Renin Activity in Black Hypertensive Patients in Rhodesia

J. J. JONES, M. GELFAND, E. KANENGONI

SUMMARY

Effective plasma renin activity was measured in 103 Black hypertensive patients admitted to Harare Hospital. Renin activity was found to be increased in all groups of hypertensive patients, and to be particularly high in patients with hypertensive or obstructive renal disease, or with cirrhosis. In the 70 patients with primary hypertension, 51% had a high renin activity which was found to be associated with renal failure, retinopathy, hyponatraemia and hypochloridaemia, but not with cardiac failure or with cerebrovascular disease. Despite the prevalence of 'high renin' hypertension in this population, ischaemic heart disease very rarely occurs.

S. Afr. Med. J., **48**, 2223 (1974).

Hypertension is one of the commonest diseases in the Black population of Africa,[1-3] and in the resident population of Salisbury hypertension (including cerebral vascular disease) accounts for 15% of the total deaths of Black adults over the age of 39 years.[4] This percentage is very similar to the corresponding figure of 16% for Whites, and is in striking contrast to ischaemic heart disease, which kills 27% of Whites, compared with 2% of Black adults over the age of 39 years.

Laragh and his colleagues[5-8] classify primary (essential) hypertension according to the plasma renin activity, and claim that a high renin activity is more commonly associated with the development of cardiac infarction, renal failure and cerebral vascular disease. They also claim that in the Black population of the USA there is a relatively high proportion of elderly 'low renin' patients who seldom develop these complications. This view has not met with general agreement,[9] and no attempt has hitherto been made to assess the renin status of the Black hypertensive patients living in Africa.

In this study, we assayed plasma renin activity in Black hypertensive patients admitted to the University's teaching hospital at Harare, to determine whether renin activity can be related either to the aetiology, or to the complications of the disease.

Godfrey Huggins School of Medicine, University of Rhodesia, Salisbury, Rhodesia

J. J. JONES, *Professor*
M. GELFAND, *Professor*
E. KANENGONI, *Technical Assistant*

Date received: 30 July 1974.

PATIENTS AND METHODS

The majority of patients with uncomplicated primary hypertension are treated as outpatients at Harare Hospital. Consequently, this study of hypertensive patients admitted to hospital includes a disproportionately large number of patients with secondary or complicated hypertension. In 1971 - 73, a total of 689 hypertensive patients was admitted. Effective renin activity was bio-assayed[10] on plasma from the 103 patients who were admitted to hospital on the Wednesday of each week, i.e. about one-seventh of the total number of patients was studied.

Renin activity in the hypertensive patients was compared with activity in a contrast group of 12 healthy Black subjects (5 women and 7 men, aged 20 to 39 years) who were nurses, messengers and technicians in the hospital. All of the 12 healthy subjects and 26 of the hypertensive patients had a second blood sample collected for renin assay 4 hours after taking 80 mg furosemide[11] by mouth. This sample was collected at 12 noon, 24 hours after the first blood sample.

Renal biopsies were not performed in this study: the value of the information likely to be obtained was considered to be insufficient to justify the possible risk to the patient.

RESULTS

Table I compares plasma renin activity in the 103 patients with renin activity in the 12 healthy subjects. Compared with the contrast group, renin activity was significantly increased in all groups of hypertensive patients, and it was significantly higher in patients with obstructive renal disease (6 bladder carcinomas, 3 schistosomal ureteric disease and 3 ureteric calculi), in patients with uraemia (serum urea $>$ 60 mg/100 ml) due to hypertensive renal disease, or in patients with cirrhosis, than in patients with cerebral vascular disease, congestive heart failure or uncomplicated primary hypertension.

The 70 patients with primary hypertension (without cirrhosis) have been considered in more detail, and their clinical and biochemical results are shown in Table II. Fifty-six per cent of them were men. Serum creatinine was raised ($>$ 2 g/100 ml) in 20%, total serum protein was low ($<$ 6 g/100 ml) in 26%, 16% were anaemic (haemoglobin $<$ 12 g/100 ml), serum sodium was low ($<$ 130 mEq/litre) in 17%, serum chloride was low ($<$ 95 mEq/litre) in 14%, and serum potassium was low ($<$ 3,7 mEq/litre) in 36%, but the excretion of urinary VMA (3-methoxy-4-hydroxy-mandelic acid) was never excessive ($>$ 8 mg/24 h).

TABLE I. EFFECTIVE PLASMA RENIN ACTIVITY IN ng/ml/h IN THE CONTROL GROUP AND IN PATIENTS WITH HYPERTENSION

	Number	Renin	
Contrast group	12	0,18	a
Primary hypertension	25	0,38	b
+ heart failure	32	0,35	b
+ uraemia	13	1,00	c
+ cirrhosis	12	1,10	c
Secondary hypertension			
Inflammatory renal*	8	0,68	d
Obstructive renal	12	1,18	c
Coarctation	1	0,30	

$P<0,05$: a<b, c, d and b< c.
(Analysis of variance of the normal score using Duncan's test for unequal groups.)
* Inflammatory renal disease: 1 patient with pyelonephritis and 7 with glomerulonephritis.

