Angiotensin II in essential hypertension

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Summary

Plasma concentrations of angiotensin II (PAC) were measured in a group of 146 hypertensive patients (diastolic pressure ≥ 105 mm Hg) who had no apparent underlying cause for their condition and 113 randomly selected normotensive controls (diastolic pressure < 90 mm Hg). There was no evidence of bimodality in the frequency distribution curves for plasma angiotensin II concentrations among the hypertensive patients. It was concluded that hypertension associated with low angiotensin II concentration and by implication "low-renin" hypertension is not a condition separate from essential hypertension.

Introduction

It has been suggested that "low-renin" hypertension represents a major sub-group of about 20% of cases distinct from essential hypertension.¹ This view is mainly based on research conducted on selected patients attending specialised centres. If "low-renin" hypertension were a separate condition, the frequency distribution curve for renin among hypertensive patients would show evidence of bimodality. In two studies of inpatients, however, no bimodality was shown.^{2,3} To settle this point we studied plasma angiotensin II concentrations (the active product of renin release) in a large unselected group of patients with hypertension.

Distribution of plasma angiotensin II concentrations among patients with hypertension and controls

	Plasma angiotensin II concentration (pmol/l)								Total
	0-5	-10	-15	-20	-25	-30	-35	-40	
<i>Patients with hypertension</i>									
Men	1	9	12	19	20	3	2	1	67
Women	3	14	19	18	10	8	4	3	79
Total	4	23	31	37	30	11	6	4	146
<i>Controls</i>									
Men		7	12	16	10	6	3	1	55
Women		10	15	13	6	5	6	3	58
Total		17	27	29	16	11	9	4	113

Conversion: SI to traditional units—Plasma angiotensin II 1 pmol/l $\approx$ 0.91 pg/ml.

Subjects and methods

The study was based on 294 hypertensive patients aged 45-64 who were detected at a screening survey in Renfrew, Scotland.⁴ Two hundred and sixty-one patients had diastolic pressures of 105 mm Hg

or more at screening, and 33 had had this level of blood pressure diagnosed previously. Sixty-seven patients were excluded, 19 because they were taking part in another study and 48 because they had become normotensive without treatment. Of the remaining 227 patients eligible for investigation, 42 defaulted, 7 died, 17 refused or were considered unfit to undergo blood sampling while untreated, and 15 had a history of renal disease. Thus plasma angiotensin II concentrations were estimated by radioimmunoassay⁵ in 146 hypertensive patients with no evidence of an underlying cause for their condition. Of these 79 were women. Specimens were taken in the untreated state, when the subject was seated, during normal outpatient clinic hours.

A group of 113 randomly selected normotensive controls with diastolic pressures below 90 mm Hg at screening were studied under the same conditions.

Results

Frequency distribution curves for plasma angiotensin II concentrations were smooth with no obvious evidence of bimodality (see table). Statistical tests (χ^2 and Kolmogorov-Smirnov (KS)) applied to the values of the hypertensive patients confirmed the absence of bimodality,² since good fits of normal distributions were obtained with the data for men ($\chi^2=2.8$; $P>0.2$; $KS=0.56$; $P>0.1$) and both sexes together ($\chi^2=5.66$; $P>0.2$; $KS=0.77$; $P>0.1$). In view of the greater skewness of the distribution of angiotensin II concentrations in women, the logarithm of the data was tested and again confirmed unimodality ($\chi^2=3.45$; $P>0.2$; $KS=0.68$; $P>0.1$).

The mean plasma angiotensin II concentrations for normal subjects were $19.6 \pm (\text{SD}) 8.0$ pmol/l (17.8 ± 7.2 pg/ml) and 18.0 ± 8.1 pmol/l (16.3 ± 7.4 pg/ml) for men and women respectively. These were similar to the normal range in our laboratory⁵: 18.8 ± 8.9 pmol/l (17 ± 8 pg/ml). The patients with hypertension had slightly lower levels than normal subjects— 18.1 ± 6.7 pmol/l (16.4 ± 6.1 pg/ml) and 16.6 ± 7.7 pmol/l (15.1 ± 7.0 pg/ml) for men and women respectively. Plasma angiotensin II concentrations below 8 pmol/l (7.2 pg/ml) were found in four men (5.7%) and seven women (9.1%) with hypertension. At the time of writing we had measured plasma renin concentrations by radioimmunoassay in 57 normotensive subjects. The values correlated well with angiotensin II concentrations ($r=0.342$; $P>0.02$).

Comment

Plasma renin or angiotensin II concentrations are usually estimated under metabolic ward conditions or with concurrent estimates of urinary sodium. Our comparison of plasma angiotensin II concentrations in patients with hypertension and controls was valid, however, as samples were taken under identical conditions, and the normal range did not differ from conventional estimates. There is a close physiological and statistical relation between renin and its active product, angiotensin, and our data provide an accurate evaluation of the renin-angiotensin system in hypertension.

The absence of bimodality in the distribution of plasma angiotensin II concentrations in our study suggests that hypertension associated with low plasma concentrations of angiotensin II, and, by implication, low renin concentrations, is not a disease separate from essential hypertension.

References

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