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Plasma angiotensin II levels in African hypertensives

W. P. LEARY AND A. C. ASMAL

Department of Clinical and Experimental Pharmacology, Faculty of Medicine University of Natal, Durban

Summary

Plasma angiotensin II levels were measured by immunoassay in twenty-seven Zulus with raised arterial pressures. Angiotensin levels were higher in patients with malignant than benign essential hypertension, mean values being 260·2 and 90·7 $\mu\mu$g/ml with standard deviations of 119·4 and 25·1 respectively ($P = < 0{\cdot}0005$).

Résumé

Le taux plasmatique d'angiotensine II a eté determiné par dosage immunologique chez 27 Zulus souffrant d'hypertension arterielle.

Le tause d'angiotensine chez les malades avec hypertension maligne était plus élevé que chez ceuse atteints d'hypertension essentielle: valeurs/moyeunes dé 260·2 et 90·7 $\mu\mu$g/ml arec deviatiens respectiment ($P = < 0{\cdot}0005$). Le valeur moyeune des dosages d'angiotensine chez 3 malades atteints de maladie renale primaire etait 215·3 $\mu\mu$g/ml.

Reports that unusual clinical and pathological presentations of hypertension occur in Africa (Seedat, 1963; Seedat & Reddy, 1971; Akinkugbe, 1968; Seftel & Kew, 1969) suggest that differences between people of various ethnic origins might be detectable in the renin-angiotensin system. No survey of plasma angiotensin II levels in African hypertensives has yet been published, although the pattern in Europe, America and Australasia is fairly well known (Boyd, Jones & Peart, 1972; Catt *et al.*, 1971; Gocke *et al.*, 1969; Düsterdieck & McElwee 1971). This paper records a pilot study in which plasma angiotensin II levels were measured in twenty-seven Zulu patients who had arterial pressures above 110 mg Hg diastolic on admission to hospital.

Correspondence: Professor W. P. Leary, Professor and Head, Department of Clinical & Experimental Pharmacology, Faculty of Medicine, University of Natal, Durban.

Methods

Twenty-seven subjects were studied at random and without special attention to electrolyte balance. All were Africans of the Zulu tribe and had diastolic pressures above 110 mm Hg on admission to the medical wards of King Edward VIII hospital, Durban. Arterial pressures were measured with the patient supine, using the standard clinical technique. Measurements were repeated at 5 min intervals, and the lowest of three recordings taken to represent blood pressure for the purposes of this study. After 6 h rest in bed, 5 ml venous blood was collected in prechilled tubes containing about 5 mg EDTA Na_2. Blood samples were taken to the laboratory in an ice bucket and centrifuged in the cold at 2000 rev/min to recover plasma. Plasma samples were stored at −20°C until assayed. Duplicate radioimmunoassays were carried out using a procedure described by Gocke *et al.*, (1969). Reagents were supplied by the CEA-CEN-SORIN association, and prepared at the Nuclear Research Centre, Sorin, Saluggia, Italy.

Each patient was subsequently classified as a case of primary (essential) or secondary hypertension on the basis of clinical, radiological and biochemical findings. Malignant hypertension was diagnosed if a combination of raised arterial pressure and neuroretinopathy was present (Pickering, 1968).

Results

Ten cases of malignant hypertension were identified and fourteen patients had neither neuroretinopathy

TABLE 1. Measurements on admission: (malignant hypertension)

Case no.	Sex	Age	Arterial pressure	Plasma angiotensin ($\mu\mu$g/ml)	Urea	Sodium	Potassium
1	M	32	260/180	315	81	138	3·0
2	F	44	240/160	470	222	133	6·8
3	F	26	210/140	191	201	133	4·4
4	M	51	175/155	110	105	135	3·3
5	M	48	210/140	433	58	139	2·8
6	F	19	210/145	140	127	139	3·9
7	M	36	270/180	350	75	135	3·4
8	F	39	250/150	210	160	131	3·5
9	F	65	210/170	235	—	—	—
10	M	38	230/170	148	56	139	3·7
Mean			226/159	260·2	120·6	135·8	3·9
s.d.			27·4/14·6	119·4	58·1	2·9	1·1

TABLE 2. Measurements on admission: (non-malignant, essential hypertension)

Case no.	Sex	Age	Arterial pressure	Plasma angiotensin ($\mu\mu$g/ml)	Urea	Sodium	Potassium
1	M	50	210/140	65	43	137	4·0
2	F	50	180/150	107	45	—	—
3	M	52	200/140	93	50	137	4·5
4	F	49	180/110	91	22	142	3·1
5	F	49	240/160	87	18	140	4·1
6	M	57	180/140	150	17	144	3·5
7	M	65	260/190	70	23	143	3·9
8	M	51	250/175	75	61	142	4·0
9	M	50	180/140	73	34	144	4·6
10	M	38	190/140	108	31	141	4·1
11	F	70	210/120	54	—	—	—
12	F	43	280/160	63	22	131	3·6
13	F	40	220/180	115	113	133	3·5
14	F	34	230/160	119	22	139	4·7
Mean			215/150	90·7	38·5	139·4	4·0
s.d.			31·18/21·4	25·7	25·2	4·0	0·5

nor obvious primary cause for their raised arterial pressures. Clear evidence of primary renal disease was found in three patients.

There was no significant difference between the ages of male ($47·3 \pm 9·2$) and female ($38·7 \pm 17·0$) patients and plasma angiotensin levels were independent of sex in the groups studied.

