Update on Continuous Glucose Monitoring (CGM) Technology in Diabetes

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November 12, 2016
Presenter Disclosure Information
Elena Toschi, MD

• No financial disclosure
Objectives:

- Use of CGM in glucose control in T1DM
- Use of CGM and hypoglycemia in T1DM
- Use of CGM in T2DM
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- Use of CGM in glucose control in T1DM
- Use of CGM and hypoglycemia in T1DM
- Use of CGM in T2DM
Trade-off Between Complications & Hypoglycemia

Continuous Glucose Monitoring and Intensive Treatment of Type 1 Diabetes

The Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group

Enrollment

Randomization

Run-in Phase

RT-CGM

SBGM

Data collection:

*NEJM* 2008
Changes in A1C in ≥25-Year-Olds

RT-CGM: -0.50

Control: +0.02

Difference: -0.53%
P value < .001

JDRF CGM Study Group, 2008.
Study Outline

- **Enrollment**
  - Randomization
    - **Run-in Phase**
    - **RT-CGM**
      - Continue RT-CGM
      - 12-mo. Outcome
    - **SBGM**
      - Start RT-CGM

0–6 months
- Data collection: *NEJM 2008*

6–12 months
- Data collection: *Diabetes Care 2010*
<table>
<thead>
<tr>
<th>CGM use in month 6</th>
<th>0 days/week</th>
<th>&gt;0–&lt;4 days/week</th>
<th>4–&lt;6 days/week</th>
<th>≥6 days/week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean change from 0–6 months in prior RCT</td>
<td>0.0 ± 0.6</td>
<td>-0.1 ± 0.5</td>
<td>+0.1 ± 0.6</td>
<td>0.0 ± 0.7</td>
</tr>
<tr>
<td>Age-group ≥25 years</td>
<td>All</td>
<td>0 days/week</td>
<td>&gt;0–&lt;4 days/week</td>
<td>4–&lt;6 days/week</td>
</tr>
<tr>
<td>n</td>
<td>51</td>
<td>4</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Baseline A1C (%)</td>
<td>7.6</td>
<td>8.0</td>
<td>7.6</td>
<td>7.5</td>
</tr>
<tr>
<td>Change in A1C from baseline to month 6</td>
<td>All</td>
<td>0 days/week</td>
<td>&gt;0–&lt;4 days/week</td>
<td>4–&lt;6 days/week</td>
</tr>
<tr>
<td>Mean change</td>
<td>-0.4 ± 0.5</td>
<td>+0.1 ± 0.9</td>
<td>-0.4 ± 0.7</td>
<td>-0.5 ± 0.3</td>
</tr>
<tr>
<td>Improved ≥0.5%</td>
<td>23 (45)</td>
<td>1 (25)</td>
<td>2 (50)</td>
<td>4 (67)</td>
</tr>
<tr>
<td>Worsened ≥0.5%</td>
<td>3 (6)</td>
<td>1 (25)</td>
<td>1 (25)</td>
<td>0</td>
</tr>
<tr>
<td>A1C &lt;7.0%</td>
<td>15 (29)</td>
<td>0</td>
<td>2 (50)</td>
<td>3 (50)</td>
</tr>
</tbody>
</table>
### CGM-Measured Time of eu-, hypo- and hyper-glycemia

<table>
<thead>
<tr>
<th>Age ≥25 years (n = 74)*</th>
<th>Baseline (blinded)</th>
<th>Month 6</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Glucose (mg/dl)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minimum/day</td>
<td>157 ± 25</td>
<td>152 ± 18</td>
<td>0.08</td>
</tr>
<tr>
<td>71–180 mg/dl</td>
<td>882</td>
<td>980</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Hypoglycemia</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minimum/day (mg/dl)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤70</td>
<td>55</td>
<td>45</td>
<td>0.02</td>
</tr>
<tr>
<td>≤60</td>
<td>20</td>
<td>17</td>
<td>0.006</td>
</tr>
<tr>
<td>≤50</td>
<td>5</td>
<td>4</td>
<td>0.02</td>
</tr>
<tr>
<td>AUC†</td>
<td>0.3</td>
<td>0.3</td>
<td>0.008</td>
</tr>
<tr>
<td>LBGI</td>
<td>0.9</td>
<td>0.9</td>
<td>0.02</td>
</tr>
<tr>
<td><strong>Hyperglycemia</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minimum/day (mg/dl)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;180</td>
<td>439</td>
<td>390</td>
<td>0.03</td>
</tr>
<tr>
<td>&gt;200</td>
<td>296</td>
<td>256</td>
<td>0.004</td>
</tr>
<tr>
<td>&gt;250</td>
<td>114</td>
<td>72</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>AUC‡</td>
<td>15.1</td>
<td>12.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HBG1</td>
<td>6.8</td>
<td>5.8</td>
<td>0.002</td>
</tr>
</tbody>
</table>
JDRF CGM Study: Similar HbA1c Reductions Observed in Pump and MDI Users*

