Four-Week Low-Glycemic Index Breakfast With a Modest Amount of Soluble Fibers in Type 2 Diabetic Men

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Low-glycemic index diets are associated with a wide range of benefits when followed on a chronic basis. The chronic effects, however, of the substitution of 1 meal per day are not well known in diabetic subjects. Therefore, we aimed to evaluate whether the chronic use of a low-glycemic index breakfast (low-GIB) rich in low-GI carbohydrates and a modest amount of soluble fibers could have an effect on lipemia at a subsequent lunch, and improve glucose and lipid metabolism in men with type 2 diabetes. A total of 13 men with type 2 diabetes were randomly allocated in a double-blind cross-over design to a 4-week daily intake of a low-GI versus a high-GI breakfast separated by a 15-day washout interval. The low-GI breakfast was composed of whole grain bread and muesli containing 3 g β-glucan from oats. Low-GIB induced lower postprandial plasma glucose peaks than the high-GIB at the beginning (baseline, $P < .001$) and after the 4-week intake ($P < .001$). The incremental area under the plasma glucose curve was also lower ($P < .001$, $P < .01$, baseline, and 4 weeks, respectively). There was no effect on fasting plasma glucose, insulin, fructosamine, or glycosylated hemoglobin (HbA_{1c}). Fasting plasma cholesterol, as well as the incremental area under the cholesterol curve, were lower ($P < .03$, $P < .02$) after the 4-week low-GIB period than after the high-GIB period. Apolipoprotein B (apo B) was also decreased by the 4-week low-GIB. There was no effect of the low-GI breakfast on triacylglycerol excursions or glucose and insulin responses at the second meal. The high-GIB, however, tended to decrease the amount of mRNA of leptin in abdominal adipose tissue, but had no effect on peroxisome proliferator-activated receptor γ (PPARγ) and cholesterylester transfer protein (CETP) mRNA amounts. In conclusion, the intake of a low-GI breakfast containing a modest amount (3 g) of β-glucan for 4 weeks allowed good glycemic control and induced low plasma cholesterol levels in men with type 2 diabetes. The decrease in plasma cholesterol associated with low-GI breakfast intake may reduce the risk of developing cardiovascular complications in subjects with type 2 diabetes.

CONCERNS ABOUT USING high-carbohydrate diets in diabetes[1] because of adverse effects on triglycerides and high-density lipoprotein-cholesterol levels,[2] are overcome by recommending carbohydrates that give low postprandial plasma glucose responses.[3,4] For over half a century, it has been postulated that the increase in blood glucose was less pronounced after the consumption of starchy foods than after the consumption of foods containing simple carbohydrates. Starchy foods have been recognized as the main candidate for reducing glycemic and insulinemic responses. However, coincidental with recommendations to increase the intake of starchy foods has been the recognition that the glycemic responses to all starches are not the same and that starches are not interchangeable.[5,6] The glycemic index (GI) of foods has, thus, been established and used to classify foods according to their blood glucose responses.

Although the use of low-GI carbohydrates in the diet of patients with type 2 diabetes is still debated,[7,8] epidemiologic studies demonstrated that the GI of the diet may be an important factor in preventing non–insulin-dependent diabetes.[9,10] Beneficial effects of such a diet have been demonstrated in diabetic and normal subjects when the diet is followed during the 3 meals of the day on a short- or long-term basis.[11-15]

For practical purposes, we aimed to change only 1 meal during the day. Breakfast was chosen because it is frequently found that at this meal, diabetic patients require more insulin than for an isocaloric midday or evening meal.[16,17] Moreover, some patients are hyperglycemic throughout the day, while others are mainly hyperglycemic in the morning (particularly after breakfast) and less hyperglycemic at noon and postlunch.[18] It has been suggested that insulin sensitivity and glucose responses during the second meal may be related to the effect from the preceding carbohydrate challenge.[19] Moreover, the magnitude of the increase in plasma triacylglycerols following a meal is recognized to be accentuated by carbohydrate-induced hyperinsulinemia.[20] Thus, decreased plasma glucose excursions and improved insulin sensitivity following a low-GI meal eaten at breakfast might enhance tolerance for carbohydrates and lipids at lunch.

