Diabetologia 18, 347–348 (1980)

Diabetologia

Letters to the Editor

Heterogeneity of Plasma IRI Responses in Patients with IGT

Dear Sir:

In their editorial, Dr. Keen and his colleagues have published new diagnositic criteria for the oral glucose tolerance test [1]. Following their criteria, we have rearranged our collected data on plasma immunoreactive insulin (IRI) and blood glucose (BG) obtained during 100 g oral glucose tolerance tests (O-GTT) performed in subjects who had visited our clinic. ΣBG shown in the Figures are the sums of the six BG values obtained before administration of glucose and at 30, 60, 90, 120 and 180 min after 100 g oral glucose. All subjects shown in Figure 1 were classified as IGT by the combined use of fasting and two hour BG levels from the O-GTT [1]. The subjects in group A (Fig. 1) were those whose fasting blood glucose were above 140 mg/100 ml initially, however, who were finally classified as IGT after a certain period of treatment. Group A patients had no conditions such as liver disease, hyperthyroidism, gastrectomy or steroid treatment which are known to impair glucose tolerance. Compared to patients with these above mentioned conditions, group A patients showed lower IRI responses to a glucose load.

In another portion of these studies, we examined data on 742 patients who had initially visited our diabetes clinic from March, 1965 to April, 1968. A total of 650 cases presented complete data on plasma IRI and BG levels from 100 g O-GTT. Of the 131 cases who were defined as having diabetes mellitus (DM) according to the criteria of Keen et al. [1], and whose fasting blood glucose values distributed between 120 and 139 mg/100 ml, 120 cases, or 91.6%, fell into the low IRI response zone, which we have defined as diabetic IRI response [2]. Thus in moderate and severe impairment of glucose metabolism, the insulin secretory response after a glucose load is recognized to be impaired.

There exists, however, some controversy with regard to insulin responses in mild glucose intolerance. There are reports that insulin response to glucose is decreased in patients with mild impairment of glucose tolerance, if the influences of hyperglycaemia and obesity are taken into account [3, 4]. Some reports claim, however, that insulin response during GTT is not decreased but may be enhanced in mild glucose intolerance [5, 6]. We have therefore ana-

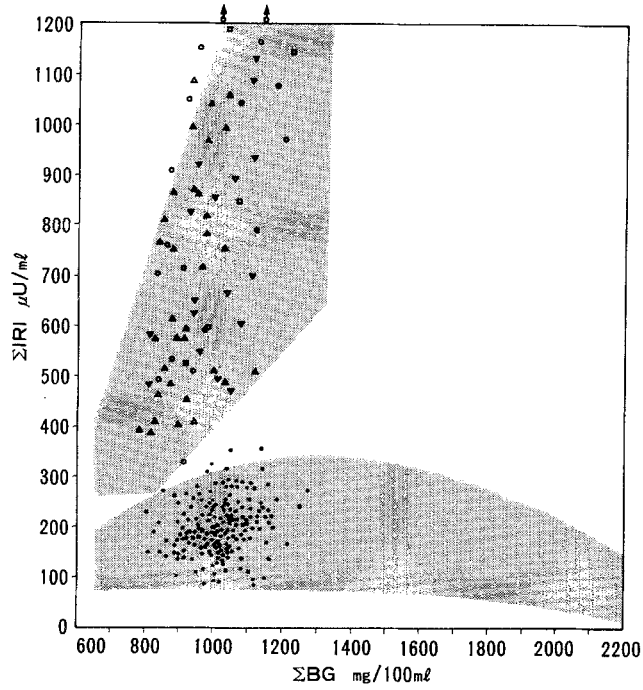

Fig. 1. Relationship between ΣBG and ΣIRI during 100 g O-GTT in IGT patients. ○ steroid treatment, △ liver disease (liver cirrhosis, acute and chronic hepatitis), ▽ hyperthyroidism, ⊐ gastrectomy. Group A patients (●) were those whose fasting blood glucose had been above 140 mg/100 ml before O-GTT was performed, and who had no known pathological conditions mentioned above. Upper shaded area: non-diabetic IRI response zone; lower shaded area: diabetic IRI response zone (2)

