No Glycemic Benefit From Guar Administration in NIDDM

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A randomized crossover study of 5-g guar minitablets against placebo, given three times per day with main meals for 8 wk, was done in 29 non-insulin-dependent diabetes mellitus (NIDDM) patients who had near-normal fasting plasma glucose concentrations on treatment with diet alone, additional sulfonylurea, or ultralente insulin. Guar did not reduce the excessive postprandial glycemic excursion, glycosylated hemoglobin values, basal plasma glucose concentrations, basal or incremental plasma C-peptide values, or body weight. There were few side effects with either guar or placebo therapy. Mean low-density lipoprotein cholesterol levels were significantly reduced ($P < .001$) by guar administration (116 ± 23 vs. 104 ± 19 mg/dl). Guar additives did not improve the excessive postprandial glycemia found in NIDDM patients in whom near-normal fasting plasma glucose levels had been obtained. *Diabetes Care* 10:68–71, 1987

Non-insulin-dependent diabetes (NIDDM) can be treated with diet alone or in combination with sulfonylurea administration (1) or a basal insulin supplement (2) to obtain near-normal fasting plasma glucose levels (<108 mg/dl) (3,4). This is a logical initial aim in reducing glycemia (2), but patients often continue to have moderately elevated glycosylated hemoglobin values (5). This probably reflects their larger-than-normal postprandial glucose excursions (1,2,6).

Increased content of dietary fiber (unabsorbable plant polysaccharides), particularly gel-forming fiber, has been shown to be effective in reducing postprandial glucose levels in diabetics (7,8). Guar has been successfully incorporated in some food products (9–12), but such preparations are not widely available. Guar minitablets taken with meals provide a convenient method of increasing dietary fiber content and reduce postprandial glucose concentrations (13). This randomized crossover study examines whether guar minitablets decrease the excessive postprandial glucose rise in NIDDM or reduce glycosylated hemoglobin levels.

METHODS

Twenty-nine NIDDM patients, selected from a clinic of the UK Prospective Diabetes Study (4), gave written informed consent to the study. All had been diagnosed diabetic, with a mean of three fasting plasma glucose levels >108 mg/dl, their actual values being 191 ± 65 mg/dl (range 110–333 mg/dl) with 21 patients having values >140 mg/dl. They were 31–71 yr old, all initially treated by diet alone, and none had ketonuria or became insulin dependent. They had subsequently achieved near-normal fasting plasma glucose levels (<108 mg/dl) after randomization (4) to therapy with diet alone (11 patients), chlorpropamide (8 patients), or basal insulin supplement (10 patients) given as a once-daily subcutaneous injection of human ultralente insulin (Ultratard HM, Novo, Copenhagen). Mean dose of chlorpropamide was 263 mg/day (range 100–500 mg/day), and mean insulin dose was 0.28 IU · kg^{-1} · day^{-1} (range 0.8–0.58 IU · kg^{-1} · day^{-1}). A full 3-day diet history was obtained in each person, but no changes were made in the diet or prescribed therapy for the duration of the study, and patients were asked not to alter their usual life-styles.

For two successive 8-wk periods, patients were asked to take in random order either guar minitablets (5 g 3 times/day, Glucotard, MCP, Livingston, UK) or placebo (Bezalip tablet base with no active ingredient). Each therapy group—diet alone, sulfonylurea, or insulin— was randomized separately; in each case, half took guar followed by placebo and half took placebo followed by guar. The prescribed therapy was taken immediately before the first mouthful of each meal and washed down with water. After 4 wk on both therapies, patients were reviewed at an outpatient clinic to monitor compliance and to complete a questionnaire relating to possible side effects. At the end of each 8-wk study period, each patient was admitted at 1700 h for a 24-h metabolic profile with blood samples taken via an indwelling Teflon cannula.

TABLE 1
Patient details at entry to the study according to their study

	Diet	Chlorpropamide	Insulin	All patients
N	11	8	10	29
Male/female	9/2	7/1	8/2	24/5
Age (yr)	52.3 ± 11.2	55.5 ± 13.3	55.2 ± 8.4	54.2 ± 10.7
	(34–67)	(31–71)	(36–65)	(31–71)
Body mass index (kg/m^2)	26.3 ± 2.0	25.1 ± 3.9	27.8 ± 3.1	26.5 ± 3.1
	(23.3–30.4)	(19.1–31.5)	(24.8–33.6)	(19.1–33.6)
Duration (yr)	2.9 ± 1.9	4.1 ± 2.3	3.9 ± 1.3	4.6 ± 1.9
	(1–6)	(2–8)	(3–6)	(1–8)
Dietary content				
Carbohydrate (g)	167 ± 49	150 ± 27	146 ± 36	155 ± 40
	(97–258)	(124–195)	(104–206)	(97–258)
Protein (g)	65 ± 13	66 ± 14	61 ± 14	64 ± 13
	(44–82)	(53–90)	(44–93)	(44–93)
Fat (g)	62 ± 25	60 ± 14	58 ± 17	60 ± 19
	(31–118)	(41–80)	(34–69)	(31–118)
Dietary fiber (g)	24 ± 5	27 ± 9	20 ± 9	23 ± 8
	(14–32)	(19–38)	(9–36)	(9–38)
Carbohydrate intake (% cal)	52 ± 3	49 ± 4	51 ± 3	51 ± 3
	(48–56)	(44–55)	(46–56)	(44–56)

Values are means ± 1 SD with ranges in parentheses.

