Comparison of a low-glycemic index vs standard diabetic diet

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Aim. There is insufficient evidence for the efficacy of a low-glycemic index (GI) diet in the management of diabetes. The goal of this study was to measure the effect of a low GI versus a standard diabetic diet in adults with diabetes type 2.
Methods. This was an open label, randomized, crossover study. Twenty persons with type 2 diabetes were randomized to two groups. Each group followed a standard diabetic diet or a low glycemic index diet for 3 months. The effectiveness of the two diets was evaluated using a hyperinsulinemic euglycemic clamp with endogenous glucose production measurement, indirect calorimetry and bioimpedance analysis. Outcome measures were body mass, BMI, body fat, glycosylated hemoglobin, fasting glucose, lipid profile, insulin sensitivity and hepatic glucose production.
Results. Body mass after 3 months following the diabetic diet was 93 kg (83-104) vs. low glycemic index diet 92 kg (85-104) $P<0.05$, BMI 31.3 kg/m^2 (27.5-35.9) vs. 30.7 kg/m^2 (27-35.3) $P<0.05$, body fat 28% (25.5-43) vs. 27% (23-43) $P<0.05$ (median and interquartile range). There was no statistically significant difference between diets for glycosylated hemoglobin, fasting glucose, lipid profile, insulin sensitivity or hepatic glucose production.
Conclusions. The results are comparable with other studies showing a modest effect of a low GI diet in the management of diabetes. We found a modestly greater weight loss, body fat and BMI reduction on the low GI diet.

Keywords: diabetes type 2, low glycemic index diet, standard diabetic diet, hepatic glucose production

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INTRODUCTION

Diet is significant in both the prevention and treatment of type 2 diabetes. People diagnosed with diabetes in the Czech Republic, are educated on diets which stress regular, optimal intake of basic nutrients, minerals, vitamins, trace elements and fiber. The aim is to establish an energy intake that prevents overweight and obesity. Diabetic diets should also assist in preventing the acute and chronic complications of the disease[1]. However, opinions on diets for diabetic patients are constantly changing and even today they are arbitrary.

Originally, dietary recommendations emphasized control of the amount of carbohydrates regardless of quality and source. Interest in the composition of carbohydrates increased with the discovery of postprandial glycaemia (PPG) as an independent risk factor for cardiovascular disease. Jenkins et al. in the early 1980s, established a standard called the "Glycemic Index (GI)" (ref.[2]), for classing carbohydrates according to their effect on PPG. GI is calculated as the ratio of the area under the blood glucose curve following ingestion of 50 g of carbohydrate to the area under the blood glucose curve following 50 g of pure glucose[3,4]. A low-GI diet is assumed to have a number of advantages such as increased blood sugar control, protection against cardio vascular disease and cancer. One meta-analysis of studies on GI showed that low GI foods significantly improve glycemic control[5]. Low GI also favourably influences the lipid profile, and according to some studies negatively correlates with insulin sensitivity[6], improves fibrinolytic activity and decreases chronic inflammation[7]. However, it has to be noted most studies on low-GI diet usually compare diets with low and high GI which may not necessarily conform to the common dietary recommendations for persons with diabetes. As the Brand-Miller meta-analysis concluded, the average GI of diets can be as high as 83 in the case of a high GI.

For this reason, the aim of this study was to compare the effect of a low-glycemic index diet with a standard diabetic diet.

MATERIALS AND METHODS

Twenty persons (12 men and 8 women) with type 2 diabetes, treated by diet and metformin, were included. The main demographic, clinical, and metabolic characteristics of the patients are summarized in Table 1. The study was approved by the Ethics Committee of the Medical Faculty of Charles University, Pilsen. All subjects were adequately informed about the purpose and any risks of the experiment and gave their informed written consent.

The initial examination included measurement of bioimpedence, hyperinsulinemic euglycemic clamp with hepatic glucose production measurement, indirect calorimetry and blood sampling. The subjects then took part

Table 1. Main demographic, clinical and metabolic data.

Variables	All (n = 20)
Men/women (n)	12/8
Age (years)	62.7±5.8
Body mass (kg)	94,5±14,5
BMI (kg/m^2)	32±4.2
HbA1c (%)	7±2.88
FPG (mmol/L)	7.4±1.61
Metformin dose (mg/day)	1626±431
Diabetes duration (years)	7±4.1

All values are mean ± SD.
BMI, body mass index, HbA1c, glycosylated hemoglobin according to Diabetes Control and complications Trial (DCCT). For International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) units use this converting equation: IFCC = (10.93*DCCT) - 23.50; FPG, fasting plasma glucose.

in an information session with a dietician. A second identical examination took place three months after following the recommended diabetic diet. The subjects were then randomly assigned to two equal groups; Group 1 continued with the unchanged diabetic diet while group two followed a low-GI diet limited to 55 (compared to glucose). After the second three-month period, the third identical examination was carried out. The groups were then crossed over according to the standard crossover design. The last examination took place at the end of the third three-month period. The study thus lasted 9 months, within which each subject underwent 4 complex examinations.

