Glycemic Effects of Spaghetti and Potato Consumed as Part of Mixed Meal on IDDM Patients

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Recently, we demonstrated that spaghetti caused a significantly lower glycemic response in isoinsulinemic insulin-dependent diabetic (IDDM) subjects than an exchangeable amount of potato. The question is, however, whether the difference of the glucose response in IDDM patients is preserved if these carbohydrate-rich foods are taken as part of a mixed meal. To answer this question, we evaluated blood glucose, free-insulin, and glucagon responses to exchangeable amounts of spaghetti and potato when ingested together with bolognese sauce in seven IDDM patients who had attained euglycemia with the artificial pancreas before meal intake. The potato (200 g raw wt) with bolognese sauce (167 g) and spaghetti (50 g raw wt) with bolognese sauce (167 g) had approximately identical caloric content (435 and 447 kcal, respectively), fat (18 g each), protein (23 and 26 g, respectively), and carbohydrate (47 and 48 g, respectively). Blood glucose increment after white spaghetti and bolognese sauce was only ~50% of that seen in response to potato and bolognese sauce. Similar constant insulin levels and increments in glucagon were seen. A major determinant of the postmeal glucose rise in IDDM patients seems to be dependent on the kind of carbohydrate in the meal. The approach by which the insulinemia was kept constant by the artificial pancreas seems to be a valuable tool for studying glycemic responses to different meals in IDDM patients who otherwise show great variations in circulating insulin and glucose levels when treated by subcutaneously administered insulin. *Diabetes Care* 10:401–406, 1987

The influence of different carbohydrate foods on postprandial blood glucose responses has been extensively studied in normal and non-insulin-dependent diabetic (NIDDM) subjects (1–8). Little information is available about the glycemic responses in insulin-dependent diabetic (IDDM) patients (8–12). This is probably due to difficulties in obtaining reproducible conditions in IDDM patients (9,10). Great variations in insulin and glucose levels within and between experiments exist in diabetic patients treated by conventional subcutaneously administered insulin (9). To circumvent this problem, the artificial pancreas has been applied in IDDM patients to attain euglycemia and isoinsulinemia before test meals (11,12), as well as a constant insulin concentration throughout the experiments (12). With the advent of this methodology, we recently found that spaghetti caused a significantly lower glycemic response than exchangeable amounts of potato in IDDM patients (12). The question arises, however, whether a major difference in blood glucose response to potato and spaghetti is also present when the two carbohydrate sources are ingested as part of a more realistic mixed meal.

Consequently, we examined the short-term effects on blood glucose levels of exchangeable amounts of spaghetti and potato when evaluated as part of a mixed meal in IDDM subjects who, by means of the artificial pancreas, had obtained near-normal blood glucose levels and isoinsulinemia before meal intake.

SUBJECTS AND METHODS

Seven IDDM patients, fully informed of the experimental nature of the investigation, were studied. The study had approval by the local ethical committee. Clinical data are given in Table 1. All patients were free of clinical signs of peripheral neuropathy and nephropathy. Five patients (A.L., A.H.C., J.J., C.L., and V.J.) had background retinopathy. Each subject consumed the two test meals randomly assigned within a 4-wk period.

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TABLE 1
Clinical data for seven insulin-dependent diabetic patients

Patient	Sex	Age (yr)	Body mass index (kg/m^2)	Duration of diabetes (yr)	Insulin requirement (U/day)	Fasting blood glucose* (mM)		HbA_{1c} (%)	
						Meal A	Meal B	Meal A	Meal B
A.L.	M	64	22.2	25	36	3.5	4.9	7.7	7.7
A.H.C.	M	36	27.4	13	64	2.9	4.4	7.4	7.4
J.J.	M	25	25.1	18	60	4.7	3.8	6.8	6.6
S.U.	M	32	22.6	6	34	6.3	6.2	7.3	7.8
T.K.	M	34	23.4	5	30	7.4	7.6	7.7	7.7
C.L.	M	28	26.3	15	48	4.7	5.1	8.4	8.6
V.J.	M	26	23.9	10	60	4.4	5.6	7.1	7.0
Mean ± SD		35 ± 13	24.4 ± 1.9	13 ± 7	47 ± 14	4.8 ± 1.6	5.4 ± 1.2	7.4 ± 0.5	7.5 ± 0.6

Meal A, spaghetti plus bolognese sauce; meal B, potato plus bolognese sauce.
*Fasting blood glucose is mean of blood glucose values at −15 and 0 min before test meal.