Patients were given their normal food intake with identical meals on the two admissions together with their usual and experimental medications. Side effects of drugs, if any, were recorded with specific gastrointestinal inquiries intermingled with less-relevant questions. The number of sachets or tablets each patient possessed at the end of the study was checked to assess compliance.

Plasma glucose was measured by a glucose oxidase method (Pye Unicam Aura spectrophotometer, Pye Unicam, Cambridge, UK, with Boehringer GOD-PAP). Glycosylated hemoglobin was measured by an isoelectrofocusing method (14), with a 5-h incubation of the dialyzed sample at 37°C to exclude short-term glucose adducts (15). The interassay coefficient of variation was 5.9% with a normal range of 5.0–8.5%. Plasma immunoreactive C-peptide was measured by radioimmunoassay (2) and cholesterol with a Technicon analyzer by the Liebmann-Burchard reaction. High-density lipoprotein (HDL) cholesterol was measured in the supernatant obtained by precipitation of the low-density lipoprotein (LDL) and very-low-density lipoprotein (VLDL) with heparin and manganese chloride (16). The LDL and HDL cholesterol were measured in the supernatant obtained after precipitation of VLDL by sodium dodecyl sulfate (17) and the LDL levels derived by subtraction.

Overnight basal values were taken as the arithmetic mean of the samples at 0300, 0500, and 0700 h. Postprandial glycemic and C-peptide excursions for each patient were quantified by taking the 24-h trapezoidal incremental area above the overnight basal value and dividing by the time interval to give the mean incremental rise in milligrams per deciliter and picamoles per milliliter, respectively. The normal C-peptide incremental rise (1) after a standard breakfast is 0.45 ± 0.15 pM. Results between guar and placebo therapies were compared by the paired *t* test for all patients and for each treatment group separately. Exact *P* values are given; the level of significance was 5%. *P* values > .05 were considered not significant.

RESULTS

Initial patient details are given in Table 1. Compliance was excellent. Counts of the number of guar sachets returned showed a median of 96% used (range 93–100%), with one patient using only 76% because of an initial misunderstanding that it was to be taken twice rather than thrice daily.

There were no significant differences among patients treated by diet alone, with additional sulfonylurea therapy, or with basal insulin supplementation with respect to mean

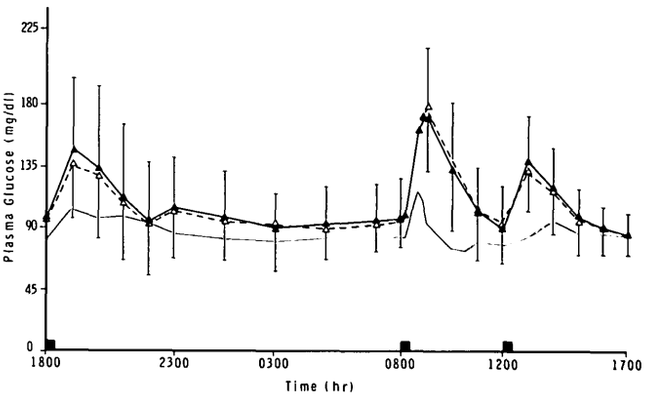

FIG. 1. Mean plasma glucose concentrations (±1 SD) over 24 h for all patients while taking guar minitablets (△) or placebo tablets (▲). Mean values for normal subjects shown for comparison (– –).

TABLE 2
Values obtained on treatment with guar and placebo therapy

	Diet	Chlorpropamide	Insulin	All patients
Weight (kg)				
Guar	79.1 ± 9.2	72.4 ± 11.1	80.2 ± 7.8	77.6 ± 9.6
Placebo	78.9 ± 8.3	72.3 ± 10.8	80.4 ± 7.6	77.6 ± 9.2
Glycosylated hemoglobin (%)				
Guar	7.5 ± 1.0	9.1 ± 3.3	8.1 ± 1.4	8.1 ± 2.0
Placebo	7.2 ± 0.9	8.4 ± 2.2	8.2 ± 2.0	7.9 ± 1.8
Basal plasma glucose (mg/dl)				
Guar	94 ± 18	90 ± 20	90 ± 27	92 ± 22
Placebo	95 ± 20	92 ± 22	88 ± 41	92 ± 29
Mean incremental glucose rise, 0800–1700 h (mg/dl)				
Guar	18 ± 14	22 ± 11	34 ± 18	25 ± 16
Placebo	14 ± 5	22 ± 11	34 ± 18	23 ± 14
Basal plasma C-peptide (pmol/ml)				
Guar	0.51 ± 0.25	0.69 ± 0.26	0.34 ± 0.26	0.50 ± 0.28
Placebo	0.55 ± 0.20	0.72 ± 0.26	0.35 ± 0.32	0.53 ± 0.29
Mean incremental C-peptide rise, 0800–1700 h (pmol/ml)				
Guar	0.57 ± 0.24	0.52 ± 0.27	0.57 ± 0.26	0.56 ± 0.26
Placebo	0.60 ± 0.26	0.56 ± 0.23	0.49 ± 0.25	0.55 ± 0.29
LDL cholesterol (mg/dl)				
Guar	101 ± 19	104 ± 23	104 ± 19	104 ± 19
Placebo	104 ± 27	116 ± 23	128 ± 19 (P = .001)	116 ± 23 (P = .001)
HDL cholesterol (mg/dl)				
Guar	43 ± 8	43 ± 12	46 ± 8	43 ± 8
Placebo	43 ± 12	46 ± 12	43 ± 8	43 ± 12
Triglycerides (mg/dl)				
Guar	275 ± 222	222 ± 168	213 ± 142	239 ± 177
Placebo	301 ± 204	168 ± 71	168 ± 62	222 ± 142

