Effect of Digestible Carbohydrates on Glucose Control in Insulin-dependent Diabetic Patients

NICOLA PERROTTI, M.D., DONATELLA SANTORO, M.D., SALVATORE GENOVESE, M.D., ANGELA GIACCO, R.D., ANGELA RIVELLESE, M.D., AND GABRIELE RICCARDI, M.D.

Recent studies have demonstrated that high-carbohydrate–high-fiber diets may improve the metabolic control in diabetes. To evaluate the influence of dietary carbohydrates separate from dietary fiber on blood glucose control, six insulin-dependent diabetic patients (IDD) were assigned in random order to two weight-maintaining diets for consecutive periods of 10 days. The diets differed in carbohydrate (41% in diet A and 60% in diet B) and fat content (41% and 20%, respectively) but were identical in calories, proteins, simple sugars, and fiber. After each dietary period blood glucose was continuously monitored for 24 h (Biostator GCIIS, Life Science Instruments, Miles Laboratories, Elkhart, Indiana). The M value was 48 ± 20 after diet A and 96 ± 27 after diet B ($t = 3.83$, $P < 0.025$); the mean daily blood glucose was 152 ± 5 mg/dl after diet A and 206 ± 11 mg/dl after diet B ($t = 7.50$, $P < 0.001$). Similarly, the blood glucose level for the 3-h period after each of the three main meals was lower after diet A than after diet B (analysis of variance: $F = 5.2$, $P < 0.05$). No significant difference in fasting serum cholesterol, triglycerides, or serum lipoprotein composition was observed between the two diets. In order to separate the influence of dietary carbohydrate and fat on postprandial blood glucose concentration, an additional test meal experiment was performed in eight insulin-dependent diabetic patients. In random order on consecutive days they were given two standard meals that were identical in carbohydrate and protein content and differed only in the amount of olive oil added to the meals (12 g versus 36 g). The average blood glucose increments calculated for the 3 h after the meal were almost identical after the high-fat and the low-fat test meal. It is concluded that increasing the amount of dietary carbohydrate leads to the deterioration of blood glucose control in IDD patients. DIABETES CARE 1984; 7:354–59.

Diet is generally considered to be an important step in the treatment of both insulin-dependent and non-insulin-dependent diabetes mellitus.[1] Although general agreement has been reached about the usefulness of hypocaloric diets for obese non-insulin-dependent diabetic patients, uncertainties still exist about the appropriate carbohydrate content in isoenergetic diets for nonobese insulin-dependent patients (IDD).

Low-carbohydrate–high-fat diets have been used for a long time but at present high-carbohydrate–low-fat diets have gained favor on the assumption that a high-lipid content may be responsible for atherogenicity in diabetes mellitus.[2,3]

A number of papers have been published[4–7] about the value of high-carbohydrate–low-fat diets for the treatment of diabetes mellitus. In some experiments nonphysiologic formula diets were used;[4] in others dietary carbohydrates and fiber were both increased.[5–7]

The benefits of a high-fiber diet for the treatment of diabetes mellitus have been demonstrated by our group and others in previous reports.[8–10] These reports have not proved that high-carbohydrate diets might be useful for the treatment of diabetes without a parallel increase in plant fiber content.

The aim of this study was to evaluate, in IDD patients, the metabolic effect of a high-carbohydrate–low-fat diet compared with a traditional low-carbohydrate–high-fat diet. Both diets were equal in plant fiber content.

Moreover, since a high-fat intake might affect the rate of glucose absorption,[11,12] an additional experiment was performed to evaluate the influence of dietary fat on blood glucose concentration in the postprandial period.

SUBJECTS AND METHODS

Patients

All patients were recruited from our outpatient clinic and gave their informed consent to participate.

Experiment 1. Six IDD patients participated in this experiment. They were aged 20–47 yr and had diabetes for at least 2 yr. For three patients a fasting C-peptide measurement was available and was below the limits of sensitivity of the assay.[13] The remaining three patients had suffered one or more episodes of ketoacidosis.[14] Their clinical data are listed in Table 1.

Experiment 2. Eight IDD patients took part in this experiment. The age of the group ranged from 15 to 32 yr, and the duration of diabetes ranged from 1 to 26 yr. Also, for these patients the diagnosis of insulin-dependent diabetes was established either on the basis of C-peptide measurements (two patients) or on the basis of their proneness to ketosis.[13,14]

Experimental Protocol

Experiment 1. Patients were given two weight-maintaining diets differing in carbohydrate content. In the low-carbohydrate diet (diet A), carbohydrates represented 41% of total calories; in the high-carbohydrate diet (diet B), they represented 60% of total calories (Table 2). The amount of soluble carbohydrates was identical in both diets: 66 g in diet A and 66 g in diet B; the difference in the carbohydrate content was due only to starch and was obtained by varying the amount of bread (80%) and pasta (20%). The amount of plant fiber was also identical in both diets and was derived mainly from cereals, leafy vegetables, and fruit. The variation in dietary fat was obtained by changes in the daily consumption of olive oil.

