Continuous glucose monitoring reduces both hypoglycaemia and HbA1c in hypoglycaemia-prone type 1 diabetic patients treated with a portable pump

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Received 27 May 2010; received in revised form 6 August 2010; accepted 10 August 2010
Available online 22 September 2010

Abstract

Aim. – This study aimed to assess the effectiveness of continuous glucose monitoring (CGM) for glucose control in type 1 diabetic patients treated by continuous subcutaneous insulin infusion (CSII) and presenting with frequent hypoglycaemic episodes.

Methods. – Thirteen patients with type 1 diabetes (diabetes duration: 25 ± 15 years; CSII duration: 5.5 ± 7.0 years), with more than six recorded capillary blood glucose (CBG) values < 60 mg/dL, according to their metres for the past 14 days, were offered the permanent use of a CGM device (Guardian RT®, Medtronic) plus ongoing self-monitoring of blood glucose (SMBG) for 12 weeks, followed by a 12-week crossover period of SMBG only, or vice versa. Glucose control, determined by recorded 14-day CBG values < 60 mg/dL and HbA1c levels, and quality of life according to the Diabetes Quality of Life (DQOL) questionnaire, were assessed at baseline, and after 12- and 24-week follow-ups.

Results. – Four patients withdrew from the study during the first period (of whom three were using CGM). In the nine study completers, the number of low CBG values decreased significantly from 13.9 ± 9.2 to 7.6 ± 6.8 (P = 0.011) when patients used CGM, that is, whether in the initial or final trial period, while a decrease in HbA1c from 8.3 ± 0.7 to 7.7 ± 0.6% (P = 0.049) was observed, in contrast to the absence of any significant differences during the SMBG-only period. DQOL scores were also essentially unaffected.

Conclusion. – This pilot observational study supports the hypothesis that CGM use can significantly improve overall glucose control while reducing hypoglycaemic episodes in hypoglycaemia-prone type 1 diabetic patients treated by CSII.

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Keywords: Type 1 diabetes; Hypoglycaemia; Continuous glucose monitoring; Insulin pump; Quality of life
Conclusions. – Cette étude pilote supporte l’hypothèse selon laquelle la mesure continue du glucose peut améliorer le contrôle glycémique tout en diminuant la fréquence des hypoglycémiées chez des patients diabétiques de type 1 à risque hypoglycémique sous traitement par pompe portable à insuline.

Mots clés : Diabète de type 1 ; Hypoglycémie ; Enregistrement continu du glucose ; Pompe à insuline ; Qualité de vie

1. Introduction

Les buts actuels de contrôle du glucose dans les patients atteints de diabète de type 1 (T1DM) comprennent le glycémique glyquemé (HbA1c) ≤ 7% associé au taux le plus faible possible de hypoglycémie. De plus, une qualité de vie (QOL) déficiente [1]. Continuous subcutaneous insulin infusion (CSII) peut conduire à des HbA1c plus faibles que SMBG seulement [6]. Cependant, ces patients ont une fréquence plus grande de détecter les deviations hyperglycémiques et hypoglycémiques [4]. Un sous-ensemble de CSII traités patients continue d’expériences fréquents hypoglycémiques en vie de tout le temps [4,5].

Néanmoins, l’augmentation de l’utilisation de la glycémie continue (CGM) est utile dans la détection de la fréquence et de la qualité des hypoglycémies qui pourraient sinon passer inaperçues [7,8]. Bien que le bénéfice de CGM ait été récemment observé, il est largement reconnu que la mise en œuvre de CGM sur une période de temps court peut être supérieure à la mesure clinique seule [9]. Pour cette raison, le présent étude a été conçu pour évaluer le contrôle du glucose avec 12 semaines CGM par rapport à la mesure clinique seul. Les patients inclus dans le groupe de CGM et six avec SMBG seulement. Quatre patients ont quitté l’étude pendant la période de SMBG seul.


2. Methods

L’étude a inclus 13 patients adultes T1DM – traités par CSII pour au moins 1 an, avec quatre visites mensuelles. Les patients ont été attendus au moins six mesures de capillaire sanguine (CBG) < 60 mg/dL, en accord avec leurs mesures de glucose de l’embaras私たち. Pendant la période de SMBG, tous les patients ont réalisé les mesures de glucose de l’embaras私たち. Pendant la période de SMBG, les patients ont également été soumis à une visites mensuelles et une auto-evaluation de leur contrôle du glucose.

