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Serum immunoreactive insulin responses to a glucose load in Asian Indian and European Type 2 (non-insulin-dependent) diabetic patients and control subjects

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Summary. The serum immunoreactive insulin response to an oral glucose load was estimated in 15 Asian Indian and 29 European non-diabetic subjects, and in 45 Asian Indian and 72 European Type 2 (non-insulin-dependent) diabetic patients. In the non-diabetic group, basal insulin values were higher in the Asian Indians than the Europeans (16.7 ± 3.0 vs. 6.9 ± 0.7 mU/l, $p < 0.001$), and remained higher throughout the glucose tolerance test. Total insulin response was also higher in the Asian Indians ($p < 0.001$), and linear regression analysis revealed basal insulin, body mass index and race to be important predictors of insulin response. Amongst the diabetic patients, basal insulin values were again higher in the Asian Indians compared with the Europeans (18.0 ± 5.0 vs. 11.5 ± 0.9 mU/l, $p < 0.05$). Total insulin response was also greater ($p < 0.01$). Linear regression analysis revealed the basal insulin value to be the only significant predictor of insulin response. The results demonstrate higher insulin levels in Asian Indians than Europeans in both normal subjects and Type 2 diabetic subjects. The insulin response to a glucose load is also greater in the Asian Indians. In the control subjects, ethnic differences contribute to this response, whereas in the diabetic patients this is a function of the elevated basal insulin values of the Asian Indians.

Key words: IRI, Type 2 diabetes, Asian Indians, Europeans, ethnic variation.

The prevalence of diabetes in migrant Asian Indian populations has been shown to be extremely high [1, 2]. A recent survey in Southall, West London showed that, in the UK, the prevalence of 'known' diabetes in those originating from the Indian subcontinent is three-fold higher compared to the local European population [3]. As a first step in elucidating differences between the two populations, we looked at serum immunoreactive insulin (IRI) responses to a glucose load in Asian Indian and European diabetic patients.

Subjects and methods

Subjects

The subjects were both obese and non-obese diabetic patients seen at the Hammersmith Hospital, London between 1 January 1981 and 31 December 1984. There were 45 Asian Indian and 72 European Type 2 (non-insulin-dependent) diabetic patients. None of the patients in the study had had ketosis at any time. All were tested within a year of first diagnosis. None of the patients had ever received insulin. Ten Indian and 8 European diabetic patients had received oral hypoglycaemic agents for a period of 1 to 4 months prior to the study, but these were withdrawn for 2 weeks prior to the test. Forty-four percent of Indian patients and 30% of European patients had a first-degree relative with diabetes.

Control subjects were healthy, non-diabetic, obese and non-obese subjects of both Asian Indian and European origin. All had normal glucose tolerance tests, and none had a family history of diabetes. Control subjects were either volonteers from hospital staff or those who had been tested to rule out diabetes and were found to have normal glucose tolerance.

The Asian Indian diabetic patients and control subjects were from the Punjab, Gujerat, Pakistan or Bangladesh. All European patients and control subjects were from western Europe. Clinical details of the study groups are shown in Table 1. The body mass index (BMI) was calculated according to the formula (weight in kg)/(height in metres)^2. Subjects over 65 years of age, and those with any intercurrent illness, were excluded. None of the study subjects were anaemic and none were taking any drugs known to intefere with carbohydrate metabolism. All diabetic patients and control subjects had normal liver and kidney function tests as shown by normal serum bilirubin, SGOT, SGPT, serum proteins, albumin: globulin ratios and normal plasma urea and creatinine levels. Informed consent was obtained from all patients and control subjects, and the approval of the hospital ethical committee was obtained.

Table 1. Details of the study groups

	Sex (m:f)		Age (years)	Mean duration of diabetes (months)	BMI (kg/m^2)
Control subjects					
Asian Indians ($n=15$)	8	7	42.3 ± 3.2	–	25.5 ± 1.4
Europeans ($n=29$)	15	13	44.5 ± 2.5	–	24.2 ± 0.8
Diabetic patients					
Asian Indians ($n=45$)	33	12	51.0 ± 1.6	10	25.1 ± 0.6[a]
Europeans ($n=72$)	50	22	53.1 ± 1.0	8	27.0 ± 0.6[a]

