Serum dopamine β-hydroxylase activity in essential hypertension

K. AOKI, K. TAZUMI, T. YOSHIDA, S. KATO, I. SATO AND K. TAKIKAWA
Second Department of Medicine, Nagoya City University Medical School, Mizuho-ku, Nagoya, Japan

Summary
1. Serum dopamine β-hydroxylase activity was determined in normotensive control subjects and patients with labile or established essential hypertension. The enzyme activity was 25.9 ± 1.9 (SEM), 29.6 ± 2.5 and 25.1 ± 1.9 μmol min⁻¹ ¹⁻¹, for control, labile and established hypertensive subjects respectively.
2. Neither blood pressure nor serum dopamine β-hydroxylase activity was changed in normotensive control subjects by administration of phentolamine; however, in patients with essential hypertension blood pressure was significantly decreased (P < 0.01) and serum dopamine β-hydroxylase activity was slightly increased. With propranolol administration, blood pressure and the serum enzyme activity were not significantly changed in normotensive or hypertensive subjects.
3. Our results suggest that there is no correlation between serum dopamine β-hydroxylase activity and blood pressure.

Key words: adrenergic receptor blockade, dopamine β-hydroxylase, hypertension.

Introduction
Recently, a sensitive assay technique for the determination of serum dopamine β-hydroxylase activity has been developed (Weinshilboum & Axelrod, 1971; Nagatsu & Udenfriend, 1972). This enzyme synthesizes noradrenaline from dopamine, and both the enzyme and noradrenaline are released into the circulation by stimulation of sympathetic nerve endings. Therefore, the serum activity of the enzyme would be an expected index of sympathetic nervous activity. In this study, serum dopamine β-hydroxylase activity was measured in patients with hypertension. The effects of sympathetic α- and β-receptor-blocking agents on blood pressure and the serum enzyme activity were also examined.

Methods
Eighty-four patients with essential hypertension and seventy-six normotensive healthy volunteer subjects were studied. The blood pressure (arm-cuff method) was measured on more than 4 days. The patients with essential hypertension consisted of twenty-eight with labile essential hypertension in whom the systolic pressure fluctuated over 160 and below 140 mmHg and fifty-six patients with established essential hypertension in whom the systolic pressure was persistently over 160 mmHg (Table 1). In these patients, urea nitrogen concentration and the serum concentrations of sodium, potassium and chloride were in the normal range, and urinalysis was normal. These patients were free from overt renal disease.

Correspondence: Dr Kyuzo Aoki, Second Department of Medicine, Nagoya City University Medical School, Mizuho-ku, Nagoya 467, Japan.
pathetic $\beta$-receptor-blocking agent, was given intravenously (0.2 mg/kg body weight). Blood samples were taken before and at 5 min, 15 min, 30 min and 60 min after the injection.

Blood pressure was measured by the auscultatory method, and heart rate was monitored by an electrocardiogram.

Serum was separated from collected blood samples by centrifugation at 10 000 g for 10 min at 0°C and measured for serum dopamine $\beta$-hydroxylase activity (Nagatsu & Udenfriend, 1972). The reaction mixture, containing serum, acetate buffer, pH 5.0, sodium fumarate, ascorbic acid, catalase, tyramine, pargyline and $N$-ethylmaleimide, was incubated at 37°C for 60 min for octopamine formation. The supernatant was transferred to a column of Dowex-50 (H$^+$). The absorbed amines were eluted with ammonia solution. Octopamine in the eluate was converted into $p$-hydroxybenzaldehyde by sodium iodate solution. Extinction at 330 nm was measured by spectrophotometer. When octopamine in ammonia solution was carried through the oxidation procedure as standard, extinction increased linearly with octopamine concentration. Serum dopamine $\beta$-hydroxylase activity was expressed as $\mu$mol of octopamine min$^{-1}$.

Results were expressed as mean value $\pm$ SEM, and statistical significance was checked by group $t$-test.

Results

Results for each group of subjects are listed in Table 1.

The average blood pressure in normotensive control subjects ($n = 76$) was 119 systolic and 72 mmHg diastolic, and in labile hypertensive subjects ($n = 28$) was 137 systolic and 85 mmHg diastolic;
Dopamine β-hydroxylase in hypertension

467s

in established hypertensive patients (n = 56) it was 166 systolic and 104 mmHg diastolic. Blood pressure in hypertensive subjects was significantly higher than that of normotensive subjects (P < 0.01).

Serum dopamine β-hydroxylase activity was 25.9 μmol min⁻¹ l⁻¹ in normotensive subjects, 29.6 in labile hypertensive subjects and 25.1 in established hypertensive subjects. These differences were not significant.

With phentolamine, neither blood pressure nor serum dopamine β-hydroxylase activity was changed in normotensive subjects (n = 5). In contrast, the blood pressure of the hypertensive group (n = 13) decreased significantly (P < 0.01) and the serum enzyme activity was increased slightly by the administration of phentolamine.

With propranolol, both in normotensive (n = 11) and in hypertensive subjects (n = 13) systolic blood pressure did not change and diastolic pressure increased slightly; serum dopamine β-hydroxylase activity remained unchanged.

Discussion

Plasma dopamine β-hydroxylase activity has been reported to be higher in patients with primary hypertension than in those with secondary hypertension (Stone, Gunnells, Robinson, Schanberg & Kirshner, 1974), and plasma concentrations of noradrenaline and dopamine β-hydroxylase activity in hypertension correlated closely with the diastolic pressure (Louis, Doyle, Anavekar, Johnston, Geffen & Rush, 1974). In other studies, however, the enzyme's activity did not correlate with blood pressure (Horwitz, Alexander, Lovenberg & Keiser, 1973) and blood pressure reduction by anti-hypertensive drugs did not induce changes in the activity (Aoki, Tazumi & Takikawa, 1975). This study shows clearly that there is no correlation between blood pressure and serum dopamine β-hydroxylase activity. However, in labile essential hypertension high serum activity of the enzyme is somewhat higher than in the other groups (Table 1). Low serum activity has been observed in patients with chronic renal failure on prolonged haemodialysis (Aoki et al., 1975).

The fall in blood pressure produced by sympathetic ganglionic blockade (pentolinium tartrate) was associated with a fall in plasma catecholamines and dopamine β-hydroxylase activity (Louis et al., 1974), because this agent blocks release of both noradrenaline and the enzyme from sympathetic nerve endings. In this study a fall in blood pressure induced by phentolamine was associated with a slight increase of enzyme activity. This may be explained by an increased release of noradrenaline and dopamine β-hydroxylase by reflex sympathetic stimulation due to abrupt fall of blood pressure. Propranolol did not change either blood pressure or the enzyme's activity in this study.

Acknowledgment

We are grateful to Professor T. Nagatsu and Professor K. Hotta for their valuable suggestions. This study was supported in part by a grant from Mitsui Life Social Welfare Foundation.

References


