

Blood pressure and plasma insulin in acromegaly

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It is well known that hypertension may be a common feature of growth hormone excess^{1,2}. To date, studies of changes in the level of, and in blood pressure sensitivity to, the hormones such as anti-natriuretic hormone^{3,4}, renin-angiotensin^{2,5,6}, and catecholamines^{7,8} are frequently contradictory in acromegalics and the mechanism of increased blood pressure in the patients remains to be fully elucidated. In recent, hyperinsulinemia (insulin resistant state) is considered to be a pathogenic factor in the hypertension associated with non-insulin dependent diabetes mellitus and possibly also in essential hypertension⁹. Hyperinsulinemia is frequently observed in acromegalic patients. These findings prompted us to investigate the correlation between blood pressure and plasma insulin level in acromegalic patients to elucidate the possible role of hyperinsulinemia in an increase of blood pressure.

Subjects and methods

Nineteen untreated acromegalic patients (nine women and ten men) were recruited from our clinic. All were inpatients and none of them were receiving drugs affecting insulin secretion and blood pressure. The age was 25-69 yr (46.6 ± 12.8 yr, means \pm SD). Systolic (first phase) and diastolic (fifth phase) blood pressures were measured to the nearest even digit on the right arm in a supine position following at least a 5-min bed rest with the use of a random-zero sphygmomanometer. Blood pressure was measured at 10:00 am for three days. Each blood pressure was scored by the mean of three measurements.

After an overnight fasting, 75g oral glucose tolerance test was performed. During the test, the subjects were in bed rest, and the blood was drawn from antecubital vein at 0, 30, 60, 120 and 180 min. Blood glucose was measured by glucose oxidase method. Plasma growth hormone (GH) and insulin (IRI) were measured by respective radioimmunoassay using a double antibody method. The sum of plasma GH or IRI at 0, 30, 60, 120 and 180 min was expressed as the Σ GH or Σ IRI. Transsphenoidal surgical treatment revealed that all patients had had acromegaly due to benign pituitary adenoma. Pearson's coefficient of correlation was applied for statistical analyses.

Results

According to the World Health Organization criteria, three subjects showed normal glucose tolerance, five showed impaired glucose tolerance, and eleven showed diabetic. Basal GH levels were 10-160 ng/ml.

No significant correlation was observed between mean blood pressure (MBP, diastolic plus one-third pulse pressure) and basal GH or Σ GH. Significant correlation was observed between MBP and IRI level at 120 min ($r = 0.57$, $p < 0.02$) or Σ IRI ($r = 0.58$, $p < 0.02$) as shown in Figs. 1 and 2, although no significant correlation was observed between MBP and basal IRI, body mass index (kg/m^2) or blood glucose level.

Discussion

In acromegaly, no direct relation has been reported between blood pressure and plasma growth hormone concentration by Davies et al²⁾ and Snow et al¹⁰⁾, whereas growth hormone level has been reported to be higher in hypertensive acromegalics by McGuffin et al.¹¹⁾ In the present study, blood pressure revealed not to be correlated with plasma growth hormone level. Therefore, it clearly demonstrated that blood pressure was higher in hyperinsulinemic acromegalics; suggesting that hyperinsulinemia may cause an increase of blood pressure in acromegalics. Insulin is known to increase renal sodium re-absorption, and direct relationship has been observed between blood pressure and amount of exchangeable sodium in untreated acromegalics²⁾. Thus insulin-induced sodium retention may contribute to the increase of blood pressure in acromegalic patients. Although Ferrannini et al¹²⁾ have reported that plasma glucose level after oral glucose load, as well as plasma insulin level, were directly related to hypertension prevalence, in the present study diabetic acromegalics who had high plasma glucose level were rather hypotensive. Hyperinsulinemia, rather than hyperglycemia, may have an important role in the increase of blood pressure in acromegalics.

The diabetic acromegalics may be slightly hypovolemic and consequently their blood pressures would be lower. In the present study the number of subjects examined was very small and the correlation between plasma insulin and blood pressure has not been examined after hypophysectomy. Further studies should be necessary.

