Original article

Ambulatory 24-hour fast using flexible insulin therapy in patients with type 1 diabetes

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Abstract

Aim. – Prolonged fasting may be necessary in life for religious, medical and other reasons. For this reason, our study investigated the feasibility and safety of a 24-h fast conducted at home for patients with type 1 diabetes.

Research design and methods. – Thirty-four patients with type 1 diabetes performed a 24-h complete fast at home. Thirteen patients were treated with multiple insulin injections using either glargine (n = 12) or NPH (n = 1) as basal insulin. The remaining patients were treated with an insulin pump. All patients received their basal insulin only, which was adjusted to 40% of their total daily dose, and were monitored by either a Gold® or Guardian® continuous glucose monitoring (CGMS) device. Capillary glucose (SMBG) was targeted at 3.9–7.8 mmol/L, with a standardized protocol for correction of hyper- and hypoglycaemia. Interstitial glucose (IG) profiles were compared with the SMBG values; the IG profiles of patients using glargine or a pump and either of the two CGMS devices were also compared.

Results. – All of the patients completed the 24-h fast with no major incident. At the end of the fast, 80% of the IG values were on target. The route by which insulin was delivered made no difference, but there were more IG values on target in patients monitored by the Guardian® device. IG was below target in 104 occurrences and above-target in 34. After a mean intake of 10 g of sucrose, below-target IG was corrected within 30 min [range: 15–40]. The mean insulin dose to correct above-target episodes was 1 U.

Conclusion. – Prolonged fasting is possible at home in patients with type 1 diabetes, provided the basal dose is adjusted. The use of CGMS is not necessary, but offers useful information on the patient’s IG profile during the fast.

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Keywords: Type 1 diabetes; Flexible insulin therapy; Continuous glucose monitoring system; Hypoglycaemia; Fast

Résumé

Jeûne de 24 heures chez des patients diabétiques de type 1 au cours d’un programme d’insulinothérapie fonctionnelle.

Objectif. – Le jeûne prolongé peut être nécessaire dans la vie, pour des raisons religieuses, médicales ou autres. Nous avons étudié la faisabilité et la sécurité d’un jeûne de 24 heures au domicile chez des patients diabétiques de type 1.

Méthodes. – Trente-quatre patients diabétiques de type 1 ont fait un jeûne calorique total de 24 heures à leur domicile. Treize étaient traités par injections multiples, avec une basale de glargine (n = 12) ou NPH (n = 1). Les autres avaient une pompe à insuline. Les patients ne recevaient que la basale de leur insuline, ajustée à 40 % de la dose totale quotidienne. Ils ont été surveillés avec un système de mesure en continu de la glycémie (CGMS), soit le Gold®, soit le Guardian®. Les objectifs glycémiques étaient entre 3,9 et 7,8 mmol/L, et pour ce faire les patients appliquaient un protocole standardisé de correction des hypo- et des hyperglycémies. Les mesures de glycémies interstielles (IG) ont été comparées aux automesures capillaires (SMBG). Nous avons aussi comparé les profils IG des patients traités par glargine ou par pompe, et avec l’un ou l’autre des CGMS.

Résultats. – Tous les patients ont terminé l’épreuve, sans incident majeur. À la fin du jeûne, 80 % des IG étaient dans les objectifs. Il n’y avait pas de différence selon les modalités d’administration de l’insuline. En revanche, plus de valeurs étaient dans les objectifs chez les patients surveillés avec le Guardian® qu’avec le Gold®. Cent quatre épisodes d’hypoglycémie ont été enregistrés et 34 d’hyperglycémie. Après une prise moyenne de 10 g de sucrose, les hypoglycémies ont été corrigées en 30 minutes [15–40]. Une dose moyenne de 1 U a corrigé les épisodes d’hyperglycémie.

