BENEFICIAL EFFECTS OF HIGH DIETARY FIBER INTAKE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

MANISHA CHANDALIA, M.D., ABHIMANYU GARG, M.D., DIETER LUTJOHANN, PH.D., KLAUS VON BERGMANN, M.D., SCOTT M. GRUNDY, M.D., PH.D., AND LINDA J. BRINKLEY, R.D.

ABSTRACT

Background The effect of increasing the intake of dietary fiber on glycemic control in patients with type 2 diabetes mellitus is controversial.

Methods In a randomized, crossover study, we assigned 13 patients with type 2 diabetes mellitus to follow two diets, each for six weeks: a diet containing moderate amounts of fiber (total, 24 g; 8 g of soluble fiber and 16 g of insoluble fiber), as recommended by the American Diabetes Association (ADA), and a high-fiber diet (total, 50 g; 25 g of soluble fiber and 25 g of insoluble fiber) containing foods not fortified with fiber (unfortified foods). Both diets, prepared in a research kitchen, had the same macronutrient and energy content. We compared the effects of the two diets on glycemic control and plasma lipid concentrations.

Results Compliance with the diets was excellent. During the sixth week of the high-fiber diet, as compared with the sixth week of the ADA diet, mean daily preprandial plasma glucose concentrations were 13 mg per deciliter (0.7 mmol per liter) lower (95 percent confidence interval, 1 to 24 mg per deciliter [0.1 to 1.3 mmol per liter]; P=0.04) and mean daily urinary glucose excretion was 1.3 g lower (median difference, 0.23 g; 95 percent confidence interval, 0.03 to 1.83; P=0.008). The high-fiber diet also lowered the area under the curve for 24-hour plasma glucose and insulin concentrations, which were measured every two hours, by 10 percent (P=0.02) and 12 percent (P=0.05), respectively. The high-fiber diet reduced plasma total cholesterol concentrations by 6.7 percent (P=0.02), triglyceride concentrations by 10.2 percent (P=0.02), and very-low-density lipoprotein cholesterol concentrations by 12.5 percent (P=0.01).

Conclusions A high intake of dietary fiber, particularly of the soluble type, above the level recommended by the ADA, improves glycemic control, decreases hyperinsulinemia, and lowers plasma lipid concentrations in patients with type 2 diabetes. (N Engl J Med 2000;342:1392-8.)

DIETARY guidelines for patients with diabetes mellitus were revised by the American Diabetes Association (ADA) earlier this year.[1] The ADA recommends that the composition of the diet be individualized on the basis of a nutritional assessment and the outcomes desired. Consistent with the previous recommendations of the ADA,[2] the new guidelines advise replacing saturated fat with carbohydrates. However, on the basis of previous studies,[3-10] an alternative approach of replacing saturated fat with cis monounsaturated fat was also included in the recommendations.[1] This new approach is further supported by epidemiologic studies that have shown the healthful effects of diets rich in cis monounsaturated fat in Mediterranean countries.[11,12]

Another, less strongly emphasized aspect of Mediterranean diets is the high intake of fruits, vegetables, and grains that are rich sources of dietary fiber.[13,14] The ADA recommended a moderate increase in the intake of dietary fiber to 20 to 35 g per day because of the cholesterol-lowering effects of soluble fiber. However, the effects of dietary fiber on glycemic control were considered inconsequential.[1] Furthermore, the expert panel of the ADA considered it difficult to achieve a high dietary intake of soluble fiber without consuming foods or supplements fortified with fiber.[1] We therefore designed the present study to determine the effects on glycemic control and plasma lipid concentrations of increasing the intake of dietary fiber in patients with type 2 diabetes exclusively through the consumption of foods not fortified with fiber (unfortified foods) to a level beyond that recommended by the ADA. In addition, we studied the effects of such an intervention on the intestinal absorption of cholesterol and the fecal excretion of sterols in an attempt to uncover the mechanisms by which a high-fiber diet lowers plasma cholesterol.

METHODS

Patients

We studied 12 men and 1 woman (9 non-Hispanic whites and 4 blacks) with type 2 diabetes at the general clinical research center of the University of Texas Southwestern Medical Center at Dallas. The protocol for the study was approved by the institutional review board of the medical center, and each patient gave written informed consent. In all patients the onset of diabetes was insidious; the disease developed in most of the patients after 40 years of age. Their mean (±SD) age was 61±9 years (range, 45 to 70). Their mean body weight was 93.5±12.7 kg, and the mean body-mass index (the weight in kilograms divided by the square of the height in meters) was 32.3±3.9. Three patients were treated with diet alone, and the other 10 patients were treated with 2.5 to 20

From the Department of Internal Medicine (M.C., A.G., S.M.G., L.J.B.) and the Center for Human Nutrition (A.G., S.M.G.), University of Texas Southwestern Medical Center, Dallas; the Department of Veterans Affairs Medical Center, Dallas (M.C., A.G., S.M.G.); and the Department of Clinical Pharmacology, Rheinische Friedrich-Wilhelms-Universität, Bonn, Germany (D.L., K.B.). Address reprint requests to Dr. Garg at the Center for Human Nutrition, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd., Dallas, TX 75390.

mg of glyburide daily in addition to diet. The dose of glyburide was not changed during the study.

