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Short Communications

Failure of Fasting to Influence the GIP Response to Oral Glucose in Non-obese Human Subjects

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Summary. The plasma GIP response to an oral 50 g glucose tolerance test has been compared in eight non-obese human subjects after 12 and 36 h of fasting. Basal plasma GIP and basal plasma insulin concentrations were similar after 12 and 36 h of fasting. Basal blood glucose was lower after 36 h fasting than after 12 h fasting ($p < 0.0125$). After 36 h fasting the oral glucose tolerance test stimulated higher blood glucose concentrations at 60, 90 and 120 min ($p < 0.0125$) and higher plasma insulin concentrations at similar time points ($p < 0.05$), but stimulated plasma GIP concentrations were similar after 12 and 36 h fasts. These findings show that the increased insulinotrophic effect of oral glucose after 36 h fasting in non-obese subjects is not due to an associated augmentation of the glucose-induced GIP response.

Key words: GIP, insulin, glucose, fasting.

Worsening of glucose tolerance after fasting was first described by Lehmann in 1873 [1] and Johansson in 1909 [2] suggested that the body has a reduced ability to oxidise administered glucose after a fast.

The capacity for the insulin response to glucose appears to be maintained after a fast [3] and it has been suggested that the delay in insulin secretion occurring, might relate to a stimulus delay [4].

As gastric inhibitory polypeptide or glucose-dependent insulinotrophic polypeptide (GIP) has been proposed as the major incretin for insulin release under physiological conditions [5], it seemed reasonable to assess a possible role for the glucose-augmented GIP response in the hyperinsulinaemia induced by short-term fasting in non-obese human subjects.

Methods

Eight non-obese subjects (three male and five female, age range 17–41 years; body mass index < 29 kg/m^2) consumed a diet containing 300 g of carbohydrate for 3 days. After a period of 12 h fasting, an oral glucose tolerance test with 50 g of glucose was performed and peripheral venous blood samples were collected at 0, 30, 60, 90 and 120 min after the oral glucose. The subjects were maintained on a 300-g carbohydrate diet for at least a further 3 days. They were then fasted for 36 h and a further oral glucose tolerance test was carried out.

Venous blood was withdrawn into ice-cold heparinized tubes. The plasma was separated by centrifuging at 1 000 *g* for 20 min at 4 °C and then divided for hormone estimation. The samples for insulin estimation were stored at −20 °C before assay.

Insulin was measured by radioimmunoassay, the details of which have been published [6]. Plasma GIP was measured by the method of Alam [7]. Natural porcine GIP (donated by J Brown, University of British Columbia, Vancouver, Canada) was used for standards, antibody production and radioactive labelling of GIP. A plasma extraction system was used [8]. GIP was labelled with ^{125}I (Radiochemical Centre, Amersham, Bucks, UK) and purified using ion-exchange chromatography. Antibody raised in sheep (S100) was used in a final dilution of 1:600. The sensitivity of the assay is in the order of 5 ng/l and cross-reactivity with related peptides, secretin, glucagon and vasoactive intestinal polypeptide (gift from V Mutt, Karolinska Institute, Stockholm, Sweden) was in the order of 1:10000 on a weight basis.

Blood glucose was measured by enzymic fluorimetric continuous flow assay [9].

Statistical Analysis

The results are expressed as mean ± SEM. Student's t-test was applied to paired and unpaired values with the level of significance set at $p < 0.05$.

Results

After the 36-h fast, the basal blood glucose fell (3.8 ± 0.1 versus 4.2 ± 0.1 mmol/l after the 12-h fast, $p < 0.0125$) but in the oral glucose tolerance test the 60-min (8.2 ± 0.4 versus 6.4 ± 0.4 mmol/l, $p < 0.0125$), the 90-min