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Conclusion. — Le jeûne prolongé au domicile est possible chez les patients diabétiques de type 1, après ajustement des doses d’insuline basale. L’utilisation du CGMS avec alarmes n’est pas nécessaire, mais donne des informations utiles sur l’évolution du profil IG pendant le jeûne.

Mots clés : Diabète de type 1 ; Insulinothérapie fonctionnelle ; Mesure en continu du glucose ; Hypoglycémie ; Jeûne

1. Introduction

The goal of flexible insulin therapy using long-acting insulin or an insulin pump is to allow patients a wider choice of food intake, provided the prandial insulin dose is adjusted. This has been the basis of structured in- and outpatients training programmes [1–4]. With stable basal insulin, patients can change the time of meals, or even skip a meal [5] or consecutive meals, although this does not appear to have been studied except in the context of religious fasts, such as Ramadan [6,7] or Yom Kippur [8]. Unlike many diabetes-education programmes, which foster too passive a role for patients, flexible insulin therapy calls for their active participation in all decisions about their treatment. To give patients the skills they need to participate in such decisions, part of our ambulatory programme asks them to undertake a 24-h fast at home. This fast has four goals: (1) to show patients it is possible to fast; (2) to make them understand the respective roles of basal and bolus insulin as well as exercise, food and life events on blood glucose; (3) to teach them the amount of carbohydrates they need to correct hypoglycaemia; and (4) to teach them the amount of insulin they need to reverse hyperglycaemia.

The present report presents the results of a 24-h fast in 34 outpatients with type 1 diabetes who were monitored using a continuous glucose monitoring system (CGMS). The aim of the study was to describe the interstitial and capillary glucose data of a prolonged fast in patients with type 1 diabetes, and to determine whether or not continuous glucose monitoring influences the behaviour of patients in this context. For this reason, patients were monitored by two different CGMS devices: the MiniMed System Gold®, which does not give patients access to interstitial glucose (IG) levels; and the Guardian® REAL-Time System (both by Medtronic, Northridge, CA, USA), which offers patients continuous access to their IG levels.

2. Patients and methods

Of the patients with type 1 diabetes involved in our intensive education programme, more than 300 have voluntarily performed a 24-h fast at home (F. Elgrably, unpublished data). For the present study, 34 agreed to be continuously monitored by either the Gold® or Guardian® CGMS devices. The Guardian® enables patients to know their glucose levels at any time, and includes both low- and high-glucose alarms. The results of the Gold®, in contrast, are not available to the patient, and the device uses no alarms. The objective of the comparison between these two devices was to determine whether or not knowing the glucose data has any influence on the behaviour of patients at times of either high or low glucose while fasting.

2.1. The 24-h fast

This was conducted at home over a weekend. On Friday evening, the patients took their usual meal at dinner, including the usual prandial insulin. After that, no food was allowed until 07:00 h on Sunday morning (24-h fast), and only calorie-free drinks were allowed. Patients were advised to stay at home and not to exercise. Patients taking long-acting insulin were asked to take the basal injection either at bedtime (glargine, \(n = 11\)) or in two injections 12 h apart [neutral protamine Hagedorn (NPH) insulin, \(n = 1\)]. The basal insulin dose was adjusted for the fast. Patients were asked to inject 40% of their usual total daily insulin dose, or up to 0.4 U/kg, as basal insulin [9]. Decreasing the total daily dose to 40% was found to be effective for the entire cohort of patients participating in the fast (F. Elgrably, unpublished data). The injection was done at the usual time. Patients using an insulin pump were requested to switch the basal rate at 06:00 h on Saturday morning to a rate providing 40% of their total daily insulin dose.

The patients were then asked to perform self-monitoring of blood glucose (SMBG), using their regular device, every 2 h from 07:00 h to 00:00 h (midnight) and twice from 00:00 h on Saturday to 07:00 h on Sunday. Any symptom suggestive of hypoglycaemia had to be checked by immediate SMBG. The target glucose level during the fast was 3.9–7.8 mmol/L, and the written standardized protocol was applied to correct any deviations from these target values (see below). All patients were provided with a phone number at which they could reach a member of the medical team around the clock, if necessary. All patients signed an informed-consent agreement to participate in the protocol, which was approved by the local ethics committee.

