Comparison of Plasma Glucose, Serum Insulin, and C-Peptide Responses to Three Isocaloric Breakfasts in Non-Insulin-Dependent Diabetic Subjects

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While differences in glucose and insulin responses to specific carbohydrate foods have been reported, few data are available for mixed meals incorporating such foods. This study compared the plasma glucose (PG), serum insulin (SI), and C-peptide (CP) responses to three different isocaloric test breakfasts given in random order to eight insulin-treated non-insulin-dependent diabetes mellitus (NIDDM) patients. The test meals were selected from a hospital food exchange list and contained similar quantities of carbohydrate, protein, fat, and dietary fiber. The postprandial PG, SI, and CP responses to two of the test breakfasts (meal A: eggs, toasted wholemeal bread, orange juice, margarine, and milk; meal B: wheatflake biscuits, toasted wholemeal bread, milk, and margarine) were similar (meal A: 104.3 ± 23.0 mg · h · dl^{-1}, 5996 ± 1108 μU · min · ml^{-1}, and 89.8 ± 25.4 pmol · min · ml^{-1}, respectively; meal B: 104.9 ± 21.6 mg · h · dl^{-1}, 6268 ± 1161 μU · min · ml^{-1}, and 99.8 ± 26.4 pmol · min · ml^{-1}, respectively). Meal C, consisting of toasted muesli and skim milk, produced smaller glycemic and insulin responses (46.8 ± 8.8 mg · h · dl^{-1}; $P < .02$, and 4369 ± 700 μU · min · ml^{-1}; $P < .05$, respectively) than meals A and B and less endogenous insulin secretion (CP response 62.8 ± 19.9 pmol · min · ml^{-1}; $P < .05$ compared with meal A, NS compared with meal B). The lower glycemic response after meal C could be explained by differences in method of food processing resulting in a decreased availability of starch to amylolytic enzymes, the higher content in meal C of sucrose, lactose, and fructose, which are associated with a low glycemic index, and by quantitative and qualitative differences in fiber. While food exchange lists are generally useful in planning diets for diabetic persons, some modification to current lists may be necessary to take into account the processing method and nature of the carboyhydrates in the food when considering the equivalence of individual food items.
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Food exchange lists are commonly used for planning the diet of a person with diabetes. The basic assumption of such lists is that isocaloric quantities of foods grouped according to their basic nutrient content can be exchanged with one another and have similar effects on postprandial glycemia. The validity of the exchange system for carbohydrate foods has been challenged by recent studies that have demonstrated that the physiologic effects of food ingestion cannot be predicted simply from their chemical composition.[1-4] Factors such as the way food is prepared or processed, the nature of the food carbohydrates, certain types of dietary fiber, interactions of carbohydrate with proteins and lipids, and the presence of antinutrients affect postprandial glycemia and insulinemia.[5-10]

While individual food items have been studied, few data are available for mixed meals.[4,11] The aim of the present study was to compare postprandial glucose (PG), serum insulin (SI), and C-peptide (CP) responses to three meals selected from food exchange lists containing similar amounts of carbohydrate, fat, and protein in insulin-treated persons with non-insulin-dependent diabetes mellitus (NIDDM).

PATIENTS AND METHODS

Eight patients (four women and four men) who fulfilled the National Diabetes Data Group criteria for NIDDM[12] and were being treated with insulin were studied. The clinical details of the patients are shown in Table 1. All subjects were being treated with twice-daily injections of insulin. Six were receiving a bovine/porcine biphasic insulin (Rapitard MC, Novo

TABLE 1
Clinical details of subjects studied

Subject	Sex	Age (yr)	BMI (kg/m²)*	Glycosylated hemoglobin (%)	Duration of diabetes (yr)	Duration of insulin treatment (yr)	Insulin binding capacity (%)
1	M	69	26.6	7.9	7	5	3
2	M	42	27.1	8.9	2	0.5	0.1
3	F	79	18.8	7.8	10	8	1.4
4	F	63	27.9	6.0	1.5	0.5	0
5	F	68	27.6	11.6	18	6	3
6	M	65	23.2	6.9	2	1	4
7	M	51	26.5	11.7	6	2	0
8	F	54	27.9	10.7	5	3	4
Mean ± SEM		61.4 ± 4.2	25.7 ± 1.1	8.9 ± 0.8	6.4 ± 2.0	3.3 ± 1.0	1.9 ± 0.6

*Body mass index.

