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PLASMA CATECHOLAMINE AND 5-HT IN PREGNANCY

(catecholamine metabolites/5-HT/pregnancy)

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The adrenergic and dopaminergic systems and 5-hydroxytryptamine levels were studied in four groups of pregnant: group I of 25 first trimester normotensives, group II of 15 second trimester normotensives, group III of 15 third trimester normotensives, Group IV of 15 with pregnancy-induced hypertension. Blood samples were taken from the fasting ambulatory women. Plasma norepinephrine (NE) levels were 196 ± 66 pg/ml, 202 ± 49 pg/ml, 188 ± 49 pg/ml, 214 ± 75 pg/ml, respectively. There was no significance among each group. Plasma 3,4-dihydroxyphenylacetic acid (DOPAC) levels were significantly higher in pregnancy-induced hypertension than in the other groups. (648 ± 196 pg/ml vs. 483 ± 102, 497 ± 92 and 501 ± 139 pg/ml). Plasma 5-hydroxytryptamine (5-HT) levels were significantly higher in case of pregnancy-induced hypertension than in the other groups. (122 ± 22 ng/ml vs. 93 ± 26, 99 ± 18 and 94 ± 22 ng/ml). These data may suggest that the serotonergic and/or dopaminergic systems may play important roles in pregnancy-induced hypertension.

The mechanism involved in pregnancy-induced hypertension is unclear. Cession (1) reported a higher urinary excretion of norepinephrine(NE) and epinephrine(E) in patients with pregnancy-induced hypertension compared with normal pregnant women. Zuspan (14) found that the urinary excretion of catecholamine increased in patients with pre-eclampsia and

eclampsia, and plasma NE and E measurements have been made to investigate the sympathetic nervous system activity (2,6,10,15). Davey and Macnab (2) suggested that the sympathetic nervous system activity may be increased in some of women who become hypertensive when pregnant.

Recently, it was found that Ketanserine, a selective 5-hydroxytryptamine(5-HT) receptor blocker depressed blood pressure (4) and thus 5-HT seems to an important role in hypertension.

In the present study, we measured plasma NE, 3,4-dihydroxy-phenylacetic acid (DOPAC) and 5-HT levels in pregnant Japanese women in pregnancy with special reference to pathogenesis of pregnancy-induced hypertension.

MATERIALS AND METHODS

Seventy patients with hypertension in pregnancy and normotensive pregnant control participated in this study. In order to know the time for occurrence of hypertension during pregnancy, we classified normotensive pregnant control into 3 trimesters, first trimester, second trimester and third trimester (Table I).

Table I. SUBJECT

	group	number	Mean age (years old)
I	normotensive women in the first trimester	25	26
II	normotensive women in the second trimester	15	28
III	normotensive women in the third trimester	15	28
IV	pregnancy-induced hypertension BP $\geq$ 140/90 mmHg	15	29

Gestational age was estimated from the date of the last menstrual period and from ultrasound examinations.

Blood samples for determination of NE, DOPAC and 5-HT in plasma were drawn in the morning with the patient fasting and in a supine position. All samples were stored at -20°C until assay.

Plasma NE and DOPAC were measured by high performance liquid chromatography with electrochemical detection described as

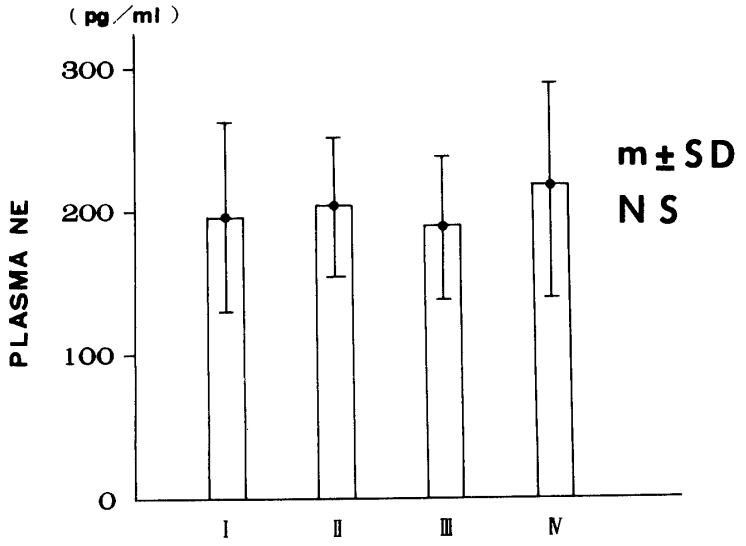

Fig.1. Plasma norepinephrine in normotensive women in the first trimester (I), the second trimester (II) and the third trimester (III) and in pregnancy-induced hypertension (IV).

Yamamoto *et al.* (14). 5-HT was measured by the o-phthalaldehyde method (5).

One way layout analysis of variance was used for statistical evaluations.

RESULTS

The plasma NE levels of normotensive pregnant control in the first trimester, the second trimester and the third trimester, and of pregnancy-induced hypertensives were 196 ± 66, 202 ± 49, 188 ± 49, 214 ± 75, (pg/ml), respectively. There was no significance between in normotensives and in patients with pregnancy-induced hypertension (Fig.1).

The plasma DOPAC levels of normotensive pregnant control in the first trimester, the second trimester and the third trimester were 483 ± 102, 497 ± 92, 501 ± 139 (pg/ml), respectively. There was no significant change. But in patients with pregnancy-induced hypertension plasma DOPAC levels were 648 ± 196 pg/ml, its levels were significantly higher than normal pregnant women ($p<0.05$) (Fig.2).