<table>
<thead>
<tr>
<th></th>
<th>Pump (n=43)</th>
<th>MDI (n=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline HbA1c, %</td>
<td>7.5 ± 0.4</td>
<td>7.9 ± 0.6</td>
</tr>
<tr>
<td>Change from baseline, %</td>
<td>−0.5 ± 0.5</td>
<td>−0.5 ± 0.8</td>
</tr>
</tbody>
</table>

*Among patients ≥25 years old.
Insulin Delivery Method

More patients use MDI…

% of Patients

Pump 28%
MDI 72%

but most CGM users are on pumps.

% of CGM Users

Pump 85%
MDI 15%

- Wisconsin Research and Education Network 2013
Adult CGM Users Have Lower HbA1c Regardless of Insulin Delivery Method (T1D Exchange)

DIaMonD Study

- Multiple Daily Injections and Continuous Glucose Monitoring in Diabetes
Study Design – Phase 1

Participants: T1DM MDI users not at HbA1c goal

ADA 2016
24 Participating Centers Across the US
## Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All Patients (N=158)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age</td>
<td>48 yrs</td>
</tr>
<tr>
<td>Mean T1D duration</td>
<td>21 yrs</td>
</tr>
<tr>
<td>Mean SMBG</td>
<td>4/day</td>
</tr>
<tr>
<td>Mean BMI</td>
<td>28</td>
</tr>
<tr>
<td>≥ 1 severe hypo in past 12 mo</td>
<td>11%</td>
</tr>
<tr>
<td>≥ 1 DKA in past 12 mo</td>
<td>1%</td>
</tr>
</tbody>
</table>
Baseline Characteristics

Age
- <45 yrs: 35%
- 45-<60 yrs: 44%
- ≥60 yrs: 22%

Gender
- Female: 56%
- Male: 44%
# Baseline Characteristics

**Race**
- White non-Hispanic: 84%
- Black non-Hispanic: 6%
- Hispanic or Latino: 9%
- More than one race: 1%
- Unknown/not reported: 1%

**Education**
- <Bachelor’s Degree: 44%
- Bachelor’s Degree: 39%
- Post-Bachelor’s Degree: 13%
- Unknown: 4%
## Baseline HbA1c by Treatment Group

<table>
<thead>
<tr>
<th></th>
<th>CGM (n=105)</th>
<th>Usual Care (n=53)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean HbA1c</td>
<td>8.6%</td>
<td>8.6%</td>
</tr>
<tr>
<td>HbA1c Range</td>
<td>7.5%-9.9%</td>
<td>7.5%-9.9%</td>
</tr>
<tr>
<td>HbA1c 7.5%-8.4%</td>
<td>45%</td>
<td>45%</td>
</tr>
<tr>
<td>HbA1c 8.5%-9.9%</td>
<td>55%</td>
<td>55%</td>
</tr>
</tbody>
</table>
Visit Completion

Randomization N=158

CGM (n=105)
- Completed: 104
- Completed: 100
- Completed: 100
- Completed: 105

Usual Care (n=53)
- Completed: 51
- Completed: 52
- Completed: 51
- Completed: 52

Week 1 Visit
- Completed: 104

Week 2 Call
- Completed: 100

Week 3 Call
- Completed: 100

Week 4 Visit
- Completed: 105

Week 12 Visit
- Completed: 103

Week 24 Visit
- Completed: 103 98%

1 Dropped

1 Dropped

Completed: 53 100%
CGM Usage ≥6 Days/Week

% of Participants

Week 4: 94
Week 12: 96
Week 24: 89

≥6 days/wk
0 days/wk
SMBG Frequency

Mean No. of Daily SMBG Checks

<table>
<thead>
<tr>
<th></th>
<th>CGM</th>
<th>Usual care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>5.1</td>
<td>5.1</td>
</tr>
<tr>
<td>Week 12</td>
<td>3.7</td>
<td>4.8</td>
</tr>
<tr>
<td>Week 24</td>
<td>3.6</td>
<td>4.6</td>
</tr>
</tbody>
</table>

*P < .001*
HbA1c Treatment Group Differences

Mean HbA1c, %

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 12</th>
<th>Week 24</th>
</tr>
</thead>
<tbody>
<tr>
<td>CGM</td>
<td>8.6%</td>
<td>7.6%</td>
<td>7.7%</td>
</tr>
<tr>
<td>Usual care</td>
<td>8.6%</td>
<td>8.1%</td>
<td>8.2%</td>
</tr>
</tbody>
</table>

