NOTE

Plasma Antidiuretic Hormone Levels in Patients with Normal and Low Renin Essential Hypertension, and Secondary Hypertension

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Abstract

In order to investigate the antidiuretic hormone (ADH) in essential hypertension and secondary hypertension, plasma ADH levels were measured in normal subjects, in patients with normal and low renin essential hypertension, and in other patients with various forms of secondary hypertension. Plasma ADH levels were significantly lower in low renin essential hypertension and higher in malignant hypertension than in normal subjects. The plasma ADH levels tended to be lower in renal hypertension and primary aldosteronism, and higher in renovascular hypertension, but these differences were not statistically significant. From these results, it appeared that ADH might play a role in malignant hypertension, but not in the other hypertensive diseases.

Antidiuretic hormone (ADH) secretion is regulated by blood pressure, plasma osmolality and plasma volume through baroreceptors (Robertson *et al.*, 1973; Berl *et al.*, 1974; Shimamoto *et al.*, 1976a), osmoreceptors (Dunn *et al.*, 1973; Robertson *et al.*, 1973; Shimamoto *et al.*, 1976b) and volume receptors (Claybaugh and Share, 1973; Dunn *et al.*, 1973), respectively.

Recently, it has been reported that ADH may play a very important role in the pathogenesis of DOCA-salt hypertension in rats (Möhrling *et al.*, 1976). In addition, in human beings, it has also been reported that plasma ADH levels are lower in patients with essential hypertension than in normal subjects (Padfield *et al.*, 1976; Shimamoto *et al.*, 1979).

However, the plasma ADH level in each form of secondary hypertension has not been clarified. Therefore, in this study, plasma

ADH levels were measured in patients with various forms of secondary hypertension.

Materials and Methods

All of the normal and hypertensive subjects of this study were examined two weeks after admission, and were maintained on a regular diet containing 200 mEq/day of sodium and 75 mEq/day of potassium. In these subjects, all drugs were withdrawn after admission. The patients with essential hypertension were divided into low and normal renin subgroups according to our previously reported method (Kikuchi *et al.*, 1979). Blood samples were taken in the early morning under an overnight dehydrated state from 42 normal controls (19 females and 23 males, aged 16 to 70 years), 17 patients with low renin essential hypertension (11 females and 6 males, aged 32 to 61 years), 25 patients with normal renin essential hypertension (8 females and 17 males, aged 21 to 64 years), 4 patients with malignant hypertension (1 female and 3 males, aged 34 to 40 years), 6 patients with renal hypertension (3 females and 3 males, aged 21 to 59 years), 5 patients with renovascular hypertension (2 females and 3 males, aged 15 to 34 years), 4 patients with primary aldosteronism (2 females and 2 males,

aged 24 to 54 years), 4 patients with pheochromocytoma (1 female and 3 males, aged 18 to 47 years) and 3 patients with Cushing's syndrome (2 females and 1 male, aged 27, 32 and 50 years). Before blood sampling, these subjects were kept in a recumbent position for at least 30 minutes.

The determination of the plasma ADH level was carried out by the radioimmunoassay method reported previously (Shimamoto *et al.*, 1976b). Plasma renin activity (PRA) was measured with the angiotensin I radioimmunoassay kit (CIS). Plasma osmolality was measured by freezing point determination (Osmette Precision Osmometer, Precision Systems, Framingham, Mass.).

A statistical analysis was performed with Student's *t*-test for unpaired data. The values were expressed as mean $\pm$ SEM.

Results

As shown in the Fig. 1, the plasma ADH levels were 4.5 ± 0.2 pg/ml, 3.6 ± 0.2 pg/ml, 4.3 ± 0.1 pg/ml, 8.7 ± 1.5 pg/ml, 3.8 ± 0.4 pg/ml, 5.5 ± 0.9 pg/ml, 3.8 ± 0.5 pg/ml, 4.7 ± 0.7 pg/ml, and 6.4 ± 1.6 pg/ml, respectively in normal controls and patients with low renin essential, normal renin essential, malignant, renal and renovascular hypertension, primary aldosteronism, pheochromocytoma and Cushing's syndrome. The plasma ADH level was significantly lower ($p < 0.01$) in low renin

essential hypertensives than in normal subjects and in normal renin essential hypertensives. The tendency toward lower levels was observed in renal hypertension and primary aldosteronism, and toward a higher one in renovascular hypertension, but these differences were not statistically significant. The plasma ADH level was significantly higher ($p < 0.01$) in patients with malignant hypertension than in normal controls.

