Slowly Digestible Carbohydrate Sources Can Be Used to Attenuate the Postprandial Glycemic Response to the Ingestion of Diabetes-Specific Enteral Formulas

Purpose

The purpose of this study is to compare the glycemic and insulinemic responses following the ingestion of recently developed diabetes-specific enteral formulas versus a standard and a high-fat formula.

Methods

Fifteen type 2 diabetes patients were selected to participate in a randomized, double-blind, crossover study. Two enteral formulas (47 energy percent [En%] carbohydrate, 34En% fat, and 4 g fiber/200 mL) were defined with either isomaltulose (formula 1) or sucromalt (formula 2) as the main carbohydrate source. For comparison, an isoenergetic diabetes-specific, high-fat (33En% carbohydrate, 50En% fat, 2.9 g fiber/200 mL) and a standard formula (55En% carbohydrate, 30En% fat, 2.8 g fiber/200 mL) were tested.

Results

Ingestion of formulas 1 and 2 and the high-fat formula resulted in an attenuated blood glucose response when compared with the standard formula ($P < .05$). In accordance, peak plasma glucose concentrations were significantly lower when compared with the standard formula (189 ± 3.6 mg/dL [10.5 ± 0.2 mmol/L], 196.2 ± 3.6 mg/dL [10.9 ± 0.2 mmol/L], 187.2 ± 3.6 mg/dL [10.4 ± 0.2 mmol/L], and 237.6 ± 3.6 mg/dL [13.2 ± 0.2 mmol/L], respectively). Plasma insulin responses were lower after

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consumption of the newly developed and high-fat formulas. Ingestion of the high-fat formula resulted in a greater postprandial triglyceride response ($P < .05$).

Conclusions

Diabetes-specific enteral formulas rich in slowly digestible carbohydrate sources can be equally effective in attenuating the postprandial blood glucose response as low-carbohydrate, high-fat enteral formulas without elevating the plasma triglyceride response.

It has been well established that improvements in glycemic control can effectively reduce the risk of developing microvascular and macrovascular complications in type 2 diabetes patients.[1-4] Recent data applying continuous glucose monitoring in well-controlled type 2 diabetes patients report that daily postprandial glucose excursions leading to hyperglycemia are much more prevalent than previously thought.[5] Such postprandial blood glucose excursions represent a direct and independent risk factor for the development of cardiovascular complications in type 2 diabetes patients.[6,7] Therefore, effective therapeutic strategies in diabetes treatment should aim to reduce postprandial hyperglycemia.

The clinical relevance of reducing postprandial hyperglycemia has been recognized by the International Diabetes Federation (IDF), and recommendations on postprandial glucose management have recently been published.[8] From a nutritional perspective, the IDF recommends diets with a low glycemic index (GI) and/or a low glycemic load to improve postprandial glycemic control. However, it should be noted that a recent long-term intervention study in type 2 diabetes patients with optimal glycemic control failed to observe substantial improvements in overall glycemic control (A1C) following 1 year on a lower GI diet (GI = 55) versus a higher GI diet (GI = 63).[9] Therefore, the proposed long-term benefits of diets low in GI remain to be established.

At present, standard enteral formulas for patients in need of nutritional support are also being used by type 2 diabetes patients. However, most of these enteral formulas have not been developed with the intention to also address their role in managing postprandial glycemia. Therefore, diabetes-specific enteral products are now available that generally contain less carbohydrate (35-40 energy percent [En%]). As such, these products typically contain more fat (40-50En%), with a large contribution from monounsaturated fatty acids, typically more than 60% of total fat content.[10] Consumption of these products has been shown to result in an attenuated rise in postprandial blood glucose concentrations when compared with standard formulas in type 2 diabetes patients.[11]