2.2. Hypoglycaemia

This was defined as a capillary glucose (SMBG) value of less or equal to 3.9 mmol/L, whether accompanied by symptoms or not. Any SMBG-confirmed hypoglycaemia had to be corrected with 10 g of sucrose if glucose was 2.8–3.9 mmol/L, or 15 g of sucrose if glucose was less than 2.8 mmol/L. SMBG was controlled 30 and 60 min later, and the same protocol applied if SMBG was still less or equal to 3.9 mmol/L. Patients using a pump were asked not to adjust the basal rate. When simultaneous SMBG and Guardian® results were discrepant, the patient had to act according to the SMBG result.

In the analysis of continuous monitoring data, asymptomatic hypoglycaemia was defined as an unrecognized episode of more than three consecutive values less or equal to 3.9 mmol/L without a simultaneous SMBG measurement (Gold®) or sugar intake (Guardian®). In such instances, the nadir was considered the start of the hypoglycaemic episode. The time to recovery was...
defined as the time elapsing from the nadir to the first interstitial glucose (IG) level greater than 3.9 mmol/L. The total duration of hypoglycaemia was measured from the first IG less or equal to 3.9 mmol/L to the first IG greater than 3.9 mmol/L. When IG was greater than 3.9 mmol/L but the SMBG was less or equal to 3.9 mmol/L, the time to recovery could not be assessed.

2.3. Hyperglycaemia

When blood glucose was 7.8–12 mmol/L, patients had to inject 1 U of a short-acting insulin analogue, or 2 U if glucose was 12.1–15 mmol/L or 3 U if glucose was greater than 15 mmol/L. SMBG was controlled after 1 and 2 h, and the same correction protocol was applied if SMBG was still off-target, but not before at least 2 h had elapsed. All SMBG values, and hypo- and hyperglycaemic episodes and their corrections, were recorded.

2.4. Continuous glucose monitoring

Patients were randomized to either the Gold® or Guardian® monitoring systems. Use of the device was started in hospital on the day before the fast. The alarms of the Guardian® were set at 3.9 and 7.8 mmol/L. Patients were asked not to enter more than four (Gold®) or three (Guardian®) calibrations per day, unless directed to do so by the device. Patients were provided with written instructions on how to use the CGMS.

2.5. Statistical analysis

Categorical values were compared with the Chi-square test. Numerical values were compared by the non-parametric Mann-Whitney U test, and by Anova (analysis of variance) for repeated measures. The threshold of significance was \( P < 0.05 \). Data were expressed as medians [range].

3. Results

Data from the continuous glucose device were unusable in six patients—one randomized to the Guardian® and five to the Gold® (Fig. S1; see supplementary material associated with this article online). The patients’ characteristics are presented in Table 1. All patients completed the 24-h fast. There were no episodes of severe hypoglycaemia (defined as requiring the assistance of another person) or of ketoacidosis. The data presented here were recorded during the period starting at 07:00 h after the first (Friday) night, as the fast was considered to have effectively started from the first skipped meal.

3.1. Interstitial glucose profiles during the fast

Fig. 1 shows the time course of the mean IG profiles recorded in patients treated with long-acting insulin compared with those using continuous subcutaneous insulin infusion (CSII; Fig. 1A), and in patients monitored with the Gold® versus Guardian® systems (Fig. 1B). Similar profiles were obtained with both treatment modalities and in patients monitored with either of the devices. From 5 h following the start of the study, mean IG levels stayed within target values throughout the fast in both patients treated with long-acting insulin and those treated with CSII. The individual patient’s profiles are shown in Figs. S2 and S3 (see supplementary material associated with this article online), including their mean IG values for each of the three time periods (07:00–00:00 h, 00:00–12:00 h and 12:00–07:00 h), corresponding to the stabilization period, daytime and nighttime, respectively. IG values were significantly higher during the first period than throughout the rest of the fast. There was no difference between patients treated with long-acting insulin and those treated with a pump (Fig. S3B; see supplementary material associated with this article online). Fig. 2 shows the percentage of individual IG values that were on target (3.9–7.8 mmol/L) over the same three time periods (Fig. 2A). By the end of the study, more than 80% of the IG values were on target, with no differences between patients using either type of treatment (Fig. 2B).