TABLE II. PERCENTAGE OF PATIENTS WITH PRIMARY HYPERTENSION IN EACH GROUP ACCORDING TO THEIR ARTERIAL PRESSURE, RETINOPATHY, PROTEINURIA, SERUM UREA, DURATION OF SYMPTOMS AND AGE

Systolic pressure (mmHg)	>200	35
	170 - 200	37
	<170	28
Diastolic pressure (mmHg)	>145	21
	105 - 145	58
	<105	21
Retinopathy (grade)	3 or 4	33
	1 or 2	39
	0	28
Symptoms (in days)	<7	36
	7 - 30	30
	>30	34
Proteinuria (g/day)	Nil	36
	0,5	22
	0,5 - 2,0	27
	>2,0	15
Serum urea (g/100 ml)	<20	19
	20 - 40	44
	>40	37
Age (years)	>60	23
	40 - 60	29
	<40	48

Thirty-two patients were admitted in congestive heart failure and 11 had cerebral vascular disease (hemiplegia in 7 and convulsions in 4). Treatment for each patient invariably combined a diuretic (ethacrynic acid or polythiazide) with a vasodilator (usually alpha-methyldopa or bethanidine).

Fig. 1 compares effective plasma renin activity in those primary hypertensive patients who did not have cirrhosis, with renin activity in the healthy members of the contrast group. It is clearly not possible to identify hypertensive patients with a renin activity that is lower than normal, since, without sodium restriction, renin activity in the contrast group was often found to be undetectable. On the other hand, 51% of the primary hypertensive patients had a renin activity greater than the highest recorded for the contrast group. Furosemide stimulation to identify the suppressed renin patient also proved unhelpful, since 33% of the healthy contrast group also appeared to be suppressed.

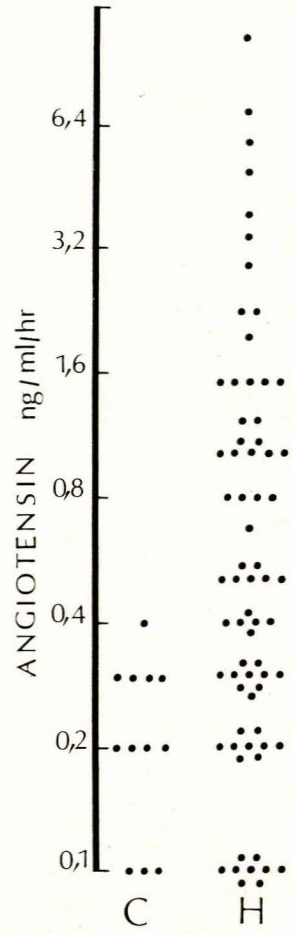

Fig. 1. Renin activity (measured as angiotensin generated in ng/ml/h) in the plasma of 12 healthy members of the contrast group (C) and in 103 patients with hypertension (H). (The scale is logarithmic.)

Since all hypertensive patients requiring admission to hospital were severely ill, it was not possible to delay treatment for a period of dietary sodium restriction before assessing their renin status. A typical diet contains 120 to 280 mEq/day of sodium, which is sufficient to make renin activity undetectable and unresponsive to furosemide stimulation.[8]

Apart from hypoproteinaemia ($P<0,005$) and renal insufficiency (increased urea, creatinine and potassium concentrations, $P<0,05$), patients admitted in congestive

heart failure showed no significant differences from the other hypertensive patients, including renin activity (high in 58% of patients in heart failure compared with high in 46% of the other patients).

Patients with cerebral vascular disease were younger than the other patients (6 years younger, $P<0,03$) and had a shorter history before admission to hospital (less than 1 week compared with 3 weeks, $P<0,05$) but there were no other significant differences, including renin activity (high in 64% of patients with cerebral vascular disease, compared with high in 49% of the other patients).

High renin activity was associated with renal failure and uraemia ($P<0,02$), and uraemia was also associated with an increase in serum creatinine ($P<0,0001$), with acidosis ($P<0,005$), hyperkalaemia ($P<0,05$), proteinuria ($P<0,07$), anaemia ($P<0,001$), retinopathy ($P<0,01$) and severe hypertension ($P<0,05$). All 5 patients who died in uraemia had a raised plasma renin activity ($P<0,08$) whereas the sixth patient who died in congestive heart failure had a normal renin activity and urea concentration.