However, nutritional guidelines for diabetes patients published by the Diabetes Nutrition Study Group of the European Association for the Study of Diabetes recommend that the fat content of a diet should not exceed 35En% and that carbohydrate intake should range between 45En% and 60En%.[12] Most diabetes-specific enteral formulas are not in line with these recommendations, as they generally contain more than 35En% fat. Therefore, 2 diabetes-specific, enteral formulas were recently defined containing less than 35En% fat and more than 45En% carbohydrate. To reduce the glycemic and/or insulinemic response to these formulas, slowly digestible carbohydrate sources such as isomaltulose and sucromalt were used. Isomaltulose is a low-GI, naturally occurring carbohydrate composed of α-1,6-linked glucose and fructose. Sucromalt is a natural sweetener with a low GI[13] comprised of oligoglucose with unique linkages, fructose, and leucrose (a natural analog of sucrose). Prior in vitro and in vivo human studies suggest that ingestion of these carbohydrate sources is accompanied by an attenuated digestion and/or absorption rate.[13-19] The present study compares the glycemic and insulinemic responses following the ingestion of a single bolus of 2 newly developed diabetes-specific enteral formulas versus a standard, fiber-enriched and a diabetes-specific, high-fat formula. This study aims to determine whether diabetes-specific enteral formulas rich in slowly digestible carbohydrate sources can be equally effective in reducing the glycemic response when compared with low-carbohydrate, high-fat enteral formulas.

Materials and Methods

Subjects

For this study, 8 male and 7 postmenopausal female type 2 diabetes patients were selected. Type 2 diabetes was verified by an oral glucose tolerance test (OGTT) according to the criteria set by the World Health Organization in 1999.[20] Exclusion criteria were acute gastrointestinal disease within 2 weeks prior to study

Table 1

Subjects' Characteristics (N = 15)

	Mean ± SEM
Age, y	63 ± 1
Gender, n	
Male	8
Female	7
Body weight, kg	83.7 ± 3.2
Height, m	1.74 ± 0.03
Body mass index, kg/m^2	27.8 ± 1.2
Fasting plasma glucose, mg/dL	159.1 ± 6.8
Fasting plasma glucose, mmol/L	8.84 ± 0.38
A1C, %	7.3 ± 0.2
Time since diagnosis, y	9 ± 2

entry, impaired liver or renal function, cardiovascular disease, and exogenous insulin therapy. All subjects were using either oral blood glucose–lowering agents (sulfonylurea derivatives with or without metformin derivatives, n = 8; thiazolidinediones with or without metformin derivatives, n = 1; meglitinides with metformin derivatives, n = 1; metformin derivatives only, n = 3) or nutrition therapy only (n = 3). Medication had not been modified during the past 2 months. Subjects' characteristics are presented in Table 1. All participants were informed about the nature and risks of the experimental procedures, after which their written informed consent was obtained. The study was approved by the Medical Ethical Committee of the Academic Hospital Maastricht and performed at the Maastricht University.

Screening

All subjects performed an OGTT before inclusion in the study. The subjects fasted overnight and arrived at the laboratory at 08:00. A Teflon catheter (Baxter Quick Cath Dupont, Ireland) was placed in the antecubital vein, and a blood sample was collected. This was followed by the ingestion of 75 g of glucose dissolved in 250 mL of water. Subjects were given 3 minutes to ingest the glucose-containing beverage. Blood samples were obtained every 30 minutes up to 120 minutes. Type 2 diabetes state was verified by measuring plasma glucose concentrations.

Study Design

Subjects visited the laboratory 4 times, with a minimum of 4 days and a maximum of 10 days between each visit. In each trial, subjects consumed a single 200-mL bolus of a different enteral formula. Two newly developed enteral formulas containing slowly digestible carbohydrate sources (formulas 1 and 2; Nutricia, the Netherlands), a standard formula (standard; Isosource® fiber; Novartis, Germany), and a diabetes-specific formula containing a high level of fat (high fat; Glucerna®, Abbott, Zwolle, the Netherlands) were tested. The macronutrient composition of the 4 enteral formulas is presented in Table 2. All formulas contained vitamins, minerals, and trace elements in accordance with the regulations for Food for Specific Medical Purposes (1999/21/EC). The formulas were stored at 4°C in sealed packing. Trials were performed in a randomized order. For each trial, nontransparent drinking bottles were prepared by a nonaffiliated researcher, and formulas were provided in a double-blind fashion.