Patients were given the two diets in random order for consecutive 10-day periods (three patients started with diet A and three with diet B). The diets were given as two main meals (midday and evening), a light breakfast, and three snacks consumed during the day.

Patients were instructed to fill a 7-day food record that was evaluated at the end of the 10-day dietary period. If the diet consumed was different from that prescribed (±15%), the patient was instructed to continue for one more week avoiding further deviations from the prescribed diet. This occurred once for diet A and three times for diet B. After the additional week of diet none of the patients showed a lack of adherence to the prescribed diet.

After each of the two dietary periods patients were admitted to a metabolic ward for 24 h of continuous blood glucose monitoring by means of the Biostator GCIIS (Life Science Instruments, Miles Laboratories, Elkhart, Indiana).

To avoid acute modifications of blood glucose concentration, during the night preceding the monitoring euglycemia was maintained by means of a glucose-controlled insulin infusion system (in addition to the usual evening dose of insulin), so that initial blood glucose values were comparable with both diets.

On the day of the experiment, patients consumed the same type of diet they had at home. Time and dosage of the insulin therapy were kept constant during the duration of the experiment and are listed in Table 1. Blood glucose concen-

TABLE 1
Patients' clinical features

Patient	Sex	Age (yr)	Duration of diabetes	BMI	Insulin dose (IU)*	
					8 a.m.	8 p.m.
			Experiment 1			
1. T.R.	F	46	6	26.5	12L	8L + 6R
2. C.A.	F	20	15	26.1	14L	4L + 8R
3. G.C.	M	27	14	24.2	25L	16L + 10R
4. A.G.	M	20	7	19.7	18L	10L + 6R
5. F.A.R.	F	19	8	27.3	30L	10L + 10R
6. S.C.	M	33	3	21.6	32L	—
Mean ± SD		27 ± 10	9 ± 5	24.2 ± 3.0	36 ± 11	
			Experiment 2			
7. U.D.	M	32	5	22.6	38L	10L + 16R
8. R.U.	M	28	3	22.0	20L	10L + 10R
9. P.D.	M	19	10	20.3	40L	8L + 10R
10. S.N.	F	18	10	24.5	6L	20L + 10R
11. P.C.	F	20	3	22.7	14L	10L + 6R
12. G.P.	M	23	3	24.7	28L	16L + 10R
13. M.I.	F	30	26	27.5	38L	18L + 10R
14. N.L.	F	15	1	19.1	32L	24L + 8R
Mean ± SD		23 ± 6	8 ± 8	22.9 ± 2.6	51 ± 14	

*Insulin type: L = lente; R = regular.

TABLE 2
Composition of the two 2000-kcal diets

	g/day	Percent	g/day	Percent
Protein	87	18	94	20
Fat				
Total	90	41	42	20
Saturated	21		11	
Polyunsaturated	8		3	
Monounsaturated	61		28	
Cholesterol	0.400		0.360	
P/S	0.4		0.3	
Carbohydrate				
Total	211	41	312	60
Simple	70		76	
Complex	140		236	
Plant fiber	28		28	

tration was measured every 10 min and used for computation of (1) the average daily blood glucose (the mean of all measurements for 24 h); (2) the average after-meal blood glucose (the mean of all measurements for a 3-h period after breakfast, lunch, and dinner); (3) the M value. This value is derived from the mathematical formula $|10 \log BG/80|$,[3] which takes into account all the deviations of blood glucose concentration from an arbitrarily selected standard value (80 mg/dl) in a 24-h period.[15]

According to this formula a normal person has an M value approaching zero, while a diabetic person has an M value that increases with the magnitude of glycemic excursions during the day. In this study the M value for each subject was calculated on the basis of 144 blood glucose measurements taken every 10 min for 24 h.

The blood glucose level at 8 a.m., after 24 h of monitoring, was used as an estimate of the fasting blood glucose concentration.