On entry into the study, the patients' plasma cholesterol and triglyceride concentrations after an overnight fast ranged from 151 to 324 mg per deciliter (3.90 to 8.38 mmol per liter) and 67 to 390 mg per deciliter (0.76 to 4.40 mmol per liter), respectively, and their fasting plasma glucose concentrations were less than 200 mg per deciliter (11.1 mmol per liter). Their glycosylated hemoglobin values ranged from 6.0 to 9.8 percent. Two patients had a history of coronary heart disease, but none had recently had a myocardial infarction, unstable angina pectoris, or congestive heart failure. Also, none had thyroid, renal, or hepatic disease. None of the patients were receiving lipid-lowering therapy.

Design of the Study

All the patients were first admitted to the general clinical research center for five days (the base-line period), during which a detailed history was taken, a physical examination was performed, and laboratory tests were performed. After the base-line period, all the patients received both the ADA diet and the high-fiber diet, each diet for a period of six weeks. Six patients received the high-fiber diet first, and the other seven received the ADA diet first. There was a median interval of seven days between the two study periods, during which the patients were instructed to consume an isocaloric diet. During the last week of each dietary period (days 36 to 42), the patients were hospitalized for evaluation.

On weekdays, all the patients ate at least one meal (breakfast, lunch, or dinner) at the general clinical research center. Other meals were supplied in packages so that they could be consumed at home. The dietitian monitored compliance by interviewing the patients. The patients were instructed to bring back any unconsumed food and to maintain a constant level of physical activity throughout the study.

Blood for lipid analyses was drawn, after an overnight fast, daily for two days before the institution of the study diet and daily on days 38 through 42 during both dietary periods. Plasma glucose was measured at 7 and 11 a.m. and at 4 and 8 p.m. each day during the base-line period and on days 38 through 42 of both dietary periods. Glycosylated hemoglobin was measured during the base-line period and at the end of each dietary period. On the last day of each dietary period, blood samples were obtained every two hours for measurements of plasma glucose and insulin. On days 38 through 42, patients collected 24-hour urine specimens for quantitative determination of glucose.

To permit us to determine fecal sterol balance and the percentage of cholesterol absorption, each patient took a capsule containing 30 mg of sitostanol, 3 mg of [26,26,26,27,27,27-$^{2}H_{6}$]-cholesterol, and 3 mg of [5,6,22,23-$^{2}H_{4}$]-sitostanol (Medical Isotopes, Pelham, N.H.) three times a day on days 36 through 42. Fecal samples were collected on day 35 or 36 and on the last three days of each dietary period. Fecal samples were frozen within 12 hours after collection and were pooled for analysis of small aliquots.

Diets

The composition of the study diets is shown in Table 1. The composition of the diets was calculated by means of a software program based on the Department of Agriculture Handbook Series 8 (Nutriplanner, Practocare, San Diego, Calif.).[15] The content of total as well as soluble and insoluble dietary fiber was estimated according to the data provided in the *CRC Handbook of Dietary Fiber in Human Nutrition*.[16] Both diets consisted of unfortified foods. The patients were allowed some choices of food items. Both diets provided 15 percent of the total energy as protein, 55 percent as carbohydrate, and 30 percent as fat; saturated, cis monounsaturated, and polyunsaturated fats accounted for 7 percent, 17 percent, and 6 percent of the total energy, respectively.

The high-fiber diet provided 50 g of total fiber per day; soluble and insoluble fiber content provided 25 g each. The ADA diet contained 24 g of total fiber per day, with 8 g as soluble fiber and 16 g as insoluble fiber. Unfortified foods, particularly those rich

Table 1. Composition of the Study Diets.

Constituent	ADA Diet*	High-Fiber Diet
Carbohydrate (% of total energy)	55	55
Protein (% of total energy)	15	15
Fat (% of total energy)	30	30
Saturated	7	7
Cis monounsaturated	17	17
Polyunsaturated	6	6
Cholesterol (mg/day)	300	297
Fiber (g/day)		
Total	24	50
Soluble	8	25
Insoluble	16	25

*ADA denotes American Diabetes Association.

