Renal Dopaminergic Activity in Patients with Primary Aldosteronism

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To clarify the role of renal dopaminergic activity in patients with primary aldosteronism (PA), urinary excretion of free dopamine (DA) and the conversion ratio of DA from l-dopa in the kidney were investigated in 8 patients with PA and 10 normotensive subjects (NT). All subjects were hospitalized and received a standard diet (Na 120 mEq, K 75 mEq/day) and 2 h renal clearance test was performed. Plasma l-dopa concentration (p-DOPA), creatinine clearance (Ccr), urinary excretion of sodium (UNaV) and DA (uDA) as well as fractional excretion of sodium (FENa) were measured. No significant difference was found in UNaV or FENa between NT and PA, or between before and after adrenalectomy (Adx) in PA. UDA was significantly higher in PA than NT, and decreased significantly after Adx. There was no difference in the product of Ccr X p-DOPA between NT and PA, or between before and after Adx in PA. The ratio of uDA/(Ccr X p-DOPA) was significantly higher in PA than NT. After Adx this ratio decreased significantly to the normal range. These results suggest that (1) renal dopaminergic activity is augmented and contributes to the escape phenomenon in PA, and (2) augmented renal DA production in PA might be caused by an increase of conversion to DA from l-dopa at the renal proximal tubules. (Hypertens Res 1995; 18 Suppl. I: S193-S195)

Key Words: primary aldosteronism, urinary free dopamine, hypertension, l-dopa, renal sodium handling

It has been recognized that dopamine (DA) exists in kidney not only as a precursor of the sympathetic neurotransmitter, norepinephrine, but also as an active hormone, and modulates the balance of sodium and fluid volume (1-7). Many previous reports (8-12) have suggested that main source of renal DA is circulating l-dopa delivered into renal tubules, which converts to DA by dopa-decarboxylase at the renal proximal tubules (13). We previously reported that suppressed renal dopaminergic activity may concern to the pathogenesis of human essential hypertension, particularly in low renin essential hypertension (14, 15), and this suppression is induced by attenuated activity of conversion step from l-dopa to DA in the kidney, which may be attributed to a decrease in dopa-decarboxylase activity at the epithelial cell of renal proximal tubules.

Primary aldosteronism (PA) is considered as a typical volume dependent hypertension. It has been indicated by Kuchel et al. (16) that renal dopaminergic activity is augmented in PA, and normalized after adrenalectomy. However it has not been clarified whether the augmented activity of renal dopaminergic system in PA is modulated by changes in production of DA in the kidney. In this study we investigated the renal dopaminergic activity and the conversion ratio of DA from its precursor l-dopa in the kidney in PA, comparing with those variables in normotensive subjects and the effects of adrenalectomy on renal dopaminergic activity.

Subjects and Methods

Eight patients with PA, and 10 normotensive subjects (NT) were employed in this study. The diagnosis of PA was recognized as a unilateral adrenal cortex adenoma based on pathological histology after surgery in all patients. All subjects were confirmed informed consent. They were all in-hospital and fed a standard diet including Na 120 mEq and K 75 mEq throughout the study. In the early morning after overnight fasting, all subjects were kept in supine position and 2 h renal clearance test was performed. Patients with PA were studied before and 4 weeks after unilateral adrenalectomy.

Blood sample was obtained and blood pressure was measured by cuff method at the endpoint of the clearance. Urine sample was collected during 2 h clearance study. Sodium and creatinine concentration were measured in serum and urine by the ion electrode method and Jaffe’s method, respectively. Plasma l-dopa concentration (p-DOPA) and urinary excretion of free DA (uDA) were measured by HPLC-ECD. During each clearance period, urinary excretion of sodium (UNaV), fractional excretion of sodium (FENa), endogenous creatinine clearance (Ccr) and uDA were determined. Plasma l-dopa de-
Results

The Table 1 shows the clinical characteristics of NT and PA. There were no significant differences in UNaV and FENa between NT and PA, or between before and after adrenalectomy in PA. UDA was significantly higher in PA than NT (488 ± 127 vs 204 ± 23 ng/min, respectively, p < 0.05), and decreased significantly (p < 0.05) after adrenalectomy in PA (177 ± 7 ng/min). No significant difference was observed in the product of Ccr × p-DOPA between NT and PA, or between before and after adrenalectomy in PA. The ratio of uDA to (Ccr × p-DOPA) was markedly higher in PA than NT (5.21 ± 1.50 vs. 1.80 ± 0.13, respectively, p < 0.05). After adrenalectomy, this ratio decreased significantly (p < 0.05) to the normal range (1.69±0.11) (Fig. 1).

Discussion

The present study showed that renal dopaminergic activity was enhanced in PA and normalized after adrenalectomy. In 1979, Kuchel et al. (16) reported...
that four patients with PA with aldosterone producing adenoma showed an elevated urinary excretion of conjugated and free DA, which decreased to normal levels after removal of the aldosteronomia; Horky et al. reported similar results in 1983. It is conceivable that two opposite actions for renal sodium handling occur in PA, sodium and volume retention with excess mineralocorticoid with some sort of escape from this sodium retaining effect in order to compensate for volume expansion. Several mechanisms for escape have been demonstrated, such as atrial natriuretic factor, renal prostaglandin, and renal adrenergic system. From our results or two previous studies, renal DA may take part in escape from sodium and volume retention in PA.

However, the mechanism of enhanced renal dopaminergic activity in PA has not been clarified up to the present. The production of DA in the kidney depends on decarboxylation of l-dopa, tubular uptake and its delivery to the kidney. This has led us to measure plasma l-dopa to estimate its rate of delivery to the kidney and the conversion rate of DA from l-dopa in the kidney. The conversion ratio of DA from l-dopa, expressed as uDA / (Ccr × p-DOPA), increased in PA and normalized simultaneously with urinary DA excretion after adrenalectomy, although the delivery of l-dopa was in the normal range before and after adrenalectomy. Therefore, the augmented renal DA was not due to change in delivery of circulating l-dopa into the kidney, but rather to an increase of conversion of DA from l-dopa in the kidney. From these data, it should be considered that enhanced renal dopaminergic activity in PA might be regulated by changes in renal dopa decarboxylase activity in the kidney.

We previously reported that the products of Ccr × p-DOPA did not differ in essential hypertensives from normotensives, whereas uDA / (Ccr × p-DOPA) was lower in essential hypertensives, particularly in low renin essential hypertensives, and urinary l-dopa was undetectable. These findings suggested that low decarboxylation activity of l-dopa at the renal tubules was responsible for attenuated renal dopaminergic activity in essential hypertensives. Since we did not measure unfortunately urinary excretion of l-dopa in the present study, therefore we were unable to completely exclude the possibility of changes in the amount of tubular uptake of l-dopa.

In conclusion, the results of the present study suggest that renal dopaminergic activity in PA is augmented and that this augmentation of DA might be caused by an increase in dopa-decarboxylase activity in renal proximal tubules.

References