Experimental protocol. Intermediate insulin was withdrawn 48 h before the experiments, and the patients were treated with soluble insulin only. The last soluble insulin dose was given at 2300 h the day before the study. At 0800 h the next morning the patients were connected to the artificial endocrine pancreas (Biostator, Miles, Elkhart, IN) to achieve normoglycemic equilibrium. The set constants of the Biostator were selected as follows: $KR = 70$, $KF = 67$, $BI = 90$, $RI = 0.2 \times$ kg body wt, $FI = 320$, $BD = 75$, $QD = 10$, $RD = 50$, and $FD = 360$. QI was set to 20 when blood glucose was >8.5 mM but increased to 40 when the blood glucose was below that value [KR, a constant for rising glucose levels; KF, a constant for falling glucose levels; BI, the preselected level of glucose (mg/100 ml) at which the basal insulin infusion rate is administered; RI, the basal insulin infusion rate at the preselected glucose level BI (mU/min); FI, maximum insulin infusion rate (mU/min); BD, the level of blood glucose at which basal glucose infusion rate is administered (mg/100 ml); QD, the reciprocal of the static gain for glucose infusion (mg/100 ml); RD, basal glucose infusion rate at the preselected glucose level BD (mg/min); FD, maximum glucose infusion rate (mg/min); QI, the reciprocal of the static gain for insulin infusion (mg/100 ml)]. By increasing the QI as blood glucose approached normal values, a smoother approximation to the preselected value of 4.7 mM was achieved. Normoglycemia was maintained for at least 1 h before the test meal was given at 1130 h. At this time the feedback control on blood glucose was terminated, and insulin infusion was continued at a fixed rate of 0.2 $mU \cdot kg^{-1} \cdot min^{-1}$.

Meals. Composition of the two mixed meals is shown in Table 2. The patients were fed according to the Danish food-exchange system (50 g spaghetti exchanged by 200 g potato; 13). The approximate contents of carbohydrate, fat, protein, and energy in spaghetti and potato were calculated according to Paul and Southgate (14), whereas the same parameters for bolognese sauce were calculated according to Helms (15). Briefly, they contained 167 g bolognese sauce in combination with either 50 g raw wt white spaghetti made from durum wheat semolina or 200 g raw wt potato. Each subject was asked to ingest the meal continuously over 10 min and drink 250 ml of water. Spaghetti and potatoes were boiled for 10 and 19 min, respectively. The bolognese sauce was prepared in one batch, divided into separate portions, and frozen until needed. Before ingestion, it was cooked for 5 min. A weight reduction of the bolognese sauce portions of 10.8% (from 187 to 167 g) was seen after cooking. Blood glucose levels ranging between 3.4 and 7.8 mM were maintained at this level for at least 1 h before starting the experiment. The subjects were asked to urinate just before meal intake. Glucose excretion was then measured in the urine collected during the test (0–240 min). Patients sat in their beds throughout the experiment.

Analytic techniques. Plasma and urinary glucose were measured by the glucose oxidase method. HbA_{1c} values were determined by a commercial kit (Bio-Rad, Richmond, CA). Normal HbA_{1c} values ranged from 3.5 to 5.5%. Serum free-insulin levels were determined as described by Nakagawa et al. (16) with modification (17). Plasma C-peptide was measured by a commercial kit (Immunonuclear, Stillwater, MN). Plasma glucagon was measured by specific radioimmunoassay (18).

Statistical analysis. Absolute incremental areas of blood glucose were calculated geometrically by subtracting the mean basal blood glucose concentration from each value. The mean basal glucose concentration was defined as the mean of the blood glucose concentrations at −15 and 0 min before ingestion of the test meal. Results of all measurements are expressed as means ± SE. Significance was calculated by Student's two-tailed t test for paired data. To correct for the effects of multiple comparisons, Bonferroni's method of adjusting the significance level was adopted; i.e., with three comparisons, the criterion of significance changed from $P < .05$ to $P < .0167$ (.05/3).