Adjusted mean difference (95% CI) -0.5% (-0.7% to -0.3%) -0.6% (-0.8% to -0.3%)
HbA1c Secondary Outcomes
Week 24

- HbA1c < 7.0%: 18% (P = 0.02)
- HbA1c < 7.5%: 38% (P < 0.001)
- HbA1c Reduction of ≥ 1%: 52% (P < 0.001)
- HbA1c < 7.0% or Reduction of ≥ 1%: 52% (P < 0.001)

Compared to usual care (4% for each category, no statistical significance indicated).
CGM-Measured Time-in-Range 70-180 mg/dL

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Minutes/Day</td>
<td>662</td>
<td>734</td>
</tr>
</tbody>
</table>

P = 0.006

- CGM
- Usual care
In Summary:

Use of CMG in adult with type 1 diabetes is efficacious in improving glucose control both pump and MDI users.
Objectives:

- Use of CGM in glucose control in T1DM
- Use of CGM and hypoglycemia in T1DM
- Use of CGM in T2DM
Percent Values ≤50 mg/dL (2.8 mmol/L) Age ≥25 Years

JDRF CGM Study Group, 2008.
A1C <7.0% and No Severe Hypoglycemia

JDRF CGM Study Group, 2008.
Severe Hypoglycemia Incidence Rate per 100 Person-Years in Adults

Overall Baseline A1C ≥7.0% Baseline A1C <7.0%

0–6 months 7–12 months

JDRF CGM Study Group, Diabetes Care 2010
CGM-Measured Hypoglycemia

- **<70 mg/dL**
  - Baseline: CGM 76, Usual Care 90
  - Week 24: CGM 75, Usual Care 53
  - **P = 0.006**

- **<60 mg/dL**
  - Baseline: CGM 44, Usual Care 56
  - Week 24: CGM 26, Usual Care 43
  - **P = 0.01**

- **<50 mg/dL**
  - Baseline: CGM 22, Usual Care 29
  - Week 24: CGM 11, Usual Care 23
  - **P = 0.005**
Percentage of Time Glucose Levels <60 mg/dL

Daytime (6 AM to 10 PM)

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time &lt;60 mg/dL, %</td>
<td>1.7%</td>
<td>1.6%</td>
</tr>
</tbody>
</table>

Nighttime (10 PM to 6 AM)

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time &lt;60 mg/dL, %</td>
<td>4.0%</td>
<td>2.4%</td>
</tr>
</tbody>
</table>

$P = .02$

$P = .005$
In Summary:

Use of CMG in adult with T1dM reduce risk of severe hypoglycemia and time spent in hypoglycemic range, especially overnight in both pump and MDI users.
Objectives:

- Use of CGM in glucose control in T1DM
- Use of CGM and hypoglycemia in T1DM
- Use of CGM in T2DM
Short- and Long-term Effects of Real-Time Continuous Glucose Monitoring in Patients with Type 2 Diabetes

Vigersky, Diabetes Care 2012
High Incidence of Hypoglycemia in Stable Insulin-Treated Type 2 Diabetes Mellitus: Continuous Glucose Monitoring vs. Self-Monitored Blood Glucose. Observational Prospective Study

Casanueva et al. Canadian Journal of Diabetes 2015
Use of novel flash glucose-sensing technology to optimize glucose control in individuals with type 2 diabetes on intensive insulin therapy

- Study design:
  - T2D on intensive insulin treatment
  - FreeStyle Libre vs SMBG
  - SMBG ≥4/d
  - Baseline A1c ≥8.8%
  - Followed over 6 month
Use of novel flash glucose-sensing technology to optimize glucose control in individuals with type 2 diabetes on intensive insulin therapy

- **Results:**
  - A1c reduction was similar at 0.3% in both groups at 6 month
  - CGM users spent 30 minutes fewer per day <70 mg/dl (p<0.001),
  - 13 minutes fewer per day <55 mg/dl (p=0.001),
  - 8.5 minutes fewer per day <45 mg/dl (p=0.001)=75% reduction
  - All measures of nocturnal hypoglycemia were also significantly lower
In Summary:

- CGM improves glucose control in T2D subject not on insulin
- CGM reduce risk of hypoglycemia in T2D on intensive insulin therapy
Conclusion:

- CGM use is recommended in adults with T1DM who have A1C levels above target and well-controlled T1DM who are willing and able to use these devices on a nearly daily basis.

- Short-term, intermittent RT-CGM use is suggested T2DM (not on prandial insulin) who have A1C levels 7% and are willing and able to use the device.

*JCEM* 2016 in press; AACE Feb 2016
Thank you