Industri A/S, Bagsvaerd, Denmark), one a biphasic porcine insulin (Mixtard, Nordisk, Gentofte, Denmark), and one a mixture of porcine regular and isophane insulins (Velosulin and Insulatard, Nordisk). Five of the eight subjects were performing self-monitoring of blood glucose. Patients gave informed consent before participation in the study. Patients were given three different meals as a breakfast (A, B, or C) in random order on each of three test days at least 48 h apart. The three test meals were based on the food exchange lists used in the hospital and represented three commonly requested breakfasts.

Meal A consisted of two (100 g) boiled eggs, two slices (59 g) toasted wholemeal bread (Tip-Top brand) with 4 g margarine, 250 ml unsweetened orange juice (Orchy brand), and 30 ml whole milk with 200 ml tea or coffee.

Meal B consisted of two (30 g) wheatflake biscuits (Weetbix brand), 1½ slices (45 g) toasted wholemeal bread with 4 g margarine, 350 ml whole milk, and 200 ml tea or coffee.

Meal C consisted of 75 g toasted muesli (Purina brand), 300 ml skim (low-fat) milk, and 200 ml tea or coffee.

Meals were prepared by a dietitian. The composition of each meal is shown in Table 2. Estimates of nutrient composition were calculated using data supplied by the food manufacturer or from a standard reference.[13] Each meal was similar with regard to carbohydrate, protein, fat, dietary fiber, and energy content. Each meal provided ~48% of energy as carbohydrate, 36% as fat, and 16% as protein.

Patients attended the Metabolic Unit of the hospital after an overnight fast. An intravenous cannula was inserted into an antecubital vein soon after arrival. At 0800 h the patient's usual morning dose of insulin was injected subcutaneously into the anterior abdominal wall, and after 30 min the test breakfast was eaten within 15 min under supervision. Blood was collected for measurement of PG, SI, and CP concentrations just before insulin administration, before eating, and at 30-min intervals for 3 h. Dietary assessment was made before entry to the study and all subjects were considered to be complying with their prescribed diet. No attempt was made to modify the diet of the subjects who continued to receive their usual diet before and during the study period.

A hexokinase method was used for measuring the PG concentration. Serum insulin concentration was determined by a standard double-antibody radioimmunoassay. The detection limit of this assay is 2–4 μU/ml; the coefficient of variation between and within assay is 5%. Insulin antibodies were measured as percent binding to iodinated porcine insulin. Nondiabetic subjects have an insulin binding capacity of 0–4%. C-peptide concentration was determined by radioimmunoassay using the M1230 antibody.[14] The fasting range for nondiabetic individuals is 0.26–0.63 pmol/ml; the intraassay and interassay coefficients of variation are 2% and 6%, respectively. Glycosylated hemoglobin was measured by ion-exchange chromatography with disposable minicolumns supplied by Bio-Rad Laboratories, Richmond, CA (range for nondiabetic persons, 5.2–8.4%).

Data are presented as means ± SEM. Peak rise of PG or

TABLE 2
Composition of test meals

	Meal A	Meal B	Meal C
Carbohydrate (g)			
Total	54	55	60
Starch and dextrins	24	38	28
Sugars	30	17	32
Glucose	10.2	0.2	3.3
Fructose	8.9	0.2	3.0
Lactose	1.4	16.2	14.3
Sucrose	9.5	0.4	11.4
Protein (g)	21	20	17
Fat (g)	18	19	19
Dietary fiber (g)	3.6	5.1	5.4
Energy (kcal)	470	470	480

TABLE 3
Mean (±SEM) concentrations of plasma glucose, serum insulin, and C peptide before and after the test meals

