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ORIGINAL ARTICLES

Influence of Oral Antidiabetic Drugs on Hyperglycemic Response to Foods in Persons with Type 2 Diabetes Mellitus as Assessed by Continuous Glucose Monitoring System: A Pilot Study

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Abstract

Background:

The purpose of this prospective open-label trial was (1) to assess the influence of oral antidiabetic drugs (OAD) on the glycemic index (GI), glucose response curves (GRCs), daily mean plasma glucose (MPG) and (2) to compare the GI of foods in persons with OAD-treated type 2 diabetes mellitus (T2DM) with the respective GI in healthy persons (HP).

Methods:

Tested foods containing 50 g of carbohydrates were eaten for breakfast and dinner after 10 and 4 h of fasting, respectively. Glycemic index, GRC, and MPG were obtained using the CGMS® System Gold™ (CGMS). In T2DM patients [n = 16; age (mean ± standard error) 56.0 ± 2.25 years], foods were tested four times: tests 1, 2, and 3 were performed within one week in which placebo was introduced on day 2, and test 4 was carried out five weeks after reintroduction of OAD. Glycemic indexes, GRC, and MPG from tests 1, 2, 3, and 4 were compared. In a control group of 20 HP (age 24.4 ± 0.71 years), the mean GIs were calculated as the mean from 20 subject-related GIs.

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Abbreviations: (CGMS) CGMS® System Gold™ continuous glucose monitoring system, (DCCT) Diabetes Control and Complications Trial, (GI) glycemic index, (GRC) glucose response curve, (HbA1c) hemoglobin A1c, (HP) healthy persons, (IAUC) incremental area under the curve, (IFCC) International Federation of Clinical Chemistry, (MPG) mean plasma glucose, (OAD) oral antidiabetic drugs, (T2DM) type 2 diabetes mellitus, (WHO) World Health Organization

Keywords: continuous glucose monitoring system, glycemic index of foods, glycemic response curve, incremental area under the curve, oral antidiabetic drugs, type 2 diabetes mellitus

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Abstract cont.

Results:

In T2DM patients, subject-related assessment of GIs, GRC, and MPG distinguished persons with and without OAD effect. Nevertheless, the group-related GIs and the MPG on days 2, 8, and 39 showed no significant difference. There was no significant difference between the GIs in OAD-treated T2DM patients (test 4) versus HP (except in apple baby food). Glucose response curves were significantly larger in T2DM patients (test 4) versus HP.

Conclusions:

Determination of GRC and subject-related GI using the CGMS appears to be a potential means for the evaluation of efficacy of OAD treatment. Further studies are underway.

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Introduction

Since the pioneering papers of Otto and colleagues[1] and Jenkins and associates,[2] who developed the concept of glycemic index (GI), many questions have been raised about its importance in the healthy as well as in the diabetes population. Diets rich in high-GI foods have been linked to a higher incidence of diabetes mellitus, coronary heart disease, cancer, and other disorders.[3] So far, the GI of many foods has been determined,[4] and the question whether GI should be a part of nutritional labels and dietary recommendations is being discussed.[5,6]

According to the World Health Organization (WHO), GI is defined as the incremental area under the blood glucose response curve (GRC) of a 50 g carbohydrate portion of a test food expressed as a percentage of the response to the same amount of carbohydrates from a standard food taken by the same subject.[7]

The beneficial effects of low-GI foods have been shown particularly in diets for persons with diabetes,[8–13] although the GI is routinely determined in healthy persons (HP). Besides the role of GI in a healthy diet in persons with diabetes, we asked whether GI and other parameters of hyperglycemic response to foods may be of importance in evaluating the effectiveness of oral antidiabetic drugs (OAD) therapy.

The purpose of this pilot prospective open-label trial was (1) to assess the influence of OAD on GI, mean plasma glucose (MPG), and GRCs, namely, the incremental area under the curve (IAUC) and (2) to compare the GIs and GRCs of four foods in type 2 diabetes mellitus (T2DM) patients treated with β-cell stimulators and/or metformin with the respective values in HP.

