The Medtronic MiniMed Gold Continuous Glucose Monitoring System: An Effective Means to Discover Hypo- and Hyperglycemia in Children Under 7 Years of Age

**Purpose**
- To assess the incidence of hypoglycemia and postprandial glycemic patterns in children under the age of 7 years with type 1 diabetes utilizing continuous glucose monitoring (CGM).

**Endpoints**
- To evaluate whether specific glycemic patterns are associated with age, HbA1c, and form of insulin therapy–multiple daily injections (MDI) or continuous subcutaneous insulin infusion (CSII).

**Methods**
- Each child wore a Medtronic MiniMed CGMS© (Continuous Glucose Monitoring System) Gold™ on 3 to 7 occasions during an approximate 6-month time period. Families decided the number of sensor wears based on the time they were able to commit.
- Parents were asked to enter at least 4 blood glucose values during the day and 1 value overnight. Parents were also asked to enter meal event markers into the CGMS and to remove the device after 3 days (based on FDA approval). However, some families continued with prolonged sensor wear if there had not been any sensor alarms.
- Any sensor worn for less than 24 hours was considered unsuccessful and discarded. Also, days with less than 3 calibrations were discarded.
- Mild hypoglycemia was defined as ≤70mg/dL and severe hypoglycemia was defined as ≤40 mg/dL.
- Meal times were defined as breakfast between 6 am and 9 am, lunch between 11 am and 2 pm, and dinner between 5 pm and 8 pm. Night was defined as 8 pm to 8 am.
- CGMS readings were paired to meter values and used for calibration by the CGMS software.

**Results**
- A total of 19 children with type 1 diabetes enrolled in the study that lasted approximately 6 months. Subjects were a mean of 4.8 years of age (range: 1.6 – 6.8) and had a mean HbA1c of 8.0% ± 0.7% (range: 6.7% – 9.6%).
- Six subjects started the study on CSII and the remaining 13 subjects started on MDI.
- The cohort used the CGMS sensor on 102 separate occasions, providing 434 days of data and 2,221 paired meter and sensor glucose values.
- During the study, 4 children initially treated with MDI switched to CSII therapy for greater insulin dosing flexibility.

**Hypoglycemia**
- All subjects had mild sensor hypoglycemia (≤70 mg/dL) and 17 of 19 had severe sensor hypoglycemia (≤40 mg/dL).
- The overall rate of mild sensor hypoglycemia was 1.1 ± 1.7 episodes per 24 hours, with an overall median duration of 40 minutes (25th-75th percentiles: 25-80 minutes).
- The frequency and duration of hypoglycemia did not change significantly over time.
- The duration of mild nocturnal sensor hypoglycemia (median 55 minutes; 25th-75th percentiles: 30-105 minutes) was significantly longer than mild daytime sensor hypoglycemia (median 40 minutes; 25th-75th percentiles: 25-65 minutes, p<0.001).
- The false-positive rate was 16% for mild sensor hypoglycemia; however, the false-positive rate for severe sensor hypoglycemia was 55%.
- No statistically significant associations with age or insulin regimen (CSII vs. MDI) were detected.

**Postprandial Hyperglycemia**
- The peak glucose (3-hour post-meal glucose) and the glucose excursion (peak glucose minus meal glucose) were higher at breakfast than at lunch and dinner.
- There were no differences in the extent of the postprandial glucose excursions based on age (<5 vs. ≥5 years), or insulin regimen (CSII vs. MDI).
• Children with HbA1c values ≥8.0% had higher mean postprandial glucose values after breakfast and lunch when compared to children with HbA1c values <8.0%.
• Children with HbA1c values >8.0% had peak post-breakfast sensor glucose values that reached, and likely exceeded, 400 mg/dL more frequently than did children with HbA1c values <8.0% (27 vs. 7, p<0.001). This also occurred after lunch and dinner and caused the peak post-prandial glucose values to be underestimated to a greater extent in children with HbA1c values >8.0%.
• There was no association between the presence of preceding nocturnal hypoglycemia and post-breakfast peak glucose values.

### Meal Results Summary*

<table>
<thead>
<tr>
<th></th>
<th>Breakfast (n=182)</th>
<th>Lunch (n=211)</th>
<th>Dinner (n=231)</th>
<th>Breakfast vs. lunch</th>
<th>Breakfast vs. dinner</th>
<th>Lunch vs. dinner</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-hour post-meal mean glucosea</td>
<td>247 ± 64</td>
<td>199 ± 67</td>
<td>194 ± 63</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>0.60</td>
</tr>
<tr>
<td>3-hour post-meal peak glucosea</td>
<td>313 ± 66</td>
<td>252 ± 78</td>
<td>257 ± 75</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>0.65</td>
</tr>
</tbody>
</table>

Data are mean ± SD values as indicated. SD represents within-subject variation. Glucose concentrations are in mg/dL.

*a The post-meal mean and peak glucose values are underestimated as there were 66 meals where the peak value was 400 mg/dL (34 at breakfast, 18 at lunch, 14 at dinner).

### Rate of Glucose Change After Meals
• The most rapid rate of rise occurred 15-30 minutes after the parental-entered meal marker.
• Rates of change did not differ significantly based on HbA1c levels.

### HbA1c and Mean Sensor Glucose Levels
• Neither HbA1c levels nor the mean sensor glucose changed meaningfully over time. The mean HbA1c value at the start of study was 8.0 ± 0.7% (n=19) compared to 8.0 ± 0.5% (n=17) at the last visit.
• The mean sensor glucose and the percentage of time with sensor glucose >200 mg/dL were significantly associated with HbA1c (p<0.001 for both).
• The percentage of time with sensor glucose ≤70, ≤60, or ≤50 mg/dL was not significantly associated with HbA1c values.

### Adverse Events
• There were no serious adverse events.
• Families occasionally reported mild irritation and rash at the insertion site; no child required therapy.
• Over 50% of the sensors were worn for greater than 72 hours and no infections occurred, despite prolonged use.

### Conclusions
• The CGMS was well tolerated by young children with diabetes.
• The near-continuous device detected more episodes of both mild and severe hypoglycemia than did home blood glucose monitoring, although the sensor false-positive rate was high for severe hypoglycemia.
• Postprandial hyperglycemia associated with a rapid rate of change in glucose was found to be the most marked after breakfast.
• Subjects with higher postprandial glucose levels were associated with higher HbA1c levels.

*Adapted from study.