Hyperinsulinemic euglycemic clamp (HEC)

Subjects arrived fasting in the morning. Bioimpedance and indirect calorimetry (see further) were performed after body mass measurement. A cannula was then inserted into an antecubital vein. A priming dose of insulin was administered after blood sampling for assessment of basic biochemical parameters, for blood glucose measurement using the glucometer (HemoCue glucose analyser; HemoCue Ltd, Ängelholm, Sweden) and for later determination of background isotope enrichment. The isotope was prepared on the same day in the hospital pharmacy according to patient body mass, i.e. at a dose of 36 mg/kg body mass. We used glucose 6,6-$^2H_2$, 99% isotope (Cambridge Isotope Laboratories, USA) for preparation of the infusion. After administration of a 15 mL bolus of the described solution of isotope (at time -180 min), a constant speed of administration of 9 mL/h of isotope solution was maintained using a syringe pump until the end of the experiment. The stabilization period took 180 min in total. At time 0, the actual one-step hyperinsulinemic euglycemic clamp of 120 min in duration was started. A blood sample was obtained for basal insulinemia assessment. The sample was frozen and later analyzed via immunoradiometric assay using a commercial kit (Immunotech SA, Marseille, France). A continuous insulin infusion (ACTRAPID HM; Novonordisk, Copenhagen, Denmark) at a rate of 100 mIU/m^2/min was then delivered by a syringe pump starting at 20% glucose 500 mL, enriched by 2.5 g of isotope infused at variable rates to maintain a target glycemia at 5 mmol/L. Blood glucose was measured by the glucometer Hemocue every 5-10 min. Blood samples were taken from a second cannula inserted peripherally in an upper extremity. Glucose solution uptake was used for calculation of the M value as a parameter of insulin sensitivity[8]. Target insulinemia was confirmed from a blood sample taken during the steady state. Blood samples for isotope enrichment analysis were collected in test tubes containing sodium fluoride for the whole examination. They were cold stored, centrifuged and frozen for later evaluation. The isotope enrichment was determined at the Anästhesiologische Pathophysiologie und Verfahrensentwicklung, Universitätsklinikum, Ulm using the instrument GC/MS Agilent 5890/5970 (USA, CA). Basal endogenous glucose production was calculated using the equation Ra = F/Ep, where Ra is a rate of glucose appearance, F is a tracer infusion rate, and Ep is the [6,6-$^2H_2$] glucose isotopic enrichment in the plasma. Steel's equation[9] was used for the calculation of endogenous glucose production (EGP) during the steady state.

Indirect calorimetry

Indirect calorimetry measurement was performed on entry and in the course of the clamp during the steady state. An open canopy method of indirect calorimetry with a duration of 45 min was used with the VMAX (Sensor Medics, Anaheim, CA, USA). REE (resting energy expenditure) and RQ (respiratory quotient) were automatically recorded in the course of system stabilization and served for further calculations. Urine was collected and urine nitrogen excretion was measured. Non-protein RQ, important for determination of the glucose oxidation rate was calculated. Glucose storage was calculated as the difference between used glucose (M - value) and oxidized glucose.

Bioimpedance

This was measured using NUTRI 4 (Data Input GmbH, Darmstadt, Germany). Prior to the clamp commencement in a supine position, 4 electrodes were placed on precise spots on the wrist and instep (dominant extremities). A constant current of approx. 0.8 mA, f 1, 5, 50 and 100 kHz was used. The bioimpedance instrument calculated body fat percentage, fat mass and total fat-free mass based on measurements of total body water (TBW), intracellular water (ICW), extracellular water (ECW), phase angle, and body cell mass (BCM).

Dietary follow-up

Subjects were instructed by a dietitian on following the standard diabetic diet. The entry caloric density was based on prior indirect calorimetry in the range 1500 - 2400 kcal (defined as 1.4 x REE), divided into 6 meals of 175 - 325 g

of carbohydrates. 40% of calories should come from carbohydrates, about 30% from protein, about 30% from fat. For carbohydrates, whole grains, legumes (beans, peas and lentils), fruits, vegetables and low-fat dairy products were recommended. Fibre-rich foods including vegetables, fruits, nuts, legumes, whole-wheat flour and wheat bran were advised with fibre intake at least 20 g per day, as well foods containing monounsaturated and polyunsaturated fats, such as walnuts, olives, olive and peanut oil, avocados, almonds. Reduced intake of saturated fats, trans fats (saturated fat intake should be <7% of total calories[10]), cholesterol (aim for no more than 200 mg of cholesterol per day) and sodium (aim for less than 4 g of sodium per day) was requested.