Table 2. Sample Menus of the Study Diets.*

ADA Diet: Food	Weight (grams)	High-Fiber Diet: Food	Weight (grams)
Breakfast			
Orange juice	220	Orange sections	300
White grits	50	Oatmeal	50
Egg substitute	40	Scrambled egg	37
Olive oil	10	Olive oil	10
Decaffeinated coffee	2	Decaffeinated coffee	2
Lunch			
Ham (5% fat)	50	Ham (5% fat)	52
Mayonnaise	6	Mayonnaise	12
Iceberg lettuce	15	Iceberg lettuce	10
Fresh tomato	30	Fresh tomato	15
Low-sodium bread	60	Whole-wheat bread	60
Corn (canned)	140	Corn (canned)	40
Cider vinegar	5	Green peas (canned)	110
Dehydrated onion	2	Dehydrated onion	2
Olive oil	10	Olive oil	10
Fresh green pepper	10	Fresh green pepper	10
Fresh celery	15	Fresh celery	15
Fruit cocktail (canned)	105	Fresh papaya	250
Instant tea	2	Instant tea	2
Oatmeal raisin cookie	20		
Dinner			
Chicken breast (skinned)	90	Chicken breast (skinned)	90
Bran flakes	10	Bran flakes	10
Low-sodium bread	20	Oat bran	5
Parmesan cheese	1	Parmesan cheese	1
Whole egg	1	Egg substitute	10
Tomato (canned)	120	Tomato (canned)	105
Low-fat cheese	11	Low-fat cheese	19
Spaghetti	45	Spaghetti	19
Green beans	75	Zucchini	195
Olive oil	17	Olive oil	19
Whole-wheat bread	21	Whole-wheat bread	30
Graham crackers	21	Fresh peaches	300
Instant tea	2	Instant tea	2
Bedtime snack			
Mozzarella cheese	30	Fruit cocktail (canned)	200
Low-sodium bread	30	Cherries (canned)	100
Pineapple juice	190	Granola	15

*Each menu provided 2308 kcal per day. ADA denotes American Diabetes Association.

in soluble fiber, such as cantaloupe, grapefruit, orange, papaya, raisins, lima beans, okra, sweet potato, winter squash, zucchini, granola, oat bran, and oatmeal, were used to achieve high-fiber intake. No fiber supplements were used. Sample menus of both the study diets are shown in Table 2. The individual foods were weighed daily during meal preparation in the research kitchen of the general clinical research center.

Biochemical Analyses

Fasting plasma total cholesterol, lipoprotein cholesterol, and triglycerides were measured according to the procedures of the Lipid Research Clinics.[17] Cholesterol and triglycerides were measured enzymatically with the use of kits (Boehringer Mannheim, Indianapolis). Very-low-density lipoproteins (VLDLs) (density, less than 1.006 g per milliliter) were removed by ultracentrifugation, and cholesterol was measured in the VLDL fraction and the infranatant. High-density-lipoprotein (HDL) cholesterol was measured enzymatically after lipoproteins containing apolipoprotein B had been precipitated with heparin–manganese. Cholesterol in the low-density lipoprotein (LDL) fraction was estimated to be the difference between the cholesterol content of the infranatant and that of the HDL fraction.

Plasma and urinary glucose were measured by the glucose oxidase method (Beckman Glucose Analyzer, Beckman Instruments, Fullerton, Calif.). Glycosylated hemoglobin was measured with ion-exchange high-performance liquid chromatography (Bio-Rad Laboratories, Hercules, Calif.). Plasma insulin was measured by radioimmunoassay.[18,19]

Pooled fecal samples collected within the last week of each dietary period were prepared for analysis of neutral and acidic fecal sterols as described previously.[20] Gas–liquid chromatography of neutral and acidic fecal sterols was performed on a gas chromatograph (model HP5890, Hewlett–Packard, Palo Alto, Calif.) equipped with an automatic sample injector. Cholesterol absorption was measured during the same period from fecal samples by gas–liquid chromatography and mass spectrometry.[21]

Statistical Analysis

To compare the two study periods and to assess the effect of the sequence in which the patients received the high-fiber and ADA diets, we used repeated-measures analysis of variance.[22] For skewed data, we used the Wilcoxon signed-rank test to compare the two dietary periods.[23]

RESULTS

The compliance with both the study diets was excellent, according to interviews with the patients and estimates of the energy content of any leftover foods. Three patients reported consuming extra food on one day during the study, two while eating the high-fiber diet and one the ADA diet. The patients commented about the larger quantities of food in the high-fiber diet, but they consumed all the food given to them. The results are presented irrespective of the order of the diets, because the sequence of the diets had no effect on the results.

