DIETARY GUAR GUM SUPPLEMENTATION DOES NOT MODIFY INSULIN RESISTANCE IN GROSS OBESITY

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Obesity is characterized by impaired glucose tolerance and hyperinsulinemia and is considered an insulin resistant state[2]. Dietary guar gum supplementation reduces blood glucose and carbohydrate-induced plasma insulin response in healthy subjects[5,6] and in type II diabetics[6-8]. In order to evaluate whether guar is able to reduce hyperinsulinemia and insulin resistance in gross obesity, we studied *in vivo* and *in vitro* insulin sensitivity after dietary guar supplementation.

MATERIALS AND METHODS

Nine obese female patients, >50% ideal body weight (Geigy Tables), aged 32 ± 6 years, with no family history of diabetes, but with impaired glucose tolerance (NDDG criteria[9]), were treated for 6 weeks with guar (4 + 4 g/day). Since no effects on insulin sensitivity parameters were recorded after treatment (see 'Results'), patients were submitted to a new guar treatment 8 + 8 g/day for 6 weeks after an interval of 3 months; only 6 patients completed this second treatment (3 dropped out because of side effects).

Guar was administered in the shape of a commercial preparation (Guargel®, Guidotti, Pisa, Italy) together with 200 ml of water at meal time (13^{00} and 20^{00}) and was added to the usual diet in order to maintain the body weight constant during the study. Compliance was checked by computing the number of envelopes of guar-dose supplied to each patient before treatment in variable excess and returned at the end of treatment. Patients received no other drugs one month before and during the study.

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At entrance to the study and at the end of each treatment, the following tests were performed starting at 08^{00}, after an overnight fast: 100 ml venous blood sample for determination of total specific insulin binding on circulating monocytes according to BECK-NIELSEN et al.[1]; D-6-3H-glucose (Amersham, U.K.) infusion (0.2 μCi/min for 240 min); euglycemic hyperinsulinemic clamp at ~ 100 μU/ml with human insulin (Humulin®, Eli Lilly Co., Indiana, U.S.A.). Tests were always performed in the first 2 weeks of the menstrual cycle. Informed consent was obtained from all patients before the beginning of the study. Plasma insulin was measured by solid-phase antibody (RIA-Korning Kit, Massachusetts, U.S.A.); glucose production and utilization were measured and calculated as previously reported elsewhere[11]. All values were expressed as means ± SEM and statistical analyses were carried out by Student's *t*-test for paired data.

RESULTS

Body weight values are reported in tab. 1: no significant variation was found between values recorded before study and after each guar treatment. Compliance with treatment was 83% at 4 + 4 g/day and 88% at 8 + 8 g/day. Side effects (flatulence, diarrhea, nausea) were reported during the 4 + 4 g/day period by 2/9 patients and during 8 + 8 g/day period by 6/6 patients.

Values for fasting plasma glucose and insulin, glucose production and glucose utilization (DE FRONZO's M value[3]) are reported in tab. 1: the difference between values recorded after each treatment versus pre-treatment values was not statistically significant for any parameter.

Glucose production during clamp was completely suppressed in all tests. Plasma glucose and insulin levels during clamp were not significantly different in the three series of tests.

Total specific insulin binding was: 2.80 ± 0.20 (pre-treatment), 2.75 ± 0.25 (4 + 4 g/day) and 2.78 ± 0.31% (8 + 8 g/day); the differences between treatment versus pre-treatment values were not statistically significant.

DISCUSSION

Guar gum supplements added to the usual diet at the dose of 8 or 16 g/day for 6 weeks did not modify insulin resistance in our series of grossly, obese patients. In particular, parameters of insulin sensitivity recorded *in vivo* (fasting

	n	body weight (kg)	fasting plasma glucose (mg/dl)	fasting plasma insulin (μU/ml)	fasting glucose production (mg/kg/min)	glucose utilization (mg/kg/min)
pre-treatment	9	101.4 ± 5.4	90.3 ± 2.7	15.2 ± 1.5	2.17 ± 0.33	3.52 ± 0.43
4 + 4 g/day guar	9	100.2 ± 6.2	87.2 ± 2.7	13.5 ± 1.9	2.18 ± 0.18	3.22 ± 0.44
8 + 8 g/day guar	6	100.5 ± 7.0	86.1 ± 3.4	13.7 ± 1.6	2.28 ± 0.14	3.49 ± 0.63
		n.s.	n.s.	n.s.	n.s.	n.s.