The acute effects of low- or high-GI breakfasts have been evaluated in normal healthy subjects. Few studies have evaluated the chronic effect of these breakfasts in type 2 diabetic subjects.[21,22]

In this perspective, therefore, we aimed to evaluate the effects of a low-GI breakfast on both glucose and lipid metabolism in men with type 2 diabetes. We aimed also to evaluate the effects of a low-GI breakfast on hyperlipidemia at a subsequent lunch. Furthermore, we determined the expression of some lipid-related enzymes: cholesterylester transfer protein (CETP), leptin, and peroxisome proliferator-activated receptor γ (PPARγ), because in a previous study from our laboratory, a similar diet for rats was found to decrease the satietogenic factor, leptin, as well as some lipid-related enzymes.[23]

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Submitted July 13, 2001; accepted January 2, 2002.

Supported by grants from the National Institute of Health and Medical Research (INSERM), Pierre and Marie Curie University, and Nestle Center, Orbe, Switzerland.

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0026-0495/02/5107-0009$35.00/0

doi:10.1053/meta.2002.33345

Table 1. Clinical Characteristics of the Subjects at the Time of Screening

Subject No.	Order Diet	Age (yr)	BW (kg)	Height (m)	BMI (kg/m^2)	Diabetes Therapy	HbA_{1c} (%)	FBG (mmol/L)	TG (mmol/L)	Cholesterol (mmol/L)
1	L/H	63	97	1.78	26	Metformin/sulfonylureas	9.5	12.2	1.9	4.9
2	H/L	58	85	1.78	27	Metformin/sulfonylureas	8.9	10.3	0.8	4.2
3	H/L	53	74	1.67	27	Metformin	7.1	7.3	1.3	5.3
4	L/H	67	89	1.81	27	Metformin/sulfonylureas	10	13.0	0.6	5.1
5	L/H	61	83	1.70	29	Metformin/sulfonylureas	9.8	12.6	1.5	5.9
6	L/H	61	100	1.66	36	Sulfonylureas	6.9	10.1	0.7	5.2
7	L/H	63	85	1.62	32	Metformin/sulfonylureas	8.9	13.0	2.5	5.1
8	H/L	66	73	1.69	26	Metformin/sulfonylureas	9.3	13.3	1.4	4.9
9	H/L	56	65	1.70	23	Metformin/sulfonylureas	7.9	12.0	2.6	5.4
10	H/L	41	84	1.65	31	Metformin	7.2	8.3	4.2	4.5
11	L/H	60	70	1.75	23	Sulfonylureas	8.1	9.9	1.4	4.8
12	H/L	66	83	1.87	24	Diet	6.6	7.1	0.9	3.7
13	L/H	44	77	1.73	26	Sulfonylureas	7.0	10.2	1.5	7.5
Mean ± SEM		59 ± 2	82 ± 3	1.72	28 ± 1		8.3 ± 0.4	10.8 ± 0.8	1.6 ± 0.3	5.1 ± 0.3

NOTE. Order: randomization of the subjects to start with a high-GI dietary period then a low-GI dietary-period (H/L) or to start with a low-GI then a high-GI dietary period (L/H).

Abbreviations: BW, body weight; BMI, body mass index; FBG, fasting blood glucose; TG, triglycerides.

SUBJECTS AND METHODS

Subjects

A total of 13 men with type 2 diabetes were recruited from patients attending the outpatient clinic of the Department of Diabetes of Hôtel-Dieu Hospital. Patients were selected on the basis of having fasting plasma glucose of 7.7 to 13.0 mmol/L, glycosylated hemoglobin (HbA_{1c}) 6.5% to 11%, and plasma triacylglycerols lower than 3 mmol/L. Due to known plasma glucose and insulin variations by estrogen and progesterone modifications, women were excluded from this study.

The clinical and biological characteristics of these subjects are given in Table 1. Patients with abnormal renal, hepatic, and thyroid functions as determined by physical examination, blood cell count, and standard blood biochemical profile were excluded. Similarly, patients suffering from gastrointestinal disorders were prohibited from entering the study. Twelve patients were taking oral antidiabetic agents (sulfonylurea and/or metformin) and 1 patient on an antidiabetic dietary regimen alone. One patient was receiving an α-glucosidase inhibitor (acarbose). He was asked to stop the treatment 4 weeks before the beginning of the study. None of the patients were being or had been treated with insulin. Four patients were being treated for hypertension with β-blockers, angiotensin-converting enzyme (ACE) inhibitors, antidiuretics, and/or calcium antagonists.

Despite the fact that sulfonylureas and metformin have very different mechanisms of action, the observed results might not be due to different therapies: all patients continued and kept constant all therapies throughout the whole study period. Moreover, the results of the low-GI period were compared with those of the high-GI period in the same patient with the same accompanied treatments.

