SHORT COMMUNICATION

PLASMA DOPAMINE β-HYDROXYLASE AND NORADRENALINE AMOUNTS IN ESSENTIAL HYPERTENSION

L. B. GEFFEN, R. A. RUSH, W. J. LOUIS AND A. E. DOYLE

Physiology Department, Monash University, Clayton, and University of Melbourne, Department of Medicine, Austin Hospital, Heidelberg, Victoria, Australia

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SUMMARY

1. Plasma dopamine β-hydroxylase (DβH) amounts were measured by radio-immunoassay in twenty-eight patients, twenty of whom had essential hypertension. There was a positive correlation between resting diastolic blood pressure and plasma DβH concentration.

2. Plasma DβH amounts also correlated significantly with those of plasma noradrenaline (NA) in individual patients.

3. These findings provide further support for the conclusions drawn from studies of plasma catecholamines that the sympathetic nervous system contributes toward the maintenance of the elevated blood pressure in essential hypertension.

Key words: plasma dopamine β-hydroxylase, plasma noradrenaline, essential hypertension, immunoassay.

Studies using a sensitive double-isotope derivative assay for plasma catecholamines have shown that plasma noradrenaline amounts are elevated in some patients with essential hypertension (Engelman, Portnoy & Sjoerdsma, 1970; de Quattro & Chan, 1972; Louis, Doyle & Anavekar, 1973). In one series of experiments (Louis et al., 1973) there was a close relationship between resting diastolic blood pressure and plasma noradrenaline amounts, and in that study after acute ganglionic blockade the decreases in resting blood pressure and plasma noradrenaline amounts correlated significantly, suggesting that the value of the blood pressure in essential hypertension is at least in part dependent on excess sympathetic activity.

Recently it has been demonstrated that the adrenal medulla and sympathetic nerves release specific proteins as well as catecholamines from their synaptic vesicles (Smith, 1971; Geffen & Livett, 1971). One of these proteins is the enzyme dopamine β-hydroxylase (DβH) that converts dopamine into noradrenaline within the vesicles. DβH enzymic activity has recently been detected in human plasma (Wienshilboum & Axelrod, 1971a; Goldstein, Freedman & Bonnay, 1971; Geffen, Rush, Louis & Doyle, 1973). Since DβH has a much longer circulating...
half-life than catecholamines (Rush & Geffen, 1972), it was of interest to measure its circulating amount as an independent index of sympathetic function in the same series of patients with essential hypertension in whom we previously reported elevated plasma NA amounts (Louis et al., 1973).

PATIENTS AND METHODS

Twenty-eight patients (eight females and twenty males) aged 26–60 were studied. The nature of the studies was explained and consent obtained. The patients were free of overt renal or adrenal disease and had never received anti-hypertensive drugs. On the third day after admission to hospital, a cannula was inserted into a forearm vein and 1 h later blood samples were taken. Blood pressure was measured in the recumbent position by the auscultatory method. At the time of study, eight of the patients had resting diastolic blood pressures of 90 mmHg or less and were considered to be normotensive or have labile hypertension, whereas the remainder were diagnosed as having essential hypertension.

Biochemical assays

Plasma samples were assayed independently in separate laboratories for noradrenaline by a double-isotope derivative assay (Louis & Doyle, 1971) and for DβH by a radioimmunoassay (Rush & Geffen, 1972) as previously described.

Statistical methods

The significance of correlations was assessed by calculating Spearman’s rank correlation coefficient ($r_s$).

RESULTS

The patients with diastolic blood pressures above 90 mmHg had significantly higher amounts of both noradrenaline and DβH than the group with diastolic pressures below this value. The mean ($\pm$ SEM) plasma noradrenaline concentrations in the two groups were 0.40 ± 0.05 and 0.16 ± 0.04 ng/ml ($t = 2.64, 0.01 < P < 0.02$), and the mean plasma DβH concentrations were 265 ± 33 and 133 ± 17 ng/ml ($t = 2.51, 0.01 < P < 0.02$) respectively. There was a close correlation between plasma DβH and plasma NA amounts in individual patients (Fig. 1) that was significant both in the hypertensive group ($r_s = 0.517, P < 0.05$) and in the total group of patients ($r_s = 0.516, P < 0.01$).

