Peak-time determination of post-meal glucose excursions in insulin-treated diabetic patients

S. Daenen, A. Sola-Gazagnes, J. M’Bemba, C. Dorange-Breillard, F. Defer, F. Elgrably, É. Larger*, G. Slama

Université Paris 5 René-Descartes, service de diabétologie, Hôtel-Dieu, AP–HP, 1, place du Parvis-de-Notre-Dame, 75004 Paris, France

Received 26 September 2007; received in revised form 7 December 2009; accepted 7 December 2009
Available online 11 March 2010

Abstract

Objective. – This study aimed to determine the optimal time to measure peak blood glucose values to find the best approach for self-monitoring blood glucose after a meal.

Design and methods. – For this retrospective analysis, 69 ambulatory continuous glucose-monitoring system (CGMS) profiles were obtained from 75 consecutive insulin-treated patients with diabetes. The parameters measured were the peak post-meal blood glucose values, peak time, and rates of increase and decrease to and from the zenith of the resulting curves.

Results. – The mean peak time after breakfast was 72 ± 23 min, which was reached in less than 90 min in 80% of the patients. The apparent glucose rate of increase from pre-meal to the maximum postprandial value was 1.23 ± 0.76 mg/dL/min, while the glucose rate of decrease was 0.82 ± 0.70 mg/dL/min. Peak time correlated with the amplitude of postprandial excursions, but not with the peak glucose value. Also, peak times were similar after breakfast, lunch and dinner, and in type 1 and type 2 diabetic patients.

Conclusion. – To best assess peak postprandial glucose levels, the optimal time for blood glucose monitoring is about 1 h and 15 min after the start of the meal, albeit with wide interpatient variability. Nevertheless, 80% of post-meal blood glucose peaks were observed at less than 90 min after the start of the meal.

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Keywords: Postprandial blood glucose value; Optimal postprandial blood glucose monitoring; CGMS; Type 1 and type 2 insulin-treated diabetic patients; Self-monitoring of blood glucose

Résumé

Délai de survenue du pic glycémique postprandial chez des patients diabétiques traités par insuline.

But. – Déterminer le moment du pic glycémique postprandial pour déterminer le meilleur moment pour l’autosurveillance postprandiale.

Méthodes. – Nous avons analysé de façon rétrospective 69 holters glycémiques (CGMS) consécutifs obtenus en ambulatoire chez 75 patients diabétiques insulinotraités. Nous avons analysé la valeur du pic glycémique postprandial, son moment de survenue après le début du repas, la courbe de croissance puis de décroissance de la glycémie après le repas.

Résultats. – Le pic glycémique postprandial est survenu en moyenne à la 72 ± 23e minutes après le petit déjeuner. Ce pic est survenu pour 80% des patients avant la 90e minute. La vitesse de croissance entre le début du repas et le pic était de 1,23 ± 0,76 mg/dL par minute. La vitesse de décroissance était de 0,82 ± 0,70 mg/dL par minute. Le moment de survenue du pic était en corrélation avec l’amplitude du pic postprandial, mais non avec la valeur du pic. Le moment de survenue du pic était similaire pour le petit déjeuner, le déjeuner et le dîner chez les patients diabétiques de type 1 ou 2 insulinotraités.

Conclusion. – Le moment de survenue du pic glycémique postprandial est en moyenne de 1 h 15 minutes après le début du repas avec cependant une large variabilité inter-sujets. Cependant, 80% des patients ont leur pic glycémique postprandial avant la 90e minute après le repas.

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Mots clés : Glycémie postprandiale ; Moment optimal de surveillance de la glycémie postprandiale ; CGMS ; Diabète de type 1 ; Diabète de type 2 ; Insulinothérapie ; Autosurveillance glycémique ; Holter glycémique

* Corresponding author.

E-mail address: etienne.larger@htd.aphp.fr (É. Larger).

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1. Introduction

The level of glycated haemoglobin (HbA1C) is the best overall parameter for evaluating glycaemic control in patients with diabetes, as it is an indicator of the average blood glucose over a period of 2–3 months. Improving postprandial hyperglycaemia is an important therapeutic goal, and treatments that specifically lower postprandial blood glucose also decrease HbA1C levels by 25–65% in patients with type 2 diabetes [1,2]. Postprandial glucose is an important determinant of HbA1C concentration in patients with relatively good glucose control, while the contribution of fasting hyperglycaemia increases as glycaemic control worsens [3–6]. Postprandial hyperglycaemia is an important contributor to late (micro- and macrovascular) complications of diabetes [7–10], whereas cardiovascular complications appear to be more dependent on blood glucose levels after a meal than on fasting blood glucose, and the effect appears to be stronger in women than in men [11]. However, in light of the negative results in the HEART2D trial [12], the question of the specific role of postprandial hyperglycaemia remains a subject of debate, except in diabetic patients who are pregnant, in whom there is considerable evidence to suggest a crucial role for postprandial hyperglycaemia [13–20]. Tools specifically designed to improve postprandial hyperglycaemia—such as dietary interventions that attempt to optimally distribute carbohydrate intakes throughout the day and include fibre-rich and/or low glycaemic-index foods, and alpha-glucosidase inhibitors, glinides and rapid-acting analogues of insulin—can work in synergy with drugs that act on fasting and interprandial, as well as postprandial, blood glucose levels. Also, the growing use of basal–bolus insulin regimens and insulin-pump administration make it easier to teach patients how to read and correct fast- ing, interprandial (basal) and postprandial (bolus) blood glucose levels.