Also, as shown in Fig. S3C (see supplementary material associated with this article online) and Fig. 2C, there was no difference in mean individual IG values in patients monitored with either the Gold® or Guardian® devices. However, more IG values were on target in patients using the Guardian® than the Gold® during both the second \( (P = 0.04) \) and third \( (P = 0.001) \) time periods.

3.2. Hypoglycaemia

All patients reported at least one episode of hypoglycaemia, as defined by the protocol (≤ 3.9 mmol/L). Altogether, there were 104 episodes of hypoglycaemia, with a mean of three episodes per patient. The median sugar intake was 10 g per episode and 20 g per patient. In patients monitored by the Guardian®, only 10 out of 50 episodes of low glucose detected by the device were not followed by an SMBG measure. In contrast, in the absence of alarms, 20 out of 54 episodes of low glucose recorded by the Gold® device remained undetected by the patient (Chi-square: 2.9, \( P = 0.09 \)). SMBG and IG values were concordant in 50 episodes (48%). However, 25 episodes, symptomatic or not but confirmed by SMBG, went unrecognized by glucose monitoring, while 29 episodes recorded by monitoring were either discordant with the simultaneous SMBG or not simultaneously measured by SMBG.

For each hypoglycaemic event, IG was recorded at 30 min before (T−30) and at the start (T0) of the episode, and over its total duration and time to recovery (Table S1; see supplementary material associated with this article online). When hypoglycaemic events were compared in patients monitored by the Gold® and Guardian® systems, there were no differences in IG at T−30, or in time to recovery or duration of hypoglycaemia. In contrast, there was a significant difference between IG values at the start and the simultaneous SMBG \( (P < 10^{-6}) \). The number of hypoglycaemic episodes did not differ between patients monitored by either CGMS device. However, the mean duration of time that each patient’s IG was less than 3.9 mmol/L was significantly higher in patients using the Gold® system \( (P < 10^{-6}; Table 2) \). No episodes of hyperglycaemia were recorded within

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Table 1
Clinical characteristics of patients participating in the 24-h fast.

<table>
<thead>
<tr>
<th></th>
<th>All (n = 28)</th>
<th>Gold® (n = 12)</th>
<th>Guardian® (n = 16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>42 [25–70]</td>
<td>37 [25–59]</td>
<td>52 [30–70]</td>
</tr>
<tr>
<td>Gender ratio (M/F)</td>
<td>20/8</td>
<td>7/5</td>
<td>13/3</td>
</tr>
<tr>
<td>Diabetes duration (years)</td>
<td>19 [1–38]</td>
<td>15 [6–30]</td>
<td>20 [1–38]</td>
</tr>
<tr>
<td>Pump/glargine (n/n)</td>
<td>16/11</td>
<td>5/6</td>
<td>11/5</td>
</tr>
<tr>
<td>Insulin dose (U/day)</td>
<td>44 [26–84]</td>
<td>44.5 [32–84]</td>
<td>40 [26–72]</td>
</tr>
<tr>
<td>HbA1c (mmol/mol)</td>
<td>56 [46–75]</td>
<td>58 [46–68]</td>
<td>54 [50–75]</td>
</tr>
<tr>
<td>Severe hypoglycaemic events in the previous year (n)</td>
<td>3</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

Data are presented as numbers or medians [range]; M: male; F: female.

