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Changes in plasma human atrial natriuretic peptide (hANP) level in normal pregnancy and pregnancy induced hypertension.

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Abstract

We determined plasma human atrial natriuretic peptide (hANP) levels in normal pregnancy and pregnancy induced hypertension (PIH). The plasma hANP levels slightly decreased in the first trimester of normal pregnancy and tended to recover as pregnancy advanced, although these changes were slight. However, the plasma hANP level in puerperium was higher than that in the third trimester of normal pregnancy. The plasma hANP level in mild PIH was not significantly higher than that in the third trimester of normal pregnancy. In contrast, the plasma hANP level in three cases of severe PIH was approximately 200% higher than those in the normal third trimester and mild PIH.

KEYWORDS: human atrial natriuretic peptide(hANP), preload, pregnancy induced hypertesion(PIH)

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Key words : **human atrial natriuretic peptide (hANP), preload, pregnancy induced hypertesion (PIH)**

Human atrial natriuretic peptide (hANP) designates a family of peptide homones secreted by specialized cells in atrial myocytes. These hormones have been shown to be potent natriuretic, diuretic and vasodilatory substances. Increased intra-atrial pressure or atrial distension stimulates secretion of hANP (1-3). The hANP is presumed to play an important role in regulating the volumes of body fluid and circulating blood in both normal pregnancy and pregnancy induced hypertension (PIH) which show marked hemodynamic changes.

Materials and Methods

We determined plasma hANP levels in normal pregnancy and PIH. Seven non-pregnant cases, 28 normal pregnancy cases (first trimester 8 cases, second trimester 8 cases, third trimester 12 cases), 5th puerperal day 7 cases, 9 PIH cases (6 mild cases, 3 severe cases in the third trimester) were used as the subjects.

Venous blood was collected in supine position with aprotinin (500 KIU/ml)-EDTA (1 mg/ml). The plasma was quickly separated by centrifugation for 10 min at 4°C and stored at −20°C until assayed. All subjects were eating a near normal diet. Water and salt intake were not particularly restricted.

Samples and standards were incubated for 24 h at 4°C with 100 μl of anti-αhANP antibody (obtained from Dr. Kenji Kangawa, Department of Biochemistry, Miyazaki Medical School). ^{125}I αhANP was then added and the tubes were incubated for additional 24 h at 4°C. The antigen-antibody complex was then precipitated with 100 μl of goat antirabbit immunoglobulin G. These tubes were incubated for 30 min at 4°C and then centrifuged for 30 min at 3,000 rpm. The supernatant was removed as

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quickly as possible using an aspirator and the tubes were inserted in a well-type gamma scintillation counter (4). The interassay coefficient of variation ranged from 10 % to 14 %, and the intraassay variation was between 6 % and 8 %. Statistical analysis was performed by Student's t test.

Results

The plasma hANP level slightly decreased in the first trimester of pregnancy and tended to recover as pregnancy advanced (Fig. 1). However there was no significant difference in the plasma hANP levels among the three trimesters of pregnancy. The plasma hANP of puerperium was significantly higher than that in the third trimester of normal pregnancy (Fig. 1).

When the plasma hANP level was compared between PIH and the third trimester of normal pregnancy, mild PIH ($n = 6$) showed slightly higher level than the normal third trimester, but there was no statistical difference between them. However, as shown in Fig. 1, the plasma hANP level in severe PIH ($n = 3$) was significantly higher than the normal third trimester and the mild PIH.

A significant positive correlation ($r = 0.814$, $p < 0.05$) was noted between the hematocrit (Ht) level and plasma hANP level in mild PIH cases (Fig. 2).

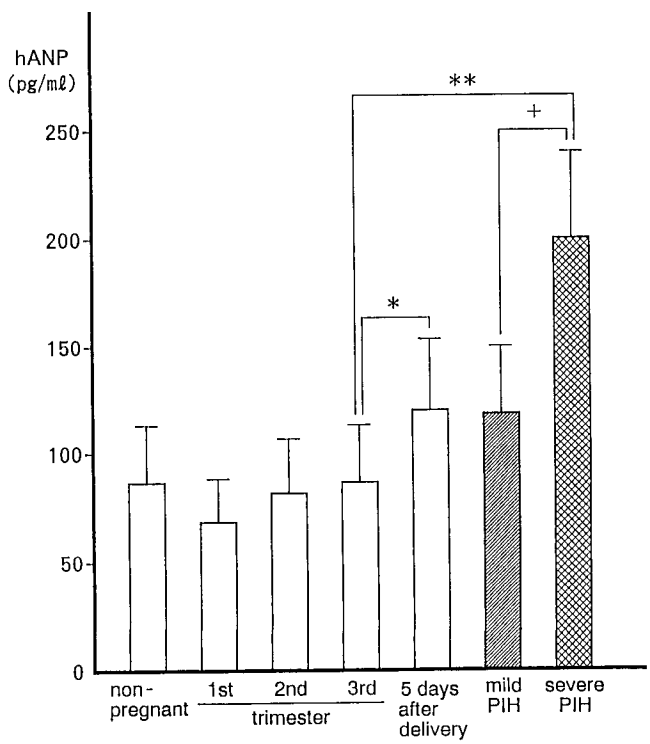

Fig. 1 Plasma hANP levels in non-pregnancy, normal pregnancy and pregnancy induced hypertension (mild and severe: 3rd trimester). Vertical bars in each column indicate SD. Significantly different from normal pregnancy (3rd trimester): *, $p < 0.05$; **, $p < 0.001$. Significantly different from mild PIH: +, $p < 0.05$ by Student's t test.

