Haemodynamic responses to exercise and acute β-receptor blockade in renin sub-types of essential hypertension

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Summary

1. Haemodynamic and renin responses to dynamic exercise before and after intravenous β-adrenoceptor blockade with propranolol were compared in twenty-one patients with essential hypertension and either high (n = 7), normal (n = 7) or low plasma renin activity (n = 7).

2. Renin and heart-rate responses to exercise and β-receptor blockade diminished from high-renin to normal and to low-renin patients, effects which were blunted with increasing age.

3. Among the renin groups cardiac output, stroke volume, diastolic pulmonary artery pressure, systemic pressure and peripheral vascular resistance as well as their changes produced by exercise and acute β-receptor blockade were not significantly different.

4. Long-term anti-hypertensive propranolol effects correlated with the pre-treatment renin status, renin stimulation and its suppression by acute β-receptor blockade as well as with the exercise tachycardia and the patient's age.

5. The results suggest different adrenergic control mechanisms in renin sub-types of essential hypertension, age being a modulating factor.

Key words: acute and chronic β-receptor blockade, exercise stimulation, haemodynamics, hypertension, propranolol, renin.

Introduction

Patients with essential hypertension can be classified into high-, normal- and low-renin groups (Laragh, Baer, Brunner, Bühler, Sealey & Vaughan, 1972). Irrespective of pressure, high-renin patients tend to be younger whereas low-renin types predominate with older age. Renin status and renin responsiveness tally with changes in plasma catecholamines induced by physiological stimuli which reflect adrenergic nerve activity (Esler & Nestel, 1973). Chronic β-adrenoreceptor blockade reduces pressure most in high-renin and least in low-renin hypertensive patients (Bühler, Laragh, Baer, Vaughan & Brunner, 1972). Thus biochemical and pharmacological observations point to a higher neurogenic component in high- as opposed to the low-renin forms of hypertension (Bühler, Burkart, Lütold, Küng, Marbet & Pfisterer, 1975).

Haemodynamic studies in established essential hypertension revealed normal cardiac output measurements, whereas supranormal values have been observed in borderline as well as in the more egregious high- as well as low-renin forms of secondary hypertension (Tarazi, Ibrahim, Dustan & Ferrario, 1974). In earlier studies correlations were found between changes in cardiac variables and changes in renin (Dustan, Tarazi & Bravo, 1972) or age (Julius, Amery, Whitlock & Conway, 1967).

In the present study haemodynamic response patterns were linked with the three renin sub-types of essential hypertension. In order to unmask possible differences among the groups, a dynamic analysis of adrenergic renin responses was combined with a simultaneous evaluation of haemodynamic changes produced by physical exercise before and during acute β-adrenoreceptor blockade. These acute renin and haemodynamic effects were then compared with the results of chronic anti-hypertensive propranolol therapy as well as the patient's age.
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<th>Renin sub-group</th>
<th>Plasma renin activity (ng h⁻¹ ml⁻¹)</th>
<th>Heart rate (beats/min)</th>
<th>Cardiac index (l min⁻¹ m⁻²)</th>
<th>Stroke index (ml/m²)</th>
<th>Diastolic pulmonary artery pressure (mmHg)</th>
<th>Mean systemic pressure (mmHg)</th>
<th>Total peripheral resistance (kPa l⁻¹ s)</th>
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Methods

Twenty-one patients with mild essential hypertension (seven from each renin group) were selected. The average age was 54 years for the low-renin, 39 for the normal-renin and 36 for the high-renin patients; there were four men and three women in each group.

At least 2 months after any therapy, the patients were admitted in the morning to an acute study, with complete right-heart catheterization. Cardiac output was determined by Fick's principle. Heart rates were measured by electrocardiogram and blood pressures were recorded non-invasively with a Physiometrics SR1. The mean systemic pressure is reported as the diastolic value plus one-third of the pulse pressure.

With the catheter in situ, the patient remained without premedication for 30 min in a supine position, after which resting measurements were obtained. Adapting a model developed earlier in normal man (Bühler, Marbet, Patel & Burkart, 1975), patients subsequently exercised sitting on a bicycle ergometer (Elema-Schönder EM 370) for three 4 min periods with work loads of 50, 75 and 100 W. Before and at the end of the exercise test, haemodynamic measurements were made and blood was sampled for renin determinations; the radioimmunoassay method of Sealey, Gerten-Banes & Laragh (1972) was used. The same test procedures were repeated 45 min after intravenous administration of propranolol (0.15 mg/kg body weight).

Chronic anti-hypertensive responses to propranolol (average 2.7 mg/kg by mouth daily) were evaluated after 9–17 (average 13.7) weeks.

Results

Haemodynamic and renin responses to exercise and acute β-receptor blockade (Table 1)

Plasma renin. Among the three renin groups plasma renin values were significantly different both at rest and during exercise (P < 0.05 or less for all). Resting and exercise-stimulated renin values fell on propranolol more in the high- and normal-renin as compared with the low-renin group (P < 0.05 or less).

