Obesity Does Not Modulate Insulin Secretion in Indian Patients with Non-insulin-dependent Diabetes in the Young

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The insulin response to a 100-g oral glucose load was studied in 40 obese (percent desirable weight ≥ 120%) and 40 nonobese (<120%) age- and sex-matched Indian patients with non-insulin-dependent diabetes in the young. There were no significant differences between the obese and nonobese patients with respect to their insulin and glucose responses. Thus, it appears that obesity does not exert a significant modulating effect on insulin secretion in patients with fasting hyperglycemia. DIABETES CARE 7: 77–79, JANUARY–FEBRUARY 1984.

In previous communications we have recorded that while insulin-dependent diabetes mellitus is rare in the South African Indian population, non-insulin-dependent diabetes in the young (NIDDY) is not uncommon.[1–5] NIDDY is characterized by an early age of onset (14–34 yr), lack of insulin dependence, and a strong familial aggregation (84% of patients have a positive family history, 75% a diabetic parent, 8% three-generation transmission of diabetes).[3–5] However, in sharp contrast to the other reports on NIDDY in which obesity is a rarity,[6] 50% of Indian patients with NIDDY are obese.[3,5] Furthermore, in response to a 100-g oral glucose challenge the patients with NIDDY displayed a delayed and attenuated insulinemic response when compared with nondiabetic controls; this hypoinsulinemia was evident by lower mean insulin responses, a lower area under the insulin curve, and decreased insulin-glucose ratios.[3,5] In this study the insulin response to an oral glucose load was compared between obese and nonobese Indian patients with NIDDY.

PATIENTS AND METHODS

The term NIDDY was adopted in preference to MODY in this communication as recommended by Keen for the new classification of diabetes.[7]

The clinical characteristics of the patients with NIDDY have been detailed previously.[3–5] Briefly, all patients had onset of symptomatic diabetes before the age of 35 yr and all had been aketonuric and asymptomatic for a minimum period of 1 yr with diet and oral hypoglycemic agents as sole therapy. While 28 nonobese patients were either on glibenclamide (Daonil, Hoechst, South Africa) or chlorpropamide (Diabinese, Pfizer, South Africa) in combination with phenformin (Insoral TD, Warner, South Africa), 32 obese patients were on a similar regimen. The remaining patients in both groups were either on glibenclamide (Daonil) or chlorpropamide (Diabinese). Eighty Indian patients with NIDDY who had no evidence of hepatic, renal, or thyroid dysfunction as determined by clinical examination and standard laboratory technique were chosen for this study. Percent desirable weight (PDW) was calculated from the medium frame ideal body weight estimates of the Society of Actuaries, and obesity was defined as a PDW ≥ 120.[8] Informed consent was obtained from all participants in this study. Precautions undertaken before glucose tolerance testing have been described previously.[3] After an overnight fast of 12–14 h, samples were obtained for glucose and insulin assays. Thereafter, 100 g of glucose was administered orally and further samples obtained at 30, 60, 120, and 180 min. Plasma glucose levels were measured by the ferricyanide method on the Technicon Autoanalyzer (Tarrytown, New York), which incorporated a dialysis step to remove non-glucose reducing substances. Serum immunoreactive insulin levels were determined by a radioimmunoassay technique in which the specific insulin antibody is covalently coupled to a solid phase (Pharmacia Diagnostics, Uppsala, Sweden). The intra- and interassay coefficients of variation for the glucose assay were 1.7% and 2.3%, respectively, while the intra- and interassay coefficients of variation of the insulin assay were 4.4% and 4.6%, respectively. The areas under the glucose and insulin curves were calculated according to Chiles and Tzagournis.[9] All data are expressed as mean ± SEM unless stated otherwise. Sta-

tistical analyses included the Mann Whitney U test and Pearson's correlation coefficient (log transformation of data). Significance was defined at the 5% level using two-tailed tests of significance.

RESULTS

As is evident from Table 1, 50% of the patients studied are obese. While the age, duration of diabetes, and sex distribution of these obese and nonobese subgroups are virtually similar, the PDW of the two subgroups are significantly different.

There were no significant differences between the two subgroups with regard to their mean glucose and insulin responses (Table 2). In addition, the computed areas under the glucose and insulin curves were not significantly different. Furthermore, the correlation between the fasting insulin concentration and PDW was not significant ($r = 0.14$; $P > 0.1$).

DISCUSSION

The finding that obesity is a major phenotypic manifestation in Indian patients with NIDDY is similar to the findings reported in young Pima Indians.[10] However, unlike the present report, a significant number of the young Pima Indians were ketosis prone and insulin dependent.

Obesity is usually associated with hyperinsulinism (fasting and stimulated) in normal individuals and those with impaired glucose tolerance.[11,12] However, in the present study obesity was not a significant factor modulating insulin secretion for there were no significant differences between the responses of the obese and the nonobese subgroups. Although no differences were observed at 180 min, insulin and glucose concentrations had not reached baseline values and, therefore, differences might have been observed if sampling had been carried out over a longer period. This finding accords with the experience of Reaven et al.[13] who failed to demonstrate any difference in insulin secretion and insulin action between obese and nonobese patients with non-insulin-dependent diabetes mellitus (NIDDM) matched for severity of diabetes. It would appear that in patients with significant hyperglycemia the effect of obesity on insulin secretion is overridden and a hypoinsulinemic response supervenes, reflecting an exhausted and inadequate secretory capacity of the beta cells.

Thus, while obesity might be a significant factor in precipitating genetically predisposed Indian patients with NIDDY into the symptomatic diabetic state, its effect on the metabolic aberrations in these patients is not evident. Further support for this proposition is that obesity has no effect on the disturbances in lipid and lipoprotein metabolism or other hormonal responses in NIDDY.[5,14]

TABLE 1
Salient clinical characteristics of Indian patients with NIDDY

	Obese		Nonobese
Number	40		40
Male:female	8:32		6:34
Age	34.3 yr (16–53)	*	31.7 yr (14–55)
Duration of diabetes	6.1 yr (1–27)	*	5.7 yr (1–32)
Percent desirable weight	139.5% (120–171)	†	104.5% (86–119)

Data are expressed as mean and (range).
*Denotes $P > 0.05$.
†Denotes $P < 0.001$.

TABLE 2
The glucose and insulin responses to a 100-g oral glucose load ($\chi \pm SE$)

	Obese		Nonobese
Glucose responses (mmol/L)			
Basal	12.6 ± 0.7	NS	11.9 ± 0.7
30 min	16.8 ± 0.5	NS	16.1 ± 0.6
60 min	20.2 ± 0.8	NS	19.8 ± 0.8
120 min	21.6 ± 0.9	NS	20.7 ± 0.9
180 min	19.7 ± 1.1	NS	19.0 ± 1.1
Glucose area (mol/180 min)	3.5 ± 0.2	NS	3.4 ± 0.2
Insulin responses (mU/L)			
Basal	26.2 ± 1.9	NS	23.0 ± 1.9
30 min	40.3 ± 2.1	NS	35.1 ± 3.4
60 min	45.2 ± 4.4	NS	40.4 ± 3.4
120 min	50.8 ± 4.5	NS	45.3 ± 5.3
180 min	48.8 ± 4.6	NS	41.1 ± 5.1
Insulin area (mU/180 min)	8.2 ± 0.7	NS	7.2 ± 0.8

NS = not significant.

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