Improved metabolic control in diabetic adolescents using the continuous glucose monitoring system (CGMS)

P Schaepelynck-Bélicar1, Ph Vague1, G Simonin2, V Lassmann-Vague1

SUMMARY

Objective: To determine the utility of the continuous glucose monitoring system (CGMS) as an outpatient procedure to improve management of diabetes in adolescents.

Research Design and Methods: Twelve adolescents (mean age: 16.2 ± 3 years) with poorly controlled type 1 diabetes (HbA1c > 8%) were included in this trial. Mean HbA1c during the previous year was 10.1 ± 1.2%. Inulin treatment consisted of 2 or 3 daily injections in 10 cases and CSII in 2. At the beginning of the study, HbA1c was determined and low blood glucose index (LBGI) was calculated. Continuous glucose monitoring was performed for three days. After downloading and analyzing data, results were discussed with the patient and insulin treatment was adjusted. Two months later testing was repeated and all parameters were reassessed.

Results: Initial CGMS profiles demonstrated glycemic excursions unrecognized by capillary measurements in all twelve patients. Glycemia before and after meals varied from < 60 mg/dL to > 200 mg/dL in 2 patients (2 episodes). Postprandial hyperglycemia exceeded 200 mg/dL in 10 patients (24 episodes). Prolonged overnight hyperglycemia was observed in 5 patients (7 episodes), dawn phenomenon in 4 patients (6 episodes) and nighttime hypoglycemia in 4 patients (4 episodes). A day-to-day reproducibility of glycemic profiles was observed in 8 patients. Then insulin treatment was adjusted according to CGMS data. Changes involved dose levels in 3 patients, insulin type in 7, number of injections, i.e. 3 instead of 2, in 5 or change from insulin injection to CSII in 1. Reassessment two months later demonstrated a significant reduction of glycemic excursions in 8 patients. HbA1c (m ± SD) decreased from 10.3 ± 2.1% to 8.75 ± 1.06% (p < 0.05). LBGI increased from 1.7 ± 0.9 to 2.4 ± 1.4 but the difference was not significant.

Conclusions: Use of CGMS in diabetic adolescent outpatients achieved a significant improvement in metabolic control not only by providing accurate data for adjustment of insulin treatment but also by promoting patient communication and motivation.

Key-words: Adolescent · Glucose Monitoring · Diabetes Management · Education.

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RESUME

Amélioration du contrôle métabolique d’adolescents diabétiques par l’utilisation du holter glycémique CGMS

But de l’étude: Préciser l’aide apportée par le Holter glycémique (CGMS) en ambulatoire dans la prise en charge thérapeutique de l’adolescent diabétique.

Méthodes: Douze adolescents d’âge moyen 16,2 ± 3 ans présentant un diabète de type 1 mal équilibré (HbA1c > 8 %) ont participé à l’étude. L’HbA1c moyenne au cours de l’année écoulée était 10,1 ± 1,2 %. Le traitement insulinique comportait 2 ou 3 injections quotidiennes d’insuline dans 10 cas ou la pompe externe dans 2. Au début de l’étude, l’HbA1c est mesuré et le LBGI (Low Blood Glucose Index) calculé. Puis l’enregistrement continu des glycémies est réalisé pendant 3 jours au moyen du CGMS. A l’issue de ces trois jours, les données sont déchargées, puis analysées et discutées avec le patient et le traitement insulinique ajusté en fonction des résultats. Deux mois plus tard les mêmes paramètres sont réévalués.

Résultats: Les premiers enregistrements donnés par le CGMS ont révélé des excursions glycémiques méconnues par l’autosurveillance capillaire chez les 12 patients. Il a été mis en évidence: chez 2 patients, 2 épisodes d’hyperglycémie (< 60 mg/L) préprandiale puis hyperglycémie (> 200 mg/L) postprandiale; chez 10 patients, 24 épisodes d’hypoglycémie postprandiale; chez 5 patients, 7 épisodes d’hypoglycémie nocturne prolongée; chez 4 patients, 6 épisodes de phénomène de l’aube; enfin, chez 4 patients, 4 épisodes d’hypoglycémie nocturne. Par ailleurs, 8 patients présentaient des profils de glycémie reproductibles d’un jour à l’autre. Le traitement insulinique a été adapté en fonction des données de ces premiers enregistrements CGMS. Ces adaptations ont consisté en: une modification des doses chez 3 patients, du type d’insuline chez 7, du nombre d’injections chez 5 ou passage à la pompe externe chez 1 patient. La réévaluation deux mois plus tard a montré une réduction significative des excursions glycémiques chez 8 patients. L’HbA1c a baissé de 10,3 ± 2,1 % à 8,75 ± 1,06 % (p < 0,05). Le LBGI est passé de 1,7 ± 0,9 à 2,4 ± 1,4 mais la différence n’est pas significative.