Plasma angiotensin levels were higher in patients with malignant than with benign essential hypertension, mean values being 260·2 and 90·7 $\mu\mu$g/ml with standard deviations of 119·4 and 25·1 respectively. This difference was highly significant ($P = < 0·0005$). The mean value of angiotensin determinations in three patients with primary renal disease was 215·3 $\mu\mu$g/ml but this sample was too small for statistical analysis or comment.

Patients with blood urea raised above 45 mg% had a higher mean plasma angiotensin (215·1 $\mu\mu$g/ml) than those whose urea was lower (119·4 $\mu\mu$g/ml). Standard deviations were 127·6 and 85·2 for these determinations, and the difference recorded was significant ($P = < 0·025$).

Low correlations ($< 0·5$) were found between plasma angiotensin II and sodium, potassium and

urea levels as well as between angiotensin II and systolic or diastolic pressures, in both malignant and non-malignant hypertension.

Discussion

Normal values for plasma angiotensin II depend, to some extent, upon the test used and vary widely among different laboratories (Boyd & Peart, 1974). With the method used in this study, depending upon the degree of sodium depletion, normal values of from 40 to 140 $\mu\mu$g/ml are recorded (Gocke *et al.*, 1969). Raised angiotensin II levels have been reported in association with malignant hypertension and renal disease, irrespective of the immunoassay method used (Boyd & Peart, 1974).

The results of this study are in broad agreement with those from laboratories outside Africa. Plasma angiotensin levels were raised in association with malignant or renal hypertension and fell within normal limits in patients with benign essential hypertension. This tendency was clearly significant despite the use of relatively imperfect clinical criteria to identify cases of malignant hypertension and uncertainty concerning electrolyte balance at the time blood samples were collected for analysis.

The lack of correlation between angiotensin, serum electrolyte levels and arterial pressures is not thought to be significant. However, future studies should include daily measurements of urinary electrolyte excretion and arterial pressures for at least 72 h before measurement of angiotensin levels.

Several apparent differences between the patterns of hypertensive disease in Africa and Western Europe have been reported. In Nigeria retinal changes are rare, even in severely hypertensive patients, and are apparently not of prognostic significance (Akinkugbe, 1968). Elsewhere in Africa diastolic pressures may fall with age, and cerebral vessels appear particularly sensitive to raised arterial pressures (Shaper, Williams & Spencer, 1961; Smith, 1966). In Southern Africa hypertension may develop at an earlier age in the Bantu and be more severe than in the White population (Becker, 1946; Uys, 1956; Schrire, 1958).

It would appear from the results reported here, that these features of hypertension in Africans cannot be explained solely on the basis of quantitative changes in circulating angiotensin II. Factors such as tissue angiotensinase levels, local prostaglandin synthesis and regional arterial sensitivity to vaso-active substances require investigation. However, before further complex biochemical investigations are carried out, the impressions of Seftel & Kew (1969) with regard to changing profiles in hypertension amongst urbanized Bantu should be studied. The results of such studies would indicate whether further attempts should be made to identify genetically or environmentally determined differences in hypertension as it affects Africa.

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References

Akinkugbe, O.O. (1968) The rarity of hypertensive retinopathy in the African. *Am. J. Med.* **45**, 401–404.

Becker, B.J.P. (1946) Cardiovascular disease in Bantu and Coloured races of South Africa; hypertensive heart disease. *S. Afr. J. med. Sci.* **11**, 107–120.

Boyd, G.W., Jones, M.B.S. & Peart, W.S. (1972) *Hypertension.* p. 583. Springer, Berlin, Heidelberg & New York.

Boyd, G.W. & Peart, W.S. (1974) *Angiotensin.* p. 222. Springer; Berlin Heidelberg, New York.

Catt, K.J., Cran, E., Zimmet, P.Z., Best, J.B., Cain, M.D., & Coghlan, J.P. (1971) Angiotensin II blood levels in human hypertension. *Lancet*, **1**, 459–64.

Düsterdieck, G. & McElwee, G. (1971) Estimation of angiotensin II concentration in human plasma by radio-immunoassay. *Europ. J. clin. Invest.* **2**, 32–38.

Gocke, D.J., Gerten, J., Sherwood, L.M. & Laragh, J.H. (1969) Physiological and pathological variations of plasma angiotensin II in man. *Circulat. Res.* **24** & **25**, 131–146.

Pickering, G.W. (1968) *High Blood Pressure*, p. 453. Churchill, London,

Schrire, V. (1958) The racial incidence of heart disease at Groote Schuur Hospital, Cape Town. *Am. Heart J.* **56**, 742–760.

Seedat, Y.K. (1963) Malignant hypertension in the Natal African and Indian. *S. Afr. med. J.* **37**, 655–666.

Seedat, Y.K. & Reddy, J. (1971) Propranolol in the South African non-white hypertensive patient. *S. Afr. med. J.* **45**, 284–285.

Seftel, H.C. & Kew, M.C. (1969) Hypertension in the African. *Lancet*, **2**, 595.

Shaper, A.G., Williams, A.W. & Spencer, P. (1961) Blood pressure and body build in an African tribe living on a diet of milk and meat. *E. Afr. med. J.* **38**, 569–580.

Smith, A.J. (1966) Arterial hypertension in the Lagos University Teaching Hospital. *W. Afr. Med. J.* **15**, 97–104.

Uys, C.J.S. (1956) The pathology of renal disease in the Bantu on the Witwatersrand; hypertensive vascular disease. *S. Afr. J. Lab. clin. Med.* **2**, 13–28.

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