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TABLE 2
Meal composition

	Weight (g)	Energy (kcal)	Carbohydrate (g)	Fat (g)	Protein (g)
Test carbohydrate					
Spaghetti (white raw)	50.0	189	42.0	0.5	6.8
Potato (old raw)	200.0	174	41.6	0.2	4.2
Bolognese sauce					
Onion	9.4	2.8	0.6	0	0.1
Beef (medium fat)	87.5	215.9	0.4	15.8	17.8
Water	75.0				
Tomato puree (concentrated)	7.2	5.1	0.8		0.4
Margarine	1.9	14.0		1.5	
Wheat flour (70% extraction rate)	6.1	19.7	4.0	0.1	0.6
Total	167.0*	258	5.8	17.4	19.0
Meal A		447	47.8	17.9	25.8
Meal B		432	47.4	17.6	23.2

Meal A, spaghetti plus bolognese sauce; meal B, potato plus bolognese sauce. In addition, each meal contained 250 ml of water.
*Weight loss by cooking 10.8%.

RESULTS

In all diabetic patients, plasma C-peptide levels were <1.1 ng/ml in the fasting state without significant elevation after the meals. The postprandial increase in blood glucose after the two test meals (bolognese sauce with cooked spaghetti or potato) is shown in Fig. 1. Before the two meals, no significant difference was seen in the mean fasting blood glucose levels, which were close to normal (Table 1). Furthermore, identical HbA_{1c} values ± SD were also present before the mixed meal with spaghetti or potato (7.4 ± 0.5 and 7.5 ± 0.6%, respectively; Table 1). Mean ± SE plasma glucose response areas to the two test meals are given in Table 3. After ingestion of spaghetti and bolognese sauce, the mean blood glucose response area was significantly smaller than after potato and bolognese sauce at 120 min ($P < .001$), 180 min ($P < .001$), and 240 min ($P < .001$). Thus, compared with the potato-plus-meat–sauce response, the response area to spaghetti with bolognese sauce was reduced by 53 ± 5% ($P < .001$) after 120 min, 49 ± 6% ($P < .001$) after 180 min, and 45 ± 8% ($P < .001$) after 240 min. The amount of glucose lost in the urine during the 4-h period was higher after the mixed meal with potato (6.3 ± 2.3 g) than with spaghetti (3.9 ± 1.7 g; $P < .05$). As seen in Fig. 2, constant and identical plasma free-insulin levels were found during the two tests. After ingestion of both test meals, a small, significant increment in plasma glucagon (area above basal) appeared (0–240 min; $P < .05$), an increment that attained the same size in the two situations (Fig. 3).

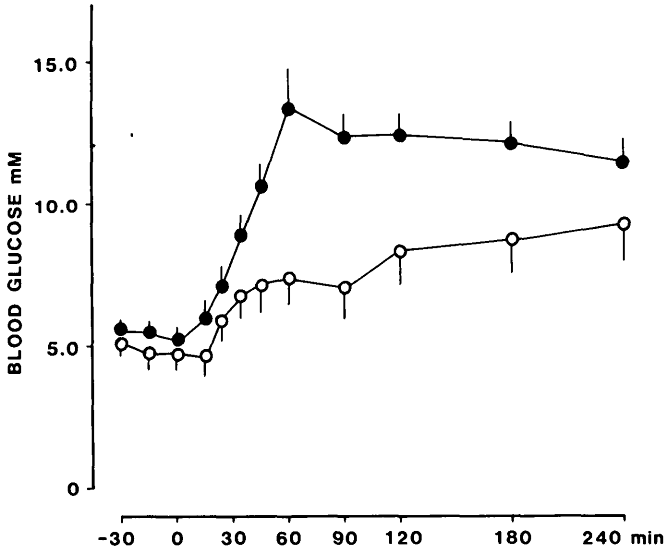

FIG. 1. Mean blood glucose variations observed after mixed meal of bolognese sauce (167 g) and cooked potato (200 g raw wt; ●) or spaghetti (50 g raw wt; ○) in 7 insulin-dependent diabetic patients receiving constant insulin infusion with artificial pancreas. Meal intake lasted 10 min. Values are means ± SE.