Cholesterol and triglycerides were measured by enzymatic methods[14,15] on a fasting serum specimen and on serum lipoproteins separated by preparative ultracentrifugation.[16]

Experiment 2. On two consecutive days, the patients were given test meals closely resembling the composition of the lunch in the high-carbohydrate diet (diet B) of the previous experiment. To this meal, on one occasion, 24 g of olive oil was added. This amount represents the difference in the lipid content between the main meals of diets A and B of experiment 1. In other words, the two test meals were different only for the lipid (18 and 42 g, respectively) and for the energy content (1100 and 1400 kcal, respectively). The other dietary components, namely, carbohydrates (186 g), proteins (50 g), and fiber (15 g), were identical.

The two meals were given in random sequence (four patients started with the high-fat and four with the low-fat meal), always at the same time (12:00 a.m.) leaving unchanged the time and the dosage of insulin administration.

Venous blood samples were taken immediately before the meal (two basal samples taken at 15-min intervals) and then every 15 min for the next 3 h. The blood collected was immediately deproteinized with perchloric acid, centrifuged, and the supernatant stored at −20°C. Blood glucose was then measured using a commercial kit (Boehringer Mannheim [Mannheim, West Germany] GOD-Perid method).[17]

Increments above basal were calculated for each subject subtracting from each blood glucose value the mean of the two basal samples.

Statistical methods. Unless otherwise stated, values are given as mean ± SE. Data have been analyzed by the Student's paired *t* test and by the two-way analysis of variance.[18]

The null hypothesis was rejected when $2P < 0.05$.

RESULTS

Experiment 1. In four cases (one for diet A and three for diet B) the composition of the diet reported in the 7-day food record was different (±15%) from the diet prescribed and therefore patients continued for one more week.

The composition of the diets calculated from the patients' records for the week preceding the experiment was as follows (respectively, for diets A and B): 1984 ± 98 and 1935 ± 102 kcal; 229 ± 12 and 308 ± 14 g carbohydrate; 85 ± 6 and 49 ± 7 g fat; 89 ± 11 and 84 ± 7 g protein.

The amount of insulin infused overnight by the Biostator was 4.8 ± 2.2 IU during diet A and 9.6 ± 5.1 IU during diet B; the difference was not significant.

Both the average daily blood glucose and the M value were significantly lower after diet A in comparison with diet B (Table 3).

Blood glucose concentrations during the day were constantly higher after diet B in comparison with diet A: the difference was statistically significant at 11:00 and 12:00 a.m., and at 3:00, 4:00, 5:00, 7:00, 8:00, and 9:00 p.m. (Figure 1).

The average blood glucose concentration for 3 h after the main meal was higher at the end of diet B (Figure 2):

131 ± 24 mg/dl versus 152 ± 22 mg/dl after breakfast
151 ± 28 mg/dl versus 242 ± 45 mg/dl after lunch
166 ± 41 mg/dl versus 239 ± 33 mg/dl after dinner

The differences, checked by the two-way analysis of variance, were significant between the two diets ($F1 = 5.2$, $P < 0.05$) but not between the different meals ($F2 = 2.0$, NS).

TABLE 3
M value, mean daily blood glucose, and fasting blood glucose (mean ± SE) after the two dietary periods

	Diet A	Diet B
M value	48 ± 20	96 ± 27*
Mean daily blood glucose (mg/dl)	152 ± 5	206 ± 11†
Fasting blood glucose (mg/dl)	118 ± 29	125 ± 24

*$t = 3.83$, $P < 0.025$; †$t = 7.50$, $P < 0.001$.

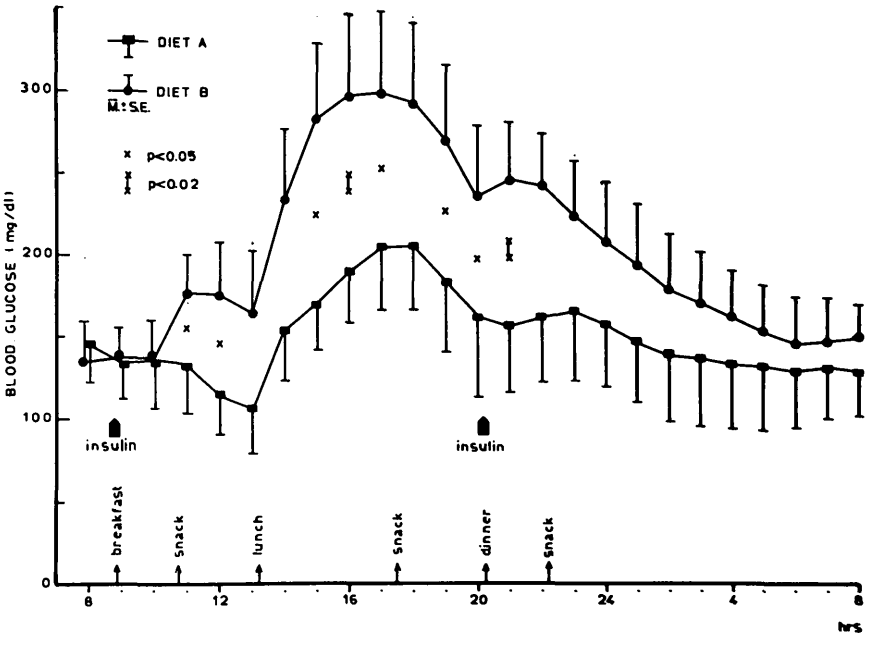

FIG. 1. Daily blood glucose profile at the end of the two dietary periods.