Conclusion: L’utilisation du CGMS a permis une amélioration significative de l’équilibre glycémique chez ces adolescents diabétiques, d’une part en donnant des informations utiles pour ajuster le schéma insulinique et d’autre part en aidant à une meilleure communication et à la motivation du patient.

Mots-clés: Adolescent · Surveillance glycémique · Prise en charge du diabète · Éducation.

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Optimal management of type 1 insulin-dependent diabetes requires intensive self-monitoring of blood glucose (SMBG) with 4 to 8 capillary blood glucose measurements per day being necessary to adjust insulin treatment to changes in plasma glucose, diet and activity. However intensive SMBG alone does not provide enough information on glycemic excursions during postprandial or overnight periods and fails to detect asymptomatic hypoglycemia.

The MiniMed Continuous Glucose Monitoring System (CGMS®, Medtronic-MiniMed, Northridge, CA, USA) is an automated device designed to measure glucose in interstitial tissue throughout the day and night [1, 2]. Measurements are made by a subcutaneously-implanted sensor containing glucose-oxidase. The sensor measures electrical current in relation to the interstitial glucose concentration. Signals are stored in a monitor that averages data every 5 minutes. The device needs about four capillary glucose readings each day for calibration. After three days, information in the monitor is downloaded to a computer and converted into glucose levels using MiniMed Solution® software version 2.0. Data presented in a graphic format are reviewed to identify glucose excursions as a basis for adjusting insulin treatment.

Results of early studies [3-5] carried out since FDA approval of the CGMS in June 1999 have established good device reliability and patient acceptance. Improved control of diabetes has been achieved in all patients with particularly promising results in difficult cases [4, 6]. As diabetic adolescents constitute a particularly difficult population for metabolic control due to physical and psychological factors related to puberty, we decided to evaluate the utility of CGMS as an outpatient procedure to achieve optimal management of type 1 insulin-dependent diabetes in adolescents.

Research design and methods

Diabetic patients

Twelve adolescents with poorly controlled type 1 diabetes (HbA1c > 8%) were consecutively included in this trial. Informed consent was obtained from both patients and parents. There were five girls and seven boys with a mean age of 16.2 ± 3 years (m ± SD). Mean duration of diabetes was 6.8 ± 2.1 years (m ± SD). Mean HbA1c during the previous year was 10.1 ± 1.2% (m ± SD). At the time of inclusion, seven patients performed regular SMBG with a mean frequency of 2.22 ± 0.41 fingerstick tests per day over the last 30 days (range: 1.65 to 2.85). In the remaining five patients the mean number of fingerstick tests per day was less than 1. Insulin treatment consisted of 2 or 3 daily injections in ten patients and CSII in two.

Study protocol

On the first day of study, patients came to the hospital for subcutaneous implantation of the sensor, programming of the monitor and instruction on the use of the CGMS. They were asked to enter a minimum of four SMBG measurements into the monitor for calibration as well as a certain number of events such as insulin injections, meals, sports activity, and manifestations. These events were programmed into the monitor in the form of code values. In addition baseline HbA1c was measured and low blood glucose index (LBGI) was calculated as an indicator of the risk of severe hypoglycemia [7]. Patients then returned home wearing CGMS in usual living conditions.

After 3 days, patients returned to the hospital. CGMS data were downloaded to a computer and glucose profiles were reviewed. The criteria for analysis of glycemic profiles were as follows:
- the “day” period was from “7:00 am to 10:00 pm” and the night period from “10:00 pm to 7:00 am”;
- the preprandial period was one hour before meals and postprandial period three hours after meals;
- glycemic excursions were defined as hypoglycemia less than 60 mg/dl and hyperglycemia greater than 200 mg/dl.

Findings were discussed with the patient and insulin treatment was adjusted if necessary.

Two months later CGMS, HbA1c assays, and LBGI were repeated in order to evaluate the effects of the adjusted treatment. Statistical analysis was performed using the Student’s t test for paired values. Probability values (p) less than 0.05 were considered as significant.

There was no control group, all included patients experienced continuous glucose monitoring using CGMS.