Methods

Subjects

Thirty-five T2DM patients treated with OAD (β-cell stimulators and/or metformin) and 30 HP were invited to participate in this study. Healthy volunteers were recruited among students of the Faculty of Medicine, Palacky University, Olomouc, and persons with diabetes were recruited among patients from two out-patient clinics. The T2DM patients fulfilled these inclusion criteria: T2DM treated with OAD, no ongoing inflammatory disease, overall good condition, and willingness to use the CGMS® System Gold™ (CGMS) continuous glucose monitoring system (Medtronic MiniMed, Northridge, CA). Healthy subjects fulfilled these inclusion criteria: good overall health (assessed by a physical and laboratory investigation), no medication, and willingness to use the CGMS. Twenty-one T2DM patients and 25 HP provided written informed consent, with participation in this study performed in accordance with the Helsinki Declaration of 1973 as revised in 2000 and approved by the local ethics committee. There were a total of 10 dropouts in both of the groups. In the T2DM patient group, the dropouts were due to incomplete data (n = 3), upper respiratory infection (n = 1), and personal request to quit the study (n = 1). In the healthy group, all dropouts were due to viral gastroenteritis (n = 5). Twenty HP and 16 T2DM patients completed the study (**Table 1**).

Laboratory Procedures

Basic anthropometric and laboratory parameters were measured at the beginning of the study. In T2DM patients, hemoglobin A1c (HbA1c) values [International Federation of Clinical Chemistry (IFCC) scale] were determined on day 1 and on day 38. The conversion of HbA1c values from the IFCC scale to the traditional National Glycohemoglobin Standardization Program/Diabetes Control and Complications Trial (DCCT) scale may be calculated using the formula: IFCC [%] = (DCCT – 2.15)/0.915.[14,15]

Table 1.
Characteristics of Type 2 Diabetes Patients and Healthy Persons at Baseline (Mean ± Standard Error)

Group	T2DM Patients (n = 16)	HP (n = 20)	Reference range
Age [years]	56.70 ± 2.25[a]	24.40 ± 0.71	n/a
Duration of diabetes [years]	6.19 ± 0.91	0	n/a
Body mass index [kg/m^2]	31.90 ± 1.18	22.30 ± 0.73	<25
HbA1c/IFCC [%] Day 1	5.31 ± 0.48[a]	2.91 ± 0.05	2.80–4.00
HbA1c/IFCC [%] Day 39	5.28 ± 0.49	n/a	2.80–4.00
Total cholesterol [mmol/liter]	5.00 ± 0.38	4.45 ± 0.19	<5.00
High-density lipoprotein cholesterol [mmol/liter]	1.25 ± 0.09[a]	1.70 ± 0.11	1.00–1.60
Low-density lipoprotein cholesterol [mmol/liter]	2.50 ± 0.26	2.28 ± 0.16	<2.60
Triacylglycerols [mmol/liter]	2.84 ± 0.58[a]	1.02 ± 0.13	<1.70
C-peptide [µg/liter]	3.55 ± 0.4[a]	1.40 ± 0.11	1.10–5.00

[a] Versus HP, Mann-Whitney, $p < 0.001$

Tested Foodstuffs

Four different foodstuffs with a known content of nutrients but unknown GI value were tested: apple baby food, dark chocolate, puffed rice squares, and strawberry yogurt. The choice of tested foodstuffs was influenced by the amount of carbohydrates provided in the nutritional label to ensure easy preparation of portions containing 50 g of available carbohydrates each. Fifty grams of glucose in the form of glucose solution in 250 ml of water was used as standard food (**Table 2**).

Study Design

Persons with Type 2 Diabetes

In T2DM patients, the study duration was approximately 40 days (**Figure 1**) and consisted of two test periods during which continuous glucose monitoring was performed using the CGMS.[16,17] The first period lasted 9 days in which, on day 2, the OAD were replaced by placebo and reintroduced on day 10 in their previously prescribed strength and dosage. Since all subjects were very compliant and were taking their OAD medication regularly; it was on purpose that they should not interrupt this rhythm even knowing it was a placebo they received. It was thus uncomplicated, after the end of the withdrawal period, to switch from the placebo to their original medication. During the 9-day period, all subjects consumed 50 g of glucose or four alternative

