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Biochemical tests for diagnosis of phaeochromocytoma: urinary versus plasma determinations

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Abstract

Fifteen patients with hypertension due to phaeochromocytoma and 35 controls with essential hypertension were studied to assess the diagnostic value of urinary and plasma biochemical determinations in phaeochromocytoma.

In every case of phaeochromocytoma the urinary concentration of vanillylmandelate, metanephrines, or adrenaline plus noradrenaline was diagnostic of the disease irrespective of whether the patient was normotensive or hypertensive at the time. Plasma determinations of adrenaline and noradrenaline, however, gave falsely negative results on three occasions.

These findings suggest that urinary biochemical deter-

minations—particularly of metanephrines—are more reliable than plasma catecholamine measurements as a test for phaeochromocytoma. The test is particularly useful in patients with intermittent hypertension.

Introduction

Diagnosing phaeochromocytoma is easy in patients with sustained hypertension: measurement of 24-hour excretion of vanillylmandelate, metanephrines, and catecholamines suffices to confirm or exclude the presence of the tumour.¹ Diagnosis is harder to establish when hypertension is intermittent, however, since tumoral secretion of catecholamines may be absent during normotensive periods. To assess the diagnostic value of urinary and plasma determinations in phaeochromocytoma, we measured urinary concentrations of catecholamine metabolites and resting plasma concentrations of catecholamines in 15 patients with phaeochromocytoma, four of whom had intermittent hypertension.

Methods

In 15 hypertensive patients the diagnosis of phaeochromocytoma was based on biochemical tests and confirmed at operation. Thirty-five other patients diagnosed by conventional methods as having essential hypertension were used as controls. No patient received any treatment for 15 days before testing. A 24-hour urine collection was assayed for vanillylmandelate, metanephrine, and adrenaline

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Plasma and urinary values in controls (patients with essential hypertension) and patients with phaeochromocytoma

						Supine blood pressure* (mm Hg)	Plasma concentrations (nmol/l)		Urinary concentrations (mmol/24 h)		
							Adrenaline	Noradrenaline	Vanillylmandelate	Metanephrines	Adrenaline + noradrenaline
							<i>Patients with essential hypertension (n = 35)</i>				
Mean $\pm$ 1SD	..	..	..	..	..	159/101 $\pm$ 25/18	0.58 $\pm$ 0.43	1.29 $\pm$ 0.67	19.60 $\pm$ 5.10	2.05 $\pm$ 0.87	0.40 $\pm$ 0.11
Range	..	..	..	..	..		0.10–2.03	0.24–3.35	7.56–32.30	0.84–3.24	0.30–0.64
							<i>Patients with phaeochromocytoma</i>				
Normotensive at time of sampling:											
1	..	..	..	..	..	93/62	0.87	1.49	30.90	7.32	0.85
2	..	..	..	..	..	108/59	2.63	11.36	27.30	53.20	1.97
3	..	..	..	..	..	124/60	1.29	1.42	43.30	4.37	1.74
4	..	..	..	..	..	140/72	0.98	1.58	50.40	19.30	1.04
Hypertensive at time of sampling:											
5	..	..	..	..	..	150/94	0.89	3.63	32.30	5.55	0.87
6	..	..	..	..	..	153/95	3.01	3.39	40.30	20.60	1.05
7	..	..	..	..	..	161/91	9.06	95.51	252.00	88.60	15.40
8	..	..	..	..	..	156/96	13.49	218.60	61.00	65.00	13.00
9	..	..	..	..	..	146/103	0.73	21.21	175.40	16.50	5.07
10	..	..	..	..	..	172/92	2.00	21.80	143.20	42.60	5.22
11	..	..	..	..	..	180/109	12.31	9.77	223.30	52.70	74.50
12	..	..	..	..	..	177/112	2.12	96.16	88.20	18.20	6.67
13	..	..	..	..	..	155/131	31.90	66.60	100.80	43.80	7.03
14	..	..	..	..	..	179/135	2.63	20.58	65.50	21.70	3.09
15	..	..	..	..	..	180/135	3.67	83.32	143.60	42.80	5.19

*Mean of values obtained before and after blood sampling.

