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PLASMA DEHYDROEPIANDROSTERONE SULFATE CONCENTRATION IN ESSENTIAL HYPERTENSION

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SUMMARY

Plasma dehydroepiandrosterone sulfate (DS) concentration has previously been reported to be elevated in hypertensive Japanese men with uncharacterized renin status. Indirect evidence suggests that some patients with low renin essential hypertension might be expected to have an elevated plasma DS concentration. The intravenous furosemide test was utilized to categorize renin status in black and white, male and female hypertensive patients, and plasma DS concentration was measured. Plasma DS concentration in the low and normal renin subgroups did not differ significantly. In addition, no difference in plasma DS concentration was noted between black and white hypertensive patients and normal subjects, though plasma DS concentration decreased with age and was lower in women. We thus conclude that plasma DS concentration is normal in the great majority of patients with essential hypertension.

INTRODUCTION

The adrenal gland has been postulated to play a role in the genesis of essential hypertension [1]. Dehydroepiandrosterone sulfate (DS) is a major secretory product of the adrenal gland [2] which appears to be regulated primarily by ACTH, though possibly, in part, by prolactin [3]. The production rate [4] and serum concentration [5] of DS have been reported to be markedly elevated in patients with essential hypertension concomitant with a markedly decreased urinary excretion rate [6]. Patients with low renin essential hypertension might be expected to have an elevated plasma DS concentration since their steroid secretory response to ACTH has suggested a mild deficiency of 11β-hydroxylase to some investigators [7]. Plasma DS concentration has not been reported in low vs normal renin hypertensive patients. We report our measurements of DS in a group of patients with essential hypertension in which renin status has been categorized.

MATERIALS AND METHODS

DS was measured by direct radioimmunoassay [8]. Plasma renin activity was determined by radioimmunoassay of generated angiotension I [9].

Experimental subjects

Blood samples were obtained between 0800 to 0900 from ambulatory normal volunteers and patients with essential hypertension, iced immediately, and centrifuged. The plasma was separated and stored at −20°C until assayed. All patients had not taken antihypertensive medications for at least two weeks before the time of study and were determined to have essential hypertension by usual clinical criteria. Patients were classified into low, normal, and high renin subgroups with the intravenous furosemide test [9], done immediately after the blood sample for DS was obtained. Statistical evaluation was accomplished using Student's *t*-test (unpaired).

RESULTS

Plasma DS concentration in normal subjects and hypertensive patients in relation to sex and age is shown in Figs. 1 and 2. There was no significant difference in plasma DS concentration of hypertensive patients in comparison to age and sex matched normotensive subjects. Plasma DS concentration was lower in women (Table 1). Plasma DS concentration of black vs white subjects was not different (Table 1). In addition, plasma DS concentration was not statistically different in low renin vs normal renin hypertensive patients (Table 1). Our normal values are comparable to those reported by others [10–13], but higher than those reported by Sekihara *et al.*[5], who reported the elevated DS levels in patients with hypertension. The previously noted decrease in plasma DS concentration with age [13] was observed (Figs. 1 and 2).

DISCUSSION

Multiple abnormalities of adrenal function have been reported in essential hypertension [1], including elevated serum DS concentration [5] in combination with a markedly decreased DS excretion rate [6].

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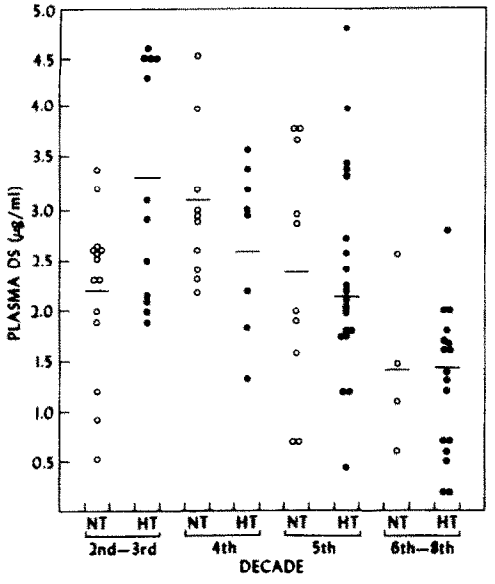

Fig. 1. Age related plasma DS concentrations in male normal subjects and hypertensive patients. Mean concentration is indicated by the horizontal bar.

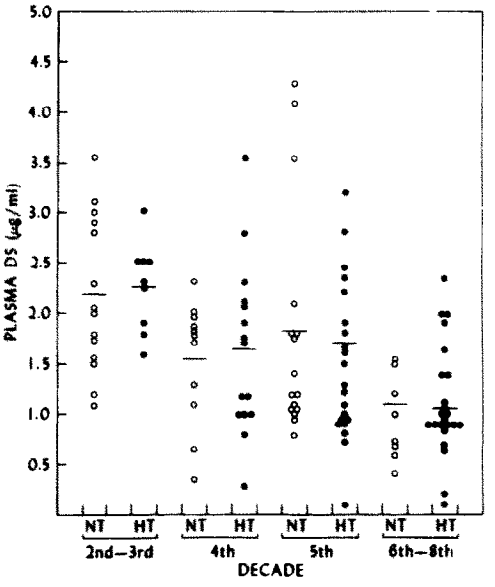

Fig. 2. Age related plasma DS concentrations in female normal subjects and hypertensive patients. Mean concentration is indicated by the horizontal bar.