Dietary and Exercise Standardization

Dietary food intake records were obtained for 2 days prior to the first test. The latter was used to standardize dietary intake prior to the other trials. Food intake was recorded, and details on energy intake and macronutrient composition of the diet before each of the 4 trials were compared. In addition, all subjects received the same standardized meal the evening prior to each of the trials (10.5 kcal [4 kJ]/kg body mass; 60En% carbohydrate, 28En% fat, and 12En% protein). All medications were continued as usual, with the last dose of medication taken before 22:00 on the evening prior to the trials. During the experimental period, the subjects maintained their normal dietary and physical activity pattern. All subjects refrained from exhaustive physical exercise training and/or manual labor for at least 3 days prior to each test.

Study Protocol

Following an overnight fast, subjects arrived at the laboratory at 08:00. A Teflon catheter (Baxter Quick Cath, Dupont, Ireland) was placed in the antecubital vein, and a blood sample was collected to determine fasting plasma glucose, insulin, free fatty acids (FFA), triglyceride, and glucagon concentrations and lipid profile. After collection of the first blood sample (t = 0 minutes),

Table 2

Macronutrient Composition of Enteral Formulas

Ingredient	Per 100 mL	Formula 1	Formula 2	Standard Formula	High-Fat Formula
Energy	Kcal	100	100	100	98
	KJ	420	420	420	411
Protein	g/En%	4.86/19	4.86/19	3.8/15	4.18/17
Milk protein		—	—	ν	ν
Soy protein		ν	ν	—	—
Whey protein		ν	ν	—	—
Carbohydrate	g/En%	11.59/47	11.59/47	13.6/55	8.14/33
Isomaltulose		ν	ν	—	—
Sucromalt		—	ν	—	—
Galactose/glucose		ν	ν	—	—
Fructose		—	—	—	ν
Oligo-/polysacchardes		—	—	ν	ν
Slowly digestible starch		ν	ν	—	—
Starch		ν	—	—	—
Other		ν	ν	—	—
Dietary fiber	g	2	2	1.4	1.44
Fat	g/En%	3.8/34	3.8/34	3.4/30	5.44/50

ν, present in formula; —, not present in formula.

subjects ingested 200 mL of each formula within 5 minutes. Thereafter, blood samples were collected at t = 15, 30, 45, 60, 75, 90, 120, 150, 180, 210, and 240 minutes to determine postprandial plasma glucose and insulin responses. Plasma triglyceride concentrations were measured in blood samples collected at t = 0, 30, 60, 90, 120, 180, and 240 minutes. Blood lipid profile and plasma glucagon concentrations were determined in plasma samples collected at t = 0, 120, and 240 minutes.

Biochemical Measurements

Blood (10 mL) was collected into EDTA-containing tubes and centrifuged at 1000*g* for 10 min at 4°C. Aliquots of plasma were frozen immediately in liquid nitrogen and stored at –80°C until analysis of glucose (Uni Kit III, La Roche, Basel, Switzerland). Insulin was analyzed by radioimmunoassay (Linco Ultra Sensitive Human Insulin RIA kit). Reagents to determine plasma triglycerides, total cholesterol, and high-density lipoprotein (HDL) cholesterol were from ABX Diagnostics (Montpellier, France). Plasma FFA concentrations were analyzed with the NEFA C test kit from Wako Chemicals (Neuss, Germany). Plasma low-density lipoprotein (LDL) cholesterol was not directly measured but calculated by LDL cholesterol = total cholesterol – HDL cholesterol – triacylglycerol/2.2 (in mmol/L). To determine blood A1C content, 3 mL of blood was collected in EDTA-containing tubes and analyzed by high-performance liquid chromatography (Bio-Rad Diamat, Munich, Germany). Commercial kits were used for determination of plasma glucagon (Euro-Diagnostica, Malmö, Sweden) and very-LDL (VLDL) cholesterol (Sebia, Evry Cedex, France) concentrations.

Statistics

In a study by Hofman et al,[11] the postprandial glucose response (incremental areas under the curve [iAUC]) following ingestion of a standard feed (200 mL; 200

kcal) averaged 307 ± 92 mmol•L/120 min. Assuming an expected reduction in the postprandial glycemic response of 30%, applying a significant level of 0.050 (2-sided) and a power of 80%, a sample size of 16 was calculated to be sufficient to detect significant differences between the new formulas and the standard formula.