During the last week of each study period, the patients in both groups had similar daily energy intakes and body weights and received a similar dose of glyburide (Table 3). The mean plasma glucose concentration was lower (by 13 mg per deciliter [0.7 mmol per liter], or 8.9 percent) when patients completed the high-fiber diet than when they completed the ADA diet (P=0.04), and mean daily urinary glucose excretion was 1.3 g lower (P=0.008). Daily plasma glucose concentrations were 10 percent lower with the high-fiber diet than with the ADA diet (values for the area under the curve, 3743±944 vs. 3365±1003 mg·hour per deciliter [207.8±52.4 vs. 186.8±55.7 mmol·hour per liter]; P=0.02), and plasma insulin concentrations were 12 percent lower (values for the area under the curve, 1107±650 vs. 971±491 μU·hour per milliliter [6642±3900 vs. 5826±2946 pmol·hour per liter]; P=0.05) (Fig. 1). Gly-

TABLE 3. METABOLIC VARIABLES DURING THE LAST WEEK OF THE STUDY PERIODS (DAYS 38 THROUGH 42).*

VARIABLE	ADA DIET	HIGH-FIBER DIET	DIFFERENCE BETWEEN DIETS (95% CI)	P VALUE†
Energy intake (kcal/day)	2308±236	2308±236	—	1.00
Weight (kg)	90.7±13.3	90.5±12.7	−0.2 (−1.1 to 0.6)	0.60
Dose of glyburide (mg/day)	10.0±8.7	10.0±8.7	—	1.00
Plasma glucose (mg/deciliter)‡	142±36	130±38	−13 (−24 to −1)	0.04
Urinary glucose (g/day)				
Mean	2.3±4.3	1.0±1.9	—	—
Median§	0.76	0.0	−0.23 (−1.83 to −0.03)	0.008
Glycosylated hemoglobin (%)	7.2±1.3	6.9±1.2	−0.3 (−0.6 to 0.1)	0.09

*Plus–minus values are means ±SD. ADA denotes American Diabetes Association, and CI confidence interval.

†An analysis of variance was used to compare the two diets, except for urinary glucose, for which the Wilcoxon signed-rank test was used.

‡The values are averages of plasma glucose concentrations measured at 7 and 11 a.m. and at 4 and 8 p.m. each day for five days during hospitalization. To convert values for plasma glucose to millimoles per liter, multiply by 0.056.

§The values are averages of five daily urine collections during hospitalization.

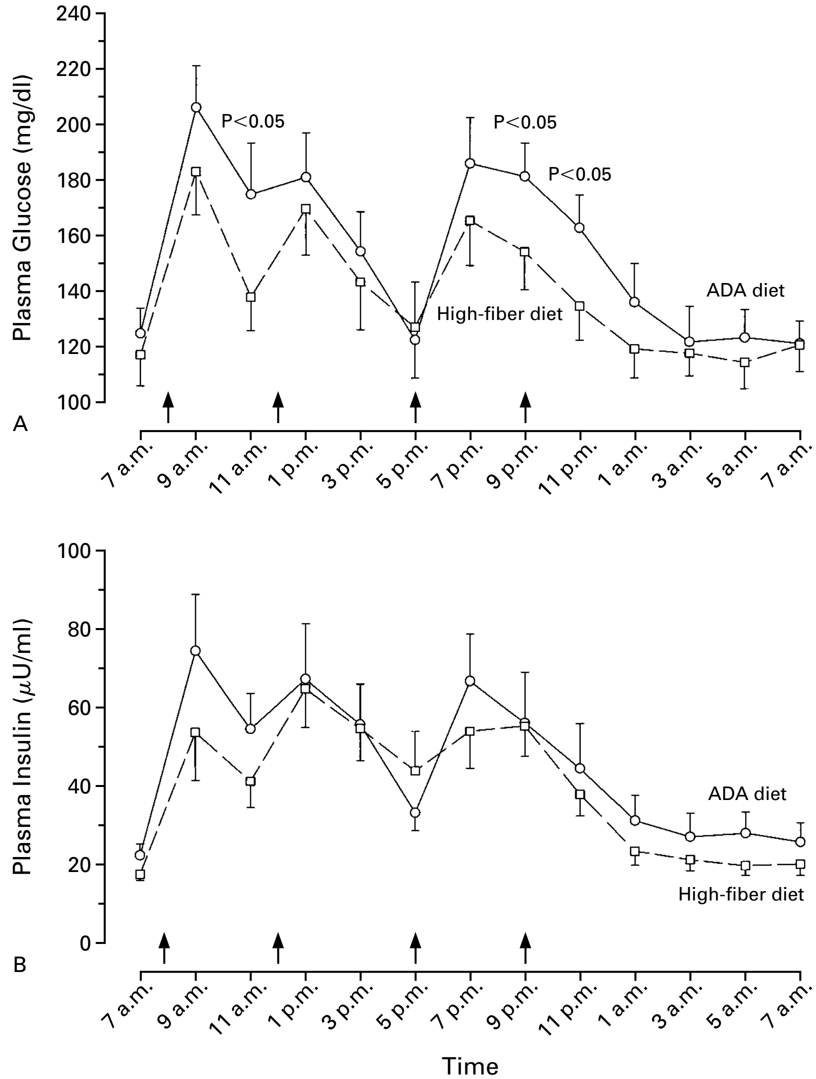

Figure 1. Mean (±SE) 24-Hour Profile of Plasma Glucose Concentrations (Panel A) and Insulin Concentrations (Panel B) during the Last Day of the American Diabetes Association (ADA) Diet and the Last Day of the High-Fiber Diet in 13 Patients with Type 2 Diabetes Mellitus.