Meal	−30 min	0 min	30 min	60 min	90 min	120 min	150 min	180 min
Plasma glucose (mg/dl)								
A	154.8 ± 23.4	145.8 ± 21.6	158.4 ± 23.4	189.0 ± 23.4	199.8 ± 27.0	190.8 ± 27.0	171.0 ± 25.2	153.0 ± 23.4
B	153.0 ± 23.4	147.6 ± 23.4	151.2 ± 23.4	192.6 ± 28.8	201.6 ± 32.4	198.0 ± 32.4	174.6 ± 30.6	158.4 ± 32.4
C	151.2 ± 21.6	140.4 ± 21.6	145.8 ± 21.6	181.8 ± 25.2	171.0 ± 27.0	153.0 ± 23.4	138.6 ± 25.2	135.0 ± 23.4
Serum insulin (μU/ml)								
A	45 ± 16	47 ± 17	62 ± 17	77 ± 21	91 ± 25	93 ± 28	84 ± 27	75 ± 22
B	49 ± 13	48 ± 12	71 ± 18	83 ± 19	96 ± 20	96 ± 20	93 ± 21	83 ± 21
C	52 ± 21	51 ± 19	64 ± 20	79 ± 19	78 ± 19	81 ± 19	74 ± 19	74 ± 19
C peptide (pmol/ml)								
A	0.52 ± 0.11	0.47 ± 0.09	0.62 ± 0.12	0.91 ± 0.20	1.09 ± 0.27	1.19 ± 0.28	1.26 ± 0.31	0.95 ± 0.21
B	0.52 ± 0.09	0.52 ± 0.09	0.69 ± 0.12	1.14 ± 0.30	1.30 ± 0.26	1.38 ± 0.26	1.24 ± 0.26	1.15 ± 0.24
C	0.57 ± 0.13	0.49 ± 0.10	0.72 ± 0.25	0.96 ± 0.27	0.94 ± 0.26	0.94 ± 0.20	0.79 ± 0.15	0.67 ± 0.14

CP was calculated as the difference between the highest postprandial concentration and the fasting value. Glycemic, SI, and CP responses were calculated as the area increment above the fasting concentration. The area increment was measured by planimetry. Results were compared using the paired *t* test.

RESULTS

The mean concentrations of PG, SI, and CP before and after each of the test meals are shown in Table 3. Basal PG on each of the test days was not significantly different. The mean PG profiles (Figure 1) after meals A and B were similar. Mean plasma concentrations of PG after meal C were similar to the other two meals over the first 60 min, but thereafter the mean PG concentrations were lower; however, these differences did not reach statistical significance. The mean peak rise of PG after meal C (30.6 ± 7.2 mg/dl) was lower than that after either meal A (48.5 ± 7.2 mg/dl, $P < .05$) or meal B (59.4 ± 10.8 mg/dl, $P < .02$). The glycemic response to meal C (46.8 ± 8.8 mg · h · dl^{-1}) was significantly lower than the response to meal A (104.3 ± 23.0 mg · h · dl^{-1}, $P < .02$) or meal B (104.9 ± 21.6 mg · h · dl^{-1}, $P < .02$) (Figure 2).

The mean concentrations of SI on each of the test days are shown in Table 3. Serum insulin concentration, which represents both endogenous and exogenous insulin, is expressed as total SI, as no subject had an insulin binding capacity exceeding the nondiabetic range (Table 1). Mean basal inslin levels were similar but above the range for nonobese, nondiabetic individuals. Although the mean SI concentrations after meal C were lower at 90, 120, and 150 min than after the other two meals, the differences were not statistically significant. The insulin responses were similar for meals A and B (5996 ± 1108 μU · min · ml^{-1} and 6268 ± 1161 μU · min · ml^{-1}, respectively) and both were significantly greater than for meal C (4369 ± 700 μU · min · ml^{-1}, $P < .05$ for both) (Figure 2).