The purpose, nature, and potential risks of the study were explained, and a written informed consent was obtained from all participants. The ethics committee of Hôtel-Dieu Hospital approved the experimental protocol.

Study Design

The patients were randomly allocated in a cross-over design to 2 periods of 4 weeks with a daily breakfast consisting of either low- or high-GI carbohydrates with a modest amount of β-glucan. The 2 nutritional periods were separated by a 15-day washout interval.

Dietary Follow-up

Before entering into the study, the subjects had been seen on a regular basis (at least every 6 months) in our department. All were well educated, especially concerning the type and quantity of foods they should consume. Each subject entered a run-in period of 1 month. Patients received individual counseling by a dietitian concerning dietary food intake. In addition, counseling sessions (in small groups) were conducted during the run-in period. During this period, we asked them to follow their usual diet more strictly. Patients were recommended to consume 55% of their caloric intake as carbohydrate, 15% as protein, and 30% as lipids. Dietary intake was prescribed individually according to data obtained from dietary questionnaires to maintain the initial caloric intake and nutrient proportions constant throughout the study.

Before the beginning of each treatment period, dietary questionnaires were obtained again (baseline data, recall technique) to maintain the initial caloric intake and nutrient proportions constant throughout the study. To assess compliance with the dietary recommendations, patients were asked to keep a food diary to be completed on the last 7 days of each treatment period. Household measuring cups or spoons and photographed food pictures were used to quantify proportion sizes of foods eaten. When each subject returned his records at the end of each 7-day period, the dietitian checked the contents of the records and clarified any ambiguous information with the subject. These records were analyzed using the computer program Profile Dossier V3 software (Audit Conseil en Informatique Médicale, Bourges, France) whose dietary database is made up of 400 foods or groups of foods representative of the French diet. French food contents were obtained from Ciqual Repertory.[24] There was approximately 10% of missing values. If a food described by a subject was not in the database, the ingredients of recipes or manufacturer's information were used to complete coding according to Ciqual Repertory.[24]

The patients were free-living and attended the department once/week. They were asked to maintain their usual habitual diet throughout the study apart from the breakfasts that were provided according to the experimental period, being low- or high-GI. During the washout, period patients followed their habitual diets throughout the day even during breakfast.

Table 2. Composition of Low- and High-GIB

	Low-GI						High-GI					
Breakfasts	Q (g)	Prot (g)	L (g)	CHO (g)	Fiber (g)	E (kcal)	Q (g)	Prot (g)	L (g)	CHO (g)	Fiber (g)	E (kcal)
Cereal*	38	5.4	2.3	21.0	7‡	126	33	3.9	0.5	20.5	6.5	109
Milk	75	2.4	1.5	4.0	0	39	75	2.4	1.5	4.0	0.0	39
Bread†	33	1.8	0.3	12.4	3	60	30	2.8	0.8	12.5	2.2	65
Butter	5	0.0	4.2	0.0	0	38	5	0.0	4.2	0.0	0.0	38
Total	150	9.5	8.3	37.4	10	263	143	9.0	6.9	37.0	8.7	249
Estimated GI%				40%						64%		

Abbreviations: Q, quantity of each product; prot, protein; L, lipids; E, energy; CHO, available carbohydrates.

*Cereal based on extruded oat bran concentrate, apple and fructose in the low-GIB period. In the high-GI period, cereals formed of whole wheat grains (Weetabix).

†Bread was pumpernickel in the low-GIB period and wholemeal bread (wheat flour) in the high-GIB period.

‡Includes, 3 g of β-glucan.

Experimental Breakfasts

The size of the meal was fixed prior to the study and based on each patient's dietary record taken before the study. Treatment foods for breakfast were provided to the subjects and prescribed to meet 20% of daily energy requirements. The composition of the 2 experimental breakfasts is shown in Table 2. In the high-glycemic index breakfast (GIB) period (calculated total GI, 64%), the cereal used was whole wheat grains (Weetabix, Burton Latimer, Kettering, Northants, UK; GI, 69%), whereas the bread used was whole meal bread (wheat flour) with a GI of 69%. In the low-GIB period (calculated total GI, 40%), the cereal used was based on extruded oat bran concentrate, apple, and fructose (muesli containing 3 g β-glucan from oats, offered by Nestle, Orbe, Switzerland; GI, 41%). The bread used was pumpernickel (GI, 41%). The breads were prepared and donated by Jackson, Eury, France.