Fasting blood glucose was also measured at the end of both diets: in all patients but one a slight increase in this parameter was observed after diet B. However, the difference was not statistically significant (Table 3).

No significant difference was observed between the two diets in fasting serum cholesterol, triglycerides, or serum lipoprotein composition (Table 4).

Experiment 2. The basal blood glucose values (average of two samples) were not statistically different between the low- and high-fat meal (105 ± 18 versus 156 ± 30 mg/dl, respectively; t = 1.58, NS).

The blood glucose increments after the two test meals are shown in Figure 3; at each point of the curve the values are very similar. Also, the hourly glycemic increments (mean of four samples during each hour) were similar after the low- and high-fat meals:

88 ± 7 mg/dl versus 97 ± 16 mg/dl during the first hour
140 ± 6 mg/dl versus 139 ± 6 mg/dl during the second hour
178 ± 4 mg/dl versus 170 ± 5 mg/dl during the third hour

None of these differences proved to be statistically significant.

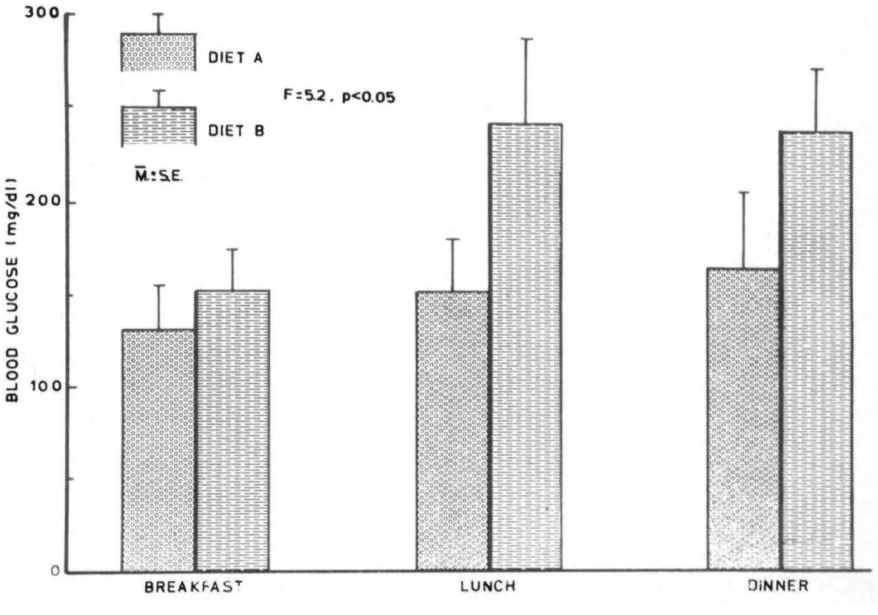

FIG. 2. Average after-meal blood glucose (the mean of all measurements for a 3-h period after the meals).

TABLE 4
Total serum cholesterol, triglyceride, and serum lipoprotein composition after the two dietary periods (mean ± SE)

	Diet A	Diet B
Cholesterol (mg/dl)		
Total	166 ± 19	162 ± 25
VLDL	11 ± 3	10 ± 3
LDL	124 ± 4	117 ± 21
HDL	34 ± 4	36 ± 3
Triglyceride (mg/dl)		
Total	98 ± 17	117 ± 19
VLDL	50 ± 7	48 ± 7

DISCUSSION

The appropriate carbohydrate content of a diet for IDD patients has been widely debated among physicians interested in diabetes.[19–26]

The data presented in this article (experiment 1) refer to the metabolic effect of diets with different carbohydrate but identical plant fiber content.

Blood glucose control as evaluated by 24 h of monitoring was significantly worse with the high-carbohydrate diet when compared with the low-carbohydrate diet as shown by measurements of the average daily blood glucose and the M value. Fasting blood glucose concentration was higher after the high-carbohydrate diet (diet B) in 5 of the 6 patients, although the difference was not significant.