However, we were unable to confirm an elevated plasma DS concentration in age and sex matched hypertensive vs normotensive subjects. Furthermore, no difference in plasma DS concentration between low renin and normal renin hypertensive patients was observed. The significance of the previously-reported decreased DS excretion [6] and the reasons why we failed to find elevated plasma DS concentration in hypertensive subjects [5] remain unknown. The report by Sekihara *et al.*[5] involved only Japanese males, age 40–58 years. There was considerable overlap in the range of values for normotensive vs hypertensive subjects so that only a few hypertensive patients were outside the normal range. It, thus, appears that plasma DS is normal in the great majority of patients with essential hypertension.

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REFERENCES

1. Genest J., Nowaczynski W., Kuchel O., Boucher R., Rojo-Ortega J. M., Constantopoulos G., Ganten D. and Messerli F.: The adrenal cortex and essential hypertension. *Rec. Prog. Horm. Res.* **32** (1976) 377–427.
2. Wieland R. G., DeCourcy C., Levy R. P., Zala A. P. and Hirchman H.: $C_{19}O_2$ steroids and some of their precursors in blood from normal human adrenals. *J. clin. Invest.* **44** (1965) 159–168.
3. Bassi F., Giusti G., Borsi L., Cattaneo S., Giannotti P., Forti G., Pazzagli M., Vigiani C. and Serio M.: Plasma androgens in women with hyperprolactinaemic amenorrhoea. *Clin. Endocr.* **6** (1977) 5–10.
4. Shao A., Nowaczynski W., Kuchel O. and Genest J.: Secretion rate of dehydroepiandrosterone and dehydroepiandrosterone sulfate in benign essential hypertesion as compared to normal subjects. *Can. J. Biochem.* **48** (1970) 1308–1313.
5. Sekihara H., Ohsawa N. and Kosaka K.: Serum dehydroepiandrosterone sulfate and dehydroepiandrosterone levels in essential hypertension. *J. clin. Endocr. Metab.* **40** (1975) 156–157.
6. Nowaczynski W., Fragachan F., Silah J., Millette B. and Genest J.: Further evidence of altered adrenocortical function in hypertension. Dehydroepiandrosterone excretion rate. *Can. J. Biochem.* **46** (1968) 1031–1038.

Table 1. Plasma DS concentration (mean ± S.E.M.) in normal subjects and hypertensive patients

	Male			Female		
	No.	Age	DS-μg/ml	No.	Age	DS-μg/ml
Normotensive						
Black	12	35.0 ± 3.0	2.02 ± 0.21	12	42.9 ± 6.3	1.77 ± 0.31
White	26	35.1 ± 2.4	2.54 ± 0.21	37	37.9 ± 1.8	1.74 ± 0.14
Hypertensive						
Black	25	45.5 ± 2.5	2.02 ± 0.25	48	44.2 ± 1.7	1.48 ± 0.15
White	27	40.5 ± 3.0	2.59 ± 0.25	21	46.8 ± 3.4	1.64 ± 0.17
Low renin	15	49.1 ± 3.7	1.89 ± 0.27	24	46.2 ± 2.4	1.42 ± 0.27
Normal renin	36	40.4 ± 2.2	2.44 ± 0.22	44	44.3 ± 2.1	1.61 ± 0.11

7. Honda H., Nowaczynski W., Guthrie G. P., Messerli F. H., Tolis, G., Kuchel O. and Genest J.: Response of several adrenal steroids to ACTH stimulation in essential hypertension. *J. clin. Endocr. Metab.* **44** (1977) 264–272.
8. Milewich L., Gomez-Sanchez C., Madden J. D., Bradfield D. J., Parker P. M., Smith S. L., Carr B. R., Edman C. D. and McDonald P. C.: Dehydroisoandrosterone sulfate in peripheral blood of premenopausal, pregnant, postmenopausal women and men. Unpublished data.
9. Kaplan N. M., Kem D. C., Holland O. B., Kramer N. J., Higgins J. and Gomez-Sanchez C.: The intravenous furosemide test: a simple way to evaluate renin responsiveness. *Ann. Int. Med.* **84** (1976) 639–645.
10. Smith M. R., Rudd B. T., Shirley A., Rayner P. H. W., Williams J. W., Duignan N. M. and Bertrand P. V.: A radioimmunoassay for the estimation of serum dehydroepiandrosterone sulphate in normal and pathological sera. *Clin. chim. Acta* **65** (1975) 5–13.
11. Wang D. Y., Bulbrook R. D., Herian M. and Hayward J. L.: Studies on the sulphate esters of dehydroepiandrosterone and androsterone in the blood of women with breast cancer. *Eur. J. Cancer* **10** (1974) 477–482.
12. Cattaneo S., Forti G., Fiorelli G., Barbieri U. and Serio M.: A rapid radioimmunoassay for determination of dehydroepiandrosterone sulphate in human plasma. *Clin. Endocr.* **4** (1975) 505–512.
13. Abraham G. E., Buster J. E., Kyle F. W., Corrales P. C. and Teller R. C.: Radioimmunoassay of plasma pregnenolone, 17-hydroxypregnenolone and dehydroepiandrosterone under various physiological conditions. *J. clin. Endocr. Metab.* **37** (1973) 140–144.