[a] $p < 0.05$

Table 2. Plasma glucose in the study groups

	Plasma glucose (mmol/l)				
	0′	30′	60′	90′	120′
Control subjects					
Asian Indians	5.4±0.2	7.9±0.3	8.6±0.4	7.6±0.4[a]	6.0±0.3
Europeans	4.9±0.1	7.7±0.3	7.6±0.3	6.6±0.3[a]	5.3±0.2
Diabetic patients					
Asian Indians	10.9±0.5	15.2±0.6	18.6±0.7	19.2±0.7	18.3±0.7
Europeans	11.8±0.4	16.7±0.5	19.4±0.5	19.6±0.6	18.0±0.6

[a] $p < 0.05$

Methods

Biochemical investigations. Oral glucose tolerance tests (GTT) were performed using 75 g glucose load. National Diabetes Data Group recomendations were used for performing GTT, for interpretation of the results and for classification of patients into Type 1 (insulin-dependent) and Type 2 (non-insulin-dependent) diabetes [4]. During the GTT, samples for measurement of immunoreactive insulin (IRI) were taken at 0, 30, 60, 90 and 120 min. The serum samples were kept frozen at -20 °C until the hormone assays were performed. Plasma glucose was estimated by the Technicon SMA II C Autoanalyser (Technicon Corporation, Tarrytown, NY, USA). IRI was estimated by double antibody radioimmunoassay [6]. Intra- and interassay coefficients of variation were 8% and 11% respectively. The lower detection limit of the assay was 2 mU/l. The antibody used had 67% crossreactivity with proinsulin.

Statistical evaluation. All values are expressed as mean ± SEM. All calculations involving IRI were carried out on log transposed data, although unlogged data is shown for the purposes of graphical representation. The area under the insulin curve (Σ IRI) was calculated by adding the logged IRI values at the five time points of the GTT. Student's unpaired t-test was used for comparison of data. In addition, Σ IRI was regressed on basal IRI, age, BMI and race separately for both control subjects and diabetic patients.

Results

Patient characteristics are shown in Table 1. The mean age of the Asian Indians and Europeans was similar in both control and diabetic groups. Amongst the control subjects, mean BMI was similar in both Asian Indians and Europeans, whereas the European diabetic patients had a significantly greater BMI than their Asian Indian counterparts. Mean plasma glucose values in the diabetic patients and in the control subjects are shown in Table 2, with similar values in both Asian Indian and European patients and control subjects.

Mean IRI levels in the control subjects during the GTT are shown in Figure 1. Basal insulin values in the Asian Indians were 16.7 ± 3.0 mU/l and in the Europeans 6.9 ± 0.9 ($p < 0.001$). Significantly higher insulin values were also seen in the Asian Indians compared with the Europeans at the time points indicated in Figure 1. The Asian Indian subjects had significantly greater $\sum$IRI values than the Europeans (345 ± 55 vs. 194 ± 19 mU/l · min, $p < 0.001$). Stepwise linear regression of $\sum$IRI on race, age, BMI, and basal IRI revealed BMI to be the most important predictor of insulin response ($t = 3.5$) followed by basal IRI ($t = 3.15$), with a further contribution by race ($t = 2.33$). Total coefficient of determination (r^2) for these predictors was 63.7%.

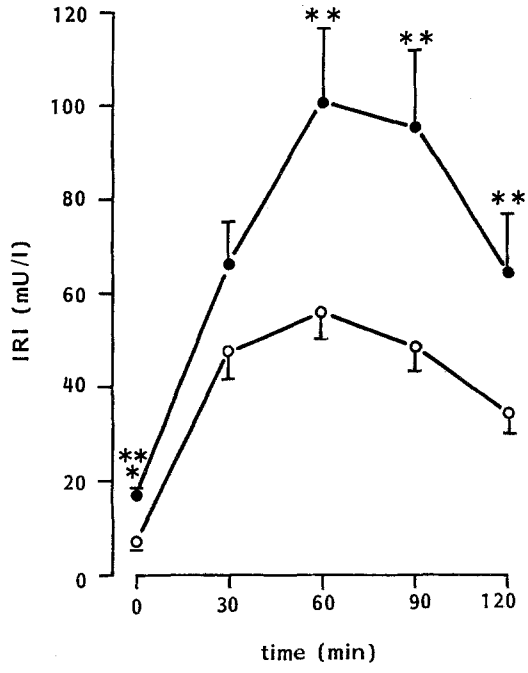

Fig. 1. Mean immunoreactive insulin (IRI) values at the five time points of the glucose tolerance (GTT) in the Asian Indian (●) and European (○) control subjects. $^{**}p < 0.01$; $^{***}p < 0.001$

