Sympathetic Nerve Activity, Plasma Renin Activity and Water-Sodium Balance in Obese Patients with Essential Hypertension

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Studies were conducted to evaluate the role of water-sodium metabolism on the hypertensive mechanisms in obese patients with essential hypertension (EHT).

The obesity index correlated positively with the mean arterial pressure, plasma volume, extracellular fluid volume or total exchangeable sodium, and negatively with plasma noradrenaline concentration or plasma renin activity in EHT. Hypotensive effects of sodium restriction (Na 35 mEq, K 75 mEq) or the natriuretic response to infused dopamine (3 μg/kg/min) was remarkable in obese EHT. Fractional excretion of sodium (FE_Na), which reflects the renal tubular reabsorption of sodium, was significantly lower in obese EHT than that in non-obese or midly obese EHT. Urinary excretion of free dopamine (UDA) had a positive relationship with simultaneously measured urinary excretion of sodium or FE_Na. In addition, UDA correlated positively with the obesity index in patients whose weight was under 115% of the ideal weight. On the contrary, the relation between the two parameters was significantly negative in patients whose weight was over 115% of the ideal weight.

These findings suggest that the expansion of body fluid volume and sodium, which might result from the blunted natriuretic ability, at least in part, due to an attenuation of the renal dopaminergic activity, play an important role of the hypertensive mechanisms in obese EHT.

MANY epidemiologic1–3 and clinical4–8 studies have clearly pointed out the relationship between obesity and hypertension; however the underlying mechanisms have not been established. Some observations indicate that the decrease in sodium intake accompanied with weight loss is a major factor in reducing blood pressure4. On the other hand, Reisin et al.9 reported that subjects who were reducing their weight had lower blood pressure than did control subjects, despite almost equivalent, unrestricted salt intake in both groups.

We have therefore evaluated the role of sympathetic nerve activity, the renin-angiotensin system and water-sodium metabolism in obese patients with essential hypertension.

The study consisted of 113 inpatients with mild or moderate essential hypertension (EHT), including 38 females and 75 males, aged 21 to 59 years old. Patients were categorized into three groups according to the level of body weight using Minowa's method9. Obese EHT had a weight of 120% or more of the ideal weight defined on the basis of age, sex and height. Mildly obese EHT had a weight between 110% and

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120%, and nonobese displayed a weight between 90% and 110% of the ideal weight. The mean of Minowa's index in obese EHT was 32.9 ± 1.6%, in mildly obese EHT 15.5 ± 0.5% and in nonobese EHT 1.5 ± 0.9%. There was no significant differences in age among the three groups. Patients were either untreated or had discontinued anti-hypertensive drugs for at least two weeks prior to hospitalization. All patients received a constant diet containing normal calories (2400Cal), 200 mEq of sodium, 75 mEq of potassium and 1.35g of inorganic phosphorus. Studies started on the fourteenth day of hospitalization.

Values were expressed by mean ± SEM. Statistical analysis was performed by the Student's t-test.

1. Plasma Noradrenaline Concentration (PNA), Plasma Renin Activity (PRA), Plasma Volume (PV), Extracellular Fluid Volume (ECFV) and Total Exchangeable Sodium (Nae) in obese EHT.

In the early morning, after overnight fasting, body weight in under wear only was determined and thereafter patients remained supine. Blood pressure was repeatedly measured by the auscultatory method immediately before blood sampling for PNA or PRA measurements. The mean arterial pressure (MAP) was calculated as the diastolic pressure plus 1/3 pulse pressure from the average of blood pressure. PNA was estimated by the HPLC-THI method, PRA by radioimmunoassay according to the method of Haber et al.10 PV11 ECFV12 and Nae13 were measured by the dilution method of 1251-RISA and 22NaCl, respectively. PV was expressed as a percentage of the mean value per height of normal men or women (ml/cm-%normal)14 ECFV and Nae were corrected by height (ml/cm and mEq/cm, respectively). There was a significant correlation between the obesity index and MAP (r = 0.378, p < 0.001). MAP in obese EHT (120.5 ± 2.8 mmHg) was greater than that in mildly obese (114.9 ± 2.7) or nonobese EHT (108.4 ± 2.3). A significant negative correlation existed between the obesity index and PNA (r = −0.527, p < 0.001) or PRA (r = −0.257, p < 0.05). The mean value of PNA (101.0 ± 6.2 pg/ml) in obese EHT was lower than that in mildly obese (142.1 ± 9.7) or nonobese EHT (181.3 ± 9.9), and a similar tendency was found in PRA (obese: 0.40 ± 0.06, mildly obese: 0.69 ± 0.11, nonobese: 0.71 ± 0.09 ng/ml/hr). On the other hand, the obesity index correlated positively with PV (r = 0.331, p < 0.001), ECFV (r = 0.245, p < 0.025) or Nae (r = 0.275, p < 0.01). The mean values of PV, ECFV, Nae (91.9 ± 2.4 ml/cm-%normal, 88.1 ± 2.0 ml/cm, 14.2 ± 0.5 mEq/cm) in obese were higher than in mildly obese (86.7 ± 1.6, 89.0 ± 2.3, 13.8 ± 0.4) or nonobese EHT (86.1 ± 1.5, 79.3 ± 1.5, 13.0 ± 0.2).