The subjects obtained the recommended diet plan with instructions to keep a detailed daily record of meal composition and ingredient weight. The records were checked biweekly by the dietitian who adjusted the diet individually. In the second three month period, the subjects were randomised to two groups. Group 1 (GI <55) was given a list of meals and cookbook for a GI content lower than 55. This group was advised to eat pasta, legumes, and wholemeal products, and at the same time, they were advised to avoid food with higher GI, such as potatoes and white bread. Food preparation was also adjusted for this group. The groups were crossed over after another three months. Computer software Nutridan (Mullerova D, Tychtl Z, Muller, Brazdova Z, Pilsen, Czech Republic) was used for evaluation of food composition. GI calculations were done by a dietitian who used publically available GI values[11]. For most mixed foods she used the average GI of the individual carbohydrates and percentage in the food for calculations[3]. The subjects received a pedometer to monitor physical activity. They were instructed and controlled in maintaining regular daily exercise.

Statistics

The data were analysed using the Friedman and Wilcoxan tests and an alpha level of $P< 0.05$ was chosen for significance. The data are presented as the median and interquartile range.

RESULTS

All 20 subjects successfully completed all diet periods. The groups were similar in baseline measures.There were no major lifestyle ganges and nody dropped out.

Diet

The composition of the diets is shown in Table 2. There was no difference in food composition as macronutrients and energy from evaluation of the diet records but the amount of fiber differed.

Anthropometric data

There was a decrease in body mass. Initial body mass 96 kg (88-1032), 92 kg (84.6-96.9) after 3 months, 92.4 kg (83.2 -98) after 6 months, $P<0.05$. After 9 months, weight 92.6 kg (85.20- 97.8). Table 3 shows the results of the diets after three months on selected parameters. There was no change in non-fat mass or body cell mass.

Lipids

The lipid profile was similar. (Table 3)

Glycemic control

There was no difference between groups in terms of glycemic control.

Insulin sensitivity and endogenous glucose production

We found no significant difference between groups in terms of insulin sensitivity or on basal hepatic glucose production. We managed to suppress endogenous glucose production to zero during the clamp.

DISCUSSION

There was a decrease in body mass in both groups, which was 1kg greater for the low GI group. There was no statistically significant difference for any of the other parameters such as HbA1c and M value but there is a good cause to believe that the weight loss was too low to be reflected in these parameters. We can only speculate, whether a low-GI diet for longer would lead to more weight loss which would manifest itself in other param-

Table 2. The diet compositions.

	Low GI diet	Common diabetic diet	*P*
Glycemic index (%)	49 (48-51)	68 (61-72)	$P<0.01$
Fat (g)	70 (58-74)	80 (65.5-93.5)	ns
Carbohydrates (g)	159 (146-179.5)	163 (128-180)	ns
Proteins (g)	74 (58-74)	80 (65.5-93.5)	ns
Energy/day (kcal)	1676 (1589-1718)	1745 (1546-19.43)	ns
Fibre (g)	20 (17-22)	18 (13-21.5)	$P<0.05$

All values are presented as median and interquartile range

Table 3. Selected parameters after 3 months of low glycemic index diet or common diabetic diet.

Variables	Low GI diet	Common diabetic diet	*P*
Body mass (kg)	92 (85-104)	93 (83-104)	*P*<0.05
BMI (kg/m^2)	30.7 (27-35.3)	31.3 (27.5-35.9)	*P*<0.05
Fat mass (%)	27 (23-43)	28 (25.5-43)	*P*<0.05
Fat free mass (kg)	65.5 (51-74)	64 (51.5-72)	ns
Body cell mass (kg)	32.9 (26.3-37.8)	30.8 (28.7-35.7)	ns
LDL – cholesterol (mmol/L)	2.71 (2.12-3.46)	2.67 (2.29-3.55)	ns
HDL – cholesterol (mmol/L)	1.1 (0.96-1.17)	1.11 (0.93-1.23)	ns
Triglycerides (mmol/L)	1.6 (1.32-1.76)	1.54 (1.11-1.8)	ns
Fasting plasma glucose (mmol/L)	6.5 (5.6-8.4)	6.7 (6.1-7.5)	ns
†HbA1c (%)	6.63 (6.08-7.0)	6.45 (6.18-6.91)	ns
M – value (mg/kg/min)	6.72 (4.91-7.7)	5.27 (3.55-7.02)	ns
Basal hepatic glucose production (mg/kg/min)	1.6 (1.39-1.84)	1.65 (1.51-1.91)	ns

All values are presented as median and interquartile range
BMI, body mass index; LDL, low-density lipoprotein; HDL, high-density lipoprotein;
HbA1c glycosylated hemoglobin according to Diabetes Control and Complications Trial (DCCT).). For International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) units use this converting equation: IFCC = (10.93*DCCT) - 23.50.