Tab. 1 - Means ± SEM of variables measured. The differences between guar treatment and pre-treatment values were evaluated by Student's *t*-test for paired data.

plasma glucose and insulin, glucose production and utilization) or *in vitro* (insulin binding on circulating monocytes) were not significantly changed by guar treatment in this study.

The efficacy of dietary guar gum supplementation (15 g/day for 15 days) in reducing blood glucose and plasma insulin after a carbohydrate meal or OGTT has been reported in a group of type II diabetics[8]. In another group of type II mild diabetics, we observed both a significant reduction of hyperinsulinemia and a decreased *in vivo* and *in vitro* insulin resistance after 6 weeks of dietary guar (4 + 4 g/day) supplementation[12].

Although insulin resistance is also a characteristic feature of type II diabetes[10], the pathogenetic mechanism seems to be different from that of gross obesity. In mild insulin resistance, such as was observed in our type II diabetics[12], the main abnormality is a reduced number of insulin receptors[10]. In patients with severe insulin resistance, as is found in gross obesity, a reduced number of insulin receptors and the post-receptor defect in insulin action coexist, but the latter is the predominant abnormality[10]. Furthermore, reversibility of insulin resistance was reported in obesity when body weight was normalized[2].

The complex relation between obesity and insulin resistance has not yet been completely elucidated[2], but, probably, hyperinsulinemia may not only give rise to loss of insulin receptors, but also to an impairment of post-receptor events[4]. Since a correlation between plasma insulin levels and body weight or insulin receptor concentration[7] has been reported, we could hypothesize that any attempt at reducing insulin resistance in obesity should involve an effort to reduce body weight, thus obtaining a decrease in plasma insulin levels.

In this sense, the reduction of energy intake and physical training could represent a reasonable approach.

The results of this study indicate that dietary guar gum supplementation *per se* is unable to reduce insulin resistance in gross obesity if overweight is maintained constant. This obervation has only pathophysiologic relevance and we cannot exclude that guar could have a rational place in an integrated therapeutic program together with restriction of food intake and systematic physical exercise.

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SUMMARY

Obesity is considered an insulin resistant state. Dietary guar gum supplementation is able to reduce blood glucose and plasma insulin response to a carbohydrate meal. In order to evaluate whether guar is able to reduce hyperinsulinemia and insulin resistance in gross obesity, we studied 9 obese patients, >50% overweight with impaired glucose tolerance before and after 4+4 g/day guar for 6 weeks. Six patients repeated the treatment with 8+8 g/day guar after a 3-month interval. Guar was added to the usual diet in order to maintain the body weight constant. Pre-treatment and post treatment study included: total specific insulin binding on circulating monocytes; 3H-glucose infusion and euglycemic hyperinsulinemic clamp at ~ 100 μU/ml. The differences between post-treatment and pre-treatment values were not significant for any of the parameters studied. Fasting glucose production was: 2.17 ± 0.33 SEM (pre-

treatment) *vs* 2.18 ± 0.18 (4+4 g/day) *vs* 2.28 ± 0.14 (8+8 g/day) mg/kg/min; glucose utilization was: 3.52 ± 0.43 *vs* 3.22 ± 0.44 *vs* 3.49 ± 0.63 mg/kg/min; total specific insulin binding was: 2.80 ± 0.20 *vs* 2.75 ± 0.25 *vs* 2.78 ± 0.31%; body weight was: 101.4 ± 5.4 *vs* 100.2 ± 6.2 *vs* 100.5 ± 7.0 kg. These results indicate that dietary guar gum supplementation *per se* is unable to reduce insulin resistance in gross obesity if overweight is maintained constant.

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