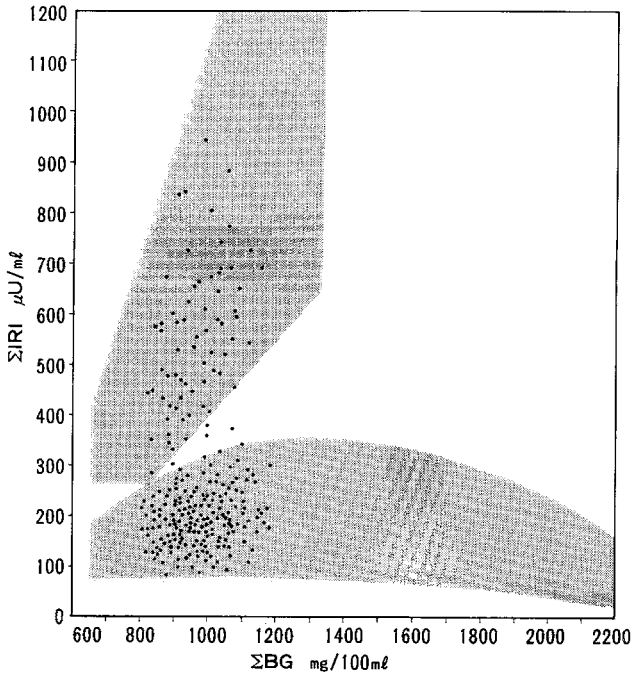

Fig. 2. Relationship between ΣBG and ΣIRI during 100 g O-GTT in IGT patients. Shaded areas are as in Figure 1

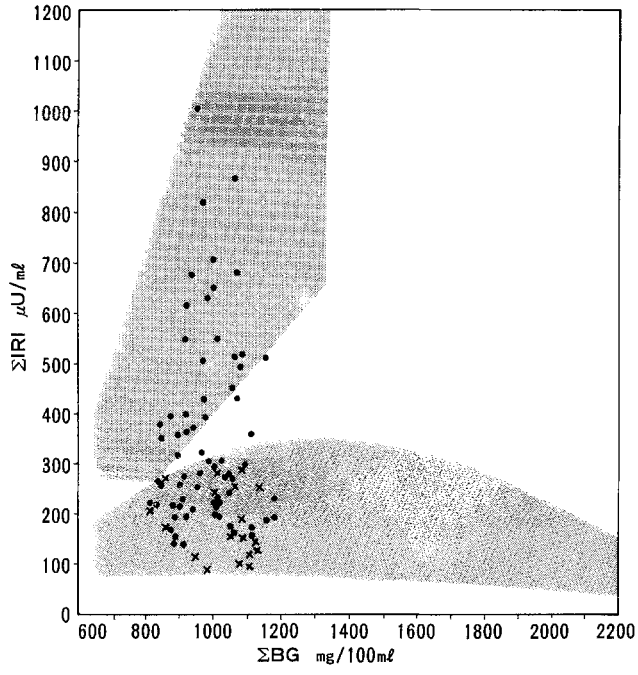

Fig. 3. Relationship between ΣBG and ΣIRI during 100 g O-GTT in IGT patients. All cases were followed at the out-patient clinic for at least ten years. Fasting blood glucose concentration was measured in each case at least once every six months. For some of these, fasting blood glucose exceeded 140 mg/100 ml during a period of follow up: these are indicated by X. Shaded areas are as in Figure 1

lyzed the relationship between ΣBG and ΣIRI during O-GTT in 243 subjects who fit the criteria for IGT (1). Diabetic IRI response was demonstrated in 171 cases, 70.4%, while the remaining showed higher IRI responses (Fig. 2). Thus, the patients with IGT are heterogenous as far as their insulin response to glucose is concerned.

We have also thought it worthwhile to analyze subjects with IGT in a prospective study. Seventy one of the 243 subjects with IGT at their first visit were subsequently followed for more than 10 years. During this period, fasting blood glucose concentrations was measured in each case at least once every six months. The patients were diagnosed as having developed clinical diabetes when their fasting blood glucose value rose to 140 mg/100 ml or greater. We found 18 such cases, all of whom belonged to the low insulin response group at their initial visit (Fig. 3).

In conclusion, patients with IGT are heterogeneous; some subsequently developed clinical diabetes whereas others did not. A low insulin response after an oral glucose load appears to be a reliable index for predicting which patients with IGT are likely to develop clinical diabetes mellitus during follow up.

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References

1. Keen H, Jarrett RJ, Alberti KGMM (1979) Diabetes mellitus: A new look at diagnostic criteria. Diabetologia 16: 283–285
2. Kosaka K, Akanuma Y, Hagura R, Kuzuya T (1979) Plasma insulin response during the 100 g glucose tolerance test in diabetic patients. International Congress Series 468: Proinsulin, insulin, C-peptide. Excerpta Medica, Amsterdam, p 283–293
3. Seltzer HS, Allen EW, Harron AJ Jr, Brennan MT (1967) Insulin secretion in response to glycemic stimulus; Relation of delayed initial release to carbohydrate intolerance in mild diabetes mellitus. J Clin Invest 46: 323–335
4. Perley MJ, Kipnis DM (1967) Plasma insulin response to oral and intravenous glucose – studies in normal and diabetic subjects. J Clin Invest 46: 1954–1962
5. Jackson WPU, van Mieghem W, Keller P (1972) Insulin excess as the initial lesion in diabetes. Lancet I: 1040–1044
6. Reaven GM, Berstein R, Davis B, Olefsky JM (1976) Nonketotic diabetes mellitus: Insulin deficiency or insulin resistance? Am J Med 60: 80–88

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