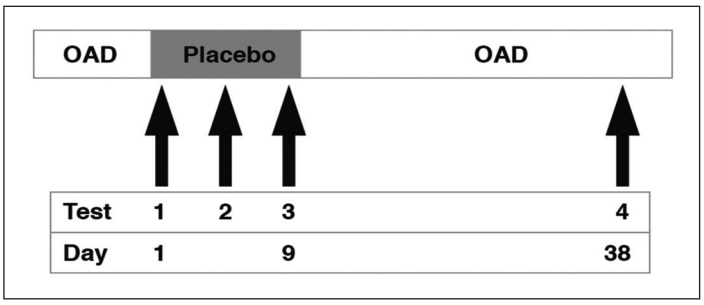

Figure 1. Scheme of the study design in T2DM patients.

Table 2.
Composition of Tested Foods

Food	Portion (50 g of Carbohydrates) [g]	Carbohydrates [g]	Carbohydrates [kJ]	Proteins [g]	Proteins [kJ]	Fat [g]	Fat [kJ]	Energy [kJ]
Glucose 20%	250.0	50	850.0	0.0	0.0	0.0	0.0	850.0
Dark chocolate	91.9	50	850.0	5.9	100.3	24.3	947.7	1898.0
Apple baby food	277.8	50	850.0	0.6	10.2	0.6	23.4	883.6
Puffed rice squares	60.3	50	850.0	4.8	81.6	0.7	27.3	958.9
Strawberry yogurt	312.5	50	850.0	10.6	180.2	6.6	257.4	1287.6

foodstuffs containing 50 g available carbohydrates for breakfast and dinner, beginning in the evening of the first day, and continued testing for the following 8 days, resulting in 15 tests (each foodstuff was tested in three replicates: tests 1, 2, and 3) performed in each of the 16 T2DM patients. The second period started with insertion of the CGMS sensor approximately 5–6 weeks after the reintroduction of OAD and lasted 3 days (days 38–40). During this 3-day period, each foodstuff was tested once more (test 4).

Healthy Persons

In HP, the study consisted of only one test period similar to the first period in T2DM patients (**Table 3**).

In both T2DM patients and HP, the CGMS sensor was inserted on day 1 of the study in the subcutaneous tissue of the buttocks or abdomen, depending on personal preference. Each participant was given exact portions of foodstuffs with a defined meal plan. The first meal test (dinner) was performed in the laboratory under the supervision of an educator who trained participants in using the CGMS and glucometers (Hypoguard Advance, Woodbridge, United Kingdom)[18] and provided them with detailed information about the study design. The CGMS was calibrated several times per day using plasma glucose values measured by personal glucometer, Advance. All participants were asked to keep a logbook with entries about their food and medication intake, physical activity, and other events. The T2DM patients were given an exact number of placebo pills and were instructed to take them. Participants were asked to fast for 10 or 4 h before breakfast and dinner, respectively, to eat up each portion of test food within 5 min, and not to perform any strenuous physical activity 120 min after food consumption. They were given the option of drinking 300 ml of water or unsweetened tea with each test meal, if desired. The subjects were asked to always enter the event "food" into the CGMS monitor just before starting to consume the tested food. During the day (except breakfast, dinner, respective postprandial 120 min periods, and preprandial periods of fast), they were free to eat any meal, provided that the total daily energy intake remained steady (± 10%). All subjects were asked to maintain a constant physical activity, not to smoke, and not to consume alcohol during the test periods. Participants were encouraged to contact a 24 h phone line in case of technical problems or any questions.

Calculation of the Glycemic Index and Statistical Analysis

At the end of the test period, CGMS data were downloaded to a personal computer and exported from the CGMS Solutions Software™ 7310 v. 3.0C (Medtronic MiniMed, Northridge, CA) to the software program DegifXL.[19,20]

The IAUC (**Figure 2**) was determined using calculus (integration, as the sum of the all 24 trapezoid areas) according to the formula IAUC = S_i, i = 1,…, 24, where

$$S_i = \frac{(G_i - G_0) + (G_{i-1} - G_0)}{2} \times \Delta t$$

G_i is the glucose concentration at a particular time, G_0 is the starting glucose concentration; and Δt = 5 min for $G_i < G_0$, $S_i = 0$.