Results

Initial CGMS profiles

As summarized in Table I, initial CGMS profiles (M0) demonstrated large excursions of glycemia unrecognized by

<table>
<thead>
<tr>
<th>Total number of glycemic excursions revealed by</th>
<th>CGMS no 1</th>
<th>CGMS no 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daytime</td>
<td>26</td>
<td>16</td>
</tr>
<tr>
<td>Nighttime</td>
<td>17</td>
<td>8</td>
</tr>
<tr>
<td>n events by patient (m ± SD)</td>
<td>3.5 ± 1.3</td>
<td>2.08 ± 1.37*</td>
</tr>
</tbody>
</table>

*p < 0.05 (M2 versus M0).
capillary measurements in all twelve patients. An example of such CGMS profile is shown on Figure 1. In two patients, two episodes of preprandial hypoglycemia followed by postprandial hyperglycemia occurred. In ten patients, a total of 24 episodes of postprandial hyperglycemia were observed. In five patients seven prolonged episodes of hyperglycemia were recorded during the night period. In four patients a total of six episodes of dawn phenomenon were observed. In four patients four episodes of asymptomatic hypoglycemia lasting up to five hours were observed. Initial CGMS findings also showed that glycemic fluctuations were reproducible from one day to the next in eight of the twelve patients as shown on Figure 2 suggesting that they depended from insulin treatment.

Treatment adjustments

Treatment was adjusted in all patients according to glycemic profiles. Changes are presented on Table II. In 3 patients treatment adjustment consisted in modifying dose levels. In 7 patients the type of insulin administered was changed. In 5 patients the number of daily insulin injections was increased from 2 to 3. In 1 patient insulin injections were replaced by CSII.

Reassessment findings

Review of CGMS profiles two months after treatment adjustment (M2) demonstrated a significant improvement in glycemic excursions in eight of the twelve patients. During the day period, one episode of preprandial hypoglycemia followed by post-prandial hyperglycemia was observed in one patient. Thirteen episodes of postprandial hyperglycemias occurred in eight patients. Two asymptomatic hypoglycemias were observed in two patients. During the night period, four prolonged episodes of hyperglycemia were observed in four patients. One dawn phenomenon oc-
occurred in one patient. Three episodes of asymptomatic hy-
poglycemia lasting up to 3.5 hours were detected in three 
patients. As shown in Table I, there was a significant de-
crease in the mean frequency of glycemic excursions from 
3.5 ± 1.3 to 2.08 ± 1.37 per patient.

As shown in Table III, metabolic control improved sig-
ificantly with HbA1c decreasing from 10.3 ± 2.1% to 8.75 ± 
1.06% (p < 0.05). When possible depending on the number 
of meter readings [7], calculation of LBGI in seven patients 
showed no significant change, i.e., 1.7 ± 0.9 versus 2.4 ± 1.4. 
Self-monitoring over the previous 30-day period was signifi-
cantly higher at the end of study. At baseline the mean num-
ber of capillary readings was 2.22 ± 0.4 per day in seven 
patients and less than one per day in five patients. Two 
months later, the mean number of capillary readings was 
2.91 ± 0.98 per day in 10 patients and less than 1 per day in 
only 2 patients.

Sensor performance

A total of 72 daily profiles were obtained from CGMS 

datas collected during the two procedures in the 12 patients

Table II

<table>
<thead>
<tr>
<th>Patient no</th>
<th>Before the 1st CGMS</th>
<th>After the 1st CGMS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Insulin dose (U/day)</td>
<td>Modality of treatment</td>
</tr>
<tr>
<td>1</td>
<td>76</td>
<td>2 injections</td>
</tr>
<tr>
<td>2</td>
<td>32</td>
<td>3 injections</td>
</tr>
<tr>
<td>3</td>
<td>52</td>
<td>3 injections</td>
</tr>
<tr>
<td>4</td>
<td>79</td>
<td>2 injections</td>
</tr>
<tr>
<td>5</td>
<td>98</td>
<td>3 injections</td>
</tr>
<tr>
<td>6</td>
<td>66</td>
<td>CSII</td>
</tr>
<tr>
<td>7</td>
<td>31</td>
<td>3 injections</td>
</tr>
<tr>
<td>8</td>
<td>68</td>
<td>2 injections</td>
</tr>
<tr>
<td>9</td>
<td>85</td>
<td>3 injections</td>
</tr>
<tr>
<td>10</td>
<td>72</td>
<td>CSII</td>
</tr>
<tr>
<td>11</td>
<td>72</td>
<td>2 injections</td>
</tr>
<tr>
<td>12</td>
<td>69</td>
<td>2 injections</td>
</tr>
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</table>