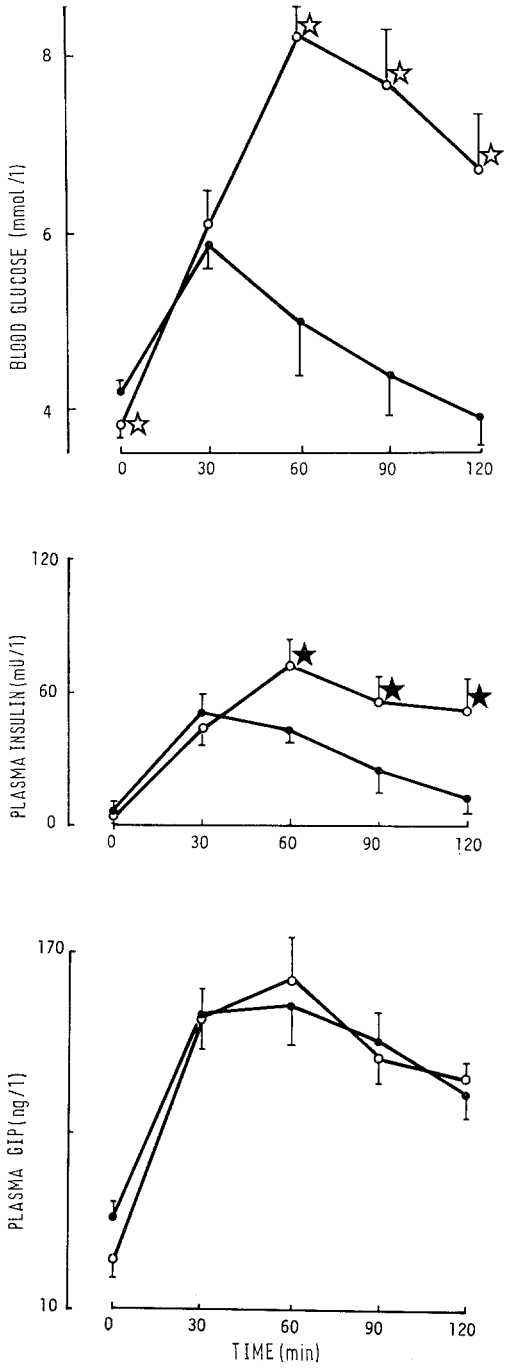

Fig. 1. Comparison of the blood glucose, plasma insulin and plasma GIP responses (mean ± SEM) to oral glucose in eight non-obese subjects after fasts for 12 h ● and 36 h ○. ☆ $p < 0.0125$ ★ $p < 0.05$

(7.7 ± 0.6 versus 5.5 ± 0.5 mmol/l, $p < 0.0125$) and the 120-min (6.7 ± 0.7 versus 4.7 ± 0.3 mmol/l, $p < 0.0125$) blood glucose levels were higher than after the 12 h fast (Fig. 1).

After the 36-h fast there was no change in basal plasma insulin (7.2 ± 3.1 versus 5.4 ± 1.0 mU/l) but in the glucose tolerance test the 60-min (72.5 ± 14.0 versus 43.4 ± 4.4 mU/l, $p < 0.05$), the 90 min (56.6 ± 12.8 versus 24.1 ± 8.8 mU/l, $p < 0.05$) and the 120 min (51.8 ± 16.2 versus 13.1 ± 5.1 mU/l, $p < 0.05$) plasma insulin responses were higher than after the 12-h fast (Fig. 1).

After both 12 and 36-h fasts, basal plasma GIP concentrations were similar (53.1 ± 7.3 versus 34.4 ± 9.0 ng/l respectively), and in the oral glucose tolerance test the 30-min (143.8 ± 13.0 versus 142.5 ± 17.5 ng/l) the 60-min (147.9 ± 16.0 versus 158.8 ± 20.4 ng/l), the 90-min (130.9 ± 14.5 versus 125.6 ± 13.8 ng/l) and the 120-min (107.9 ± 12.0 versus 113.6 ± 7.8 ng/l) plasma GIP concentrations were also similar (Fig. 1).

Discussion

The effect of starvation on the GIP response to oral glucose or a test meal is controversial. Willms et al have reported a fall in the oral glucose and test meal stimulated GIP response after 21 days' starvation in obese subjects [10]. However, as improvements in glucose tolerance and reductions in stimulated insulin levels accompanied the decreased GIP responses, the significance of these data in comparison with our results is unclear. More recently, another group has found an increased 2-h GIP response to a test meal after a 34-h fast in lean, healthy subjects [11]. These findings suggest that fasting in non-obese subjects may influence the GIP response to a test meal containing fat, protein and carbohydrate, but does not influence the response to oral glucose alone. This conclusion is in accord with Williams et al [12] who were also unable to demonstrate any change in glucose-stimulated GIP secretion after a 112-h fast in dogs. In summary, this study shows that in non-obese subjects the hyperinsulinaemia elicited by oral glucose after fasting is not due to any associated augmentation of the glucose-induced GIP response.

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