The arrows indicate the times at which the main meals and a snack were consumed during the day. To convert values for glucose to millimoles per liter, multiply by 0.056. To convert values for insulin to picomoles per liter, multiply by 6.

cosylated hemoglobin values were slightly lower after the high-fiber diet (P=0.09).

As compared with the ADA diet, the high-fiber diet resulted in a lower fasting plasma total cholesterol concentration (by 6.7 percent, P=0.02), a lower plasma triglyceride concentration (by 10.2 percent, P=0.02), and a lower plasma VLDL cholesterol concentration (by 12.5 percent, P=0.01) (Table 4). The fasting plasma LDL cholesterol concentration was 6.3 percent lower with the high-fiber diet (P=0.11). There were no significant differences between the two diets in terms of the fasting plasma HDL cholesterol concentration.

As compared with the ADA diet, the high-fiber diet decreased gastrointestinal absorption of cholesterol by 10 percent (48.5±9.6 vs. 43.7±7.4 percent; 95 percent confidence interval for the decrease, 0.6 to 9.0 percent; P=0.03) and increased fecal acidic sterol excretion by 41 percent (895±301 vs. 1258±458 mg per day; 95 percent confidence interval for the increase, 137 to 589 mg per day; P=0.005), but did not significantly affect the excretion of neutral

TABLE 4. FASTING PLASMA LIPID AND LIPOPROTEIN CONCENTRATIONS DURING THE LAST WEEK OF THE STUDY PERIODS (DAYS 38 THROUGH 42).*

VARIABLE	ADA DIET	HIGH-FIBER DIET	DIFFERENCE BETWEEN DIETS (95% CI)	P VALUE†
	mg/dl			
Plasma total cholesterol	210±33	196±31	−14 (−27 to −2)	0.02
Plasma triglycerides	205±95	184±76	−21 (−37 to −4)	0.02
Plasma VLDL cholesterol	40±19	35±16	−5 (−9 to −1)	0.01
Plasma LDL cholesterol	142±29	133±29	−9 (−22 to 3)	0.11
Plasma HDL cholesterol	29±7	28±4	−1 (−4 to 3)	0.80

*Plus–minus values are means ±SD. To convert values for cholesterol and triglycerides to millimoles per liter, multiply by 0.026 and 0.011, respectively. ADA denotes American Diabetes Association, CI confidence interval, VLDL very-low-density lipoprotein, LDL low-density lipoprotein, and HDL high-density lipoprotein.

†An analysis of variance was used to compare the two diets.

sterols (1052±375 vs. 1122±565 mg per day; 95 percent confidence interval for the difference, −194 to 334 mg per day; P=0.60).

DISCUSSION

The intake of dietary fiber among people living in Western countries remains low, and according to the Third National Health and Nutrition Examination Survey (NHANES), it averages 17 g per day in the United States.[24] Although patients with diabetes are advised to increase their intake of dietary fiber, in the NHANES study, their average daily intake was found to be only 16 g.[24] Why the intake of dietary fiber in patients with diabetes remains low — despite its well-documented effect of lowering plasma cholesterol concentrations — remains unexplained. It is possible that the controversy about whether there are beneficial effects of dietary fiber on glycemic control reduces the enthusiasm of physicians and dietitians for recommending high-fiber diets. The main purpose of our study was to investigate the effects on glycemic control of increasing the intake of dietary fiber. To avoid the confounding effects of concomitant changes in energy and macronutrients, the two study diets were isocaloric and the macronutrient composition of the diets was identical. Furthermore, unfortified foods were used as the source of dietary fiber.

Most important, we found that the high-fiber diet improved glycemic control, as evidenced by decreases in the mean daily preprandial and 24-hour plasma glucose concentrations. Urinary glucose excretion was also lowered by the high-fiber diet. The high-fiber diet lowered glycosylated hemoglobin values slightly but not significantly. The high-fiber diet also lowered 24-hour plasma insulin concentrations.