The subject-related GI for a particular test food was calculated in every individual separately according to the formula

$$GI = \frac{\text{average IAUC}_{\text{test food}}}{\text{average IAUC}_{\text{glucose}}} \times 100[\%]$$

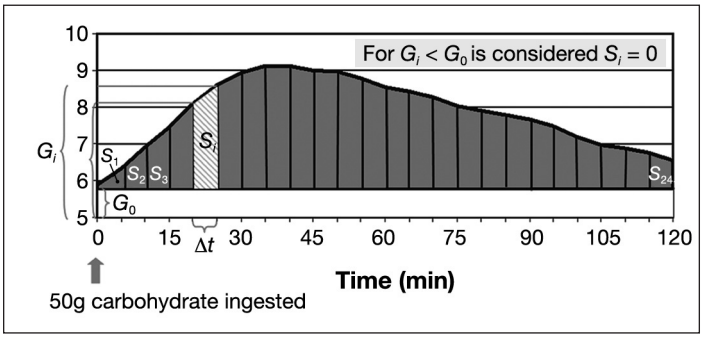

Figure 2. Calculation of the IAUC.

Table 3.
The Eight-Day Standard Meal Plan for Healthy Persons Testing Five Different Foods (Four Test Foods and One Standard Food) for Breakfasts and Dinners

Day	1	2	3	4	5	6	7	8
Breakfast		Glucose	Puffed rice squares	Dark chocolate	Apple baby food	Strawberry yogurt	Glucose	Puffed rice squares
Dinner	Dark chocolate	Apple baby food	Strawberry yogurt	Glucose	Puffed rice squares	Dark chocolate	Apple baby food	Strawberry yogurt

Plasma glucose curves were constructed from 25 glucose values obtained by the CGMS within 120 min after the Plasma glucose curves were constructed from 25 glucose values obtained by the CGMS within 120 min after the meal in 5-min intervals. Each food was tested three times within 8 days in HP and four times in T2DM patients in two test periods.

Whenever the Shapiro–Wilk test revealed non-normal distribution of values, nonparametric tests (Friedmann test, Wilcoxon signed rank test, and Mann–Whitney test) were applied.

In T2DM patients, individual GIs from tests 1, 2, 3, and 4 were calculated and compared using the Friedmann test followed by the Wilcoxon signed rank test; Bonferroni correction was performed to obtain the final significance p. The GI of test 4 was compared to HP using the Mann–Whitney test.

In HP (n = 20) first, the mean from tests 1, 2, and 3 was calculated for each individual, and then the group-averaged GI was calculated as the mean of the sample. Out of a total of 60 tests, 8 had to be excluded from the statistical evaluation due to nonadherence to the study protocol (as registered in the log books).

In T2DM patients, the values of preprandial glycemia before test meals in tests 1, 2, 3, and 4 were compared using analysis of variance (ANOVA). The daily MPG values as calculated by CGMS Solutions Software (mean sensor glucose value) of days 2, 8, and 39 were compared using ANOVA. Wilcoxon signed ranks test was applied to compare the HbA1c values of days 1 and 38. The GRC was assessed by the IAUC. The IAUC (mmol/liter·h) was calculated for each foodstuff in tests 1, 2, 3, and 4, and the comparison between individual tests was performed using Wilcoxon signed ranks test. Subject-related GIs of tests 1, 2, 3, and 4 were evaluated in each T2DM patient. No tests were excluded due to nonadherence to the study protocol. Microsoft Excel, software DegifXL, and SPSS v. 15.0 were used to analyze data.

Results

The group-related GI values in T2DM patients (tests 1, 2, 3, and 4) and in HP (mean of three tests ± standard error) are shown in **Table 4**.