Mean basal CP concentrations (Table 3) on each of the test days were not significantly different. All patients had detectable endogenous insulin secretion in the basal state (range of CP concentrations, 0.12–0.90 pmol/ml). Six subjects recorded postprandial CP concentrations of 0.28–2.25 pmol/ml, whereas two subjects with the lowest basal CP values had an insignificant alteration of CP concentration after ingestion of the meals. The mean peak rise in CP was lower

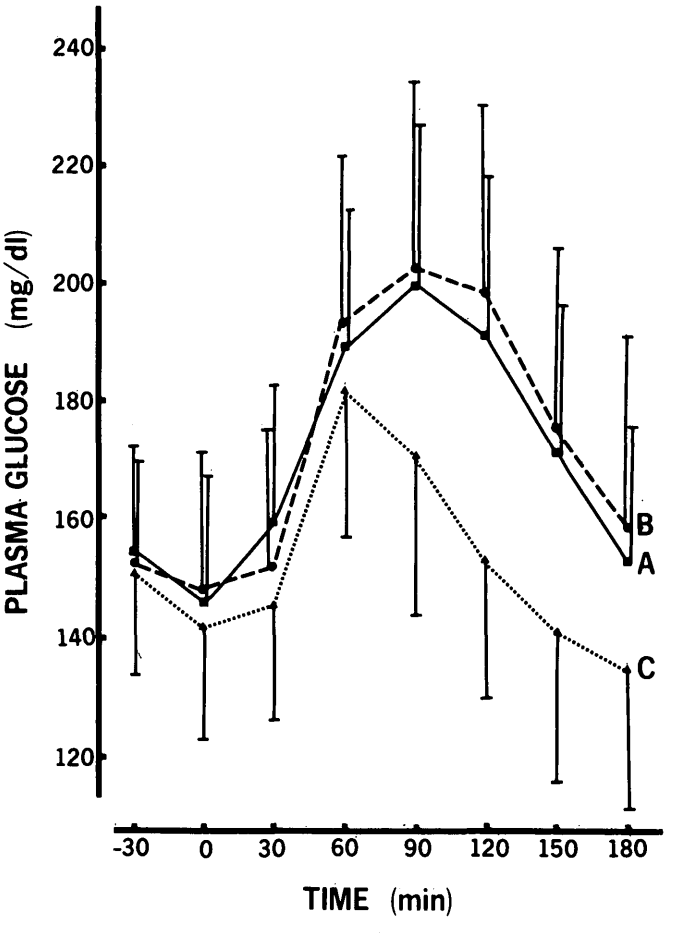

FIG. 1. Plasma glucose response to 3 different breakfast meals.

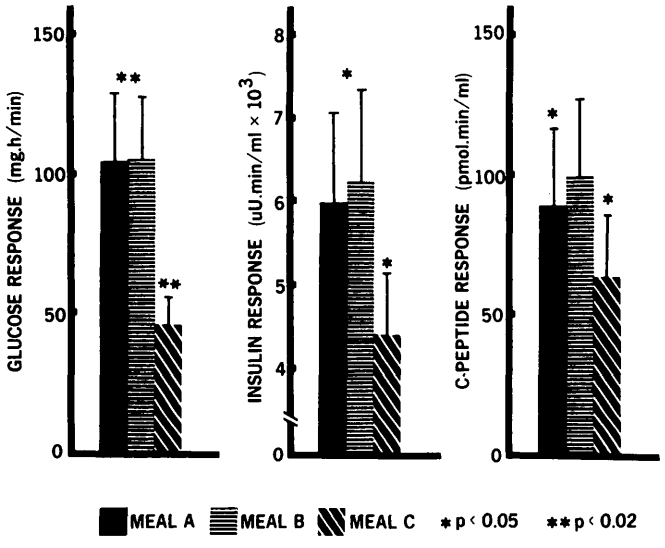

FIG. 2. Glycemic, insulin, and C-peptide responses to 3 different breakfast meals.

after meal C (0.54 ± 0.18 pmol/ml) than after meal A (0.88 ± 0.27 pmol/ml, NS) or after meal B (1.07 ± 0.29 pmol/ml, $P < .02$). Figure 2 shows the CP response to each meal. Meals A and B produced similar responses (89.8 ± 25.4 and 99.8 ± 26.4 pmol · min · ml^{-1}, respectively). The CP response after meal C (62.8 ± 19.9 pmol · min · ml) was significantly less than that after meal A ($P < .05$). The CP response paralleled the glycemic responses to meals.