The relationship between diastolic blood pressure and plasma DβH amounts in individual patients is also shown in Fig. 1. There was a positive correlation between resting recumbent diastolic blood pressure and plasma DβH concentrations ($r_s = 0.622, P < 0.001$) in the hypertensive group, as has previously been reported for plasma noradrenaline amounts (Louis et al., 1973). Insufficient patients were normotensive at the time of study to test statistically whether a similar relationship between plasma DβH and diastolic blood pressure occurred in patients with blood pressures below 90 mmHg, but the correlation was similarly significant for the total group ($r_s = 0.697, P < 0.001$; Fig. 1).

DISCUSSION

The validity of serum DβB as an index of sympathetic activity depends on the following experimental observations in animals. DβH is localized in the synaptic vesicles of sympathetic
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erves (Potter & Axelrod, 1963) and stimulation of the sympathetic nerves to isolated perfused organs releases \( \Delta DBH \) into the perfusate (see Smith, 1971; Geffen & Livett, 1971). After release in vivo, \( \Delta DBH \) enters the circulation (Weinshilboum & Axelrod, 1971a; Goldstein et al., 1971). \( \Delta DBH \) activity in rat blood has been shown to be increased by sympathetic stresses such as

forced immobilization (Weinshilboum, Kvetnansky, Axelrod & Kopin, 1971) and decreased by chemical sympathectomy with 6-hydroxydopamine (Weinshilboum & Axelrod, 1971b). In sheep, circulating \( \Delta DBH \) is cleared with a half-life of approximately 3 h mainly by the liver, lungs and kidney (Rush & Geffen, 1972).

In humans, the serum dopamine \( \beta \)-hydroxylase activity is much greater than in other species studied. Previous studies of human serum \( \Delta DBH \) have used an enzymic assay of serum \( \Delta DBH \) that gives a wide normal range of activity, making detection of pathological deviations difficult (Axelrod, 1972; Goldstein, Fuxe & Hokfelt, 1972; Nagatsu & Udenfriend, 1972). In the present study, a radioimmunoassay was used that is both specific and sensitive and gives a narrower range of normal values (Rush & Geffen, 1972; Geffen et al., 1973). The close correlation found between plasma noradrenaline and \( \Delta DBH \) values (Fig. 1) in individual patients with essential hypertension strongly supports the other evidence that radioimmunoassay of plasma \( \Delta DBH \) is a potentially useful index of sympathetic function. A similar relationship between plasma noradrenaline and \( \Delta DBH \) is not seen in patients with phaeochromocytoma, presumably because the excessive catecholamine release is not primarily from the storage vesicles of the tumour (Geffen et al., 1973).

![Graph](image)

**Fig. 1.** Relationships between (a) plasma dopamine \( \beta \)-hydroxylase (\( \Delta DBH \)) and noradrenaline amounts, and (b) resting recumbent diastolic blood pressure (BP) and plasma \( \Delta DBH \) concentrations in individual patients (see the text).

The proportionate increases in both plasma \( \Delta DBH \) and noradrenaline amounts with elevations in resting diastolic blood pressure constitute independent evidence in support of the conclusion drawn from previous studies that increased sympathetic nervous activity contributes to the elevated blood pressure in essential hypertension (Engelman et al., 1970; de Quattro &
Chan, 1972; Louis et al., 1973). Since circulating DβH, unlike noradrenaline, does not appear to be taken up by sympathetically innervated tissue not cleared by the kidney (Rush & Geffen, 1972), these results decrease the likelihood of changes in uptake, metabolism and renal clearance of circulating noradrenaline being responsible for its elevation in hypertension (Louis et al., 1973). The present results, however, do not permit any conclusion to be drawn as to whether the increased sympathetic activity is a primary or a sustaining cause of the hypertension, nor do they distinguish between abnormal release of catecholamines with a normal sympathetic activity and an increased central sympathetic drive.

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REFERENCES