Yet, surprisingly, there are scant data available to help patients determine the optimal time for assessing their postprandial blood glucose levels, a topic that is not even covered in textbooks [21]. In its consensus statement, the American Diabetes Association (ADA) expert committee stated that “measurement of plasma glucose 2 h after the start of a meal is practical, generally approximates the peak value in patients with diabetes, and provides a reasonable assessment of postprandial hyperglycaemia”. However, in situations such as gestational diabetes, the 1-h, rather than 2-h, postprandial blood glucose value is a better predictor of the obstetric outcome [22]. The International Diabetes Federation (IDF) recommends tighter control of blood glucose levels after meals in diabetics [23], and recommends a post-meal blood glucose of less than 140 mg/dL at 2 h following a meal.

The continuous glucose-monitoring system (CGMS) is a useful tool for obtaining precise postprandial peak values, whereas sporadic, hourly or even every half-hourly capillary or venous sampling permits only an interpolation of glucose values. For this reason, the present study analysed the CGMS data obtained from 75 insulin-treated diabetic patients to determine the times at which postprandial blood glucose concentrations are at their peak, and the rates of postprandial interstitial glucose increment and decrement.

2. Study design and methods

The present study retrospectively assessed CGMS recordings obtained in ambulatory settings from 75 consecutive patients. All patients were being treated with insulin, irrespective of whether they had type 1 (n = 39) or type 2 (n = 30) diabetes. In addition, 79% of the patients were taking at least three insulin injections per day or using continuous subcutaneous insulin infusion (CSII), while 82% were injecting aspart or lispro insulin before meals.

2.1. Continuous glucose-monitoring system procedure

A subcutaneous electrode was inserted in our study patients as an outpatients-procedure, and all recordings were obtained under ambulatory conditions, with the patients having their usual, non-standardised, meals. To make the results comparable, we first studied one meal per patient. The most representative meal for which recordings were available in all of our patients was breakfast. To be eligible, the recording had to clearly indicate the start of the meal, and had to have no missing values or temporary interruptions over the subsequent 3-h period. A total of 69 out of 75 recordings fulfilled these requirements. Also, using the same criteria, only 33 patients had eligible recordings for all three meals (subpopulation A). In addition, the profiles that were recorded after breakfast were checked to ensure that they were comparable to those recorded after the other meals in these patients. In a second subgroup of 36 patients (subpopulation B), the recordings of the same meal on two different days—such as two breakfasts or two lunches—allowed an assessment of intrapatient variability. Table 1 shows the characteristics of all of the study patients as a whole and as subpopulations.

Peak time was defined as the time elapsing from the start of a meal to the highest recorded glucose value. The apparent rate of increase (r1) was the glucose increment divided by the peak time, expressed as mg dL/min, and represented the rate of increase as it would appear to a patient measuring blood glucose values before and after a meal. The actual rate of increase (r2) was the blood glucose increment during the 60-min period preceding the highest glucose value. This measure is more precise than the apparent rate of increase, as the glucose increment is delayed, but is not accessible to the patient in a clinical situation. The rate of decrement (r3) was, likewise, the decrease in blood glucose during the first 60 min following the highest glucose value (Fig. 1). The coefficient of variation (CV) of the peak time was calculated as $CV = 100 \times \frac{\text{variance}}{\text{mean peak time}}$.

2.2. Statistical analysis

Student’s t test for paired data was used to compare numerical values, and the results are expressed as means ± standard error of the mean (SEM).

3. Results

3.1. Post-breakfast curve analysis

Analysis of the post-breakfast glucose values for the total study population (Table 2) showed that the peak glucose value
Table 1
Clinical characteristics of the study population as a whole and as subpopulations.

