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Diabetologia

Letter to the editor

Patients with insulinoma show insulin resistance in the absence of arterial hypertension

Dear Sir,

Hypertension and Type 2 (non-insulin-dependent) diabetes mellitus are associated with obesity [1, 2]. Hypertension is more frequently seen in diabetic than in non-diabetic subjects [3]. In addition, hyperlipidaemia is commonly found in both diabetic [4] and hypertensive subjects [5]. Modan et al. [6] first suggested that hyperinsulinaemia is the common element accounting for obesity, Type 2 diabetes, and hypertension. Since all three conditions are characterized by insulin resistance [7, 8], it has been hypothesized that hyperinsulinism, through insulin resistance, is the key mechanism eventually leading to cardiovascular disease [9, 10]. However, obesity, Type 2 diabetes, and hypertension all have a strong genetic, familial background. To address the possible role of pure, non-genetically determined hyperinsulinaemia in the development of hypertension, we evaluated blood pressure in 13 patients with surgically-confirmed insulinoma and in six patients with non-tumoural hypoglycaemia and hyperinsulinaemia. Insulin resistance (M/I = glucose metabolized divided by prevailing insulin levels) was evaluated during a 24-h fasting period in 16 of the above patients (10 with insulinoma, six with non-tumoural hypoglycaemia) [11] and during a euglycaemic hyperinsulinaemic clamp in three patients with insulinoma [12]. Blood pressure was measured twice a day during the hospitalization period, and for each patient the mean value was calculated. Only three patients were hypertensive, and two of them had family history of hypertension. Figure 1 shows that in the 16 patients studied during the 24-h fasting period there was a direct relationship between serum insulin levels and insulin resistance ($p < 0.001$); on the contrary, there was no relationship between blood pressure and insulin levels or between M/I index and blood pressure; insulin levels were significantly higher (43.5 ± 4.77 vs 10.8 ± 1.17 μU/ml, $p < 0.01$), and the M/I index was significantly lower (0.04 ± 0.003 vs 0.12 ± 0.02, $p < 0.01$) in insulinoma patients than in patients with non-tumoural hypoglycaemia [11].

Thus, only three out of 19 hyperinsulinaemic patients (15.8%) were hypertensive and the percentage is reduced to 1 of 19 (5.3%) if patients with familial history of hypertension are excluded. This figure does not exceed that anticipated for the general population. These results indicate that in the absence of a genetic trait for hypertension or for Type 2 diabetes, pure hyperinsulinaemia is associated with insulin resistance but not with hypertension. This is in agreement with two recent reports [13, 14]. In conclusion, either pure, non-genetically determined hyperinsulinaemia plays little or no role in the genesis of hypertension, or it takes a long time to show an effect.

Yours sincerely,

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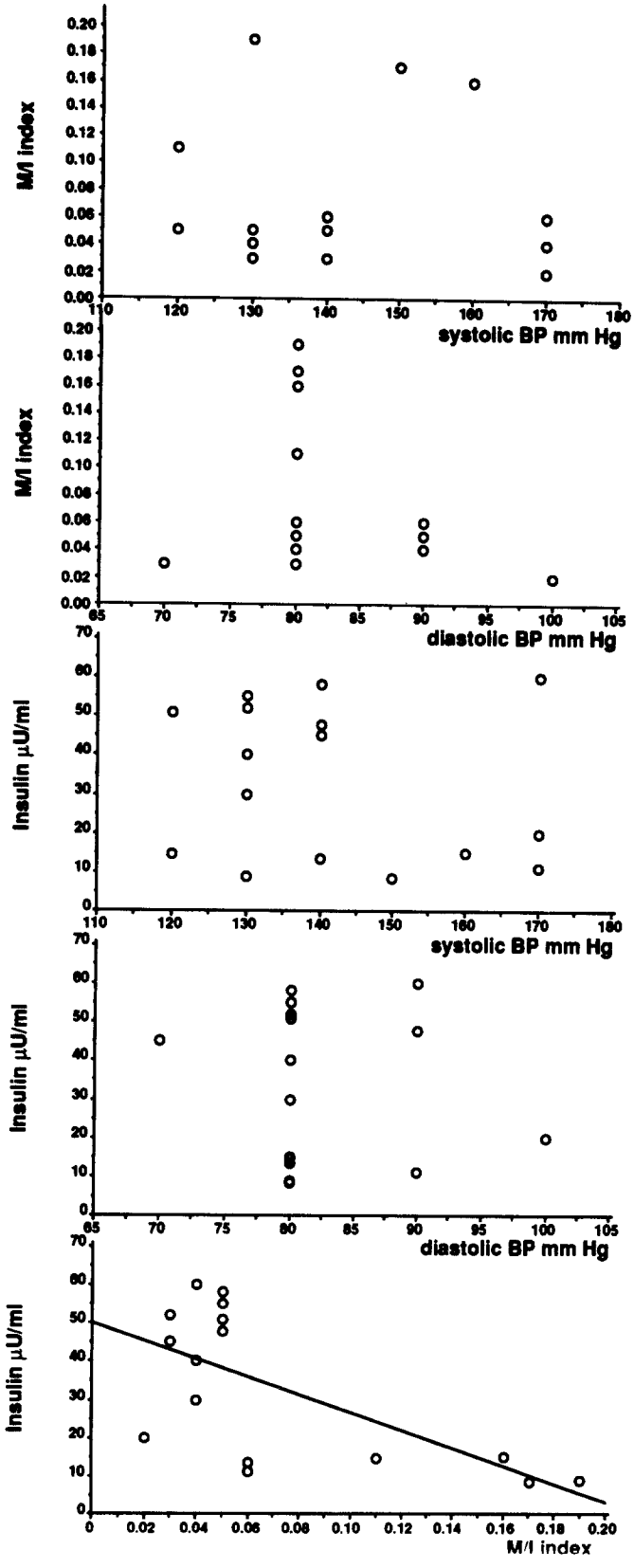

Fig. 1. Pair-wise relationships between insulin resistance (M/I index) and systolic ($r = 0.24$, NS) or diastolic ($r = 0.22$, NS) blood pressure (BP, mm Hg); between insulin levels (μU/ml) and systolic ($r = 0.20$) or diastolic ($r = 0.28$) BP; between insulin levels and the M/I index ($r = 0.65$, $p < 0.001$) in 16 patients with insulinoma or with non-tumoural hypoglycaemia studied during a 24-h fasting period. Each circle represents an individual patient

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