Heart rate. At rest heart rate tended to be lower in the low-renin patients. During exercise heart rates increased more in high- than in normal-renin and significantly more than in low-renin patients (P < 0.05); all differences narrowed after acute β-receptor blockade. There was a correlation between the propranolol reduction of the activated heart rates and renin values (r = 0.49; P < 0.05).

Cardiac index. At rest this was equally high. During exercise the steepest increase was observed in the high-renin group. Propranolol reduced output at rest as well as during exercise in all groups (slightly more in high-renin patients). However, none of these effects reached significance.

Stroke index. This was very similar at rest and changed little with exercise in the groups. Propranolol blockade produced a significant reduction in resting values only in high-renin patients (P < 0.05), whereas it merely affected the exercise-stimulated stroke indices in all groups. Changes in cardiac output were therefore due to changes in rate rather than stroke volume.

Diastolic pulmonary artery pressures. These pressures were normal at rest and increased with exercise in all groups (P < 0.01), slightly more in the older low-renin patients. After propranolol both resting and exercise pressures tended to rise.

Systemic mean arterial pressure. This exhibited a greater increase during exercise in the high- and normal-renin groups than in the low-renin patients, who also had higher resting pressure. After propranolol, the fall in exercise pressure was more pronounced in the high-renin patients but they subsequently all reached similar pressures.

Total peripheral resistance. This was within normal limits, though relatively high for the high cardiac indices. After β-receptor blockade resting resistance rose more in high- and low-renin patients, whereas the exercise-reduced resistance remained unchanged after propranolol.

Acute responses in relation to chronic propranolol therapy and age

Long-term propranolol therapy produced only minor changes in systemic pressure in the low-renin patients (172/106 to 177/103 mmHg), but significant reductions were achieved in the normal- and high-renin groups (167/106 to 136/88 and 177/110 to 141/88 mmHg respectively; P < 0.05). Individual chronic reductions in systemic mean arterial pressure were directly related to the increment and the level of renin produced by exercise (r = 0.66, P < 0.01 and r = 0.52, P < 0.05 respectively), as well as its suppression by propranolol (r = 0.62, P < 0.01). Among the haemodynamic variables only the
acute exercise tachycardia before β-receptor blockade correlated with the chronic anti-hypertensive effects of propranolol \( (r = 0.45; P < 0.05) \). Moreover, with increasing age acute renin and heart rate responses decreased \( (r = 0.52 \text{ and } r = 0.47 \text{ respectively}; P < 0.05 \text{ for both}) \). In addition, the chronic anti-hypertensive efficacy of propranolol diminished with age \( (r = 0.59; P < 0.05) \).

**Discussion**

Dynamic exercise and acute β-receptor blockade exposed different responses in heart rate and renin, which diminished from the younger high- and normal-renin to the older low-renin patients with essential hypertension. This suggests a different adrenergic control of both cardiac and renal β-receptor functions, which decrease with age.

No other single haemodynamic variable exhibited a significantly different response to physiological stimulation or propranolol blockade in either renin group. However, in a combined analysis some trends emerge. Thus, in high-renin patients, the lower diastolic pulmonary artery pressures, the increase in stroke volume with exercise and the reduction in stroke volume by propranolol blockade also point to a relatively higher adrenergic reactivity and myocardial contractility. Vice versa, the failure of an increase in stroke volume during exercise, associated with a greater increase in diastolic pulmonary artery pressure, makes hypo-responsive low-renin hypertensive patients more prone to left ventricular failure, especially when systemic pressure does not fall with chronic β-receptor-blocking therapy.

In addition to the pretreatment renin status and age, the increment in renin and the exercise-activated value as well as exercise tachycardia—a reflector of cardiac β-receptor function (Epstein, Robinson, Kahler & Braunwald, 1965)—all correlated with the chronic blood pressure reduction by propranolol. However, no relation was found to supine resting renin values, which indicates the need for at least slight renin activation (e.g. seated position) for such a comparison.

As blood pressure changes little after acute β-receptor blockade with propranolol, the decreases in cardiac output are reflected in an increase in peripheral vascular resistance. In high-renin subjects, who exhibit greater acute adrenoceptor responses and reduce blood pressure with chronic propranolol treatment, the initial increase in resistance can be counteracted by superimposed α-receptor blockade, which indicates additional adrenergic adaptive mechanisms during renin suppressive β-receptor blockade (F. R. Bühler, F. Burkart, B. E. Lütold & M. Pfisterer, unpublished observations). In contrast, the persistence of an increased vascular resistance in low-renin patients which respond little to anti-hypertensive β-receptor blockade supports the assumption of a structurally reduced arteriolar distensibility in these patients.

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**References**