Table 4.
Glycemic Index of Foods in Type 2 Diabetes Patients and in Healthy Persons

Food	Value	T2DM patient Test 1	T2DM patient Test 2	T2DM patient Test 3	T2DM patient Test 4	Significance[a]	Healthy persons	Significance[b]
No. of days without OAD		0–2	2–5	5–8	38-50 days after OAD reintroduction		n/a	
Glucose	Median Mean Standard error *n*	100 100 — 16	100 100 — 16	100 100 — 16	100 100 — 15		100	
Apple baby food	Median Mean Standard error *n*	48.0 69.6 15.9 16	40.5 46.5 6.6 16	47.9 95.8 45.6 16	21.4 28.0 6.4 15	**0.012**[c]	46.6 53.8 8.4 20	**0.002**
Puffed rice squares	Median Mean Standard error *n*	77.4 90.6 9.0 16	88.0 86.6 9.2 16	90.7 200.6 113.3 16	63.1 75.5 11.7 15	0.154	77.3 76.9 6.3 19	0.615
Strawberry yogurt	Median Mean Standard error *n*	41.5 47.1 5.5 16	58.5 63.4 8.8 16	47.4 77.5 25.8 16	45.6 51.3 7.8 15	0.428	32.3 37.7 4.8 20	0.089
Dark chocolate	Median Mean Standard error *n*	41.4 48.0 7.0 16	48.5 58.4 7.2 16	45.3 57.8 16.4 16	43.8 56.1 14.5 15	0.098	38.6 44.0 4.9 20	0.790

[a] Friedman test for comparing GI in test 1 versus test 2 versus test 3 versus test 4.
[b] Mann–Whitney test for comparing GI in HP versus test 4 with T2DM patients
[c] Test 3 versus test 4 (Wilcoxon signed rank test)

Influence of Oral Antidiabetes Drugs on Hyperglycemic Response to Foods

The comparison between the GI values of tests 1, 2, 3, and 4 for each foodstuff in T2DM patients using Wilcoxon signed ranks test showed no significant differences. However, in some persons, the subject-related GI value increased during the placebo period and returned toward baseline after reintroduction of OAD.

There were 60 GI pairs (test 4 versus test 3) obtained from 15 T2DM patients after consumption of four different foods. A reduction of GI in test 4 was observed in 36/60 pairs: in four persons in all four foods (16/16), in three persons in three foods (9/12, meaning 9 reductions in a total of 12 pairs obtained from these three persons), in four persons in two foods (8/16), and in three persons in one food (3/12). The number of persons with GI reductions for individual tested foods (15 pairs each) was as follows: there were 12 reductions out of 15 GI pairs in apple baby food, 10/15 in puffed rice squares, 8/15 in strawberry yogurt, and 6/15 in dark chocolate.

The comparison of IAUC of tests 1, 2, 3, and 4 for each foodstuff using Wilcoxon signed ranks test showed significant difference in apple baby food only (**Figure 3**), where the IAUC of test 3 was larger than the IAUC of test 4 (4.38 versus 2.20 mmol/liter·h, respectively, $p = .012$).

The ANOVA showed no significant differences either in preprandial plasma glucose values of tests 1, 2, 3, and 4 or in the daily MPG values of days 2, 8, and 39 (11.04 ± 0.77 versus 11.82 ± 0.83 versus 10.74 ± 1.02 mmol/liter, respectively, mean ± standard error). Wilcoxon signed ranks test revealed no significant difference in HbA1c values between the beginning (day 1) and the end (day 38) of the study (5.31 ± 0.48% versus 5.28 ± 0.49%, respectively, mean ± standard error).

Comparison of Glycemic Index and Glucose Response Curves in Persons with Type 2 Diabetes and Healthy Persons

There were no significant differences in GIs between HP and T2DM patients except in apple baby food (**Figure 4**), which had a significantly lower GI in T2DM patients (test 4) than in HP (28.0 ± 6.4 versus 53.8 ± 8.4, respectively, $p = .002$).

The comparison of GRCs between OAD-treated T2DM patients (test 4) and HP showed significant differences in all foods except in apple baby food (**Figure 3**, **Figure 5**, and **Table 5**).