DISCUSSION

Recently, several laboratories, including our own, have demonstrated differences in glucose responses to various unmixed carbohydrate-rich foods. Thus, spaghetti produced a significantly smaller rise in blood glucose in a heterogenous group of IDDM and NIDDM subjects than other starch sources such as bread (19), rice (12,20), or potato (12,20). Because patients do not usually consume carbohydrate-rich foods alone, but as part of mixed meals, the potential therapeutic relevance of these findings in management of diabetes is disputable. In this study we attempted to see if the marked difference in glycemic responses to spaghetti and potato observed in IDDM patients (12) was also present when the carbohydrate sources were ingested as part of a mixed meal with bolognese sauce. With the artificial pancreas, we obtained reproducible, near-normal blood glucose concentrations before test-meal adminis-

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TABLE 3
Blood glucose response (area above basal) after two meals in seven insulin-dependent diabetic patients

Patient	Blood glucose response to meal A (mM/min)			Blood glucose response to meal B (mM/min)		
	A 120 min	B 180 min	C 240 min	D 120 min	E 180 min	F 240 min
A.L.	196	331	481	494	863	1196
A.H.C.	253	520	871	622	1048	1462
J.J.	225	480	822	617	1118	1643
S.U.	383	734	1109	864	1452	2025
T.K.	428	749	1022	582	903	1131
C.L.	281	542	887	619	1030	1405
V.J.	190	196	239	376	682	940
Mean ± SE	279 ± 35	507 ± 76	776 ± 117	596 ± 56	1014 ± 91	1400 ± 136

Meal A, 50 g spaghetti plus 167 g bolognese sauce; meal B, 200 g potato plus 167 g bolognese sauce. $P < .001$ for A vs. D, B vs. E, and C vs. E.

tration, concomitantly avoiding variation in subcutaneous insulin depot absorption; i.e., insulinemia was kept constant throughout the experiments. We used the Danish food-exchange system to calculate the amounts of spaghetti and potato (13). The two test meals contained ~50 g available carbohydrate, 25 g protein, 18 g fat, and were approximately isocaloric (440 kcal) (Table 2).

We found that when potato was substituted for spaghetti as part of a mixed meal, a 50% reduction in blood glucose rise was observed in IDDM subjects over a 4-h period. In a mixed group of IDDM and NIDDM subjects, Parillo et al. (21) also looked at the glycemic response to a meal with a 50-g carbohydrate portion of spaghetti or potato. They found that the glycemic response was significantly lower after a spaghetti meal than after a potato meal (21). Because premeal blood glucose levels were not normalized in these experiments, strict comparison is difficult. Most of their patients had retained insulin production, implying that differences in blood glucose profiles may partly be due to a difference in ability to respond to insulin stimulatory gut factors.

Our findings are consistent with those observed when comparing the glycemic responses to spaghetti and potato per se

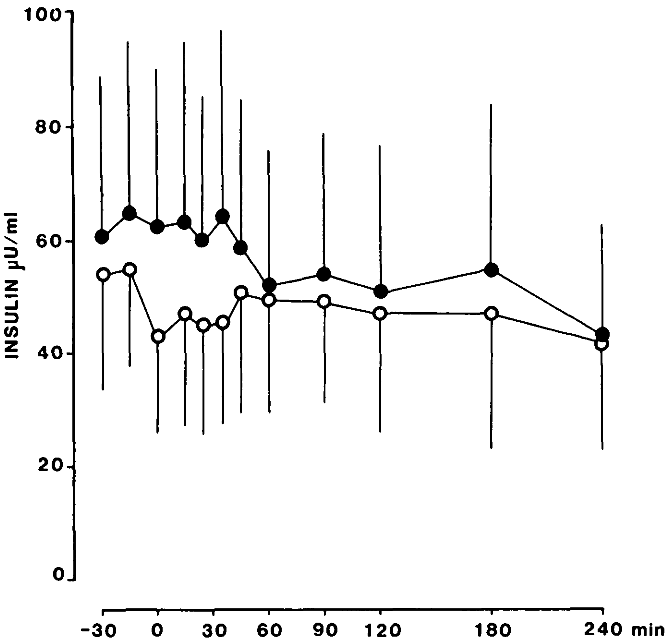

FIG. 2. Plasma free-insulin levels (means ± SE) in 7 insulin-dependent patients receiving constant insulin infusion with artificial pancreas. The test meals consisted of bolognese sauce with either cooked potato (●) or spaghetti (○).