The plasma 5-HT levels of normotensive pregnant control in the first trimester, the second trimester and the third trimester were 93 ± 26, 99 ± 18, 94 ± 22, (ng/ml), respectively. The plasma 5-HT levels were 122 ± 22 ng/ml in patients with pregnancy-induced hypertension, to compared with normotensives, its levels were significantly higher ($p<0.05$) (Fig.3).

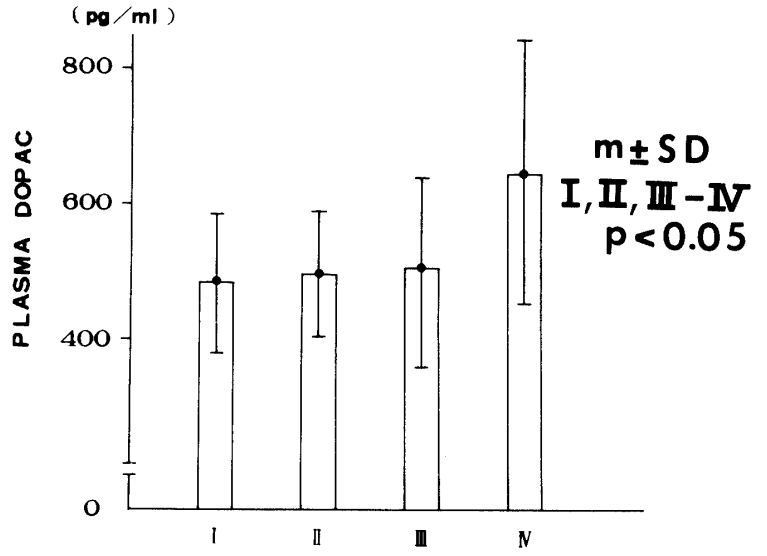

Fig.2. Plasma 3,4-Dihydroxyphenylacetic acid in normotensive pregnant women in the first timester (I), the second trimester (II) and the third trimester (III) and in pregnancy-induced hypertension (IV).

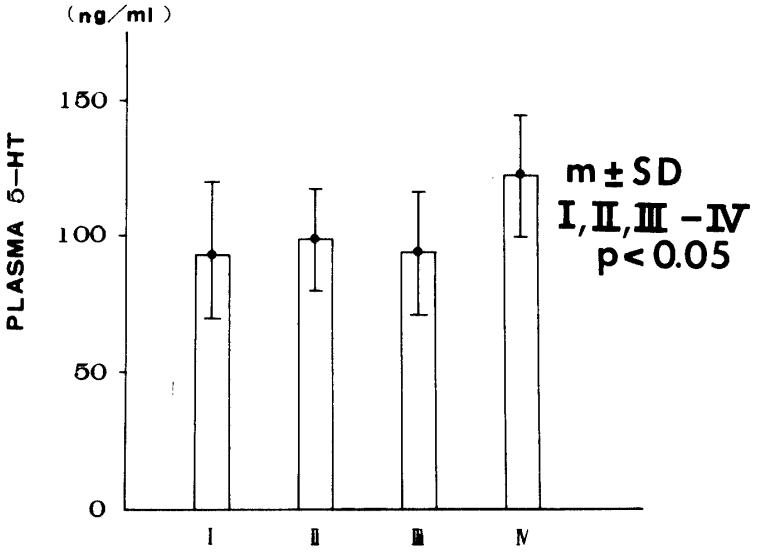

Fig.3. Plasma 5-Hydroxytryptamine in normotensive pregnant women in the first trimester (I), the second trimester (II), and the third trimester (III) and in pregnancy-induced, hypertension (IV).

DISCUSSION

Spasms of the peripheral vessels may be involved in pregnancy-induced hypertension. Catecholamines which have a vasoconstrictive effects, have been measured by several investigator. Zuspan (14) reported that urinary secretion of catecholamine significantly increased in patients with eclampsia

and pre-eclampsia, and that plasma NE, E levels were significantly increased in patients with pregnancy-induced hypertension (15). He hypothesized that increased activity of the adrenergic nervous system was an importnat factor in the development of pregnancy-induced hypertension.

On the other hand, Davey and Macnab (2) found that the plasma E/NE ratio was significantly increased in some pregnant hypertensives, and Tunbridge and Donnai (10) have shown that plasma NE levels decline with progression of the pregnancy, and that NE levels were lower in patients who had developed hypertension in late pregnancy.

In the present study, compared with normotensive pregnant control, plasma NE levels were not significantly higher in patients with pregnancy-induced hypertension.

Dopamine may play an important role in regulating blood pressure (7,8,9,11). Sowers *et al.* (8) suggest that dopaminergic control of NE secretion may be altered in essential hypertension. And dopaminergic activity decrease in essential hypertension. In the present study, DOPAC levels (dopamine metabolite) were high in patients with pregnancy-induced hypertension, but there was no correlation between plasma NE and plasma DOPAC. It is unclear whether depaminergic activity is related to pregnancy-induced hypertension.

5-HT has a vasoconstrictive effects, mediated S_2 receptor and the activity enhances the effects of angiotensin II and prostaglandins.

Recently, it is reported that ketanserine, S_2 receptor blocker is a hypotensor. Weiner (12) *et al.* demonstrated that pre-eclamptic hypertension could be controlled by ketauserine. In the present study, plasma 5-HT levels is elevated in patients with pregnancy-induced hypertension. So we support their demonstration.

Though the high level of 5-HT may be a secondary factor, there seems to be some link of this amine with pregnancy-induced hypertension.

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