In the high-GIB, we have used breads and cereals with only a mean GI of 64% and not higher. Breads and cereals with higher glycemic indices have lower fiber content than those used in the low-GIB. In an attempt to keep constant the amount of fibers in the 2 breakfasts, we used high-GI cereals and breads with a fiber content comparable to those in the low-GIB.

Breads and cereals used were analyzed for fat, protein, and dietary fiber using standard Association of Analytical Communities (AOAC) methods, with available carbohydrate calculated by difference. β-glucan in the cereal products was analyzed following the method described by McCleary.[25]

One-Day Metabolic Profile

At the beginning and the end of each nutritional period, subjects were hospitalized from 7:30 AM to 4:00 PM after an overnight fast. A sample of abdominal subcutaneous adipose tissue was obtained by needle biopsy using a 14-gauge needle and a 30-mL syringe under local anesthesia with xylocaine 10% without adrenaline. The tissue obtained was rapidly frozen in liquid nitrogen and stored at -80°C. Then, during the same day, an indwelling cannula was inserted into an antecubital vein. This cannula served for the hourly withdrawal of blood samples during the metabolic profile. At 9:00 AM, each subject consumed a breakfast (low- or high-GI) that was the same as during the chronic period. At 12:00 PM, a standard meal was served providing 45% of energy as carbohydrate, 40% as lipids, and 15% as proteins. The standard meal was of the same quantity and composition for all of the subjects at all times. Blood samples were collected in the fasting state at time 0 and then hourly during the 7 hours of metabolic profile. Blood samples were centrifuged and plasma was frozen (-20°C) for further measurements of plasma glucose, insulin, and lipids (triglycerides, cholesterol, and free fatty acids). At time 0, HbA_{1c}, high-density lipoprotein (HDL) and apolipoprotein (apo) A1 and B were also measured.

Nondietary Follow-up

Patients were asked to maintain a constant lifestyle throughout the study. Physical activity was assessed by recall questionnaires. The kind of activity and its frequency, as well as the mode and duration of transportation to and from work, were questioned. Patients' physical activity remained constant during the study.

Biological Assays

Plasma glucose was measured by the glucose-oxidase method with a glucose analyzer (Beckman, Fullerton, CA). Plasma insulin was determined by radioimmunoassay. The antiserum used in the test showed a cross-reactivity of 100% with human insulin. Triglycerides and free fatty acids were determined by using Biomérieux kits (Marcy-l'Etoile, France). Total, free, and esterified cholesterol were also measured using Labintest kits (Aix-en-Provence, France). Apo AI and apo B were determined by an immunochemical assay with Behring kits (Mauburg, Germany). Samples were taken in triplicate for the measurements of plasma glucose and insulin; for other measurements, single samples were used.

Gene Expression of CETP, Ob, and PPARγ

RNA preparation. The RNA from adipose tissue (about 80 to 100 mg of frozen tissue) was obtained by using the Rneasy total RNA kit (Qiagen, Courtaboeuf, France) as previously indicated.[26] The absorption ratio 260 to 280 nm was between 1.7 and 2.0 for all preparations. RNA integrity was verified on agarose gel electrophoresis. Average yields were similar in samples obtained after the low- (17 ± 3 μg of RNA/g/tissue) and the high-GI breakfast (16 ± 4 μg of RNA/g/tissue). Total RNA was stored at −80°C for less than 1 month before analysis.

Quantification of target mRNAs. Human PPARγ, leptin, and CETP mRNAs were quantified by reverse transcriptase (RT)-competitive polymerase chain reaction (PCR), which consists of coamplification of target cdNA with known amounts of a specific DNA competitor molecule added in the same PCR tube.[27] The RT reactions were performed from 0.1 μg total RNA/g/tissue in the presence of 1 of the specific antisense primers and 2.5 U of a thermostable RT (Tth; Promega, Charbonnières, France) as previously described.[27] Fluorescent dye-labeled sense primers were used in the PCR, and the amplified products were separated and analyzed on an ALFexpress DNA sequencer (Pharmacia, Uppsala, Sweden) using the Fragment Manager software (Pharmacia).[28] Absence of contamination with genomic DNA was checked by omitting RT in the reaction. The construction of the competitor

DNA molecules, the sequence of the primers, and the validation of the RT-competitive PCR assay for PPAR[28] and leptin[26,27] mRNAs have been described elsewhere.