Fig. 1. Mean interstitial glucose (IG) profiles recorded by sensor over the 24-h fasting period: (A) patients monitored by the Gold® (solid line) and Guardian® (dotted line) systems; and (B) patients treated with long-acting insulin (solid line) or a pump (dotted line).

Table 2
Hypoglycaemic events according to self-monitored blood glucose (SMBG) compared with glucose sensor (S) readings.

<table>
<thead>
<tr>
<th>Hypoglycaemia (all episodes)</th>
<th>SMBG and S concordant (≤ 3.9 mmol/L)</th>
<th>SMBG ≤ 3.9 mmol/L and S &gt; 3.9 mmol/L (discordant)</th>
<th>SMBG NA and S ≤ 3.9 mmol/L (undetected)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (n)</td>
<td>104</td>
<td>50</td>
<td>24</td>
<td>29</td>
</tr>
<tr>
<td>SMBG T₀ min (mmol/L)</td>
<td>3.3</td>
<td>3.3 [3.0–3.6]</td>
<td>3.3 [3–3.6]</td>
<td>NA</td>
</tr>
<tr>
<td>IG T₀ min (mmol/L)</td>
<td>3.6</td>
<td>3.6 [3–3.9]</td>
<td>4.4 [4.3–4.9]</td>
<td>3.6 [3–3.6]</td>
</tr>
<tr>
<td>IG T₋30 min (mmol/L)</td>
<td>4.0</td>
<td>3.9 [3.3–4.2]</td>
<td>4.67 [4.5–5.1]</td>
<td>4 [3.7–4.3]</td>
</tr>
<tr>
<td>Time to recovery (min)</td>
<td>30</td>
<td>30 [19–40]</td>
<td>NA</td>
<td>30 [15–50]</td>
</tr>
<tr>
<td>Duration (min)</td>
<td>55</td>
<td>55 [30–120]</td>
<td>NA</td>
<td>57 [28–83]</td>
</tr>
</tbody>
</table>

Data are presented as numbers or means [range]; IG: interstitial glucose; T₀ min: start of event; T₋30 min: 30 min before event; NA: not available.

* Concordant versus undetected.
3.3. Hyperglycaemia

Six patients had no episodes of hyperglycaemia (SMBG ≥ 7.8 mmol/L), while 22 patients experienced at least one such episode. Of the patients with hyperglycaemia, two did not take an extra injection. Altogether, there were 34 episodes during which patients took an extra bolus of ultra-rapid insulin, and six patients had to take two or more successive insulin boluses (two using Gold®, and four using Guardian®). The mean rapid-insulin dose was 1 U per episode and 2 U per patient. The monitor and sensor were concordant in 23 episodes, SMBG was higher in 11 episodes, and one episode was considered a false-positive (Table S2; see supplementary material associated with this article online). Of the 23 concordant episodes (eight patients monitored by Gold®, and 12 by Guardian®), the SMBG value was on target within 120 min in 11 patients and within 180 min in 17. No episodes of hypoglycaemia were recorded within the 180 min after the extra insulin bolus.

4. Discussion

In our programme of flexible intensive insulin therapy, fasting was used as a tool to study basal insulin and correction of off-target glucose as, during fasting, patients are in a steady state—in other words, when high or low glucose occurs, any imbalance between rapid insulin and the amount of carbohydrates cannot be responsible.

The present study was designed to evaluate the contribution of CGMS in an extreme context. The study also aimed to evaluate its utility for making fasting at home safer. Therefore, we studied the results of a 24-h fast at home in patients monitored by either Gold® or Guardian® CGMS devices. Analysis of the results has provided important information about fasting per se. The study has also shown that a 24-h fast is possible at home for type 1 diabetic patients, provided that an accurate amount of basal insulin is administered. No major incidents were recorded, although a significant number of instances of hypoglycaemia occurred. All patients completed the protocol and, at the end of the fast, more than 80% of IG values were within the stringent 3.9–7.8 mmol/L target level.