Les patients inclus dans l’étude ont été attendus au moins six mesures de glucose de l’embaras私たち. Pendant la période de SMBG, les patients ont également été soumis à une visites mensuelles et une auto-evaluation de leur contrôle du glucose. Les patients ont également été soumis à une visites mensuelles et une auto-evaluation de leur contrôle du glucose.
the study within the first 2 weeks. The three patients who dropped out while using CGM did so because of skin reactions at sensor-insertion sites, an inability to manage CGM data and the discomfort of wearing the CGM system during sports activities, respectively. The single patient who withdrew from the study during the SMBG-only period wished to have an implantable insulin-pump system because of severe blood glucose variability despite CSII. No statistically significant differences in baseline characteristics between the nine patients who completed the study and the 13 who were initially randomized were found in terms of age (47.4 ± 10.0 vs 47.1 ± 11.0 years, respectively), diabetes duration (25 ± 15 vs 26 ± 16 years, respectively), CSII duration (5.5 ± 7.0 vs 5.6 ± 7.0 years, respectively), baseline HbA1C (8.3 ± 0.4% vs 8.2 ± 0.4%, respectively), number of capillary glucose tests in the 14 days prior to randomization (87 ± 35 vs 91 ± 39, respectively) and number of CBG values < 60 mg/dL during the last 14 days of each study period (15.0 ± 8.6 vs 16.0 ± 8.9, respectively).

CGM use and sensor insertions were both well tolerated by the nine study completers. Compliance with the recommended permanent use of the CGM device and sensor changes every 3 days were close to 100%, according to the checked sensor-use count and analysis of the recordings for the last 2 weeks prior to the control visit. No ketoacidosis or severe hypoglycaemia was seen at any time during the study.

Whereas all of the study patients had more than six recorded CBG values < 60 mg/dL in their metre memory for the 14 days before entering the study (baseline), six of the nine completers had six or less such CBG values for the last 14 days of CGM use (two of four patients who started with CGM use, and four of five patients who ended with CGM use); in contrast, only one patient achieved such a result during the SMBG-only period (in the starting period in this case). No statistically significant period effect could be found. The number of low CBG values decreased significantly when patients used CGM, whereas there was no significant difference during the SMBG-only period (Table 1). The number of patients with less than six hypoglycaemic values for the last 14 days rose from 0 (baseline) to six with CGM, and from 0 to one with SMBG only. No influence of previous CSII duration was noted. Direct comparison of all three conditions showed 15.3 ± 8.6 CBG values < 60 mg/dL (out of 87 ± 35 measurements) for the last 14 days at baseline, 7.6 ± 6.8 values < 60 mg/dL (out of 79 ± 46 measurements) for the last 14 days of CGM (P = 0.0076 vs baseline) and 11.1 ± 4.5 values < 60 mg/dL (out of 81 ± 39 measurements) for the last 14 days of SMBG only (not significant vs baseline).

HbA1C levels decreased significantly with CGM use, but not with SMBG only (Table 1). In addition, the basal rate of insulin delivery showed no significant changes between the two study periods from baseline. However, most patients reported making corrections with insulin when CGM indicated hyperglycaemia, a behaviour that most likely played a role in the improvement of HbA1C levels seen during the CGM period.

Furthermore, diabetes QOL scores were not significantly different at the end of each study period vs baseline in terms of global scores (Table 1), as well as those for each specific item under study (satisfaction, personal impact, social and vocational worry, diabetes worry and well-being; data not shown).

### 4. Discussion

Our study demonstrates the benefits of permanent CGM for 12 weeks with the reduction of low blood glucose values in a subset of T1DM patients prone to hypoglycaemia during CSII. Moreover, the reduction of hypoglycaemic values while using CGM was associated with improvement of HbA1C levels, an unusual finding in patients with T1DM for whom the intensification of insulin therapy to lower HbA1C levels is generally associated with a higher rate of hypoglycaemic episodes [1]. The importance of glucose variability and the positive effect of CSII have previously been emphasized in this regard [14].