The time curves of plasma glucose, insulin, triglyceride, total cholesterol, HDL, VLDL, FFA, and glucagon concentrations were analyzed using 2-way repeated-measures analysis of variance (ANOVA) with treatment and time as within-subjects factors. Contrasts were defined to locate main effects of treatment and/or time. When significant time × treatment interactions were observed, separate analyses were performed to determine treatment effects at specific time points and/or time effects within specific treatments. Plasma glucose, insulin, and triglyceride responses were calculated as positive iAUC above baseline levels (t = 0 minutes). The iAUC were calculated according to the trapezoidal method.[21] iAUC and peak plasma concentrations were analyzed using 1-way repeated-measures ANOVA with treatment as a factor. Contrasts were defined to locate treatment effects. When data were not normally distributed, the Wilcoxon signed ranks test was used for statistical analysis. Statistical significance was set at $P < .05$. Bonferroni adjustment was used when multiple testing was performed. All calculations were performed using the Statistical Package for the Social Sciences 15.0.

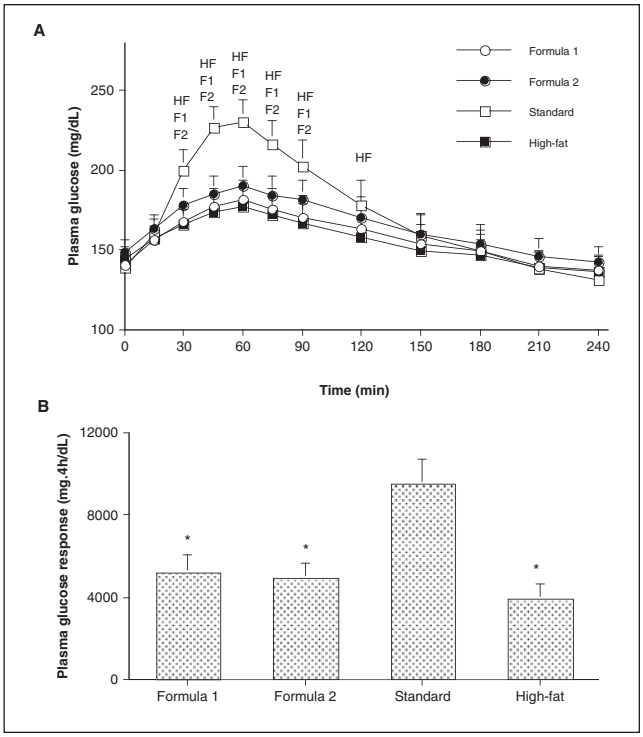

Figure 1. Plasma glucose concentrations (A) and glucose responses (incremental areas under the curve [iAUC]) (B) over a 4-hour period following the ingestion of 4 enteral formulas in type 2 diabetes patients (n = 15). (A) A significant time × treatment interaction was observed, $P < .05$. Specific differences compared with the standard formula are indicated with capital letters (HF, high-fat formula; F1, formula 1; F2, formula 2; $P < .05$). (B) There was a significant difference in plasma glucose response between treatments (iAUC). *Significantly different from the standard formula, $P < .05$.

Results

Energy intake and macronutrient composition of the diet did not differ between treatments. Daily energy intake averaged 22.6 ± 1.9 kcal/kg (95 ± 8 kJ/kg) body mass, with 46 ± 2En% carbohydrate, 34 ± 2En% fat, and 17 ± 1En% protein. Based on a 10-question tolerance questionnaire, all enteral formulas were reported to be well tolerated, and no differences were observed between scores for gastrointestinal symptoms experienced either prior to or after ingestion of the enteral formulas.

Glucose Response

A significant time × treatment interaction was observed for the plasma glucose concentrations over the 4-hour postprandial period ($P < .05$; Figure 1A). At several time points between t = 30 and 240 minutes after ingestion, plasma glucose concentrations were significantly lower following ingestion of formulas 1 and 2 and the high-fat formula when compared with the standard formula (Figure 1A). The plasma glucose response, calculated as the iAUC above baseline levels, differed between treatments ($P < .05$; Figure 1B). The plasma glucose response following ingestion of the standard formula was greater compared with the response observed after ingestion of formulas 1 and 2 and the high-fat formula ($P < .05$). In accordance, peak plasma glucose concentrations also differed between treatments ($P < .05$). Ingestion of the standard formula resulted in higher peak plasma glucose concentrations (237.6 ± 3.6 mg/dL [13.2 ± 0.2 mmol/L]) compared with formula 1, formula 2, and the high-fat formula (189 ± 3.6 mg/dL [10.5 ± 0.2 mmol/L], 196.2 ± 3.6 mg/dL [10.9 ± 0.2 mmol/L], 187.2 ± 3.6 mg/dL [10.4 ± 0.2 mmol/L]; $P < .05$).