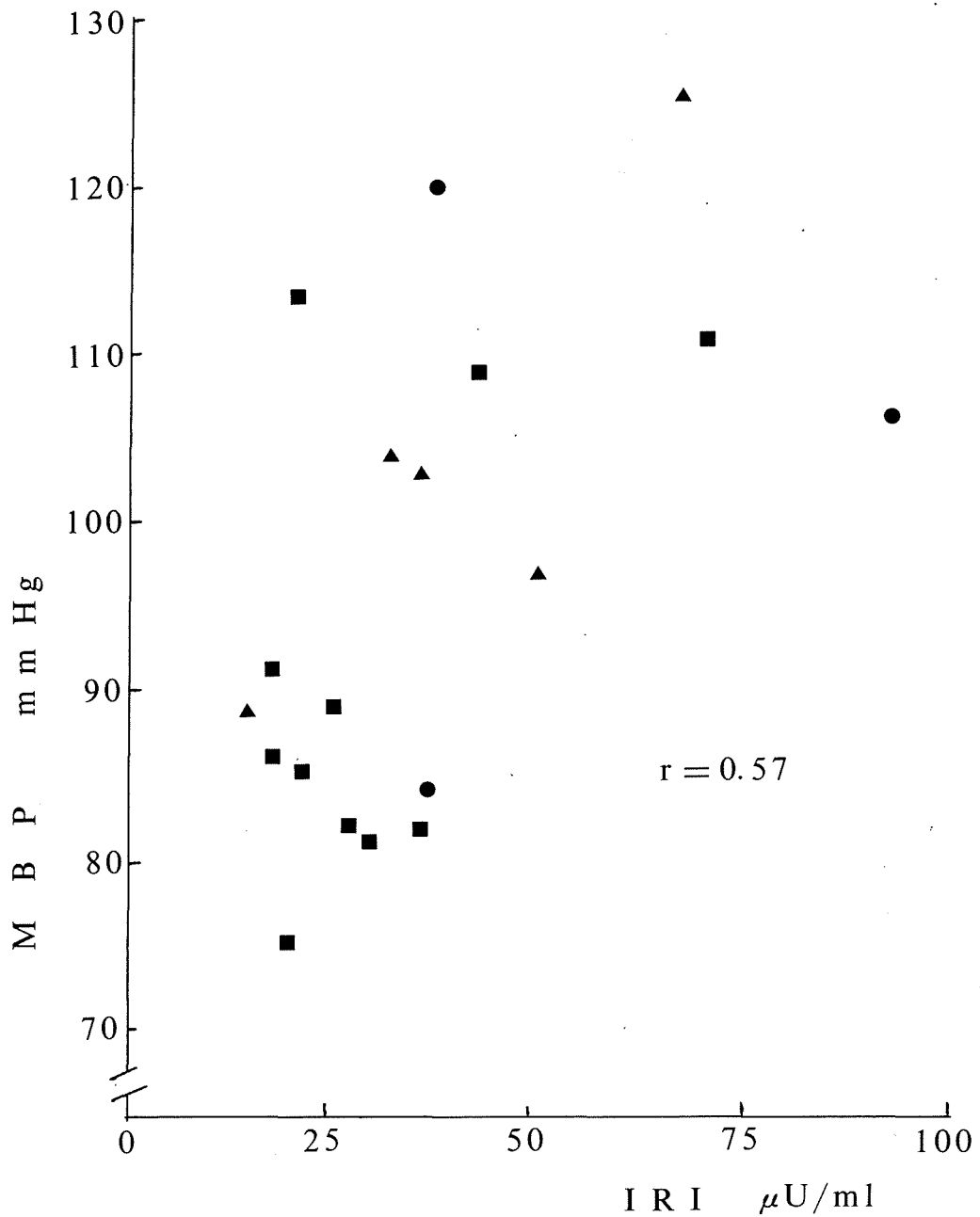


Fig. 1 Correlation between mean blood pressure and plasma insulin level at 120 min

MBP : mean blood pressure, IRI : Plasma insulin

● acromegalics with normal glucose tolerance

▲ acromegalics with impaired glucose tolerance

■ diabetic acromegalics

Significant correlation was observed between MBP and IRI ($r = 0.57$, $p < 0.02$).