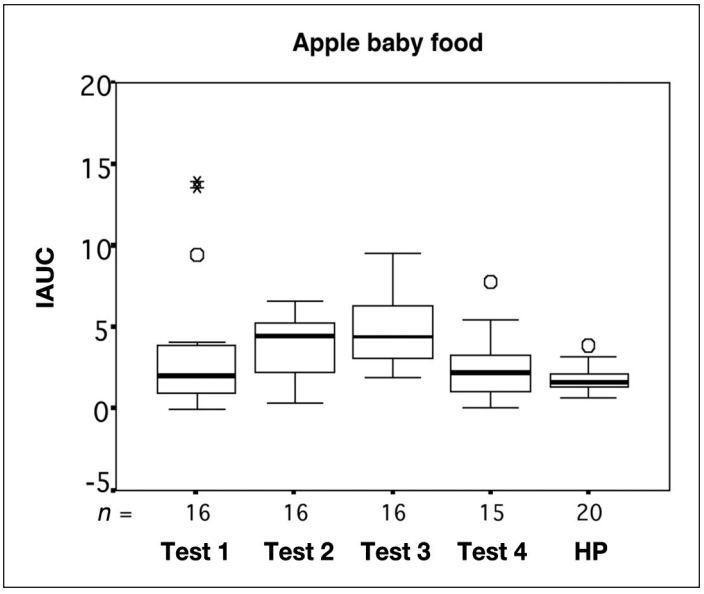

Figure 3. Glucose response curves expressed as IAUC (mmol/liter·h) after ingestion of a portion of apple baby food containing 50 g carbohydrates in T2DM patients (test 1, performed within 2 days after the withdrawal of OAD; test 2, performed 2 to 5 days after the withdrawal of OAD; test 3, performed 5 to 8 days after the withdrawal of OAD; test 4 performed 38 to 50 days after the reintroduction of OAD) and HP. $p = .012$ for test 3 versus test 4.

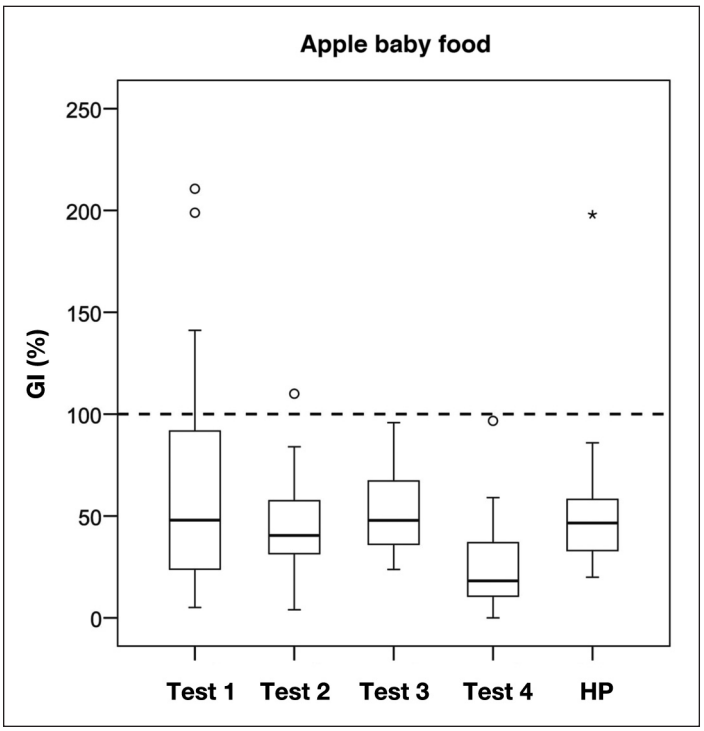

Figure 4. Apple baby food GI values for T2DM patients treated with OAD (test 1, performed within 2 days after the withdrawal of OAD, $n = 16$; test 2, performed 2 to 5 days after the withdrawal of OAD, $n = 16$; test 3, performed 5 to 8 days after the withdrawal of OAD, $n = 16$; test 4, performed 38 to 50 days after the reintroduction of OAD, $n = 15$) and HP ($n = 20$). Test 4 versus HP, $p = .002$