<table>
<thead>
<tr>
<th>Patient groups</th>
<th>Total population</th>
<th>Subpopulation A</th>
<th>Subpopulation B</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>69</td>
<td>33</td>
<td>36</td>
</tr>
<tr>
<td>Age (years)</td>
<td>49 ± 15</td>
<td>51 ± 17</td>
<td>47 ± 17</td>
</tr>
<tr>
<td>Diabetes duration (years)</td>
<td>16 ± 12</td>
<td>15 ± 10</td>
<td>13 ± 8</td>
</tr>
<tr>
<td>Diabetes types 1 and 2 (n/n)</td>
<td>39/30</td>
<td>18/15</td>
<td>17/19</td>
</tr>
<tr>
<td>HbA1c (%)a</td>
<td>7.8 ± 1.1</td>
<td>7.6 ± 1.3</td>
<td>7.7 ± 1.2</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>25 ± 5</td>
<td>25 ± 5</td>
<td>25 ± 5</td>
</tr>
</tbody>
</table>

All data are expressed as means ± standard error of the mean (SEM) unless otherwise stated; HbA1c: level of glycated haemoglobin.

Subpopulation A: complete records of three meals during the same day were available; Subpopulation B: records of the same meal were available for two consecutive days.

a normal range: 4–6%.

Fig. 1. Mode of calculation of the apparent and actual rates of blood glucose increases to peak time, and the rate of decrease afterwards. r1: apparent rate of increase of blood glucose levels after a meal i.e the slope of the line drawn between the start of the meal and the highest of the curve in mg\(^{-1}\) dL\(^{-1}\) min. r2: actual rate of increase of blood glucose levels after a meal i.e the slope of the curve within the hour before reaching the highest value expressed in mg\(^{-1}\) dL\(^{-1}\) min. r3: actual rate of decrease of blood glucose levels after a meal i.e the slope of the curve within the hour following the highest of the curve expressed in mg\(^{-1}\) dL\(^{-1}\) min.

was, on average, 227 ± 60 mg/dL, and occurred at 72 ± 23 min (range: 20–140 min) after the start of the meal, with r1 of 1.23 ± 0.76 mg dL/min and r3 of 0.82 ± 0.70 mg dL/min. There were no significant differences between type 1 and type 2 diabetic patients in terms of either peak value (P = 0.85) or peak time (P = 0.64), or r1 and r3 values (P = 0.29 and P = 0.12, respectively). Fig. 2 shows the distribution of peak times for the study population as a whole. After breakfast, 80% of patients reached their peak value in less than 90 min after the start of the meal.

Fig. 2. Distribution of peak times for the whole of the study population.

Also, there was no correlation between peak time and post-prandial glucose peak value (P = 0.60). However, there was a significant correlation between the peak time and glucose increment (r² = 0.14; P = 0.015; Fig. 3). The CV of the peak time was 32%, and the intrapatient variability of peak time, measured after the same meal on two consecutive days, was 49%.

3.2. Same-day reproducibility of the curve profile

Peak time, apparent and actual glucose rates of increase and decrease, were analysed in the subpopulation of 33 patients who had curves available for all three main meals–breakfast, lunch and dinner—in one CGMS recording (Table 3). Peak time did not

Table 2
Peak value, peak time, and apparent rates of increase and decrease of interstitial glucose concentrations, recorded after breakfast in 69 insulin-treated patients.

<table>
<thead>
<tr>
<th></th>
<th>Peak value (mg/dL)</th>
<th>Peak time (minutes)</th>
<th>Rates of subcutaneous glucose variation up to and after peak values</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r1 (mg/dL/min)</td>
<td>r2 (mg/dL/min)</td>
<td>r3 (mg/dL/min)</td>
</tr>
<tr>
<td>Total population</td>
<td>227 ± 60</td>
<td>72 ± 23</td>
<td>1.23 ± 0.76</td>
</tr>
<tr>
<td>Type 1 patients</td>
<td>228 ± 64</td>
<td>73 ± 24</td>
<td>1.32 ± 0.83</td>
</tr>
<tr>
<td>(n = 39)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type 2 patients</td>
<td>226 ± 55</td>
<td>71 ± 22</td>
<td>1.10 ± 0.64</td>
</tr>
<tr>
<td>(n = 30)</td>
<td>0.85</td>
<td>0.64</td>
<td>0.29</td>
</tr>
</tbody>
</table>