Conversion: SI to traditional units—Plasma adrenaline: 1 nmol/l $\approx$ 0.18 ng/ml. Plasma noradrenaline: 1 nmol/l $\approx$ 0.17 ng/ml. Urinary vanillylmandelate: 1 mmol $\approx$ 0.198 mg. Urinary metanephrines: 1 mmol $\approx$ 0.190 mg. Urinary adrenaline + noradrenaline: 1 mmol $\approx$ 0.169 mg.

plus noradrenaline concentrations. Normal values in our laboratory ($\pm$ 1 SD) are respectively 17.6 $\pm$ 5.5 mmol (3.5 $\pm$ 1.1 mg), 1.70 $\pm$ 0.66 mmol (0.32 $\pm$ 0.13 mg), and 0.37 $\pm$ 0.15 mmol (0.06 $\pm$ 0.03 mg)/24 h. On the same day resting plasma adrenaline and noradrenaline concentrations were measured by radioenzyme assay.² Blood samples were taken between 8 and 10 am through a microcatheter one hour after venepuncture and lying supine. Blood pressure was measured immediately before and after blood sampling and the two measurements averaged.

Results

Urinary metanephrine excretion in both normotensive and hypertensive patients with phaeochromocytoma was above the range for essential hypertension, and values for one or more of the three urinary metabolites were high in every case (table). In patients with phaeochromocytoma who were hypertensive at the time of sampling the plasma noradrenaline or adrenaline concentration, or both, was also high. Of the four normotensive patients (cases 1–4), one (case 2) had high resting plasma catecholamine values and the other three had values within the range for essential hypertension. In case 3 a symptomatic paroxysm occurred a few hours after measuring the resting plasma catecholamine concentration. At that time supine blood pressure was 148/116 mm Hg and adrenaline and noradrenaline concentrations 7.25 and 4.71 nmol/l (1.33 and 0.80 ng/ml) respectively, above the range for essential hypertension (see table).

Comment

Our data confirm reports^{1,3} that urinary tests are a highly sensitive method for diagnosing phaeochromocytoma; urinary concentrations of catecholamine metabolites—particularly metanephrines—are high in over 95% of patients, the overlap with control values being negligible when specific methods are used.³ As regards plasma determinations, two distinct clinical settings must be considered: when hypertension is present, and presumably the tumour is actively secreting, plasma catecholamine values are high; their measurement is as useful as and more convenient than that of metanephrines in a 24-hour urine collection. On the other hand, when the patient is normotensive at the time of blood sampling plasma values may be falsely negative.⁴ Of our four normotensive patients, three had normal plasma adrenaline and noradrenaline concentrations, whereas their urinary concentrations of catecholamine metabolites were high enough to permit diagnosis. This dissociation of plasma and urinary values might be due to brief secretory paroxysms in any 24-hour period in such patients,¹ such as occurred in case 3. In case 2 a high plasma noradrenaline

concentration was found despite normal blood pressure, confirming the lack of correlation between blood pressure and plasma catecholamine values in phaeochromocytoma.^{1,5} As expected, this patient also had high urinary catecholamine metabolite values, like the normotensive patients with high plasma catecholamine concentrations observed by Bravo *et al.*⁵

Our results suggest that urinary measurements are more reliable for diagnosing phaeochromocytoma; there were no falsely negative results in our urine determinations but three occurred in our resting plasma measurements. Plasma sampling during paroxysmal attacks may be helpful, but values obtained by direct venepuncture of patients under stress should be interpreted with great caution.

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ONE HUNDRED YEARS AGO The President of the Pharmaceutical Society of Liverpool, exhibited last week a sample of eugenol, which had been placed in his hands on the previous day. He said it had recently been noticed as a very energetic antiseptic, and it was also said to be a remedy for toothache. Both these properties could be readily understood, as oil of cloves, from which it was obtained, as well as oil of peppermint, had long been used to prevent ink, starch, paste, etc, from becoming mouldy. The oils had also been long regarded as remedies for toothache. It was also known as eugenin or caryophyllin acid, having a formula $C_{10}H_{12}O_2$, and forming salts with bases. He said, it would be interesting to determine its rotatory power as compared with oil of cloves, which he would do before the next meeting. (*British Medical Journal*, 1881.)