In the present study, there were 104 episodes of low blood glucose, but no severe hypoglycaemias. Recent data have shown that hypoglycaemic episodes are frequent and can be prolonged over more than 2 h in patients with type 1 diabetes under ordinary circumstances [10,11]. SMBG and IG were concordant in 50 of the 104 episodes in our study. This high rate of discordance could stem from the unreliability of CGMS devices for low glucose values, as has been reported for spurious hypoglycaemia [12–15], and might explain the large number of episodes found in patients using the Gold® device. However, this is still a subject of debate, as one study has suggested that CGMS is reliable during hypoglycaemic episodes [16], while other studies have found that glucose-monitoring devices have low sensitivity.
for the detection of hypoglycaemic episodes [11,17–20]. In the present study, when SMBG and IG were discordant at below-target values, it was always the IG that was on target and the SMGB below-target. When low-glucose episodes were detected and corrected by the patient according to protocol, blood glucose was on target within 60 min and greater than 7.8 mmol/L in only five episodes (data not shown). This suggests that 10–15 g of sucrose is usually enough to correct hypoglycaemia and that it can be recommended as the average dose. A reference textbook [21] states that the recommended dose is 15–20 g, but with no citations, and the issue does not appear to have been recently revisited. Brodows et al. [22] have shown that 20 g was enough to correct moderately severe hypoglycaemia, whereas a previous study from our group showed that 15 g of sucrose was effective [7].

The time needed to correct hypoglycaemia was 30 min and was, surprisingly, not significantly different whether the patient had taken sucrose or not. To our knowledge, this has not yet been studied in patients using a CGMS device, and could be the subject of a forthcoming study. One weakness of our present study arises from the fact that patients used their usual meters for SMBG and these were not all the same. Another study weakness is that we failed to ask patients to record whether they had symptoms or not when low glucose was observed on SMBG, or the IG values in those using Guardian®.

Hyperglycaemia (defined as blood glucose greater than 7.8 mmol/L, according to our protocol) was not frequently observed, and 11 episodes (out of 23) were corrected within less than 2 h. Successive doses of rapid insulin were necessary on five occasions, and one patient, using a pump, after three ineffective shots had to change his cannula, which was thereafter followed by normoglycaemia. Apart from these six patients, IG was on target in all patients after 3 h. This suggests that, in everyday life, if a rapid-insulin shot intended to correct high blood glucose is ineffective, it is because the patient either has a full stomach or is sick. More than 80% of IG values were on target at the end of fasting, which confirms the effectiveness of the suggested protocol for correcting off-target values.

When patients taking glargine were compared with patients using a pump, no ‘tool effect’ was found, as there were as many patients on target in the glargine group as in the pump group over the three time periods of the fast. As regards the ‘sensor effect’, there were more patients on target during the second and third time periods of the fast among those using the Guardian®. It is possible that the device’s alarms permitted otherwise undetected high or low glucose to be avoided in these patients.

Thus, the present study shows that it is possible for type 1 diabetic patients to carry out a prolonged total fast. Within the framework of our functional intensive therapy training programme, this also yielded information on the individual amounts of sugar or insulin needed to correct hypo- and hyperglycaemia as well as how to adjust basal insulin. Indeed, all of the information gathered is of considerable value for improving flexibility in meals and allowing fasting for personal, medical or religious reasons. The use of CGMS was not mandatory for the safety of fasting at home. These data extend what has already been published on the safety of fasting and show that not only is a fast of more than 24 h possible in type 1 diabetic patients using glargine or a pump, but that it can also be a useful educational tool to help patients make decisions about their own treatment.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

Appendix A. Supplementary materials

Supplementary material (Figs. S1–S3, and Tables S1 and S2) associated with this article can be found at http://www.sciencedirect.com at doi:10.1016/j.diabet.2011.06.002.

References


