

SAFETY OF NEW ALGORITHMS FOR PREMEAL INSULIN BOLUSES IN HIGH GLYCAEMIC INDEX MEALS IN PERSONS WITH TYPE 1 DIABETES MELLITUS USING INSULIN PUMPS

Natalia Lippaiova^{a*}, Maria Pallayova^b, Galina Kuzmina^a, Karolina Peterson^a,
Lucie Fajkosova^a, Jiri Luza^a

^a Department of Physiology, 2nd Department of Medicine, Faculty of Medicine and Dentistry, Palacký University, 775 15 Olomouc, Czech Republic

^b Department of Physiology, 1st Department of Medicine, Faculty of Medicine, P. J. Šafárik University, Košice, Slovak Republic

e-mail: natalia.lippaiova@seznam.cz

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Aims: Consumption of glucose or foodstuffs with high glycaemic index (GI) in persons with type 1 diabetes mellitus (PWD1) is a hot topic in present diabetology. The aim of our pilot prospective study was to assess the efficiency of empirically suggested simple algorithms for premeal boluses in PWD1 using insulin pumps and continuous glucose monitoring (CGM).

Methods: Six PWD1 (aged 46.2±15.09 y, diabetes duration 14.5±9.65 y, HbA1c/IFCC 6.3±1.59%, BMI 23.6±1.67 kg/m², mean±SD) on insulin pumps Paradigm 522/722 with RT-CGMS sensors (Medtronic MiniMed, Northridge, CA) underwent a 12-week CGM. In one week, subjects consumed 50g of carbohydrates in eleven alternative meals (rice squares, dark chocolate, white bread, honey, glucose, ravioli with meat and Eidam cheese, mashed potatoes with fish fingers, apricot dumplings with butter, spa waffles, spalta squares, and tomato soup with pasta) eaten for breakfasts, lunches, snacks and dinners in order to calculate their GI. The insulin boluses were adjusted according to empirically defined algorithms. Average glucose levels and daily insulin doses over three one-week periods (before testing, testing and after testing) were compared.

Results: During the observational period, the weekly averages of glucose levels (9.1±2.33 mmol/l vs. 9.2±2.30 mmol/l vs. 9.0±2.43 mmol/l, respectively) and daily insulin doses (39.1± 8.14 IU/d vs. 39.7±10.7 IU/d vs. 38.6±9.97 IU/d, respectively) were similar. One-week consumption of high GI foodstuffs had only a negligible effect on average glucose levels.

Conclusion: The suggested algorithms for premeal insulin boluses appear to limit the risk of potential hyperglycaemia resulting from intake of high GI foodstuffs.

INTRODUCTION

Glycemic index (GI) is a measure of the ability of a food to raise glucose levels after the food consumption. GI is defined by the incremental area under the blood glucose curve (AUC or IAUC) after the ingestion of a test food containing 50g of carbohydrates, expressed as the percentage of the AUC of a reference food containing equal amount of carbohydrates (generally glucose or white bread)¹.

The foodstuffs with low GI are preferred in diabetic diets in order to avoid postprandial and postabsorption hyperglycemia and to achieve improvements in overall plasma glucose control²⁻⁵. On the other hand the advances in intensive insulin therapy with fast-acting insulin analogs^{6, 7} and integrated real-time continuous glucose monitoring system and insulin pump (Medtronic Mini-Med Paradigm REAL-Time System; Medtronic MiniMed, Inc., Northridge, CA, USA)⁸, allow more flexible meal plans with the potential to revolutionise diabetic care.

However, to date we still lack data on the consequences of high GI foodstuff consumption on glucose control in PWD1 on insulin pump therapy. Even though the glycemic indexes in persons with diabetes type 1 or type 2 and in healthy persons appear to be identical⁹, it is useful to perform independent GI determination for both groups. There is the question as pure glucose taken in order to calculate the GI of foods is acceptable in PWD1. Therefore, the aim of our pilot study was to evaluate changes in average glucose levels and assess the effect of a one-week consumption of meals with higher GI on glucose control in PWD1 treated by an insulin pump and real-time glucose sensor.

MATERIALS AND METHODS

The study was conducted between January 2007 and June 2007 at the Faculty of Medicine and Dentistry, Palacký University, Olomouc, Czech Republic (as a part of project Degif - IGA NR 7825-3).