Insulin and Lipid Responses

No significant time × treatment interactions were observed for the changes in plasma insulin (Figure 2A)

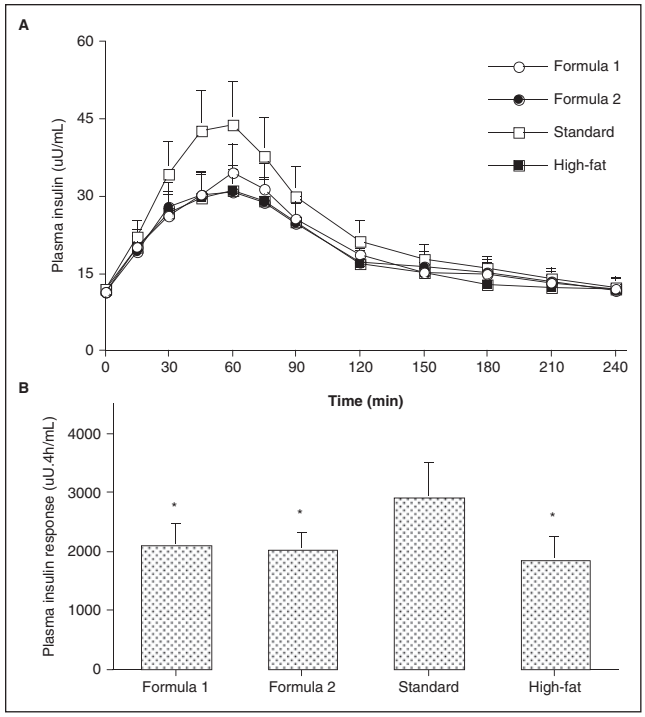

Figure 2. Plasma insulin concentrations (A) and insulin responses (incremental areas under the curve [iAUC]) (B) over a 4-hour period following the ingestion of 4 enteral formulas in type 2 diabetes patients (n = 15). (A) No significant time × treatment interaction was observed, $P > .05$. (B) There was a significant difference in plasma insulin response between treatments (iAUC). *Significantly different from the standard formula, $P < 0.05$.

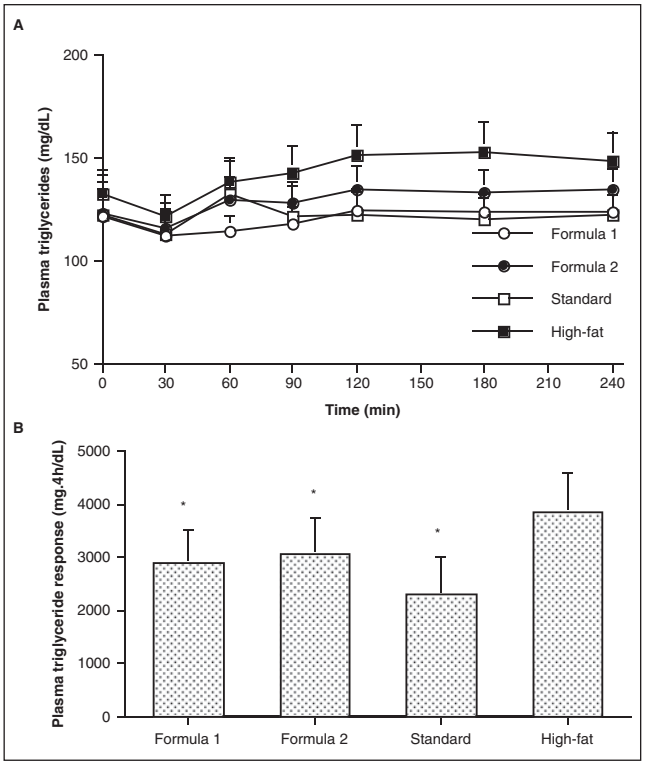

Figure 3. Plasma triglyceride concentrations (A) and triglyceride responses (incremental areas under the curve [iAUC]) (B) over a 4-hour period following the ingestion of 4 enteral formulas in type 2 diabetes patients (n = 15). (A) No significant time × treatment interaction was observed, $P > .05$. (B) There was a significant difference in plasma triglyceride response between treatments (iAUC). *Significantly different from the high-fat formula, $P < 0.05$.

