Plasma Prolactin Levels in Patients with Essential Hypertension, Malignant Hypertension and Secondary Hypertension

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Plasma prolactin level and plasma renin activity were determined in normal subjects and patients with low and normal renin essential hypertension, renal hypertension, renovascular hypertension, primary aldosteronism, Cushing syndrome, pheochromocytoma and malignant hypertension. In both normal subjects and the normal renin essential hypertensives, plasma prolactin was significantly higher in females than in males. Plasma prolactin was also significantly higher in the normal renin essential hypertensives than in normal subjects of both sexes, while no significant difference was found between the low renin group and normal subjects of either sex. A significantly positive correlation was observed between plasma renin activity and the plasma prolactin level in male essential hypertensives, but not in females. Although no significant difference in plasma prolactin level could be detected between patients with secondary hypertension and normal subjects, this level was significantly higher in malignant hypertensives than in normotensives. From these results, it was shown that significant differences of plasma prolactin levels exist between normal renin essential hypertensives, and low renin essential hypertensives or normal subjects, and that these differences may partly depend on renin status which might be related to the central dopaminergic activity. In malignant hypertensives, the high level of plasma prolactin may be caused by diminished renal function, but the suppression of central dopaminergic activity cannot be excluded in the mechanism of plasma prolactin increment.

Key Words: Prolactin, Renin, Essential hypertension, Malignant hypertension, Secondary hypertension, Central dopaminergic activity

Regarding plasma prolactin in essential hypertension, Stumpe et al. described in 1977 that plasma prolactin level is significantly higher in essential hypertensives, especially in the normal renin subgroup, than in normal controls. Similar results have also been reported by some laboratories, whereas other studies have failed to demonstrate any increase in plasma prolactin level in essential hypertension. Thus, some controversy has remained as to whether plasma prolactin level is higher or not in essential hypertensives as compared to normotensives. Moreover, the investigations in all the above mentioned reports were performed with only male subjects. No reports have been found concerning the role of prolactin in patients with secondary and malignant hypertension.

In this study, plasma prolactin levels were determined in normal controls, low and normal renin essential hypertensives, and patients with...
secondary or malignant hypertension, in relation to plasma renin activity.

MATERIALS AND METHODS

The subjects of the present study included 22 normal controls, 10 females and 12 males, ranging in age from 18 to 64 (34.3 ± 2.4, mean ± SE) years; 16 patients with low renin essential hypertension, 8 females and 8 males, from 22 to 55 (39.0 ± 2.6) years; 17 patients with normal renin essential hypertension, 7 females and 10 males, from 21 to 56 (40.9 ± 1.7) years, in whom renal function was within the normal limits; and 26 patients with secondary or malignant hypertension, i.e., 7 patients with renal hypertension (aged 21 to 59 years), 4 patients with renovascular hypertension (aged 15 to 34 years), 7 patients with primary aldosteronism (aged 24 to 54 years), 2 patients with Cushing syndrome (27 and 32 years), a patient with pheochromocytoma (47 years) and 5 patients with malignant hypertension (aged 34 to 60 years).

Patients with uncomplicated essential hypertension were divided into low, normal and high renin subgroups according to our previously reported procedure. All normotensives and hypertensives except for malignant hypertensives, were given a regular diet of 200 mEq/day of sodium and 75 mEq/day of potassium, and were examined 2 weeks after admission. None of the subjects except for the malignant hypertensives had taken medication for at least 14 days before the measurements were performed. Blood samples were drawn in the recumbent position in early morning after overnight dehydration, and blood pressure was simultaneously measured by the auscultatory method.

Plasma prolactin was estimated by a homologous radioimmunoassay method for human prolactin utilizing materials kindly provided by the National Institute of Arthritis, Metabolism and Digestive Diseases, United States of America. Plasma renin activity was determined by a radioimmunoassay using the Haber's method.

Statistical analysis was performed with Student's t-test for unpaired data.

RESULTS

Fig. 1 shows the plasma prolactin levels in normal subjects, and low and normal renin essential hypertensives of both sexes. In the normotensives and normal renin group, plasma prolactin levels were significantly higher in females than in males, but no sex difference was found in the low renin group. The patients with normal renin essential hypertension showed significantly higher levels than normal controls in both sexes, but those with low renin essential hypertension did not. In the comparison between normal renin group and low renin group, plasma prolactin levels were significantly higher in normal renin group than in low renin group in females, but not significantly in both renin groups in males.

Fig. 2 shows the values in patients with secondary or malignant hypertension. There was no significant difference in plasma prolactin levels
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Fig. 2. Plasma prolactin levels in secondary and malignant hypertensives. F: female subjects, M: male subjects.

Fig. 3 shows the correlation between plasma prolactin level and plasma renin activity in males (upper panel) and female patients with essential hypertension (lower panel). A significantly positive correlation (p < 0.02) was observed in males, but not in females.

**DISCUSSION**

It is well known that prolactin release is regulated primarily by the prolactin inhibiting factor (PIF)\(^{10,11}\) and that dopamine and its agonist stimulate PIF activity.\(^{10-13}\) Furthermore, it has been indicated that central dopaminergic activity may be involved in blood pressure regulation.\(^{14-16}\) Thus, it seems possible that plasma prolactin levels may reflect central dopaminergic activity.

In the present study, a significantly higher level of plasma prolactin was observed in the patients with normal renin essential hypertension than in normal subjects of both sexes, while no

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In the present study, a significantly higher level of plasma prolactin was observed in the patients with normal renin essential hypertension than in normal subjects of both sexes, while no
difference was observed between the normal subjects and the patients with low renin essential hypertension. These results are consistent with the data reported previously from other laboratories,\textsuperscript{1-4} and suggest a possibility that central dopaminergic activity is suppressed in normal renin essential hypertensives. The significantly positive correlation between plasma prolactin level and plasma renin activity in male essential hypertensives also suggests that plasma renin is partly affected by central dopaminergic activity through peripheral sympathetic nerve activity, as reported by Saruta et al.\textsuperscript{4}

It is well known that prolactin release is controlled not only by central dopaminergic activity, but also by sex steroids and other hormones. In fact, it was also observed in this study that plasma prolactin levels are significantly higher in females than in males. Therefore, some factors other than central dopaminergic activity seems to be more important in the prolactin release in females.

No significant difference of plasma prolactin level was found between patients with secondary hypertension and normotensives, and a clear elevation of prolactin level was observed in malignant hypertensives as compared to that in normotensives. Regarding malignant hypertension, it should be considered that high plasma prolactin levels observed in these patients may be caused by renal failure, since a significant augmentation of plasma prolactin level have been demonstrated\textsuperscript{15-18} and renal function was markedly suppressed in these patients with malignant hypertension. However, the possibility cannot be completely excluded that central dopaminergic activity might be suppressed in malignant hypertensives.

Although central dopaminergic activity has been involved in the mechanism of hypertensive diseases, an appropriate index to reflect the central dopaminergic activity has not been made available, particularly in a clinical study. If the plasma prolactin level reflects the central dopaminergic activity, the measurement of that level seems to be very useful. Prolactin release is controlled not only by central dopaminergic activity but also by other factors as shown in the female subjects of this study. Further studies will be necessary to clarify whether the peripheral prolactin level strictly reflects the central dopaminergic activity or not.

REFERENCES

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