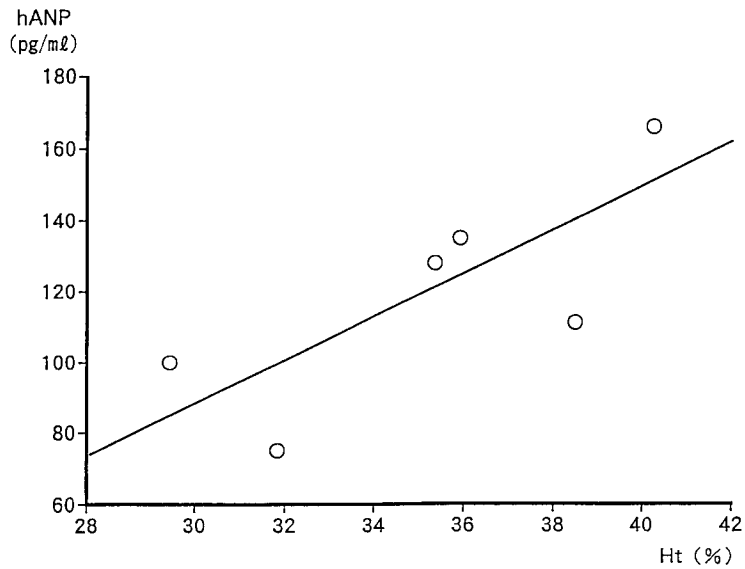

Fig. 2 Relationship between plasma hANP levels and hematocrit (Ht) in mild pregnancy induced hypertension cases ($n = 6$). Correlation coefficient, $r = 0.814$; $p < 0.05$; regression equation, $Y = -100.31 + 6.2429X$.

Discussion

The hANP is secreted by stretching of the atrial wall and shows high values under various pathophysiological conditions in which an abnormally high preload is imposed on the heart (5). Accordingly, the physiological significance of hANP is presumed to regulate body fluid homeostasis (6). The result of our present study will be interpreted from such a view point as follows.

The slight decrease in the plasma hANP level in the first trimester of normal pregnancy may imply dehydration resulting from emesis (7). The circulating blood volume increases gradually as pregnancy advances after the second trimester in the normal course, and this may become a considerable volume load (8). However, the plasma hANP level showed no significant difference from the non-pregnant control. It suggests that this increase in circulating blood volume may be compensated for by a simultaneous increase in the vascular capacity, namely, a decrease in systemic vascular resistance in normal pregnancy, thus imposing no extra preload on the heart.

On the contrary, reports from other laboratories have suggested that normal pregnant women showed higher hANP levels compared with non-pregnant control (9,10). The difference of hANP levels in the third trimester of normal pregnancy between our study and others' is explained, at least in part, by methodological consideration. Our assay was done by the competitive two-site direct radioimmunoassay using specific antibody kindly given by Dr. Kenji Kangawa, and the reliability of this method is widely recognized at present. Additionally, the values of hANP are generally thought to vary with the conditions of blood sampling such as posture, diet, and so on (3). This may be also one of the mechanisms causing the difference.

The high plasma hANP level appeared in the

puerperal stage. This suggests that the vascular capacity decreases after the termination of pregnancy and the circulating blood volume that had increased during pregnancy then becomes an increased preload on the heart, causing secretion of hANP. This may be considered as a physical change of the cardiovascular system which implies a phenomenon of involution after delivery.

In general, the increase in circulating blood volume is considered to be disturbed in PIH compared with normal pregnancy (11). Decreased circulating blood volume and increased vascular resistance with impaired perfusion of various organs, including the uteroplacental unit, are recognized as important pathologic features of PIH. Especially, decreased plasma volume and accompanied hemoconcentration have also been noted as hemorheological disturbance in PIH related to peripheral microcirculation insufficiency (12).

The high plasma hANP level shown in PIH, particularly in severe cases means a heavy volume load on the heart. This result suggests that there is no concurrent increase in the vascular capacity in proportion to an increase of the circulating blood volume in PIH. Thus it is suggested that a decrease in plasma volume is augmented, causing the hemoconcentration because hANP is secreted by an atrial load in PIH. This may be the mechanism of the positive correlation between hANP and Ht levels noted in mild PIH.

In conclusion, our present study demonstrated that the plasma hANP levels showed no significant change in normal pregnancy compared with non-pregnant control, but they were elevated in pregnancy complicated with hypertension. The pathophysiologic state in PIH is generally recognized as increased systemic vascular resistance. Consequently increased hANP levels in PIH are speculated to be caused by relative volume load resulting from a decreased vascular capacity. Some factors other than preload may also regulate the hANP levels in PIH. These factors remain to be investigated furthermore.

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