These findings suggest that the attenuated activity of sympathetic nerve or renin-angiotensin system and the expansion of body fluid volume or sodium might exist in obese EHT.

2. Relationship between The Obesity Index and Hypotensive Effect of Sodium Restriction in EHT.

Forty-one patients received a sodium restricted diet containing normal calories, 35 mEq of sodium and 75 mEq of potassium for a week after a constant diet described above. The mean value of MAP and body weight were significantly decreased (p < 0.001, and p < 0.001) by sodium restriction. A significant negative correlation was observed between the obesity index in basal state and changes in MAP (r = −0.347, p < 0.05) or in body weight (r = −0.573, p < 0.001) following sodium restriction.

These results imply that the expanded body fluid volume and sodium play important roles in the hypertensive mechanisms in obese EHT.


In the morning, each patient was examined for renal clearance. Fractional excretion of sodium (FENa) was calculated from values of blood and urine samples, by means of the formula: FE (Na) (%) = (C × Ccr) × 100, where the fractional excretion of Na. A negative correlation (r = −0.652, p < 0.001) existed between the obesity index and FE in obese EHT, and a similar tendency (r = −0.353, p < 0.1) was found in mildly obese but not in nonobese EHT. We reported previously that FENa correlated positively with MAP and negatively with Ccr in EHT. Then, FENa in obese EHT was compared to that in MAP- and Ccr-matched nonobese or mildly obese EHT. The mean value of FeNa in obese EHT was significantly lower than that in nonobese (p < 0.05) or mildly obese EHT (p < 0.025).

These findings suggest the possibility that the blunted natriuretic ability of the kidney may be present in obese patients with essential hypertension.

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4. Natriuretic Response to Infused Dopamine and Urinary Excretion of Free Dopamine in Obese Essential Hypertensives.

Thirty-seven patients were examined for their natriuretic response to intravenous infusion of dopamine (3 μg/kg/min, for 60 min). Urinary excretion of sodium (UNa V) or FENa was significantly increased by dopamine infusion. There was a significant correlation between the obesity index and change in UNa V (r = 0.544, p < 0.001) or FENa (r = 0.476, p < 0.005). Changes in UNa V (444.8 ± 43.4 μEq/min) and EFNa (21.4 ± 0.33%) induced by infused dopamine in obese EHT were greater than those (230.9 ± 32.5 μEq/min, 1.32 ± 0.19%) in nonobese EHT. This natriuretic response to infused dopamine was negatively correlated with urinary excretion of free dopamine (UDA) just before dopamine infusion.

In 32 patients, UDA was measured by the HPLC-ECD method. UDA correlated positively with simultaneously measured UNa V (r = 0.567, p < 0.001) and FENa (r = 0.546, p < 0.005), and correlated positively (r = 0.539, p < 0.01) with the obesity index in patients whose weight was under 115%. A significant negative correlation (r = −0.798, p < 0.01) between the two parameters was found in patients whose weight was over 115% of the ideal weight.

These results suggest that the renal dopaminergic activity is attenuated in obese essential hypertensives, and also suggest that this attenuation causes the blunted natriuretic ability in obese patients with essential hypertension.

REFERENCES
2. TYROLER HA, HEYDEN S, HAMES CG: Weight and hypertension: Evans County studies of blacks and whites. In Epidemiology and control of hypertension, ed by O. PAUL, 1975, p 177