eters. A diet period of 3 months is longer than that used in some other studies. It has been proven that a low GI diet can reduce weight more than the common diabetic diet. This is explained by several factors: low GI food is usually rich in complex carbohydrates and fiber. These increase the feeling of satiety and reduce excessive energy intake[12]. High GI food causes a more distinct postprandial increase in glycaemia. This leads to secretion of large amounts of insulin and a reduction in glucagon concentration (increasing the insulin/glucagon ratio). As a result insulin-regulated processes are prominent. Lipolysis and gluconeogenesis can decrease, and glycogenesis and lipogenesis increase. Two hours after a meal the amount of nutrients absorbed from the gastrointestinal tract decreases. However, the level of insulin remains elevated. This results in a faster decrease in blood glucose and creates a counterregulatory response. This in turn may cause a feeling of hunger and increased food intake. It causes increase in glycogenolysis and gluconeogenesis and elevation of other metabolic substrates in blood, such as free fatty acids, which further increase insulin resistance and act toxically on β-cells[13].

Endogenous glucose production was measured at baseline and we examined suppressibility of endogenous glucose production during hyperinsulinemic euglycemic clamp. The results showed no significant difference of the diets on endogenous glucose production. The baseline value of endogenous glucose production was similar to a healthy population[14]. Our results thus demonstrate that the dominant contribution to glycemic control was PPG and not fasting glucose, as basal endogenous glucose production was not disrupted. These findings are in accordance with Monnier et al., who showed that 70% of total glycemic control is, in well-controlled diabetics with an HbA1c under 5.6%, achieved by postprandial glycemia and conversely, in persons with HbA1c above 8.6% the glycemic control is in 70% influenced by fasting glucose, which is mostly determined by hepatic sensitivity[15]. We based the HEC methods on findings from our former study on insulin resistant individuals[8]. We assumed high insulin resistance and therefore we chose a higher target hyperinsulinemia value of 250 mU/L. Even so, we managed to fully suppress the endogenous glucose production in this experiment and hence we cannot comment on the effects of individual diets on endogenous production during the clamp which may simultaneously simulate a state after saccharide load.

There is a wide variability in GIs used in studies that compare different GIs (ref.[4]). In our study, we only used a low-GI. We were also interested in the GI value of a commonly recommended diabetic diet. Our data show that this was around 68, which is a medium GI value. The low-GI diet, used in this study was 49. No statistical difference was found in a number of parameters in spite of the fact that the difference in GI between groups was statistically significant and the diets differed moderately in fiber content. Whether a greater difference in GI between diets would produce different results remains unanswered. However, our aim was to compare a low GI diet with a diet used in practice by persons with diabetes.

Currently, glycemic index is classified as level E for diabetes prevention according to the American Diabetes Association guidelines. This means that there is not enough reliable evidence to confirm that a low GI diet pre-

vents the onset of diabetes. On the other hand, this diet is generally rich in fiber and other important nutrients and therefore to be recommended. The GI is currently classified as level B for the treatment of diabetes. According to the ADA it can mildly increase benefits over a diet based on mere total saccharide intake calculation[1]. The glycemic index is an important dietary measure but it should not be recommended alone in a diabetic diet. The concept of GI takes into account only the quality of carbohydrates, not the quantity and possibly content of other nutrients and calories. Despite these limitations, the GI has a number of qualified supporters in the medical world.

This study has some limitations. Although our subjects were regularly checked and guided by a dietitian, it is possible that not all recommendations were followed exactly. The aim of the diet records, however, was to create a realistic picture of ingested food and the results show that our recommendations were mostly followed. In our experience the method of diet records is the best.

We can conclude that compared with a standard diabetic diet, diets with low glycemic index produce some albeit small additional weight loss and body fat reduction. The question certainly is, whether the weight loss is proportional to the effort exerted on the education of persons with diabetes or to problems of the availability of some foodstuffs with low GI.

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ABBREVIATIONS

PPG, Postprandial glycaemia; GI, Glycemic Index; HEC, Hyperinsulinemic euglycemic clamp; EGP, Endogenous glucose production; REE, Resting energy expenditure; RQ, Respiratory quotient; TBW, Total body water; ICW, Intracellular water; ECW, Extracellular water; BCM, Body cell mass; Ra, Rate of glucose appearance; F, Tracer infusion rate; Ep, Glucose isotopic enrichment in the plasma; HbA1c, Glycosylated hemoglobin; DCCT, Diabetes Control and Complications Trial; IFCC, International Federation of Clinical Chemistry and Laboratory Medicine; BMI, Body mass index; LDL, Low-density lipoprotein; HDL, High-density lipoprotein.

CONFLICT OF INTEREST STATEMENT

None declared.

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