The results of previous studies that evaluated the role of dietary fiber on glycemic control in patients with type 2 diabetes were inconsistent. In some of the studies, the lack of control for concomitant changes in the intake of macronutrients makes the data difficult to interpret. For example, in the study by Kiehm et al.[25] and in that by Simpson et al.,[26] the high-fiber diet had a lower fat and higher carbohydrate content than the low-fiber diet. In other studies, the interpretation of the results was confounded by the short duration of the dietary intervention,[27-29] the lack of random assignment of the sequence of the high-fiber and low-fiber diets,[27,29] and unexplained weight loss during the high-fiber diet.[29]

Only a few well-controlled studies have evaluated the glycemic effects of increasing the intake of dietary fiber with the use of either preparations of refined concentrated fiber or unfortified food, and the results have been inconsistent.[1,30] For example, diets that included 15 to 21 g of guar-gum fiber or oat-bran concentrate per day had no effect on glycemic control[31,32] or resulted in only a slight improvement.[33,34] In randomized, crossover trials of six weeks' duration in which the intake of dietary fiber was increased by 16 g per 1000 kcal through the consumption of foods prepared in a research kitchen or by 14 g per day through dietary instruction, there was no improvement in glycemic control.[35,36] In contrast, increasing dietary fiber by 23 g for three weeks and by 30 g for six weeks resulted in decreased fasting and postprandial plasma glucose concentrations.[37,38] We found that an increase in the intake of total dietary fiber, which consisted predominantly of soluble fiber, significantly improved glycemic control and decreased the degree of hyperinsulinemia in patients with type 2 diabetes.

Our study also demonstrates the feasibility of achieving a high intake of dietary soluble fiber by consuming unfortified foods. Our patients accepted the high-fiber diet well and had few side effects; therefore, we recommend that patients with diabetes be encouraged to use unfortified foods instead of less palatable purified-fiber preparations and supplements to increase their intake of dietary fiber.

The mechanisms of the improved glycemic control associated with high fiber intake remain undefined. Whether this effect is due to an increase in soluble fiber, insoluble fiber, or both is unclear. Besides causing increased fecal excretion of bile acids, dietary fiber may cause malabsorption of fat.[39] However, in our study, the patients' weight did not change with the high-fiber diet, which suggests that the degree of reduction in the absorption of fat was insignificant. Another possibility is that dietary fiber improves glycemic control by reducing or delaying the absorption of carbohydrates.

As expected, the high-fiber diet reduced plasma total cholesterol concentrations by 6.7 percent, a finding consistent with the results of previous reports of the cholesterol-reducing effects of soluble but not insoluble fiber.[40,41] Therefore, the lowering of cholesterol can be attributed primarily to an average increase of 17 g in the intake of soluble fiber. Previous studies in normal subjects have reported no effects of the amount of dietary fiber on plasma triglyceride concentrations.[42] In our study, the decrease in plasma triglyceride and VLDL cholesterol concentrations during the high-fiber diet could have been due to the improvement in glycemic control.

The mechanisms of the reduction in plasma cholesterol concentrations induced by the increased dietary fiber intake are controversial, however. The increase in bile-acid excretion probably explains most of the reduction, and the reduction in cholesterol absorption may also have contributed to this finding. Previous studies have also reported a variable increase in bile-acid excretion resulting from the consumption of pectin,[39,43] oat bran,[44,45] bagasse,[46] and diets with a mixture of soluble fiber and insoluble fiber,[47] but not psyllium.[48] In contrast, Kesaniemi et al.[47] reported that a high-fiber diet did not change cholesterol absorption in normal subjects. However, the high-fiber diet they used included 26 g of fiber, and it did not lower plasma cholesterol concentrations.[47]

In conclusion, an increase in the intake of dietary fiber, predominantly of the soluble type, by patients with type 2 diabetes mellitus improved glycemic control and decreased hyperinsulinemia in addition to the expected lowering of plasma lipid concentrations. Therefore, dietary guidelines for patients with diabetes should emphasize an overall increase in dietary fiber through the consumption of unfortified foods, rather than the use of fiber supplements.

Supported in part by grants (M01-RR00633 and HL-29252) from the National Institutes of Health and by research grants from the Bundesministerium für Bildung, Forschung, Wissenschaft und Technologie (01EC9402) and the Deutsche Forschungsgemeinschaft (BE 1673/1-1).

We are indebted to Angela Osborn, Travis Petricek, and the nursing and dietetic service of the General Clinical Research Center of the University of Texas Southwestern Medical Center, Dallas, for their excellent technical support and to Beverley Adams-Huet, M.S., for statistical analysis.

REFERENCES

1. Nutrition recommendations and principles for people with diabetes mellitus. Diabetes Care 2000;23:S43-S46.

2. American Diabetes Association. Nutritional recommendations and principles for individuals with diabetes mellitus: 1986. Diabetes Care 1987;10:126-32.