Statistical Analyses

The analyses take into account the design of the experiment, the type, and the distribution of the variables.[14,29] For continuous variables with normal distribution, a multiple analysis of variance followed by a post hoc test (LSD) was used using CSS statistical package (StatSoft, Tulsa, OK). The main factors considered in the analysis were the following: treatment (with 2 levels: low-GIB and high-GIB), time (with 2 levels: baseline and 4-week diet), and order (with 2 levels). The mean value at the end of each diet minus the baseline value before each diet was used as the basis of a test of different carryover effects between the 2 diets. For continuous variables with normal distribution, a test for different carryover effects at the 10% level was used. If the test was not significant, a *t* test for different treatment effects at the 5% level was used. If the carryover test was significant, only data from the first dietary period were used in comparisons of treatment effects. If the usual assumption for *t* test did not hold or if the data were on an ordinal scale, the Mann-Whitney *U* test replaced the *t* test. Results are expressed as mean ± SEM.

RESULTS

Patients followed the 2 dietary periods without any difficulty. The 2 breakfasts were well tolerated, without any complaints or side effects. According to self-report, subjects' lifestyles remained unchanged throughout the entire study. There was no effect of crossover design (low- or high-GIB) or diet by period interaction for any of the parameters studied.

Diets and Body Weight

Results of the 7-day records at the end of the 2 nutritional periods demonstrated that daily intakes of total energy and macronutrients were unchanged. Concomitantly, body weight was comparable after the 2 periods of low- and high-GIBs (results not shown).

Metabolic Profiles

Fasting plasma glucose, insulin, and HbA_{1c} were not affected by the chronic changes in the type of breakfast (Table 3). However, there were some differences in the plasma glucose and insulin profiles between the 2 breakfasts at the beginning and the end of the chronic periods. With the high-GIB, plasma glucose increased more rapidly to give high peaks in the beginning (baseline data, high-GIB *v* low-GIB, $P < .001$) and at the end (4 weeks, $P < .001$) of the nutritional period. Plasma insulin peaks showed the same profiles (but not significantly different). After these postprandial peaks, blood glucose concentrations decreased with the high-GI starch breakfast dipping below the fasting values in some patients (results not shown). The area under the glucose curve after breakfast was significantly greater for the high-GIB than after the low-GIB at the beginning and the end of the nutritional period ($P < .01$) as shown in Table 3. These results validate the use of 2 breakfasts with different postprandial plasma glucose responses. There was no significant difference in plasma glucose and insulin excursions after lunch during the the 2 nutritional periods.

As shown in Tables 4 and 5, a 4-week consumption of the low-GIB induced a 10% decrease (total relative difference) in fasting total cholesterol ($P < .03$). Fasting cholesterol before the 4-week low-GIB period was found to be slightly higher (but still in the normal range) than before the high-GI dietary period, despite the cross-over design of the study. Consequently, it is more physiologic to compare statistically the differences during each period (baseline data-4-week data, high-GIB *v* low-GIB) rather than the effect at the end of the 4-week period. This

Table 3. HbA_{1c}, Plasma Glucose, and Insulin Concentrations at Baseline and After 4 Weeks of Low- and High-GIB

	Low-GI		High-GI		Chronic Effect
	Baseline*	4 Weeks	Baseline*	4 Weeks	(4 week-baseline)†
HbA_{1c} (%)	8.3 ± 0.5	7.8 ± 0.4	8.1 ± 0.3	7.9 ± 0.4	NS
Glycemia					
Fasting (mmol/L)	10.9 ± 0.6	10.6 ± 0.3	10.4 ± 0.7	10.1 ± 0.7	NS
AUC (3 h)	4.8 ± 1.1	5.5 ± 0.8	8.2 ± 1.2[a‡]	8.6 ± 1.3[b§]	NS
Peaks (increment after breakfast)	2.9 ± 0.4	3.1 ± 0.3	5.0 ± 0.4[a‡]	5.1 ± 0.5[b‡]	NS
Insulinemia					
Fasting (pmol/L)	97 ± 12	117 ± 14	97 ± 10	102 ± 12	NS
AUC (3 h)	130 ± 27	116 ± 25	159 ± 27	159 ± 25	NS
Peaks (increment after breakfast)	75 ± 13	81 ± 18	105 ± 16	100 ± 14	NS

NOTE. Data are mean ± SEM (n = 13).

Abbreviation: NS, not significant.

*Results during the 1-day metabolic profile taken just before (data in the fasting state) or after the respective breakfast.

