Continuous Subcutaneous Glucose Monitoring Improved Metabolic Control in Pediatric Patients With Type 1 Diabetes: A Controlled Crossover Study

Purpose
- To investigate whether a Continuous Glucose Monitoring System (CGMS) can improve metabolic control in pediatric subjects with type 1 diabetes.

Endpoints
- The endpoints for the study were HbA1c reduction and the duration and the frequency of hypoglycemia and hyperglycemia.

Methods
- A total of 32 subjects enrolled in the 24-week, controlled crossover study; study subjects were 12.5 ± 3.3 years of age (range: 5-19 years) and had an average duration of type 1 diabetes for 7.0 ± 3.9 years (range: 2-15 years).
- Subjects had an HbA1c of ≥6.8% at the beginning of the study.
- All subjects were treated with intensive insulin therapy; 14 subjects were treated with multiple daily injections (MDI) and 13 subjects were treated with insulin infusion pumps.
- The subjects were randomly placed into either an open or a blind study arm; both arms had subjects who used MDI therapy and pump therapy.
- Subjects in both arms wore the CGMS for 3 days every 2 weeks and were instructed to complete at least 2 self-monitoring blood glucose (SMBG) measurements and a 7-point SMBG once every week.
- The CGMS monitored interstitial glucose levels in subcutaneous tissue every 10 seconds and recorded an average value every 5 minutes.
- In the open arm, CGMS profiles were used to adjust insulin therapy at follow-up visits every 6 weeks.
- In the blinded arm, both the subjects and the diabetes team were masked to the CGMS profiles. Insulin therapy adjustments were based solely on 7-point blood glucose profiles performed by the subjects.
- After 3 months, the open and blinded study arms crossed over.

Results

HbA1c
- Twenty-seven subjects completed the study; the mean baseline HbA1c value was 8.0% ± 1.1% (range 6.8% - 10.8%).
- During the first 3-month period, there was a decrease in HbA1c levels in both the open and blinded study arms.
- After the 3-month crossover, the now open study arm had a further decrease in HbA1c levels, and the now blinded arm had an increase in HbA1c levels.
- During the open arm, subjects had a mean HbA1c reduction from 7.70% to 7.31% (p=0.013), which was significant. In comparison, the blinded arm had a mean HbA1c reduction from 7.75% to 7.65% (p=NS).

Hyperglycemia
- On average, there were 1.5 episodes per day of daytime high subcutaneous glucose (>270 mg/dL or >15 mmol/L; duration 126 ± 33 minutes, 19.4% of total time) and there were 0.6 episodes per night (duration 177 ± 83 minutes, 25.5% of total time).
Hypoglycemia

- Twenty-six of 27 subjects experienced daytime low glucose values. These subjects, on average, experienced 0.8 episodes per day (<54 mg/dL or <3.0 mmol/L, duration 58 ± 29 minutes, 5.5% of total time) and all subjects had at least 1 night-time episode of low glucose.
- There was no difference in hypoglycemia frequency between the open and blinded arms, nor between the MDI and infusion pump subjects.
- Two subjects experienced severe hypoglycemia during the study; 1 occurred during the blinded arm and one occurred during the open arm.

Hypo- and Hyperglycemic Episodes
(Hypoglycemia is defined as <3.0 mmol/L or <54 mg/dL;Hyperglycemia is defined as >15 mmol/L or >273 mg/dL)

<table>
<thead>
<tr>
<th>Event</th>
<th>Number of episodes</th>
<th>Mean duration (minutes)</th>
<th>% of total time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daytime hypoglycemia</td>
<td>0.8</td>
<td>58</td>
<td>5.5%</td>
</tr>
<tr>
<td>Daytime hyperglycemia</td>
<td>1.5</td>
<td>126</td>
<td>19.4%</td>
</tr>
<tr>
<td>Night-time hypoglycemia</td>
<td>0.4</td>
<td>132</td>
<td>10.1%</td>
</tr>
<tr>
<td>Night-time hyperglycemia</td>
<td>0.6</td>
<td>177</td>
<td>25.5%</td>
</tr>
</tbody>
</table>

Conclusions

- Adjustments to insulin therapy based on CGMS profiles improved metabolic control in pediatric subjects with type 1 diabetes.
- Subjects in the open arm reduced their HbA1c levels significantly without increasing their frequency of hypoglycemia.
- Improvements in HbA1c levels for subjects initially randomized to the blinded arm may be attributed to a study effect related to more frequent clinic visits and enthusiasm to see CGMS profiles in the future open arm.
- The use of CGMS may benefit patients with elevated HbA1c levels, a worrying increase of HbA1c levels, known or suspected hypoglycemia, a lack of motivation and/or understanding of blood glucose self-monitoring, and those who want to learn more about the effect of meals and/or physical exercise on their blood glucose.