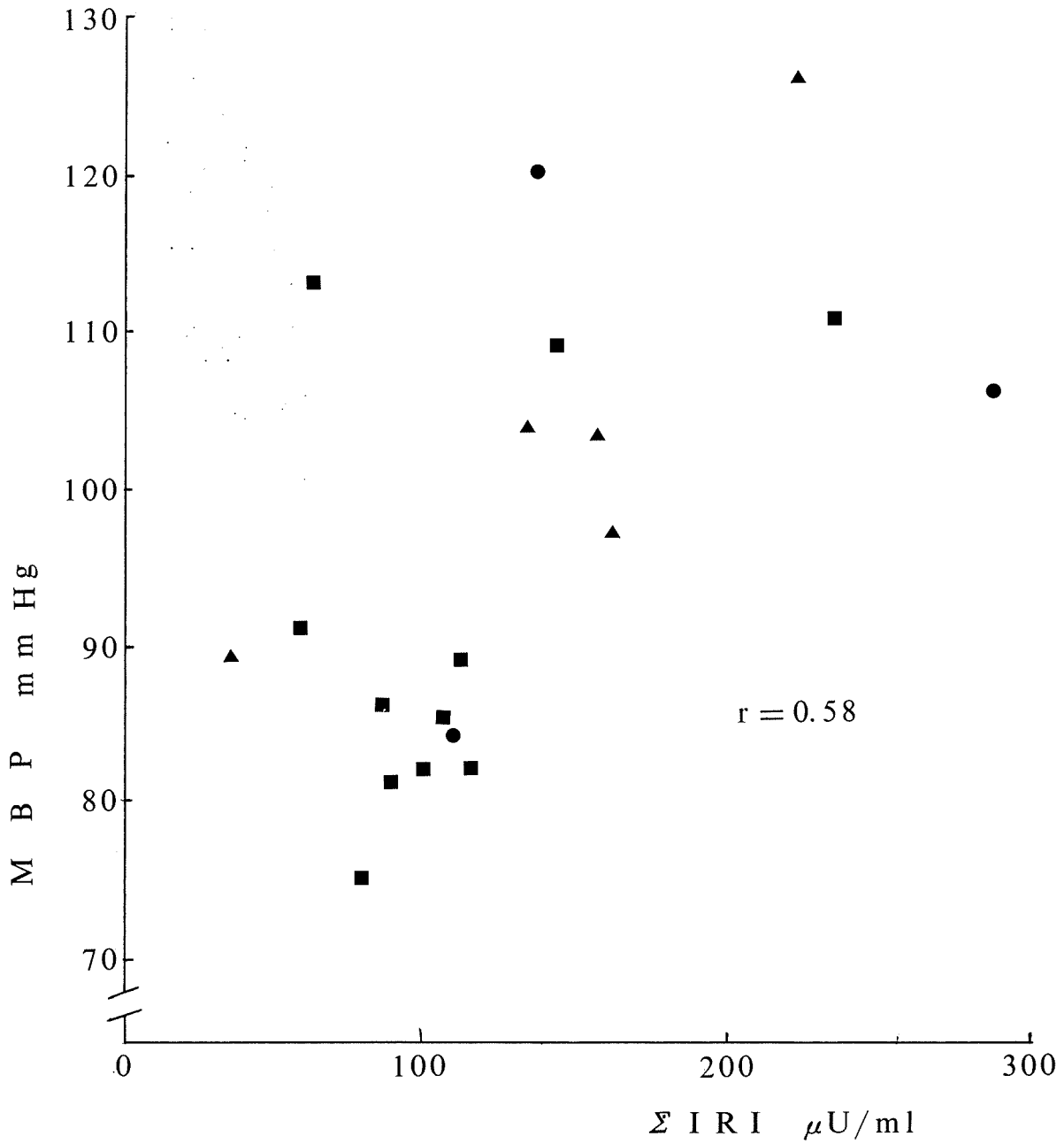


Fig. 2 Correlation between mean blood pressure and sum of plasma insulin level
 MBP : mean blood pressure, Σ IRI : sum of plasma insulin at 0, 30, 60, 120, and 180 min
 ● acromegalics with normal glucose tolerance
 ▲ acromegalics with impaired glucose tolerance
 ■ diabetic acromegalics
 Significant correlation was observed between MBP and Σ IRI ($r = 0.58$, $p < 0.02$).

Summary

Levels of plasma growth hormone (GH) and plasma insulin (IRI) were measured in 19 untreated acromegalic patients (aged 25-69 years) during the 75g oral glucose tolerance test. No significant correlation was observed between mean blood pressure (MBP, diastolic plus one-third pulse pressure) and basal GH, Σ GH (sum of plasma GH at 0, 30, 60, 120 and 180 min) or basal IRI. However, significant correlation was observed between MBP and IRI at 120 min ($r=0.57$, $p < 0.02$) or Σ IRI (sum of plasma insulin at 0, 30, 60, 120 and 180 min, $r=0.58$, $p < 0.02$). These results suggest that hyperinsulinemia may be involved in an increase of blood pressure in active acromegalics.

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