†Real chronic dietary effect: the delta (4-week data-baseline data) during the high-GI dietary period was compared with the delta during the low-GI period.

[a]Significant acute dietary effect after a single breakfast at the beginning of the chronic dietary period (baseline data, high-GI *v* low-GI). [b]Significant effect after a single breakfast at the end of the chronic dietary periods (4-week data), high-GI *v* low-GI. ‡$P < .001$, [§]$P < .01$. These results validated the fact that the 2 breakfasts had different glycemic responses at the beginning (a) and the end of the study (b) AUC is expressed as mmol · h/L.

Table 4. Circulating Lipid and Lipoprotein Concentrations at Baseline and After 4 Weeks of Low- and High GIB

	Low-GI		High-GI		Chronic Effect (4 wk- baseline)†
	Baseline	4 Weeks	Baseline	4 Weeks	
HDL (g/L)	0.36 ± 0.02	0.37 ± 0.03	0.37 ± 0.03	0.36 ± 0.03	NS
Apo A (g/L)	1.5 ± 0.06	1.5 ± 0.08	1.6 ± 0.06	1.5 ± 0.08	NS
Apo B (g/L)	1.3 ± 0.08	1.2 ± 0.08	1.3 ± 0.08	1.3 ± 0.08	<.03
Total cholesterol					
Fasting (mmol/L)	5.4 ± 0.2	5.1 ± 0.2	5.0 ± 0.2	5.2 ± 0.2	<.03
Mean (7 h)*	5.3 ± 0.7	5.0 ± 0.7	5.0 ± 0.8	5.0 ± 0.8	<.02
Free cholesterol					
Fasting (mmol/L)	1.6 ± 0.1	1.5 ± 0.1	1.6 ± 0.1	1.6 ± 0.1	NS
Mean (7 h)*	1.7 ± 0.1	1.63 ± 0.05	1.6 ± 0.1	1.6 ± 0.1	<.04
Esterified cholesterol					
Fasting (mmol/L)	6.4 ± 0.3	5.9 ± 0.3	5.6 ± 0.4	5.9 ± 0.4	<.05
Mean (7 h)*	6.1 ± 0.9	5.6 ± 1.0	5.6 ± 0.9	5.7 ± 1.0	NS
Free fatty acids					
Fasting (mmol/L)	0.48 ± 0.06	0.49 ± 0.01	0.57 ± 0.02	0.55 ± 0.01	NS
Mean (7 h)*	0.36 ± 0.04	0.34 ± 0.03	0.35 ± 0.03	0.36 ± 0.03	NS
Triglycerides					
Fasting (mmol/L)	1.6 ± 0.2	1.7 ± 0.2	1.9 ± 0.1	1.7 ± 0.1	NS
Mean (7 h)*	2.2 ± 0.3	2.2 ± 0.2	2.4 ± 0.4	2.2 ± 0.3	NS

NOTE. Data are mean ± SEM (n = 13).

Abbreviation: NS, not significant.

*Responses to a single low-GI or high-GI breakfast during the 1-day meiabolic profile before (baseline data) or after the 4-week dietary periods (4-week data).

†Real chronic dietary effect: the delta (4-week data -baseline data) during the high-GI dietary period was compared with the delta during the low-GI period.

comparison reflects correctly the effect of the dietary interventions and eliminates the influence of nonspecific baseline variations. The same situation was found for mean cholesterol and mean free cholesterol after a single low-GIB during the 1-day metabolic profile, before the beginning of the chronic period (baseline data). This finding might be due simply to initially slightly higher fasting levels. Again, it was the delta (baseline data-4-week data) that was compared taking into consideration the order of the 2 interventions. The changes (baseline-4 week) in the incremental area under the plasma total and free cholesterol response curves during the 7-hour profile day were also lower ($P < .02$ and $< .04$, respectively) after the period with the low-GIB than after the high-GIB (Table 4).

There was no significant difference in the fasting levels or the area under the curves for triacylglycerols and free fatty acids (baseline-4 week) after breakfasts. Similarly, there was no detectable effect of the low-GIB on triacylglycerol and free fatty acid excursions at the lunch meal. Apo B was found to be lower ($P < .03$) after 4 weeks of the low-GIB compared with the high-GIB (basal–4 week) as shown in Table 4.