Our results suggest that a simple increase in dietary carbohydrate content, without a parallel increase in fiber, leads to a deterioration of blood glucose control in IDD patients. The negative effect of high-carbohydrate diets is more clear in the postprandial period. These findings are in partial contradiction to previous studies in which an improvement of blood glucose control was gained in diabetic patients by increasing the amount of dietary carbohydrate to very unusual levels (75–85% of total calories).[4,5] However, these studies have been criticized[19] either because nonphysiologic formula diets were used[4] or because the amount of available carbohydrate was increased together with dietary fiber.[5]

On the other hand, it does not appear to be of any clinical value to affirm that a diet composed almost exclusively of carbohydrate is better than complete carbohydrate deprivation. The real question is whether the carbohydrate content of a diabetic diet should approximate 45% or 65% of total calories.[2] According to our data the answer is that a carbohydrate content of about 45% gives better blood glucose control in IDD patients as long as the fiber content is similar.

Our findings are somewhat different from those obtained in similar experimental conditions in non-insulin-dependent diabetic patients by Simpson et al.[26] This group found lower after-meal blood glucose levels but higher fasting blood glucose levels after a low-carbohydrate diet while the average daily blood glucose, determined hourly, was not modified. The different results might be due to differences in the selection of patients participating in the two studies: IDD patients in our study and non-insulin-dependent patients in that of Simpson and co-workers. Diets might have different metabolic consequences in patients with and without residual insulin production.[19]

In order to keep the diet isoenergetic, variations in the amount of carbohydrates must be accompanied by corresponding changes in the amount of fat. It is possible that dietary fat might affect blood glucose metabolism by slowing gastric emptying and reducing the rate of absorption of the nutrients.[11,12] If this is the case, the metabolic deterioration induced by the high-carbohydrate–low-fat diet in our experiment 1 might be due in part to its reduced fat content. To test this possibility we performed a test meal experiment in which only the amount of fat was changed (experiment 2).

The results clearly demonstrate that increasing the olive oil intake from 12 to 36 g without any change in the meal composition has no effect on postprandial blood glucose concentrations. This suggests the possibility that the high-fat content is not contributing to any significant extent to the improvement of blood glucose control after the low-carbohydrate–high fat diet.

Despite the fact that in our experiment 1 the two diets were different in carbohydrate and in fat content, no clear effect of these diets on serum lipoprotein composition was found. A possible explanation is that the diets were almost identical in simple sugar and saturated fat content, which are the dietary components having the major influence on VLDL and LDL, respectively.[27–29] Alternatively, the duration of the experiment was too short and the patients were too few to make an observation of possible differences in serum lipoproteins.

In conclusion, our results suggest that increasing the dietary carbohydrate content without increasing the fiber content for IDD patients causes deterioration of blood glucose control without any significant improvement in blood lipid composition. The deterioration of metabolic control seems to be mainly due to hyperglycemia in the postprandial period.

According to this study and to the available evidence,

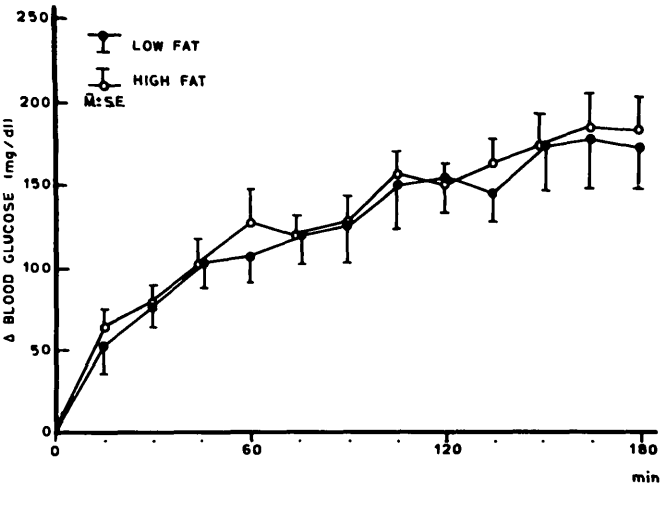

FIG. 3. Blood glucose increments after the low- and high-fat test meals.

there is no justification to recommend the use of high-carbohydrate diets to patients with insulin-dependent diabetes mellitus. A high-carbohydrate consumption is justified only if associated with a parallel increment in the consumption of dietary fiber.

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From the Institute of Internal Medicine and Metabolic Diseases, Second Medical School, University of Naples, Naples, Italy.

Address reprint requests to Nicola Perrotti, M.D., Diabetes Branch, NIADDK, National Institutes of Health, Bldg. 10, Room 8S243, Bethesda, Maryland 20814.

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