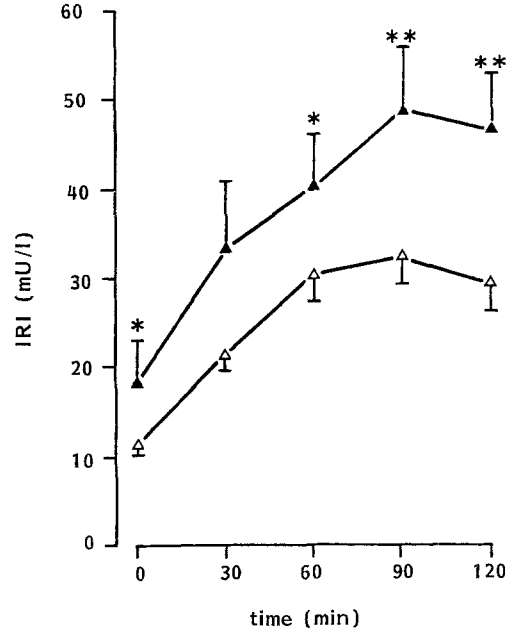

Fig. 2. Mean immunoreactive insulin (IRI) values at the five time points of the glucose tolerance test (GTT) in the Asian Indian (▲) and European (△) diabetic patients. $^{*}p < 0.05$; $^{**}p < 0.01$

Figure 2 shows the mean IRI levels in the diabetic patients. Basal insulin values in the Asian Indian patients were 18.0 ± 5.0 mU/l and in the European patients 11.5 ± 0.9 mU/l ($p < 0.05$), with further significant differences at the time points indicated in Figure 2. $\sum$IRI was also significantly greater in the Asian Indian patients than the Europeans (187 ± 29 vs. 125 ± 12 mU/l · min, $p < 0.01$). Stepwise linear regression of $\sum$IRI on age, basal IRI, BMI and race revealed that basal IRI

was the only significant predictor of insulin response ($t = 16.4$, $r^2 = 70.1\%$).

Discussion

This study shows significant differences in plasma insulin levels of Asian Indians and Europeans. Basal IRI was significantly higher in Asian Indians, whether normal subjects or non-insulin dependent diabetic patients. Regarding the insulin response to a glucose load, the Asian Indians again had a greater IRI response than the Europeans, but statistical analysis suggests that this may represent similar responses in the two ethnic groups superimposed on differing basal levels. Only in the normal subjects did race contribute to the IRI response to glucose. Clinical characteristics of the Asian Indian and European subjects were similar, suggesting a true variation in basal insulin levels between the two ethnic groups. The significantly greater BMI in the European diabetic patients compared with the Asian Indians might have been thought to lead to greater IRI values in European patients. This did not, however, appear to influence the results on statistical analysis.

Ethnic variability in IRI response has been reported in other populations. Higher insulin concentrations after glucose load were reported in both normal and diabetic Navajo Indians compared with Pennsylvania Amish of similar weight [6]. Aronoff and coworkers [7] reported that stimulated plasma insulin concentrations in the Pima Indians were two to three times higher than in the White population. Pima Indians also have higher serum gastrin levels [8] and pancreatic polypeptide responses [9] than Europeans. Recently Zimmet et al. [10] showed that Micronesians had higher plasma IRI concentrations than Polynesians. To our knowledge, there is only one study comparing IRI responses of Asian Indian and European non-diabetic subjects [11] and none comparing Asian Indian and European diabetic patients. Rubenstein et al. [11] reported that while non-diabetic Asian Indian subjects had higher IRI values than matched African subjects, there was no difference between Indians and Europeans. However, their study was based on very small numbers and the body weights of the two groups were not identical. Finally, since the glucose load used was 1 g/kg body weight, the Asian Indian patients obviously received a smaller glucose load than the Europeans. These factors might explain the differences between their study and the present report.

Recent studies have confirmed that both young and old Asian Indian diabetic patients have higher IRI values than matched groups of African diabetic patients [12]. A study from India on pancreatic B-cell function in maturity onset diabetes of the young (MODY) suggested that the IRI values seen in these patients were much higher than those reported in western countries [13]. However, no comparison was made with European patients. The present study, dealing with a population of Asian Indian and European patients studied in the same clinic by the same laboratory method, confirms that Asian Indian patients do have greater insulin secretion than European patients.

The high immunoreactive insulin levels seen in Asian Indian patients resemble those seen in Pima Indians. The mechanisms responsible for this are not clear. Studies using the euglycaemic clamp technique are now in progress to assess insulin resistance in Asian Indian and European diabetic patients. Differences in insulin clearance and hepatic extraction of insulin might also exist. Simultaneous assays of IRI and C-peptide might throw further light on this question, and such a study is now in progress.

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