Effect of Dexamethasone on Plasma Free Dopamine: 
Dopaminergic Modulation in Hypertensive Patients

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To investigate the peripheral dopaminergic modulation in the pathogenesis of human hypertension, we examined the responses of plasma free dopamine (DA) to dexamethasone (Dx) administration, which is suggested to activate dopaminergic activity. We administered Dx 2 mg intravenously to patients with primary aldosteronism (PA), essential hypertension (EH), and normotensive controls (NT). Plasma free DA was increased significantly in all groups and the responses were more remarkable in PA than in EH and NT. Plasma epinephrine (E) showed a gradual increase while plasma norepinephrine (NE) tended to decrease in all groups. The responses of both plasma DA and E were completely blocked by 250 mg of α-methyl-p-tyrosine, a tyrosine hydroxylase (TH) inhibitor, suggesting that Dx may stimulate peripheral dopaminergic activity by increasing catecholamine synthesizing enzyme (probably TH) activities. These data suggest that DA itself plays an inherent role in the sympathoadrenal regulation rather than only as a precursor of NE and that dopaminergic hyperresponses may be involved in the pathophysiology of PA. (Hypertens Res 1995; 18 Suppl. I: S197–S198)

Key Words: glucocorticoid, dopamine, α-methyl-p-tyrosine, primary aldosteronism

Several lines of evidence suggest that peripheral dopaminergic involvement may be one of the important pathogenetic factors in various types of human hypertension (1-4). Dopaminergic sodium handling has been reported to be attenuated in salt-sensitive essential hypertension (5, 6). However, the interaction between peripheral dopaminergic system and glucocorticoid, which is known to modulate dopaminergic activity (7, 8), remains still uncertain. To investigate the peripheral dopaminergic modulation in the pathogenesis of human hypertension, we examined the response of plasma free dopamine (DA) to dexamethasone (Dx) administration in hypertensive patients.

Materials and Methods

Informed consent was obtained from each subject before the study. The subjects consisted of patients with primary aldosteronism (PA, n = 9, age: 44 ± 4) and essential hypertension (EH, n = 6, 44 ± 3). The healthy volunteers were also studied as normal controls (NT, n = 8, 38 ± 3). In the morning after overnight fast, each subject rested at least 30 min in the supine position. Dx 2 mg or saline was then administered intravenously. Blood samples for measuring catecholamines, adrenocorticotropic hormone (ACTH), cortisol (F), prolactin (PRL), renin (PRA) and aldosterone (PAC) were taken before and at the every 30 min after 150 min after Dx administration. Urinary specimens for catecholamines and electrolytes were also collected before and at the 150 min after Dx administration. One week later, 250 mg of α-methyl-p-tyrosine (α-MPT, Merck Sharp & Dohme, West Point, PA, USA), a tyrosine hydroxylase (TH) inhibitor, was administered orally at the 60 min before Dx treatment, and the same protocol was repeated. Catecholamines were measured using a highly sensitive radioenzymatic assay (9), and ACTH, F, PRL, PRA and PAC were determined by radioimmunoassay.

Results

Plasma DA concentrations in all groups were increased gradually (p < 0.05) at the 90-150 min after Dx administration (Fig. 1). The response was more remarkable in PA than in EH and NT groups (PA: 206 ± 26.4%, EH: 158 ± 12.6%, NT: 153 ± 11.1% at 150 min). Plasma epinephrine (E) showed a gradual increase while plasma norepinephrine (NE) tended to decrease after Dx administration (Fig. 1). The responses of both plasma DA and E to Dx were completely abolished by concomitant administration of α-MPT (Fig. 1). Urinary DA and sodium excretion showed no significant changes by Dx administration in all groups. In each group, PAC was decreased significantly (p < 0.05) after Dx treatment but PRL and PRA showed no changes.
The main findings of the present study were: Dx administration induced a gradual increase in plasma DA and E associated with a decrease in plasma NE and the responses of both plasma DA and E were completely abolished by concomitant administration of α-MPT. These results indicate that Dx may stimulate peripheral dopaminergic activity by enhancing the activities of catecholamine synthesizing enzyme, probably TH, in the sympathoadrenal tissues. Our results are compatible with previous animal studies reporting that glucocorticoid stimulates TH activity in the sympathetic ganglia (10) and the brain (11). However, the action site of TH stimulation by Dx can not be determined in the present study.

The increases in plasma DA concentration by Dx administration were more remarkable in PA than in EH and NT groups. There have been some reports to demonstrate that DA inhibits aldosterone secretion (12, 13). The enhanced DA responses to Dx treatment in patients with PA may suggest a counteractive effect of DA against aldosterone excess state.

Our present findings support the view that DA itself is not only a precursor of NE but plays an inherent role in the sympathoadrenal regulation and that dopaminergic mechanisms may be involved in the pathophysiology of aldosterone excess state.

**Discussion**

The main findings of the present study were: Dx administration induced a gradual increase in plasma DA and E associated with a decrease in plasma NE and the responses of both plasma DA and E were completely abolished by concomitant administration of α-MPT. These results indicate that Dx may stimulate peripheral dopaminergic activity by enhancing the activities of catecholamine synthesizing enzyme, probably TH, in the sympathoadrenal tissues. Our results are compatible with previous animal studies reporting that glucocorticoid stimulates TH activity in the sympathetic ganglia (10) and the brain (11). However, the action site of TH stimulation by Dx can not be determined in the present study.

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**References**