As shown in table 1, mean blood pressure was significantly higher in patients with low renin essential, normal renin essential or malignant hypertension than in normal controls ($p < 0.01$), and also significantly higher in patients with malignant hypertension than in patients with low renin or normal renin essential hypertension ($p < 0.05$). PRA was significantly lower in patients with low renin essential hypertension than in normal controls and patients with normal renin essential or malignant hypertension ($p < 0.01$), and significantly higher in patients with malignant hypertension than in normal controls or patients with normal renin essential hypertension ($p < 0.05$). Plasma osmolality showed no significant difference between these groups.

Fig. 1. Plasma ADH levels in normal controls and patients with low and normal renin essential hypertension, malignant hypertension, renal hypertension, renovascular hypertension, primary aldosteronism (P. A.), pheochromocytoma (Pheochro.) and Cushing's syndrome (Cushing). H. T.: hypertension.

Table 1. Mean blood pressure (mBP), plasma renin activity (PRA) and plasma osmolality (Osm.) in normal controls, patients with low renin essential hypertension (LRH), normal renin essential hypertension (NRH) and malignant hypertension (malignant HT). Each value represents the mean $\pm$ SEM.

		mBP (mmHg)	PRA (ng/hr/ml)	Osm. (mosm/kg)
normal controls	(n=42)	84 $\pm$ 3	0.98 $\pm$ 0.20	283.0 $\pm$ 1.0
LRH	(n=17)	117 $\pm$ 4	0.20 $\pm$ 0.03	281.2 $\pm$ 2.3
NRH	(n=25)	120 $\pm$ 4	0.99 $\pm$ 0.15	280.6 $\pm$ 2.1
malignant HT	(n=4)	166 $\pm$ 13	11.18 $\pm$ 3.53	280.0 $\pm$ 3.1

Discussion

Although it has recently been reported that ADH might play a causative role in DOCA-salt hypertension in the rat (Möhring *et al.*, 1976), the regulation of ADH secretion and its relation to changes in blood pressure are not well understood in patients with essential hypertension. In our previous study, it was reported that ADH secretion was suppressed in patients with essential hypertension, and that this might be caused by the elevation of blood pressure.

In this study, in order to investigate further the mechanism of the lowered plasma ADH level in essential hypertension, plasma ADH levels of low and normal renin essential hypertensives were compared. As shown in Fig. 1, a significantly lower level was observed in the low renin group than in normal controls or in the normal renin group of essential hypertensives. No significant difference was observed, however, between normal controls and the normal renin group of essential hypertensives. Since plasma osmolalities were the same in all these groups, plasma osmolality can be excluded as the cause of the lower level of plasma ADH in the low renin essential hypertensives. We have already reported that the plasma volume in low renin and normal renin essential hypertensives was approximately 102% and 90% of that of normal controls, respectively (Kikuchi *et al.*, 1979). The influence of the volume factor on the ADH secretion

has been controversial (Claybaugh and Share, 1973; Goetz *et al.*, 1974; Robertson and Athar, 1976). However, Claybaugh and Share reported (1973) that a 2.6 to 5.2% reduction in blood volume increased plasma ADH levels significantly in an experiment on non-hypotensive hemorrhage in dogs. From our data, it seems that the suppressed plasma ADH levels in the low renin group are mainly attributable to high blood pressure and that absence of any significant difference in the plasma ADH level between the normal renin group and normal controls may be explained by cancellation of the decreasing action of high blood pressure by the increasing action of low plasma volume. Moreover, the significant difference between plasma ADH levels in low and normal renin groups might be explained by the difference in plasma volume, since the same levels of blood pressure and plasma osmolality were found in both groups. In addition, since it has been reported that angiotensin II stimulates ADH secretion (Bonjour and Malvin, 1970; Mouw *et al.*, 1971; Keil *et al.*, 1975), the possibility cannot be excluded that the low plasma angiotensin II level in the low renin group is partly attributable to the low plasma ADH level.

These data also suggest that the lower level of plasma ADH in essential hypertensives might be mainly due to its lower level in the low renin group.

In the patients with malignant hypertension, the plasma ADH level was significantly higher ($p < 0.01$) than that in normal subjects, suggesting that ADH might play

some pathophysiological role in this disease. The decrease in renal function in the patients with malignant hypertension should be considered as one of the factors affecting the elevation of plasma ADH, since uremic patients have a significantly higher plasma ADH level (Shimamoto *et al.*, 1977). In addition, the possibility cannot be excluded that a high plasma angiotensin II level is partly responsible for the high plasma ADH level in malignant hypertension.

On the other hand, in other hypertensive diseases, significant differences in plasma ADH levels were not observed when compared to those in normal subjects. Therefore, it might be concluded that among the human hypertensive diseases, perhaps ADH plays an important pathophysiological role only in malignant hypertension.

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