Subjects

Six PWD1 on insulin pump therapy (3 males, 3 females, aged 46.2 ± 15.09 years, diabetes duration 14.5 ± 9.65 years, HbA1c 6.3 ± 1.59 %, BMI 23.6 ± 1.67 kg/m²) provided written informed consent with participation in this study, which was approved by the Local Ethics Committee and performed in accordance with the guidelines of the Helsinki Declaration on human experimentation. Subjects were involved in a 12-week continuous glucose monitoring using insulin pump Paradigm RT 522/722 and RT-CGMS sensors with transmitters, Medtronic MiniMed, Northridge, CA, USA. This insulin pump enables to read the actual glucose concentration on its display any time. (Figs. 1, 2)



Fig. 1. Paradigm RT 522/722 and RT-CGMS sensor with transmitter, Medtronic MiniMed, Northridge, CA, USA.



Fig. 2. Paradigm RT 522/722.

Study design

During the assigned week, subjects consumed eleven alternative meals, each serving containing 50g of carbohydrates (rice squares, 70% dark chocolate, rolls, honey, glucose, ravioli with meat and Eidam cheese, mashed potatoes with fish fingers, apricot dumplings with butter, spa waffles, wheat squares, and tomato soup with pasta) eaten for breakfasts, lunches, snacks and dinners. Foodstuffs for breakfasts and dinners were consumed at 7 a.m. and 8 p.m., respectively, foodstuffs for lunches at 12 a.m. and

foodstuffs for snacks at 4 p.m. Each foodstuff was consumed in three replicates, except tomato soup with pasta, which was consumed twice only.

The defined meal plan including daily intake of nutrients and energy was the same as in a similar study with healthy persons^{10, 11}. The foodstuffs were selected by the following criteria: (1) carbohydrate content in each portion should be $50g \pm 5$ %; (2) daily energy intake ranging from 6000kJ to 9000 kJ; (3) carbohydrates, lipids and proteins should be in the ratio 5:1, 5:1,5; and (4) simple preparation of servings and reasonable costs making the meal plan flexible.

In every subject, average glucose levels were evaluated and compared over the period of three weeks, comprising the week before, during, and after the GIs testing.

One hour before and immediately before each meal test, subjects were encouraged to read the plasma glucose concentration on the display of insulin pump and to adjust the insulin boluses according to the empirically defined algorithms (Table 1, Table 2). The subjects were also instructed to enter the boluses in a log-book and keep recordings about any hypoglycaemia, food intake, meal times, exercise, and level of stress. Glucometer Advance (Hypoguard, Woodbridge, UK) was applied twice a day to calibrate the sensor.

Table 1. Algorithms for adjustment of insulin boluses 1 hr before meal test.

Plasma glucose levels 1hr before a meal-test [mmol/l]	Correction bolus [IU]
10.0 – 11.9	1
12.0 – 13.9	2
≥ 14.0	3

Table 2. Algorithms for adjustment of insulin boluses immediately before meal test.

Plasma glucose levels immediately before a meal-test [mmol/l]	Pre-meal insulin bolus [IU]	Test
< 10.0	5	perform
10.0 – 11.9	6	perform
12.0 – 13.9	7	perform
≥ 14.0	3	Wait 1hr

RESULTS

Table 3 gives the results of CGM over the study period. Average glucose levels during the week before, during, and after GIs testing were similar. Average total daily

Table 3. Characteristics of 6 PWD 1 and influence of GI testing on insulin doses and average glucose levels.

No.	Person	Age	Dia- betes dura- tion [years]	BMI [kg/m ²]	HbA1c [%]	Average total daily dose of insulin [IU/day]			Average glucose levels during the week [mmol/l]		
						before GIs testing	during GIs testing	after GIs testing	before GIs testing	during GIs testing	after GIs testing
1	♂ J.M.	40	26	26.28	9.4	54.5	57.3	55.4	12.8	11.8	12.5
2	♂ L.L.	51	9	24.03	5.8	39.2	36.6	41.5	10.0	9.2	8.9
3	♀ S.J.	60	2	23.62	6.3	31.7	27.7	27.0	10.1	12.0	11.3
4	♀ Z.M.	65	13	23.91	5.5	33.1	33.2	32.0	7.2	7.4	6.7
5	♂ S.J.	35	26	22.34	5.0	37.4	36.3	34.2	6.6	6.4	6.8
6	♀ M.P.	26	11	21.37	5.6	38.5	47.1	41.5	7.8	8.3	7.6
Avg		46.2	14.5	23.59	6.3	39.1	39.7	38.6	9.1	9.2	9.0
SD		15.09	9.65	1.67	1.59	8.14	10.70	9.97	2.33	2.30	2.43