and triglyceride concentrations (Figure 3A). Significant differences in plasma insulin and triglyceride responses (iAUC) were observed (Figures 2B and 3B, respectively). Ingestion of formula 1, formula 2, and the high-fat formula resulted in lower insulin responses compared with the standard formula (Figure 2B). The triglyceride response after ingestion of the high-fat formula was greater than the response following the standard formula and formulas 1 and 2 (Figure 3B).

Plasma lipid profile (FFA, total cholesterol, HDL, LDL, and VLDL) and glucagon concentrations at t = 0, 120, and 240 minutes are presented in Table 3. No significant time × treatment interactions were observed for any of these variables.

Discussion

The present study compares glycemic and insulinemic responses following the ingestion of a single bolus of 2 recently developed diabetes-specific enteral formulas versus a standard, fiber-enriched and a diabetes-specific, high-fat formula. The newly developed enteral formulas and the diabetes-specific high-fat formula were equally effective in attenuating the postprandial glycemic and insulinemic response when compared with a standard enteral formula.

Improving postprandial glycemic control forms a primary target in type 2 diabetes treatment. The latter is not surprising as postprandial glucose levels contribute from 30% to as much as 70% to overall glycemic control in diabetes patients in the highest (>10.2%) and lowest (<7.3%) A1C quintiles, respectively.[22] Furthermore, postprandial blood glucose excursions seem to represent a direct and independent risk factor for the development of cardiovascular complications in patients with type 2 diabetes.[6,23-25] Recent data applying continuous glucose monitoring in well-controlled type 2 diabetes patients

Table 3

Impact of Enteral Formula Ingestion on Blood Lipid Profile and Glucagon Concentrations[a]

	Formula 1			Formula 2			Standard Formula			High-Fat Formula		
Variable	**0 min**	**120 min**	**240 min**	**0 min**	**120 min**	**240 min**	**0 min**	**120 min**	**240 min**	**0 min**	**120 min**	**240 min**
FFA, mmol/L	501 ± 35	306 ± 22	509 ± 52	505 ± 33	316 ± 26	536 ± 44	536 ± 38	289 ± 24	504 ± 49	561 ± 57	366 ± 32	600 ± 46
Cholesterol, mg/dL	215 ± 14	210 ± 14	214 ± 15	210 ± 14	205 ± 13	210 ± 13	204 ± 13	202 ± 14	206 ± 14	212 ± 13	208 ± 13	214 ± 14
Cholesterol, mmol/L	5.55 ± 0.37	5.43 ± 0.37	5.53 ± 0.38	5.44 ± 0.35	5.31 ± 0.34	5.44 ± 0.34	5.28 ± 0.34	5.22 ± 0.36	5.33 ± 0.35	5.49 ± 0.34	5.38 ± 0.34	5.53 ± 0.36
HDL, mg/dL	53.8 ± 3.1	53.4 ± 3.1	53.4 ± 3.1	53.0 ± 3.1	52.2 ± 3.1	52.6 ± 3.1	52.6 ± 3.1	52.2 ± 3.1	53.0 ± 3.1	52.2 ± 2.7	51.4 ± 2.7	51.8 ± 3.1
HDL, mmol/L	1.39 ± 0.08	1.38 ± 0.08	1.38 ± 0.08	1.37 ± 0.08	1.35 ± 0.08	1.36 ± 0.08	1.36 ± 0.08	1.35 ± 0.08	1.37 ± 0.08	1.35 ± 0.07	1.33 ± 0.07	1.34 ± 0.08
LDL, mg/dL	137 ± 13	132 ± 12	136 ± 13	133 ± 12	127 ± 11	131 ± 12	127 ± 12	126 ± 12	129 ± 11	133 ± 10	127 ± 11	133 ± 11
LDL, mmol/L	3.53 ± 0.34	3.42 ± 0.31	3.52 ± 0.33	3.44 ± 0.30	3.27 ± 0.29	3.39 ± 0.30	3.29 ± 0.30	3.25 ± 0.31	3.33 ± 0.29	3.45 ± 0.27	3.27 ± 0.28	3.44 ± 0.29
VLDL, mg/dL	9.9 ± 1.1	9.7 ± 0.9	10.2 ± 0.8	9.6 ± 0.7	10.2 ± 0.5	10.5 ± 0.6	8.9 ± 0.7	10.4 ± 0.8	10.4 ± 0.5	9.2 ± 0.7	10.6 ± 0.9	10.1 ± 0.5
VLDL, µmol/L	255 ± 29	252 ± 22	264 ± 21	247 ± 18	263 ± 14	271 ± 16	230 ± 19	269 ± 20	269 ± 12	238 ± 19	275 ± 23	262 ± 13
Glucagon, pg/mL	71.4 ± 3.0	73.3 ± 3.0	69.0 ± 3.0	73.0 ± 3.9	71.4 ± 4.4	73.0 ± 4.3	71.9 ± 5.7	70.5 ± 4.5	74.2 ± 5.1	74.4 ± 5.5	74.9 ± 4.5	73.3 ± 5.1