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Glucose control and Diabetes Quality of Life (DQOL) total score for the nine study completers with continuous glucose monitoring (CGM) and self-monitoring of blood glucose (SMBG).</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before CGM</td>
</tr>
<tr>
<td>HbA1C (%)</td>
<td>8.3 ± 0.7</td>
</tr>
<tr>
<td>Number of hypos&lt;sup&gt;a&lt;/sup&gt;</td>
<td>13.9 ± 9.2</td>
</tr>
<tr>
<td>Patients without hypos&lt;sup&gt;d&lt;/sup&gt;</td>
<td>0/9&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td>DQOL total score&lt;sup&gt;b&lt;/sup&gt;</td>
<td>64.7 ± 11.0</td>
</tr>
<tr>
<td></td>
<td>Before SMBG only</td>
</tr>
<tr>
<td>HbA1C (%)</td>
<td>7.9 ± 0.5</td>
</tr>
<tr>
<td>Number of hypos&lt;sup&gt;a&lt;/sup&gt;</td>
<td>11.8 ± 7.1</td>
</tr>
<tr>
<td>Patients without hypos&lt;sup&gt;d&lt;/sup&gt;</td>
<td>1/9&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td>DQOL total score&lt;sup&gt;b&lt;/sup&gt;</td>
<td>65.1 ± 11.0</td>
</tr>
</tbody>
</table>

Hypos: hypoglycaemic episodes; NS: not significant.

<sup>a</sup> Capillary blood glucose values < 60 mg/dL during the last 14 days.

<sup>b</sup> On a scale of 0–100, the higher the DQOL score, the better the quality of life.

<sup>c</sup> Assessed at baseline.

<sup>d</sup> Two of four patients who started the study with CGM, and four of five who ended the study with CGM (no statistically significant period effect).

<sup>e</sup> One patient who started the study with SMBG only.

<sup>f</sup> Chi<sup>2</sup> test vs baseline.
However, the sustained benefits of CGM use have been controversial in clinical practice so far [8,15]. Permanent use of the Guardian RT device for 3 months significantly improved HbA1c levels compared with SMBG, while intermittent CGM use showed no significant benefit [6]. The recent Juvenile Diabetes Research Foundation (JDRF) trial reported that CGM for 6 months led to significant HbA1c improvement vs SMBG use only in young patients who showed good compliance with sensor use [16], although the incidence of severe or biochemical hypoglycaemic events was not significantly altered. In the recent French multicentre REAL Trend study, CGM-enabled insulin-pump therapy improved glycaemia more than conventional pump therapy during the first 6 months of pump use in T1DM patients who wore CGM sensors at least 70% of the time, but had no impact on hypoglycaemia [17]. However, in none of these studies was patient enrolment based on a previous high incidence of documented biochemical hypoglycaemia.

In contrast, in the present pilot study, T1DM patients were selected because of frequently detected low glucose levels (six or more values < 60 mg/dL within the past 14 days). This rate of biochemical hypoglycaemia was considerably higher than that reported in other studies, such as the recent report by the UK Hypoglycaemia Study Group comparing the frequency of biochemical hypoglycaemia in adults with T1DM with and without impaired awareness of hypoglycaemia [18]. The permanent use of CGM in our present patients treated by CSII and presenting with such a high incidence of hypoglycaemia was associated with significant reductions in both the incidence of hypoglycaemic episodes and HbA1c levels. In spite of intensive SMBG use and recently reinforced training on adaptation of insulin delivery, no significant reduction of hypoglycaemic values was obtained during the study period without CGM. Being informed of the potential risk of hypoglycaemia via the CGM system most likely helped these patients to anticipate the need for countermeasures to avoid the occurrence of hypoglycaemia [5]. The concomitant reduction in HbA1c levels may also indicate the patients’ greater self-confidence in adapting insulin doses to reduce hyperglycaemia safely because of the CGM information.

Nevertheless, the currently available CGM devices still need to be improved and made easier to use in everyday life, as revealed by the rather high initial dropout rate in our study. The lack of improvement in QOL despite the better glucose control with CGM use, including less-frequent hypoglycaemic episodes, may be related to the constraints of wearing and managing the CGM system, although the patients who completed the study all showed excellent compliance with sensor use. In a recent study, users of the integrated real-time CGM/CSII system reported more treatment benefits, greater treatment satisfaction and better QOL than SMBG + CSII users [12].

In conclusion, diabetic patients who remain prone to hypoglycaemia in spite of CSII treatment appear to be good candidates for CGM use, and such patients warrant further investigation in larger-scale trials with similar features to confirm our present findings.

Conflict of interest statement

No relevant conflict of interest to declare.

Acknowledgments

We thank the patients, nurses and physicians at our clinic who participated in our investigation. Also, the study was financially supported in part by the Fonds Léon-Fredericq (Leon Fredericq Foundation) at the University of Liège, Belgium. Some of the data from this study were presented at the 44th Annual Meeting of the European Association for the Study of Diabetes, held in Rome, Italy, 7–11 September 2008.

References