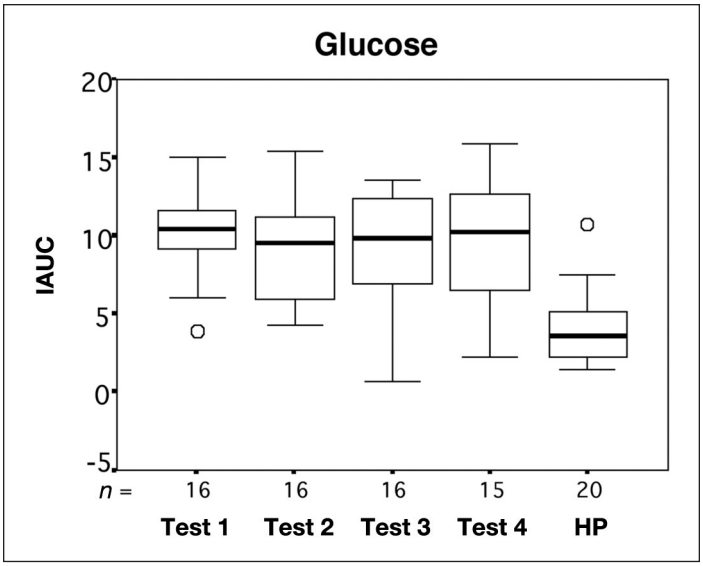

Figure 5. Glucose response curves expressed as IAUC (mmol/liter·h) after ingestion 50 g glucose in T2DM patients (test 1, performed within 2 days after the withdrawal of OAD; test 2, performed 2 to 5 days after the withdrawal of OAD; test 3, performed 5 to 8 days after the withdrawal of OAD; test 4, performed 38 to 50 days after the reintroduction of OAD) and HP. $p = .012$ for test 3 versus test 4.

Discussion

Many studies report the effects of high/low-GI diets on the control of T2DM,[8,9,11,12,21–23] but the number of studies reporting GI determination in T2DM patients is rather sparse.[24] However, it was shown that a long-lasting low-GI diet intervention leads to a reduction of anti-hyperglycemic medication and to HbA1c reduction in T2DM patients.[25] To our knowledge, data on the influence of OAD on the GI of foods have not been reported.

Specific methodologies[7,19,26,27] applied in different centers (e.g., capillary versus venous blood versus interstitial fluid sampling) make comparison of GIs more difficult. Interindividual and intraindividual variability of GIs also contribute to differences in GI values.[28] Not only the quality of available carbohydrates in the food, but also other factors such as the amount and type of protein, fat, starch, particle size, food storage, and processing may influence the GI value.[29,30]

The energetic value and content of nutrients varied in the tested foodstuffs, as it was our intention to test foods

Table 5.
Glucose Response Curves Expressed as Incremental Area Under the Curve (mmol/liter·h) in Type 2 Diabetes Patients and Healthy Persons

Food	Value	T2DM patient Test 1	T2DM patient Test 2	T2DM patient Test 3	T2DM patient Test 4	Significance[a]	Healthy persons	Significance[b]
No. of days without OAD		0–2	2–5	5–8	38-50 days after OAD reintroduction		n/a	
Glucose	Median Mean Standard error *n*	10.4 10.1 0.67 16	9.5 9.2 0.86 16	9.8 9.3 0.91 16	10.2 9.5 1.01 15	0.878	3.6 4.0 0.52 20	**0.0001**
Apple baby food	Median Mean Standard error *n*	3.9 7.2 2.02 16	4.4 3.9 0.48 16	4.4 4.9 0.59 16	2.2 2.5 0.54 15	**0.001**[c]	1.6 1.8 0.19 20	0.386
Puffed rice squares	Median Mean Standard error *n*	7.8 8.7 0.81 16	7.5 7.9 1.13 16	9.0 8.5 1.20 16	6.3 6.4 1.15 16	0.154	2.8 3.2 0.36 20	**0.042**
Strawberry yogurt	Median Mean Standard error *n*	4.1 4.7 0.66 16	5.5 5.6 0.73 16	4.2 4.9 0.85 16	4.6 4.5 0.77 16	0.428	1.5 1.6 0.22 20	**0.002**
Dark chocolate	Median Mean Standard error *n*	4.2 4.6 0.69 16	5.5 5.3 0.70 16	3.7 3.9 0.49 16	3.3 4.7 3.69 16	0.098	1.9 2.0 0.23 20	**0.006**