3. Garg A, Bonanome A, Grundy SM, Zhang Z-J, Unger RH. Comparison of a high-carbohydrate diet with high-monounsaturated-fat diet in patients with non-insulin-dependent diabetes mellitus. N Engl J Med 1988; 319:829-34.

4. Rivellese AA, Giacco R, Genovese S, et al. Effects of changing amount of carbohydrate in diet on plasma lipoproteins and apolipoproteins in type II diabetic patients. Diabetes Care 1990;13:446-8.

5. Parillo M, Rivellese AA, Ciardullo AV, et al. A high-monounsaturated-fat/low-carbohydrate diet improves peripheral insulin sensitivity in non-insulin-dependent diabetic patients. Metabolism 1992;41:1373-8.

6. Rasmussen OW, Thomsen C, Hansen KW, Vesterlund M, Winther E, Hermansen K. Effects on blood pressure, glucose, and lipid levels of a high-monounsaturated fat diet compared with a high-carbohydrate diet in NIDDM subjects. Diabetes Care 1993;16:1565-71.

7. Campbell LV, Marmot PE, Dyer JA, Borkman M, Storlien LH. The high-monounsaturated fat diet as a practical alternative for NIDDM. Diabetes Care 1994;17:177-82.

8. Lerman-Garber I, Ichazo-Cerro S, Zamora-Gonzalez J, Cardoso-Saldana G, Posadas-Romero C. Effect of a high-monounsaturated fat diet enriched with avocado in NIDDM patients. Diabetes Care 1994;17:311-5.

9. Garg A, Grundy SM, Unger RH. Comparison of effects of high and low carbohydrate diets on plasma lipoproteins and insulin sensitivity in patients with mild NIDDM. Diabetes 1992;41:1278-85.

10. Garg A, Bantle JP, Henry RR, et al. Effects of varying carbohydrate content of diet in patients with non-insulin-dependent diabetes mellitus. JAMA 1994;271:1421-8.

11. Keys A, Menotti A, Karvonen MJ, et al. The diet and 15-year death rate in the Seven Countries Study. Am J Epidemiol 1986;124:903-15.

12. Menotti A, Keys A, Aravanis C, et al. Seven Countries Study: first 20-year mortality data in 12 cohorts of six countries. Ann Med 1989;21:175-9.

13. Nestle M. Mediterranean diets: historical and research overview. Am J Clin Nutr 1995;61:Suppl:1313S-1320S.

14. Kromhout D, Keys A, Aravanis C, et al. Food consumption patterns in the 1960s in seven countries. Am J Clin Nutr 1989;49:889-94.

15. Department of Agriculture, Agricultural Research Service. Composition of foods. Agriculture handbook No. 8. Series 8-1 to 8-16. Washington, D.C.: Government Printing Office, 1976-1987.

16. Schakel S, Sievert YA, Buzzard IM. Dietary fiber values for common foods. In: Spiller GA, ed. CRC handbook of dietary fiber in human nutrition. 2nd ed. Boca Raton, Fla.: CRC Press, 1993:567-93.

17. Public Health Service. Manual of laboratory operations: lipid research clinics program: lipid and lipoprotein analysis. 2nd ed. Washington, D.C.: Government Printing Office, 1982.

18. Herbert V, Lau KS, Gottlieb CW, Bleicher SJ. Coated charcoal immunoassay of insulin. J Clin Endocrinol Metab 1965;25:1375-84.

19. Yalow RS, Berson SA. Immunoassay of endogenous plasma insulin in man. J Clin Invest 1960;39:1157-75.

20. Czubayko F, Beumers B, Lammsfuss S, Lutjohann D, von Bergmann K. A simplified micro-method for quantification of fecal excretion of neutral and acidic sterols for outpatient studies in humans. J Lipid Res 1991; 32:1861-7.

21. Lutjohann D, Meese CO, Crouse JR III, von Bergmann K. Evaluation of deuterated cholesterol and deuterated sitostanol for measurement of cholesterol absorption in humans. J Lipid Res 1993;34:1039-46.

22. Jones B, Kenward MG. Design and analysis of crossover trials. London: Chapman & Hall, 1989.

23. Conover WJ. Practical nonparametric statistics. 2nd ed. New York: John Wiley, 1980:288-92.

24. National Health and Nutrition Examination Survey III, 1988-94. NCHS CD-ROM series 11. No. 2A. ASCII version. Hyattsville, Md.: National Center for Health Statistics, April 1998.

25. Kiehm TG, Anderson JW, Ward K. Beneficial effects of a high carbohydrate, high fiber diet on hyperglycemic diabetic men. Am J Clin Nutr 1976;29:895-9.

26. Simpson HCR, Simpson RW, Lousley S, et al. A high carbohydrate leguminous fibre diet improves all aspects of diabetic control. Lancet 1981; 1:1-5.

