propranolol. The effect of propranolol in higher doses on these less-accessible receptors may be responsible for its anti-hypertensive effects (Zanchetti, Leonetti, Morganti, Terzoli, Chidsey, Bianchetti & Morselli, 1977).

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References