[a] Friedmann test for comparing IAUC in test 1 versus test 2 versus test 3 versus test 4
[b] Mann-Whitney test for comparing IAUC in HP versus test 4 in T2DM patient
[c] Test 3 versus test 4 (Wilcoxon signed rank test)

with different expected GI values. From this point of view, apple baby food and puffed rice squares are similar in their characteristics; both have a low fat and protein content (**Table 2**), yet their GIs fall in the low- and high-GI group of foods, respectively.[31,32] A reduction of GI after the reintroduction of OAD was more frequent in low-fat and low-protein foods (apple baby food, puffed rice squares) than in foods with higher content of fat and protein (strawberry yogurt, dark chocolate).

In this study, the CGMS was used to determine the GI. Even though this approach differs from the traditional method recommended by the WHO,[7] previous studies have shown high correlation in GI outcomes between both methods,[32,33] and the accuracy of the CGMS was proven.[34–37] The fact that test meals were eaten both for breakfast and for dinner led to a higher number of tests in one test period.[19] In addition, at-home food testing provided a more relaxed atmosphere for all subjects compared to the traditional laboratory setting. Using the software program DEGIF XL for GI determination made GI calculation easy and fast.[19,38] The CGMS sensors were well tolerated in all subjects, even when used continuously for more than three days.[34,39]

The strength of this pilot study is that it demonstrates the subject-related glycemic effects of OAD therapy. On the other hand, our results are undoubtedly weakened by the fact that the group of T2DM patients was not homogenous and different OAD were used.

Our results have shown no significant difference in group-related GIs between healthy subjects and T2DM patients except in apple baby food, which had a significantly lower GI in OAD-treated T2DM patients (test 4) than in HP. Apart from this observation, the IAUC after the consumption of apple baby food was significantly larger in test 3, i.e., after the 8-day OAD withdrawal, compared to the IAUC of test 4, which was assessed 39 days after the OAD reintroduction. This is the only significant difference revealing the potential group-related effect of OAD treatment on the GRC. On the other hand, it is clearly shown that the IAUC in test 4 is larger than the IAUC in HP in all foods except in apple baby food, where there is no significant difference.

The time elapsed from the last dose of OAD until test 1 was not identical in all foods due to technical reasons. Test 1 with chocolate was performed 12 h after the last OAD dose, and the remaining tests 1 with glucose, apple baby food, puffed rice squares, and strawberry yogurt were performed within 48 h of placebo introduction. However, the comparison between healthy subjects and T2DM patients was done with test 4, which was performed under regular OAD treatment.

Our findings have shown no significant changes in preprandial plasma glucose values and in daily MPG concentration before and after the OAD withdrawal. This statistical conclusion was surprising and leaves the question of whether this is due to OAD failure in some of the study participants. Nevertheless, the evaluation of individual subjects revealed potential influence of OAD on GIs in some persons and some foodstuffs and no or even adverse influence in others. Considering the already known large interindividual variability of GI due to various factors,[22] and recent findings on extended prandial glycemic profiles of foods,[40,41] this observation appears to be worthy of further investigation. In addition, the OAD withdrawal lasted only 8 days, which is a relatively short time, and the effects of OAD may have persisted during this interval.[42,43]

The length of the OAD withdrawal was based on the recommendation of the ethics committee in order to avoid threatening hyperglycemia. Because the results of our study do not show any deterioration in metabolic control after an 8-day placebo treatment, we believe that a longer period of OAD withdrawal in combination with continuous glucose monitoring may bring more evidence about the influence of OAD therapy on GI and GRCs without unnecessary hazard for the tested persons. In addition, nonresponders to OAD may be identified and become candidates for a more efficient therapeutic option.

Conclusions

Influence of OAD on hyperglycemic response to foods remains worthy of further investigation.

Even though the statistical methods used in this study failed to support our hypothesis that the administration of OAD influences the hyperglycemic response to foods, the subject-related individual assessment of GI and MPG revealed persons with and without OAD effect. Therefore, determination of subject-related GI and GRCs using the CGMS appears to be a potential means to the evaluation of efficacy of OAD treatment. Further studies are underway.

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