Abbreviations: FFA, free fatty acids; HDL, high-density lipoprotein; LDL, low-density lipoprotein; VLDL, very low-density lipoprotein.

[a] Values represent means ± SEM, n = 15. Plasma FFA, cholesterol, and LDL concentrations declined significantly from baseline to t = 120 minutes, after which values returned to baseline values ($P < .05$). No significant time × treatment interactions were observed for any of the variables.

report that daily postprandial glucose excursions leading to hyperglycemia are much more prevalent than previously thought.[5] From those data, it seems evident that standard pharmaceutical treatment with oral blood glucose–lowering medication is not sufficient to reduce postprandial blood glucose excursions. Therefore, dietary and exercise interventional strategies are warranted to further improve postprandial blood glucose homeostasis in patients with type 2 diabetes.[26]

Standard enteral products for patients in need of nutritional support are also being used by type 2 diabetes patients. However, such enteral formulas have not been developed to limit postprandial glycemia. Some diabetes-specific enteral products are available that generally contain less carbohydrate and more fat.[10] As a consequence, the macronutrient composition of these products generally does not comply with current nutritional guidelines for diabetes patients, which recommend that the fat content of a diet should not exceed 35En%.[12] The application of so-called slowly digestible carbohydrate sources may represent an effective tool to reduce fat intake and increase carbohydrate content without elevating postprandial glycemia and insulinemia. In the present study, 2 diabetes-specific enteral formulas were defined that contain such slowly digestible carbohydrate sources: isomaltulose and sucromalt. Comparison of the postprandial glycemic and insulinemic responses following ingestion of these formulas and a standard and high-fat enteral formula (Figures 1 and 2) shows that both enteral formulas 1 and 2 combine the characteristics of a carbohydrate-rich enteral formula with a low postprandial glycemic (Figure 1) and insulinemic (Figure 2) response when compared with the standard formula. The glycemic and insulinemic responses were similar to the high-fat treatment, in which an isocaloric formula was provided that contained less carbohydrate.

In formula 1, isomaltulose was used as the main slowly digestible carbohydrate source. In vitro studies using human small intestinal mucosa homogenates show that human intestinal enzymes hydrolyze isomaltulose at a much slower rate when compared with sugars such as maltose or sucrose.[14,15] This slower hydrolyzation process during gastrointestinal passage is likely responsible for the attenuated postprandial rise in blood glucose and insulin concentrations following isomaltulose versus sucrose ingestion in both healthy subjects[16-18] and type 2 diabetes patients.[17] The major carbohydrate source used in formula 2 was sucromalt. In a recent human in vivo study, Grysman et al[13] showed that ingestion of 50 g of sucromalt (containing 21 g of fructose, 25 g of gluco-oligosaccharides, and 4 g of leucrose) results in substantially lower plasma glucose and insulin responses when compared with the ingestion of 50 g of high-fructose corn syrup (containing 21 g of fructose and 29 g of glucose). No rise in hydrogen content of the expired breath was observed after sucromalt ingestion, suggesting that little if any sucromalt escaped digestion in the small intestine and entered the colon. In accordance, it was recently observed that >97% of the ingested sucromalt is absorbed from the small intestine in ileostomy patients (unpublished observations).