Six patients had malignant hypertension with a diastolic pressure over 130 mmHg, proteinuria (> 1 g/24 h) and grade 3 or 4 retinopathy (2 with papilloedema). Serum urea was increased (> 50 mg/100 ml) in 5 of them and in all 6 the plasma renin activity was increased (> 0,9 ng/ml/h ; $P<0,01$). Although these 6 patients were not significantly hyponatraemic, an increase in plasma renin was found to be associated both with hyponatraemia and with a low serum chloride concentration ($r = -0,41$; $P<0,001$). Finally, renin activity was significantly higher in male than in female patients (median : 0,92 ng/ml/h in men, compared with 0,69 in women; $P<0,05$).[12]

DISCUSSION

The high proportion of patients with renal hypertension, cardiac or renal failure, and with cerebral vascular disease in the group of hypertensive patients studied, is probably not typical of the population as a whole, but represents the pattern of disease only in those patients requiring admission to hospital. Nevertheless, the high proportion (9%) of patients with obstructive renal disease resulting from vesical schistosomiasis and carcinoma, is of considerable interest. In contrast, hypertension could be attributed to schistosomiasis in only one patient in a recent study of 500 Black patients in Durban.[3]

Without salt restriction, it is impossible to identify 'low renin' primary hypertensive patients,[7] but the proportion (51%) of 'high renin' patients in this study is unusually high,[6,7,13] even for a hospital population. As expected, it was found that patients with hypertensive[6,7] or obstructive[14] renal damage, and those with cirrhosis[15] showed significantly higher renin activity than patients with uncomplicated primary hypertension, or with congestive heart failure.[16] Unexpectedly,[5,6] cerebral vascular disease was not found to be associated with a high renin activity; there have also been a number of other reports[17,18] showing that renin is not as valuable in predicting complications as had originally been claimed.[6] Despite the high prevalence of 'high renin' hypertension in this population, ischaemic heart disease is almost unknown.[4] A bad prognosis was found to be associated with 'high renin' activity[5,6] : 5 of the 6 patients who died in hospital were in the 'high renin' group.

High renin activity in patients with primary hypertension was particularly associated with uraemia and retinopathy,[5,6] suggesting that renin release by the kidney is the result of hypertensive renal arteriolosclerosis, which could also account for the high proportion (37%) of primary hypertensive patients with a raised serum urea concentration. Only 6 patients had malignant hypertension (two with papilloedema), so that renal damage in the other patients is probably the result of 'benign' nephrosclerosis, which is known to be common in the Black population of the USA.[19]

High renin activity and a large response to furosemide stimulation were both correlated with hyponatraemia[20] and hypochloridaemia, indicating that a failure in renal salt conservation was the stimulus for renin release in this group of hypertensive patients. It also suggests that in the 51% of primary hypertensive patients with a 'high renin' status, hypertension is the result of arteriolar constriction and an increased peripheral resistance, rather than being due to salt retention, with an expansion of the extracellular fluid and blood volumes, and a consequent increase in cardiac output.[5]

REFERENCES

1. Akinkugbe, O. O. (1972): *High Blood Pressure in the African*. Edinburgh: Churchill.
2. Scotch, N., Gampel, B., Abramson, J. H. and Slome, C. (1961): Amer. Heart J., **61**, 173.
3. Seedat, Y. K. and Reddy, J. (1974): S. Afr. Med. J., **48**, 816.
4. Stamps, T. J. (1972): Sequential report from the Medical Officer of Health, Salisbury, Rhodesia, Vital Statistics.
5. Laragh, J. H. (1973): Amer. J. Med., **55**, 261.
6. Brunner, H. R., Laragh, J. H., Baer, L., Newton, M. A., Goodwin, F. T., Krakoff, L. R., Bard, R. H. and Bühler, F. R. (1972): New Engl. J. Med., **286**, 441.
7. Brunner, H. R., Sealey, J. E. and Laragh, J. H. (1973): Amer. J. Med., **55**, 295.
8. *Idem* (1973): Circulat. Res., **32**, suppl. 1, 99.
9. Wisenbaugh, P. E., Garst, J. B., Hull, C., Freedman, R. J., Matthews, D. N. and Hadady, M. (1972): Amer. J. Med., **52**, 175.
10. Kritzinger, E. E., Kanengoni, E. and Jones, J. J. (1974): S. Afr. Med. J., **48**, 499.
11. Spark, R. F. (1972): New Engl. J. Med., **287**, 343.
12. Crane, M. G., Harris, J. J. and Johns, V. J. (1972): Amer. J. Med., **52**, 457.
13. Jose, A., Crout, R. and Kaplan, N. M. (1970): Ann. Intern. Med., **72**, 9.
14. Belman, A. B., Kropp, K. A. and Simon, N. M. (1968): New Engl. J. Med., **278**, 1133.
15. Ayers, C. R. (1967): Circulat. Res., **20**, 594.
16. Brown, J. J., Davies, D. L., Lever, A. F. and Robertson, J. I. S. (1966): Brit. Med. J., **1**, 505.
17. Doyle, A. E., Jerums, G., Johnston, C. I. and Louis, W. J. (1973): Brit. Med. J., **2**, 206.
18. Mroczek, W. J., Finnerty, F. A. and Catt, K. J. (1973): New Engl. J. Med., **288**, 1077.
19. Pillay, V. K. G., Wang, F., Gandhi, V. C., Lee, H. J. and Dunea, G. (1974): S. Afr. Med. J., **48**, 953.
20. Brown, J. J., Davies, D. L., Lever, A. F. and Robertson, J. I. S. (1965): Brit. Med. J., **2**, 144.