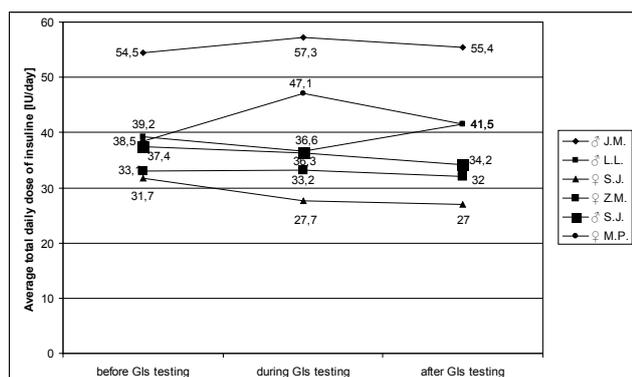


Fig. 3. Average total daily dose of insulin during the week before, during, and after GIs testing.

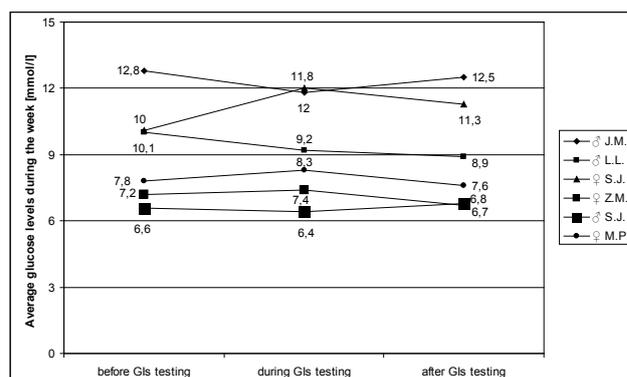


Fig. 4. Average glucose levels during the week before, during, and after GIs testing.

dose of insulin during the week before, during, and after GIs testing were similar as well (Table 3, Figs. 3, 4).

There were no disturbances in general condition and meal plan; no serious hypoglycaemia was registered.

DISCUSSION

This pilot study deals with six case reports focused on the potential hazards of consumption of pure glucose in order to investigate the glycaemic indexes of foods in PWD1.

Awareness of GIs of various foodstuffs is an important part of diabetes management, particularly in persons with type 1 diabetes mellitus. It has been suggested that mean GI values for foods are very similar in persons with type 1 and type 2 of diabetes mellitus⁹⁻¹⁸.

Accurate measurement of GI requires a standardized protocol; glucose concentrations are measured using whole blood or serum/plasma samples obtained from a

vein, artery, or capillary taken at baseline and at 15- and 30-minute intervals for two hours after the food consumption. Most recent studies have utilized capillary blood to determine glucose values and calculate the AUC and, subsequently, the GI. Recently, a study conducted by Chlup^{19, 20} found that there was no significant difference between GI determined using the continuous glucose monitoring (CGMS; Medtronic MiniMed, Northridge, CA) as compared to conventional methods. The long-lasting use of transcutaneous sensors had no serious adverse events²¹⁻²⁴.

In our six case reports, the CGMS results show similar average glucose levels during the period of GIs testing (even after glucose and honey consumption) compared to week before and after GI testing. However, the intensive instruction of PWD1 carried out by professional persons should be emphasized²⁵.

Based on these preliminary findings we might assume that consumption of pure glucose by PWD1 involves only little risk for diabetes control. On the other hand, not only

the average glycemia, but also glucose variability should be taken into consideration. Several studies have shown glucose variability is a risk factor for complications independent of HbA1c in PWD^{1,26,27} as well as in type 2 diabetes^{28,29}. Study by Monnier et al. demonstrated that glucose fluctuations during postprandial periods and, more generally, during glucose swings exhibited a more specific triggering effect on oxidative stress than chronic sustained hyperglycemia³⁰.

Our results suggest that insulin boluses adjustment according to actual blood glucose values is necessary in order to maintain normal or nearly normal glucose control. The findings also show that real-time continuous glucose monitoring helps PWD1 on insulin pump therapy to make more informed treatment decisions and supports their confidence in diabetes management.

Hence, one-week consumption of foodstuffs with high GI does not seem to increase the risk of reduced diabetes control in informed PWD 1 using insulin pumps and sensors. Further studies are in progress.

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