Furthermore, both newly defined formulas also contained slowly digestible starch. This digestible starch is formed after sterilization of a resistant starch source (modified high-amylose starch). It was recently shown that heating of this resistant starch source in liquid increases the slowly digestible starch fraction at the expense of the resistant starch portion.[27] After intragastric administration of this slowly digestible starch to cannulated male rats, this starch source was shown to significantly attenuate the postprandial glycemic response when compared with a control starch, consisting of digestible maltodextrins.[27]

Interestingly, the glycemic and insulinemic responses following the ingestion of formula 1 and 2 did not differ from the diabetes-specific, high-fat formula (Figures 1 and 2). This strongly supports the proposed efficacy of slowly digestible carbohydrate sources as a means to reduce the glycemic and/or insulinemic response to food intake. The latter does not increase the fat intake at the expense of carbohydrate ingestion, as generally observed in diabetes-specific, enteral products. The total amount of fat in formulas 1 and 2 was set in line with nutritional guidelines on the preferred macronutrient composition for type 2 diabetes patients (ie, 35En% fat maximally). Furthermore, a greater fat content of a meal is generally associated with higher postprandial plasma triglyceride levels.[28-31] In accordance, a significantly greater postprandial triglyceride response following ingestion of the high-fat formula was observed when compared with formulas 1 and 2 and the standard enteral formula. In accordance, elevated triglyceride levels were observed during continuous tube feeding for 6 hours with a high-fat (49En%) versus a standard formula (35En% fat) in type 2 diabetes patients.[31]

In the present study, different available enteral formulas, which contain more ingredients than merely different

carbohydrate sources, were compared. Although this allows a more clinically relevant comparison, it needs to be underlined that other food components might be, at least partly, responsible for the observed differences in glycemic and insulinemic responses between treatments. For example, it has been well established that protein co-ingestion with carbohydrate can further enhance the postprandial insulin and glucose responses.[32-36] Therefore, protein content as well as the protein source[37,38] being used in the formulas could have modulated the insulinemic and/or glycemic responses. Furthermore, differences in dietary fiber content and/or fiber type may contribute to the differences in the postprandial plasma glucose responses between treatments.[39] Nonetheless, the present study clearly shows that slowly digestible carbohydrate sources can be applied to design type 2 diabetes–specific enteral formulas that attenuate the postprandial rise in plasma glucose and insulin concentrations in type 2 diabetes patients when compared with standard, high-carbohydrate formulas and diabetes-specific, high-fat enteral formulas.

In the present study, habitual food intake was standardized prior to the various experimental trials. In addition, all subjects received the same standardized meal the evening prior to each test day. Despite such rigorous dietary standardization, it is evident that postprandial glucose and insulin responses can vary substantially on a day-to-day basis. The fact that all formulas were tested only once in each subject might, therefore, represent a limitation of the presented work. Furthermore, it should be noted that the clinical relevance of these findings when applied in more long-term conditions remains to be established. Clearly, more research is warranted to study the impact of the GI of different formulas on long-term glycemic control.

In conclusion, diabetes-specific enteral formulas rich in slowly digestible carbohydrate sources can be equally effective in attenuating the postprandial glycemic response as low-carbohydrate, high-fat enteral formulas, without elevating plasma triglyceride responses.

Implication

For diabetes patients in need of nutritional support, diabetes-specific enteral formulas are available. The present study results show that enteral formulas containing slowly digestible carbohydrates and a moderate amount of fat are equally effective in reducing the postprandial glycemic response as the currently available diabetes-specific, high-fat formulas (compared with a standard enteral formula). However, in contrast to a diabetes-specific, high-fat formula, the enteral formulas with slowly digestible carbohydrates do not elevate postprandial triglyceride levels and may be preferred for patients with diabetes.

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