Values are means ± 1 SD; P values are not significant except where given.

age, mean body mass index, mean duration of diabetes, and proportion of dietary carbohydrate, protein, fat, or dietary fiber content.

Results obtained on guar or placebo therapy are given in Table 2. Mean weight for all patients was identical with either therapy. Mean glycosylated hemoglobin values were at the upper end of the normal range and did not alter with guar (8.1%) or placebo (7.9%) administration.

Mean basal plasma glucose level (Table 2 and Fig. 1) was within the normal range (63–99 mg/dl) for all patients and identical on guar and placebo therapy (92 mg/dl). The mean 24-h incremental plasma glucose rise was also not different between therapies but was greater on guar (25 ± 16 mg/dl) and placebo (23 ± 14 mg/dl) than in normal subjects (5 ± 2 mg/dl).

Mean basal and incremental plasma C-peptide levels (Table 2 and Fig. 2) were not different between therapies. In patients receiving placebo therapy, mean basal plasma C-peptide values were higher in the sulfonylurea-treated group compared with those on ultralente (0.72 ± 0.26 vs. 0.35 ± 0.32 pM, P = .014), but neither differed significantly from patients on diet alone (0.55 ± 0.20 pM). These changes do not correlate with the degree of obesity, the mean body mass index of the three groups being in the opposite order.

Mean serum LDL cholesterol levels for all patients were

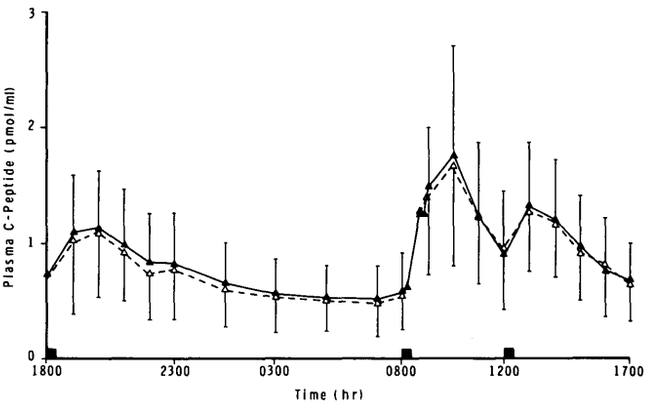

FIG. 2. Geometric mean plasma C-peptide concentrations (± 1 SD) over 24 h for all patients while taking guar minitablets (△) or placebo tablets (▲).

reduced when taking guar (104 ± 19 vs. 116 ± 23 mg/dl, $P = .001$); this effect was most marked for the insulin-treated group. Mean serum HDL cholesterol and triglyceride values were not significantly altered.

In the questionnaire, 13 and 7% of guar and placebo patients, respectively, noted increased bowel action; 7 and 17% noted constipation. Bloating or excessive wind was noted by 72% of patients on guar and 10% on placebo.

DISCUSSION

Addition of 15 g guar/day to meals made no difference to any aspect of glycemic control in these NIDDM patients in whom near-normal fasting plasma glucose levels had already been obtained on therapy with diet alone or with additional sulfonylurea or a basal insulin supplement (1,2). Aro and colleagues (18) showed 21 g/day to be effective in a 3-mo crossover study of less well controlled NIDDM patients. The minitablets of guar used in this study have been shown to be effective at the same dose in less well controlled diabetic patients (13), and guar may be more effective when blood sugar levels are high. However, the logical primary aim of therapy is fasting near normoglycemia (1,2); if this is achieved, it would appear that guar may not have any additional beneficial effect.

There is little doubt that these well-motivated and compliant patients adhered to their treatment schedules, as evidenced by the significant reduction in mean LDL cholesterol levels while taking guar, as previously reported (8,18,19), and the sachet count. Other lipids did not change.

All patients had received regular dietary advice since diagnosis, but their daily fiber intake of 23 g was not unusually high. The addition of 15 g guar, taken before meals as a granule designed to dissolve and disperse promptly in the stomach, did not delay the absorption of carbohydrate. Doubling the dose would probably not be beneficial, because there was not even a trend hinting at a beneficial glycemic effect. Guar might be useful as a means of reducing plasma LDL cholesterol levels.

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