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Comparison of two liquid nutritional supplements designed for patients with diabetes: Effect on glucose and insulin metabolism in healthy subjects

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ABSTRACT

Aim: To compare the effect of the single administration of two liquid nutritional supplements designed for diabetic patients and administered to healthy subjects to determine glucose and insulin metabolism.
Methods: A randomized, double-blind, crossover clinical trial as a pilot study was carried out in 10 healthy young volunteers. Each individual received a single administration of Enterex Diabetic or Boost GC. At the beginning of each administration and after 30, 60, 90 and 120 min, glucose and insulin concentrations were measured. Area under the curve (AUC) of glucose and insulin was calculated. First phase (Stumvoll index) and total insulin secretion (insulinogenic index) as well as insulin sensitivity (Matsuda index) were assessed.
Results: Boost GC compared with Enterex Diabetic showed a lower AUC of glucose (9496 ± 897 vs. $10{,}996 \pm 842$ mg/dl, $p = 0.004$), AUC of insulin (2253 ± 910 vs. 3924 ± 1468, $p = 0.008$) and Stumvoll index (1160 ± 233 vs. 1384 ± 295, $p = 0.049$) as well as a higher Matsuda index (31.2 ± 39.5 vs. 9.9 ± 2.6, $p = 0.001$).
Conclusion: A single administration of Boost GC in healthy individuals showed lower insulin secretion and higher insulin sensitivity compared with Enterex Diabetic.

1. Introduction

In type 2 diabetes mellitus the medical nutrition therapy in accordance with patient-specific characteristics is essential for metabolic control [1]. Many international publications establish strategies to allow the implementation of suitable nutritional recommendations in these patients [2]. Within the scope of medical nutrition therapy for diabetes, use of liquid nutritional supplements designed especially for the patient with diabetes mellitus have been an alternative to achieve, in some cases, the amount and proportion of recommended nutrients [3]. These supplements have been available for a number of years and contain specific ingredients and have shown different effects on glucose and insulin metabolism, which could impact on metabolic control [4].

A systematic review [5] showed that use of diabetes-specific formulas is associated with improved glycemic control compared with standard formulas, however, there are several nutritional formulas without scientific evidence for demonstrating preference of one over another and that show the optimal concentration of nutrients. Therefore, the aim of this study was to compare the effect of the single administration of two liquid nutritional supplements (Enterex Diabetic and Boost GC) designed for the patient with diabetes mellitus and administered to healthy individuals to determine glucose and insulin metabolism.

2. Methods

A randomized, double-blind, crossover clinical trial as a pilot study was carried out in 10 healthy, nonobese [body mass index (BMI) < 25 kg/m^2], young (18–30 years old) volunteers with similar demographic and socioeconomic characteristics. All were non-smokers and their body weight remained stable for at least 3 months prior to the study, and there were no modifications in their physical activity. All volunteers were in good health, as assessed by medical history and physical examination, including

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fasting glucose concentration of <5.5 mmol/l and blood pressure <130/80 mmHg. No history of hypertension, hepatic and renal disease, coronary artery disease, and type 1 or 2 diabetes mellitus was reported. Exclusion criteria included use of drugs with known effects on glucose metabolism and allergy to cow or soy milk.

The study was approved by the ethics committee of the participating hospital and fulfilled all requirements for human research, including Declaration of Helsinki and Good Clinical Practice; all participants provided written informed consent.

Before testing, an isocaloric diet of at least 250 g of carbohydrates per day was given for 3 days, confirmed by dietary history. Testing was initiated at 8:00 AM after a 12-h fast. Height and weight were measured wearing light clothes and without shoes. Height was measured and rounded off to the nearest centimeter, with the subjects standing. Values were used to calculate BMI according to the formula: weight (kg)/height (m^2). Waist circumference was taken at the midline between the highest point of the iliac crest and the lowest rib. Blood pressure was evaluated by the investigator after a resting period of 5 min with the subject sitting on a chair, using a standard mercury sphygmomanometer. Systolic and diastolic pressures were considered in Korotkoff phase I and V, respectively. Venous blood was obtained with the subject lying supine in a quiet room. Samples of venous blood at 0, 30, 60, 90 and 120 min were obtained and centrifuged. Serum was separated into two aliquots: the first was used for determination of glucose and the second was frozen at −20 °C for insulin measurement within the following 30 days.

After random allocation of the intervention, each individual ingested a volume equivalent to 191 kcal, gauged with water at 300 ml, which corresponded to 191 ml of Enterex Diabetic (Victus Inc., Miami, FL, USA) or 237 ml of Boost GC (Nestlé HealthCare Nutrition Inc., Minneapolis, MN, USA). The nutrient contents of Enterex Diabetic and Boost GC are carbohydrates 45.0% (maltodextrin, 21.7 g) vs. 33.5% (16 g of tapioca dextrin); lipids 35.0% (7.2 g) vs. 33.0% (7.0 g); proteins 20.0 % (9.6 g) vs. 33.5 % (16 g); and fiber 3.4 g (soy) vs. 3.0 g (guar gum), respectively. Three days after the first test, the second intervention was performed in a crossover manner. During this period, the customary diet of each subject was not modified.