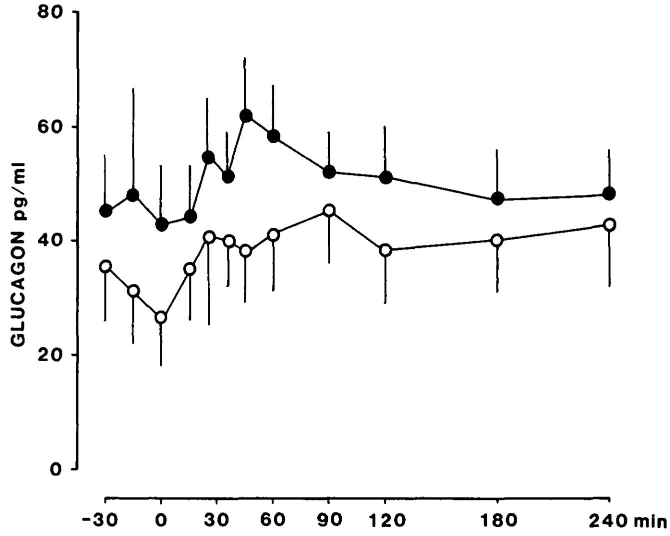

FIG. 3. Plasma glucagon concentrations (means ± SE) in 7 insulin-dependent patients receiving constant insulin infusion with artificial pancreas. Test meals consisted of bolognese sauce with either cooked potato (●) or spaghetti (○).

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in an IDDM population (12). Thus, based on our previous data we would have anticipated that spaghetti during a 180-min observation would produce ~70% of the blood glucose response observed with potato (12), whereas the relative difference that was actually observed when the starch source was taken in combination with bolognese sauce was even greater, reaching ~50% difference. However, when comparing the absolute incremental glucose response areas, these were decreased when the carbohydrates were taken as part of a mixed meal. The explanation for this can only be speculated, but various possibilities exist. First, fat content probably plays a key role for the attenuation of the glycemic response. Thus, coingestion of fat with a carbohydrate meal reduces the postprandial glucose response to the carbohydrate load (22) due to its delaying effect on gastric emptying (23). Second, the protein components might temper and/or dilute the effects of carbohydrate. Ingested protein does not alter the blood glucose level in normal individuals but causes a suppression of the blood glucose response to carbohydrate in NIDDM patients due to stimulation of insulin secretion (24). Because our diabetic patients had no preserved endogenous insulin secretion, this mode of action can be ruled out. Furthermore, it is unlikely that the very modest increment in circulating glucagon could account for any variation in blood glucose. A third, important factor participating in the glucose handling is the degree of insulinization of the patients (25). A constant insulinemia was kept throughout the experiments. Apparently the average free-insulin levels were ~3 times higher in these experiments (Fig. 2) than in our previous studies with carbohydrate alone (12). However, this difference and the large interindividual variation could be ascribed to extremely high levels of free plasma insulin in two (A.H.C. and J.J.) of our seven patients, which we cannot explain. The insulin level of the five others were similar to those seen in our previous study (12). In keeping with this, A.H.C. and J.J. received the same insulin amount, had glucose responses to the two mixed meals similar to the other diabetics, and retained similar high circulating insulin levels when checked later.

We conclude that the glycemic response to spaghetti in the context of a mixed meal is significantly lower than the exchangeable amount of potato taken as part of a mixed meal, findings that are in agreement with previous experiments on the effects of the carbohydrate per se in IDDM subjects. Note that the difference in glycemic responses observed may be dampened if the observation period had been prolonged. Furthermore, the results may not necessarily apply to individuals with NIDDM who maintain insulin secretion in response to meals. A major determinant of the postmeal glucose rise in IDDM subjects seems to be the carbohydrate source of the meal. The approach by which the important variable insulinemia is kept constant by the artificial pancreas seems to be a valuable tool for studying glycemic responses to different meals in IDDM patients and may allow an appraisal of the role of different factors influencing the blood glucose responses to food, e.g., the possible influence of different initial blood glucose and insulin levels.

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