Discussion

The recent development of the CGMS has provided clini-
cians and patients with a new monitoring tool. Most trials 
designed to establish the utility of the CGMS in clinical prac-
tice have been carried out in adults. Findings clearly show 
that the continuous monitoring provides information that 
can be used not only to improve diabetes control [3] but also 
educate patients [5, 8]. Few studies have been conducted in 
specific subgroups of diabetic patients. Results in pediatric 
cases [4, 6] indicated that CGMS is well accepted and toler-
ated and could greatly improve glycemic control. A major 
advantage of CGMS demonstrated in these pediatric studies 
is the identification of nocturnal hypoglycemia and post-
prandial hyperglycemic episodes that meter data had not 
detected even in patients with acceptable HbA1c and 
preprandial glucose levels. Nevertheless a recent study [9] 
suggests that, in patients with tightly controlled diabetes 
(HbA1c: 6.6 ± 0.6%), asymptomatic hypoglycemias reported 
by CGMS should be interpreted with caution. CGMS re-
ports could be more accurate in our patients as they experi-

Table III

<table>
<thead>
<tr>
<th>M0</th>
<th>M2</th>
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<tbody>
<tr>
<td>HbA1c (%)</td>
<td>10.3 ± 2.1%</td>
</tr>
<tr>
<td>LBGI(1)</td>
<td>1.74 ± 0.9</td>
</tr>
<tr>
<td>n SMBG(2)</td>
<td>2.22 ± 0.4 (n = 7)</td>
</tr>
<tr>
<td>&lt; 1 (n = 5)</td>
<td>&lt; 1 (n = 2)</td>
</tr>
</tbody>
</table>

* p < 0.05 (M2 versus M0), (1) in 7 patients, (2) number of capillary 
measurements per day over the previous 30 days period.
ence poor metabolic control (HbA1c: 10.3 ± 2.1%) and large daily glucose excursions.

Treatment of type 1 diabetes is particularly difficult in adolescents due to physical and psychological factors occurring at puberty. Hormonal and morphological changes may lead to various degrees of insulin resistance. In addition, factors such as teenage rebellion and need of freedom often lead to poor compliance with SMBG and/or insulin treatment. Due to a lack of communication with medical staff, therapeudic decision-making in diabetic adolescents is frequently based on a limited number of capillary blood glucose measurements. Hospitalization usually is an unsuitable alternative because it is refused by most adolescent patients and fails to reproduce the teenage living conditions.

The present study was conducted to evaluate CGMS as an outpatient procedure to improve management of diabetes in adolescents. All included patients used CGMS and encouraging results were obtained at each step of the study. Initial CGMS profiles in our patients confirmed that CGMS allows detection of previously unrecognized glycemic excursions. In most cases (8 out of 12 patients), CGMS data also indicated day-to-day reproducibility of glycemic trends. After downloading to a computer, visualization of data in a graphic format facilitated analysis and evaluation of therapy. In addition to allowing adjustment of insulin treatment based on continuous monitoring under normal living conditions, graphic representation of data provided an easily understandable communication tool between clinicians and adolescents.

Analysis of results two months later demonstrated improved diabetic control. A significant decrease in HbA1c from 10.3 to 8.75% was observed. Improvement of HbA1c persisted 6 months later. Mean HbA1c at 6 months was 8.93 ± 1.34% and remained significantly lower than at M0. LBG1 indicated that the risk for severe hypoglycemia was low [7] and did not significantly change from M0 to M2. However interpretation of these results is delicate due to the limited number of capillary measurements before the first CGMS. Furthermore this index was not validated in diabetic patients treated by pump and/or insulin analogs.

The CGMS was useful in several respects. The improvement in metabolic control observed in these diabetic adolescents clearly resulted from adjustment and/or intensification of insulin treatment as CGMS allowed adjustment of insulin dosage or type based on a better understanding of glycemic patterns. The management approach did not differ and the frequency and duration of consultations did not change. Visualization of glycemic profiles given by CGMS and discussion with the clinician helped patients to understand and accept the need to intensify treatment. Furthermore it increased patient awareness of the necessity for regular SMBG and motivated them to become more involved in management of their disease. Even if moderate the frequency of SMBG became more frequent in 10 out 12 adolescents.

From a technical standpoint, our findings demonstrate that the CGMS is compatible with current clinical practice. But it must be underlined that sensor performance was suboptimal due to patient- or device-related causes in about 40% of cases. Similar problems were described by Meyer et al. [10] who also reported malfunction in 40% of cases. Sensor performance could be improved by better patient training and use of the newly available software version 1.7.A.

In conclusion our experience with the CGMS in adolescent outpatients with type 1 diabetes was promising. Use of the CGMS led to a significant improvement in middle-term metabolic control not only by supplying more accurate data for treatment planning but also by promoting patient communication and motivation.

References