The Madrid scale [6] was used to evaluate the preferences of volunteers with regard to liquid nutritional supplements. This scale consists of eight questions referring to eight attributes of the supplement: appearance, smell, impression in the mouth (texture), taste, sensation of fullness, sweetness, taste after swallowing, and overall impression. With the above-mentioned evaluation, a range (8–24 points) is obtained, which is adjusted to percentage – the higher the score, the higher the preference.

Glucose concentration was measured using the glucose-oxidase technique (Ortho-Clinical Diagnostics, Rochester, NY, USA) with an intra- and interassay coefficient of variation <1%. Insulin was measured by immunoradiometric assay (CIS Bio International, Cedex, France) with an intra- and interassay coefficient of variation of 3.8 and 7.0%, respectively. Area under the curve (AUC) of glucose and insulin was calculated with the polygonal formula. Total insulin secretion was evaluated with the insulinogenic index (ΔAUC insulin/ΔAUC glucose). The first phase of insulin secretion was estimated with Stumvoll index ($1283 + 1.829 \times$ insulin 30 min $- 138.7 \times$ glucose 30 min $+ 3.772 \times$ insulin 0 min) and the insulin sensitivity with Matsuda index [$10{,}000/\sqrt{}$(glucose 0 min $\times$ insulin 0 min) (mean glucose, oral glucose tolerance test [OGTT] $\times$ mean insulin, OGTT)].

Sample size was calculated with the formula for clinical trials [7] with a confidence level of 95% and power of 80%. A standard deviation (SD) of 0.6 mmol/l with an expected difference of 0.8 mmol/l was used for postprandial glucose for a total of 10 subjects. SD of 0.12 pmol/l with an expected difference of 0.15 pmol/l was calculated for insulin secretion for a total of 10 individuals. SD of 1.5 with an expected difference of 2.5 was used for insulin sensitivity for a total of six subjects. Values are presented as mean ± SD. Between-group differences were analyzed by Mann–Whitney *U* test. Wilcoxon test was used for differences before and after the intervention in the same group.

3. Results

The group consisted of five females and five males with ages of 21.9 ± 1.5 years, weight of 61.4 ± 7.1 kg and BMI of 21.6 ± 1.2 kg/m^2. Waist circumference in women was 74.2 ± 5.4 and in men 83.2 ± 8.1 cm.

As shown in Table 1, lower glucose and insulin concentrations at 30 min were observed with Boost GC administration. AUC of glucose and insulin, as well as the first phase of insulin secretion, were lower (Fig. 1), and insulin sensitivity was higher (Fig. 2) with Boost GC administration.

According to the evaluation of preferences of volunteers towards liquid nutritional supplements, impression in the mouth (texture) obtained a higher statistical tendency with Boost GC (2.4 ± 0.8 vs. 1.5 ± 0.8, $p = 0.052$). The remaining preferences were similar for both interventions. Overall impression for both supplements was 60.6% ($p = 0.971$).

4. Discussion

Patients with diabetes mellitus frequently require nutritional support. Usefulness of nutritional supplements is currently a major topic of discussion. In recent years, various liquid nutritional supplements specifically designed for the patient with diabetes have been marketed. These are complete nutritional products that can be used as a snack or as a meal substitute. These supplements have demonstrated a clear superiority to the standard nutritional formulas that are used to normalize fasting and postprandial glucose concentrations. In some cases, these supplements improve lipid profile when administered several times daily. They also increase insulin sensitivity and, with long-term administration, may reduce complications of diabetes, mainly cardiovascular [8–11].

Scarce information exists about the effect of liquid nutritional supplements for diabetic patients on glucose and insulin metabolisms. In a previous study, Glucerna SR administration in healthy individuals decreased postprandial glucose and insulin concentrations with increased insulin sensitivity in comparison with Ensure High Calcium (standard formula) and 75 g of dextrose [3]. Another study describing administration of Enterex Diabetic showed a decrease in postprandial glucose and

Table 1
Glucose and insulin concentrations between interventions.

	Enterex Diabetic	Boost GC	*p*
Glucose 0 min, mmol/l	4.2 ± 0.5	4.2 ± 0.4	0.970
Glucose 30 min, mmol/l	5.5 ± 0.5	4.4 ± 0.6	0.002
Glucose 60 min, mmol/l	4.5 ± 0.9	3.9 ± 0.5	0.069
Glucose 90 min, mmol/l	4.3 ± 0.7	4.1 ± 0.4	0.595
Glucose 120 min, mmol/l	4.2 ± 0.5	4.4 ± 0.3	0.053
ΔGlucose 0–120 min, mmol/l	−0.0 ± 0.8	0.2 ± 0.4	0.150
Insulin 0 min, pmol/l	56 ± 22	39 ± 19	0.082
Insulin 30 min, pmol/l	280 ± 165	145 ± 68	0.023
Insulin 60 min, pmol/l	129 ± 49	96 ± 53	0.142
Insulin 90 min, pmol/l	76 ± 47	57 ± 19	0.545
Insulin 120 min, pmol/l	50 ± 30	41 ± 16	0.571
ΔInsulin 0–120 min, pmol/l	−5 ± 22	2 ± 16	0.257
Insulinogenic index	1.5 ± 1.2	0.6 ± 5.3	0.705