DISCUSSION

This study has shown that breakfast meals selected from food exchange lists and containing similar amounts of carbohydrate, protein, and fat do not necessarily produce equivalent PG responses in insulin-treated persons with NIDDM. The glycemic responses to meals A and B were almost identical, but the response to the muesli and milk breakfast (meal C) was approximately half that observed with the other two test meals. These differing responses in insulin-treated patients were associated with changes in SI and CP responses, which indicated diminished endogenous insulin secretion during meal C.

Differences in the methods of processing, the nature of the carbohydrates, and the type of dietary fiber of the food items included in the test meals may account for the observed differences in PG, SI, and CP responses.

During processing, the wheat starch in bread (meals A and B) and wheatflake biscuits (meal B) is fully gelatinized (hydration and swelling of the starch granule) and partially digested by native and exogenous amylases (dextrinization).[15] In contrast, the starch in the rolled oats, which is the major ingredient of the muesli (meal C), is only partially gelatinized, despite the heat treatments applied during processing.[15] Milling of oats to produce rolled oats results in less mechanical disruption of the oat grain compared with the disruptions caused by the milling of wheat to produce flour for use in breadmaking and the cooking at high temperatures and pressure and flaking of wheat used in the making of the wheatflake biscuit.[15] Gelatinization of starch and mechanical disruption of grain structure increase the digestibility of starch presumably by increasing the availability of starch to amylolytic enzymes during both processing and digestion.[6,9] The lower PG and endogenous insulin effects of the muesli and milk breakfast may in part be due to the reduced availability of the starch in the rolled oats. Our finding is consistent with other studies that have indicated that the nature of starch is an important determinant of blood glucose and insulin responses to foods in normal and diabetic individuals.[1,5,7] For example, Collings et al.[7] demonstrated a greater glycemic response to cooked (i.e., gelatinized) starch compared with raw ungelatinized starch.

Although the total carbohydrate intake provided by each meal was similar, there were differences in the proportion of simple and complex carbohydrate among the test meals. Meal C contained more simple carbohydrate in the form of lactose, sucrose, and fructose than the other meals. These sugars have less effect on PG than either glucose or cooked starch and the proportionately higher content of these sugars in meal C may have contributed in part to the lower glycemic response after that meal.[11,16] However, comparison of the glycemic responses to meals A and B demonstrates that other factors are operative. Meal B, which contained the largest amount of complex carbohydrate and the least amount of simple carbohydrate, produced an equivalent glycemic response to meal A, which contained the least amount of complex carbohydrate.

While dietary fiber intakes provided by the test meals were similar, oats contain oat gum.[17] This storage polysaccharide hydrates to produce an extremely viscous solution like guar. Fibers of this type delay the absorption of carbohydrates and result in less postprandial hyperglycemia.[18] Although fiber intakes were small in our study compared with those that have shown such effects, the difference in the type of dietary fiber in meal C may have made a minor contribution to the lower glycemic response to this meal.

The validity of currently available exchange lists for carbohydrate foods has been challenged on the basis of the glycemic index of individual food items. However, Coulston et al.[19] have questioned the use of the glycemic index of individual food items in predicting the glycemic response to mixed meals incorporating these foods. Nuttall et al.[11] noted only small differences when comparing the glycemic effects of four test breakfasts selected using the American Diabetes Association Food Exchange Lists in untreated NIDDM patients. The demonstration that one of our test breakfasts did not produce the predicted response does not undermine the general usefulness of exchange lists. However, some modification may be necessary to take into account the processing method and the nature of the carbohydrates when considering the equivalence of individual items. Until the results of further studies are available, individuals who use self-monitoring of blood glucose are in a position to identify potentially equiv-

alent mixed meals that may not produce the theoretically equivalent PG response and make the necessary and important adjustments to their diet.

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