Table 5. Individual Changes in Circulating Total Cholesterol Concentrations at Baseline and After 4 Weeks of Low- and High-GIB

		Low-GI			High-GI		
Subject No.	Diet Order	Baseline	4 Weeks	Difference	Baseline	4 Weeks	Difference
1	L/H	4.92	4.71	−0.21	4.64	4.61	−0.03
2	H/L	4.51	4.04	−0.47	4.17	3.8	−0.37
3	H/L	6.37	6.55	0.18	5.31	5.85	0.54
4	L/H	5.10	5.13	0.03	4.61	5.08	0.47
5	L/H	5.88	5.78	−0.10	5.52	5.28	−0.24
6	L/H	5.18	5.57	0.39	5.18	5.26	0.08
7	L/H	5.41	4.58	−0.83	3.91	4.61	1.30
8	H/L	5.26	4.17	−1.09	4.99	5.23	0.23
9	H/L	6.29	4.84	−1.95	5.36	6.22	0.76
10	H/L	4.79	5.02	0.23	4.53	4.40	−0.13
11	L/H	4.81	4.71	−0.10	5.65	5.72	0.07
12	H/L	4.66	4.14	−0.52	3.63	3.63	0
13	L/H	7.54	6.66	−0.88	7.43	7.40	−0.03
Mean ± SEM		5.4±0.2	5.1±0.2	−0.41±0.18[a]	5.0±0.2	5.2±0.2	0.23±0.12[b]

NOTE. Total cholesterol values are expressed as mmol/L. Results during the 1-day metabolic profiles taken just before (data in the fasting state) the respective breakfasts. Different letters in the same row indicate significant difference ($P < .03$).

PPARγ, Leptin, and CETP mRNAs

Due to technical problems, adipose tissue aspiration was successfully performed for 6 patients after the 2 dietary periods. There was no difference in the amount of PPARγ (16.8 ± 4 *v* 17.3 ± 3.7 amol/μg total RNA) or CETP (2.1 ± 0.5 *v* 2.3 ± 0.6 amol/μg total RNA) mRNAs at the end of the low-GIB and the high-GIB periods, respectively. The RNAm of ob, however, showed a trend toward a decrease in most of the subjects (n = 6) when the end of the high-GIB period was compared with the end of the low-GIB period (3.5 ± 1.0 *v* 1.3 ± 0.7 amol/μg total RNA, respectively), (amol = attomol = 10^{-18}mol).

DISCUSSON

The replacement of a high-GIB by a low-GIB for 4 weeks in type 2 diabetic patients in the present study lowered postprandial plasma glucose peaks, as well as plasma glucose and insulin responses. The effect of a low-GIB was found after the consumption of the breakfast meal (during the 1-day profile) at the beginning of the study, as well as at the end of the 4-week nutritional period. These daily dietary changes over 4 weeks was insufficient to improve either HbA_{1c} or fructosamine, but were quite enough to improve plasma cholesterol levels.

The present study demonstrated for the first time reduced cholesterol levels by 4 weeks of a low-GI meal taken once a day in the morning in normocholesterolemic subjects. This decrease in plasma cholesterol levels (-10%) might be due to changing the type of carbohydrates (in bread and cereals) from high-GI to low-GI during the breakfast meal for 4 weeks. In the literature, there is an important body of evidence in support of a therapeutic potential of a low-GI carbohydrate diet taken during the 3 meals, but not only once at breakfast, in subjects with type 2 diabetes and dyslipidemia.[11,14,30,31] However, few studies demonstrated positive effects by changing only the breakfast composition. In hypercholesterolemic type IIa patients, replacing a conventional continental breakfast by a single oat bran cereal (muesli) for 3 weeks induced a decrease in total cholesterol (-11%), as well as HDL- and low-density lipoprotein (LDL)-cholesterol levels.[32] Golay et al,[21] however, found that switching from standard cereals (cornflakes) to slow release starch cereals (muesli) at breakfast for only 2 weeks improved carbohydrate metabolism and reduced insulin requirements in type 2 insulin-treated diabetic patients, but no effect on cholesterol levels was detected. A 2-week dietary period might be insufficient to decrease plasma cholesterol as in our study. Furthermore, in normal subjects, a high carbohydrate/low-GIB meal reduced free fatty acid responses to breakfast when compared with a low-carbohydrate breakfast. The investigators did not mention any effect on cholesterol levels.[33] Recently, in type 2 diabetic subjects, the same group[22] did not find an effect on plasma cholesterol levels after 6 months of low-GIB cereal compared with high-GIB cereal. The difference between this study and the present one might be due to the incorporation of more than 1 type of low-GI food in the breakfast (cereals and bread) with a modest amount of soluble fibers.