27. Rivellese A, Riccardi G, Giacco A, et al. Effect of dietary fibre on glucose control and serum lipoproteins in diabetic patients. Lancet 1980;2: 447-50.

28. Riccardi G, Rivellese A, Pacioni D, Genovese S, Mastranzo P, Mancini M. Separate influence of dietary carbohydrate and fibre on the metabolic control in diabetes. Diabetologia 1984;26:116-21.

29. O'Dea K, Traianedes K, Ireland P, et al. The effects of diet differing in fat, carbohydrate, and fiber on carbohydrate and lipid metabolism in type II diabetes. J Am Diet Assoc 1989;89:1076-86.

30. Nuttall FQ. Dietary fiber in the management of diabetes. Diabetes 1993;42:503-8.

31. Holman RR, Steemson J, Darling P, Turner RC. No glycemic benefit from guar administration in NIDDM. Diabetes Care 1987;10:68-71.

32. Uusitupa M, Siitonen O, Savolainen K, Silvasti M, Penttila I, Parviainen M. Metabolic and nutritional effects of long-term use of guar gum in the treatment of noninsulin-dependent diabetes of poor metabolic control. Am J Clin Nutr 1989;49:345-51.

33. Aro A, Uusitupa M, Voutilainen E, Hersio K, Korhonen T, Siitonen O. Improved diabetic control and hypocholesterolaemic effect induced by long-term dietary supplementation with guar gum in type 2 (insulin-independent) diabetes. Diabetologia 1981;21:29-33.

34. Pick ME, Hawrysh ZJ, Gee MI, Toth E, Garg ML, Hardin RT. Oat

bran concentrate bread products improve long-term control of diabetes: a pilot study. J Am Diet Assoc 1996;96:1254-61.
35. Hollenbeck CB, Coulston AM, Reaven GM. To what extent does increased dietary fiber improve glucose and lipid metabolism in patients with noninsulin-dependent diabetes mellitus (NIDDM)? Am J Clin Nutr 1986; 43:16-24.
36. Manhire A, Henry CL, Hartog M, Heaton KW. Unrefined carbohydrate and dietary fibre in treatment of diabetes mellitus. J Hum Nutr 1981; 35:99-101.
37. Karlstrom B, Vessby B, Asp NG, et al. Effects of an increased content of cereal fibre in the diet of type 2 (non-insulin-dependent) diabetic patients. Diabetologia 1984;26:272-7.
38. Hagander B, Asp NG, Efendic S, Nilsson-Ehle P, Schersten B. Dietary fiber decreases fasting blood glucose levels and plasma LDL concentration in noninsulin-dependent diabetes mellitus patients. Am J Clin Nutr 1988; 47:852-8.
39. Kay RM, Truswell AS. Effect of citrus pectin on blood lipids and fecal steroid excretion in man. Am J Clin Nutr 1977;30:171-5.
40. Jenkins DJ, Newton C, Leeds AR, Cummings JH. Effect of pectin, guar gum, and wheat fibre on serum-cholesterol. Lancet 1975;1:1116-7.
41. Hillman LC, Peters SG, Fisher CA, Pomare EW. The effects of the fiber components pectin, cellulose and lignin on serum cholesterol levels. Am J Clin Nutr 1985;42:207-13.
42. Brown L, Rosner B, Willett WW, Sacks FM. Cholesterol-lowering effects of dietary fiber: a meta-analysis. Am J Clin Nutr 1999;69:30-42.
43. Cummings JH, Southgate DAT, Branch WJ, et al. The digestion of pectin in the human gut and its effect on calcium absorption and large bowel function. Br J Nutr 1979;41:477-85.
44. Kirby RW, Anderson JW, Sieling B, et al. Oat-bran intake selectively lowers serum low-density lipoprotein cholesterol concentrations of hypercholesterolemic men. Am J Clin Nutr 1981;34:824-9.
45. Zhang JX, Hallmans G, Andersson H, et al. Effect of oat bran on plasma cholesterol and bile acid excretion in nine subjects with ileostomies. Am J Clin Nutr 1992;56:99-105.
46. Walters RL, Baird IM, Davies PS, et al. Effects of two types of dietary fibre on faecal steroid and lipid excretion. BMJ 1975;2:536-8.
47. Kesaniemi YA, Tarpila S, Miettinen TA. Low vs high dietary fiber and serum, biliary, and fecal lipids in middle-aged men. Am J Clin Nutr 1990; 51:1007-12.
48. Abraham ZD, Mehta T. Three-week psyllium-husk supplementation: effect on plasma cholesterol concentrations, fecal steroid excretion, and carbohydrate absorption in men. Am J Clin Nutr 1988;47:67-74.