r1: apparent rate of increase of blood glucose levels after a meal. r2: actual rate of increase of blood glucose levels after a meal. r3: actual rate of decrease of blood glucose levels after a meal.
Postprandial blood glucose is becoming more and more an issue of concern in the treatment of patients with diabetes for a number of reasons. First, postprandial blood glucose excursions contribute significantly to overall hyperglycaemia. It is estimated that postprandial glucose constitutes 25–60% of the HbA1c increase above normal values, with the lower proportions seen in poorly controlled patients—those with HbA1c levels greater than 8–9% and the higher ones in better controlled patients, with HbA1c less than 7.0% [1,5,6]. Second, postprandial metabolic disturbances not only involve blood glucose excursions, but also lipids, coagulation modification and oxidative stress [1]. Third, there are specific means nowadays to improve postprandial blood glucose levels, including dietary modifications, alpha-glucosidase inhibitors, glinides, rapid-acting insulin analogues, glucagon-like peptide-1 (GLP-1) analogues and dipeptidyl peptidase-4 (DPP-4) inhibitors, all of which can add their effects to those of other antidiabetic drugs (such as metformin, sulphonylureas, thiazolidinediones and long-acting insulin analogues). However, these therapeutic means are underused for this specific indication in part because, often, not enough attention is given to the importance of postprandial blood glucose and of postprandial blood glucose self-monitoring, which is also not widely enough prescribed to patients.

Nevertheless, a basic condition for a proper appreciation of the importance of postprandial blood glucose would be to determine the optimal time to measure it after a meal. Convincing studies have shown that a 1-h, rather than 2-h, interval is a better predictor of the outcome of pregnancy in women with diabetes [12–19]. In contrast, there are few indications in the literature for the optimal sampling time in the general population of diabetics. Continuous blood glucose monitoring appears to be the only valid way to precisely determine postprandial peak occurrences, whereas intermittent sampling, at best, permits only a rough approximation. In our present group of 75 consecutive insulin-treated patients, including both type 1 and type 2 diabetics, the peak blood glucose value—specifically, the peak subcutaneous glucose value—was observed at 72 ± 23 min after the beginning of breakfast. There were, however, wide intrapatient variations, with the peak occurring at less than 30 min in 4% compared with greater than 120 min in 3% of patients. However, the peak time distribution followed a roughly normal curve, with 80% of peak times being less than 90 min. Also, the peak times were similar after each meal and did not differ according to the type of diabetes.

The apparent glucose increase rate was steeper than the decrease rate, while the actual mean increase rate, not accessible to patients in the usual clinical situation, was even steeper. Both the increase and decrease rates differed significantly after breakfast compared with lunch and dinner, but the composition of meals may have contributed to these results: in France, breakfast is mostly glucidic and liquid, whereas the other meals are more varied and solid. Also, although the peak value was higher after breakfast than after the other meals, the rates of decrease did not correlate with the peak value, although it was close to being statistically significant (P = 0.055). However, the peak time and postprandial blood glucose increases were positively correlated. It may be argued that subcutaneous blood glucose is only a reflection—and not, strictly speaking, the equivalent—of blood glucose value. Indeed, when venous blood glucose and

### Table 3

<table>
<thead>
<tr>
<th>Peak value (mg/dL)</th>
<th>Peak time (minutes)</th>
<th>Rates of subcutaneous glucose variation up to and after peak values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breakfast</td>
<td>223 ± 65</td>
<td>83 ± 30</td>
</tr>
<tr>
<td></td>
<td></td>
<td>r1 (mg/dL/min) 1.13 ± 0.57</td>
</tr>
<tr>
<td></td>
<td></td>
<td>r2 (mg/dL/min) 1.20 ± 0.68</td>
</tr>
<tr>
<td></td>
<td></td>
<td>r3 (mg/dL/min) 1.15 ± 0.64</td>
</tr>
<tr>
<td>Lunch</td>
<td>185 ± 60</td>
<td>88 ± 35</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.84 ± 0.47</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.90 ± 0.57</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.52 ± 0.58</td>
</tr>
<tr>
<td>Dinner</td>
<td>189 ± 67</td>
<td>82 ± 33</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.76 ± 0.56</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.84 ± 0.56</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.41 ± 0.64</td>
</tr>
<tr>
<td>P value</td>
<td>0.03</td>
<td>0.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.03</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

r1: apparent rate of increase of blood glucose levels after a meal. r2: actual rate of increase of blood glucose levels after a meal. r3: actual rate of decrease of blood glucose levels after a meal.
subcutaneous glucose were directly compared, a ‘push–pull’ phenomenon was observed: interstitial glucose increased before venous blood glucose did, whereas decreases in venous blood glucose were observed before being seen in the interstitial glucose. The lag time, however, was small, with only minutes between the peak time values in these two compartments [24,25].

5. Conclusion

The optimal time to measure peak postprandial blood glucose values is around 1 h and 15 min after the beginning of a meal, and a variation of 15 min in either direction would result in a relatively negligible under- or overestimation of around 15 mg/dL. Thus, a good estimation of peak glucose can be obtained at 1–1.5 h after the start of a meal. This finding is also more consistent with the observations made in women with gestational diabetes than with the current recommendations of the ADA.

Conflict of interest

The authors do not have any conflict of interest to declare.

References