Increasing the fiber content of the diet whether soluble or not might lead to low postprandial glycemic responses, as well as low cholesterol levels. In the present study, the fiber content of the 2 breakfasts was the same. Consequently, the quantity of fiber could not be implicated in the observed low postprandial glycemic responses found or in the low cholesterol levels induced after 4 weeks of such a breakfast. However, the low-GIB contained 3 g of β-glucan. Jenkins et al[34] showed that the increase in postprandial glucose and insulin concentrations were reduced after meals containing viscous soluble fibers. Guar, psyllium, β-glucan, and pectin were all found to flatten postprandial glycemia more consistently than wheat bran and other insoluble particulate fibers.[35] The decrease of cholesterol levels by the addition of soluble fibers present in oat bran was found in many studies. In a meta-analysis of the literature of clinical trials of free living subjects,[36] reduction in cholesterol levels was found in subjects who had initially high blood cholesterol levels (> 5.9 mmol), particularly when a daily dose of 3 g soluble fiber was used. The reduction was on average 6%. A single dose of oat bran cereal containing approximately 4g β-glucan taken by hypercholesterolemic patients for 3 weeks produced an 11% decrease in total serum cholesterol.[32] A lack of an effect, however, was reported by Lovegrove et al[37] in a UK population. In our study with only 3 g β-glucan, a 10% reduction of cholesterol was found after a 4-week intake. β-glucan might decrease cholesterol levels by increasing fecal steroid secretion or short chain volatile fatty acid production.[38] Whatever the mechanism might be, the decrease in cholesterol found in our study was due likely to the association of β-glucan with low-GI carbohydrates in the same meal.

Changing breakfast from a high-GI to a low-GI had no impact on postprandial plasma glucose, insulin, or triacylglycerol excursions after the second slightly hyperlipidemic meal (lunch). Several factors influence triacylglycerol in the postprandial state. Improving insulin sensitivity was demonstrated to decrease postprandial triacylglycerol levels,[39] whereas increasing insulin levels induced by carbohydrates was found to accentuate postprandial triacylglycerol excursions.[20] In the present study, the fact that insulin peaks were not significantly decreased by the low-GIB might explain the absence of any effect on postprandial triacylglycerol levels. This might be also due to the absence of any effect of the low-GIB on insulin resistance or chronic glucose control.

Since high-GI diets and subsequent postprandial plasma glucose responses might predispose to cardiovascular complications, as well as other metabolic diseases, such as obesity,[40,41] we also aimed to evaluate the effect of this type of breakfast on the expression of some genes implicated in lipid metabolism. In a previous study from our laboratory, a chronic period of high-GI diet was able to decrease both plasma leptin and ob gene expression in epididymal adipose tissue in normal rats before any detectable modification in weight gain or adipose tissue mass.[23] This decrease was considered as a marker that predicts further weight gain.[42] In the present study, however, 1 meal per day of a low-GI diet in patients with type 2 diabetes led to a trend towards a decrease of ob gene expression that did not reach significant values. Differences of results between rat and man might be due to the difference in quantity of low-GI food consumed during the day and/or the presence of diabetes.

The PPARγ, which is one of the key messengers responsible for the translation of nutritional and pharmacologic stimuli into changes in gene expression and differentiation pathways, did not change during the nutritional modifications in our study. A third gene implicated in the cholesterol ester transfer from LDL to very–low-density lipoprotein (VLDL)-cholesterol is the CETP, which plays a crucial role in modifying lipoprotein patterns, as well as LDL size distribution. The changes in total cholesterol in the present study were not associated with changes in either HDL-cholesterol or CETP gene. Thus, in the present study, changing 1 meal per day (breakfast) from a high to low-GI for 4 weeks in non–insulin-dependent diabetes mellitus patients was not sufficient to modulate genes implicated in lipid metabolism.

Using cereals and breads of low-GI carbohydrates and with modest doses of soluble fibers would be of benefit to patients with type 2 diabetes. Intervention to reduce plasma lipids and postprandial glycemia in patients with diabetes could reduce the risk of patients developing atherosclerotic heart diseases. Dietary intervention might be one of the major approaches in patients with diabetes and might be useful in normal nondiabetic individuals.

ACKNOWLEDGMENT

We express our gratitude to Professor B. Guy-Grand (Nutrition Department, Hôtel-Dieu Hospital) for the opportunity to perform lipid and lipoprotein measurements in his laboratory.

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