Using CGM for Non-Diabetic Endocrine Issues – A Useful Weapon?

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PENS Conference
May 16, 2018

• I have no conflicts of interest to disclose
Objectives

• Define hypoglycemia & glycemic variability
• Identify non-diabetes endocrine disorders causing glycemic variability
• Review components of CGM
• Review the role/use of CGM for non-diabetes related glycemic variability management
• Identify benefits and challenges of CGM in non-diabetes settings

Pediatric Hypoglycemia

• Hypoglycemia—<70mg/dL
• Whipple’s triad
  – Symptoms
  – Low blood glucose
  – Relief after treatment

Glycemic Variability

• Glycemic variability (GV), which refers to swings in blood glucose levels, has a broader meaning because it alludes to blood glucose oscillations that occur throughout the day, including hypoglycemic periods and postprandial increases, as well as blood glucose fluctuations that occur at the same time on different days. 
  Suh & Kim, JH (2015)
NON-DIABETES ENDOCRINE DISORDERS CAUSING GLYCEMIC VARIABILITY

Glycogen Storage Disease

- Glycogen Storage Disease (GSD)
  - Impaired production of glucose from gluconeogenesis and glycogenolysis
  - Defects in glucose 6-phosphate enzyme system [liver, kidney, intestines] (1a)
  - Defect of the G6P transporter, G6P translocase [leukocytes] (1b)
  - Kasapkara, Demir, Hasanoglu, & Turner (2013)

GSD

- Clinical Manifestations
  - Failure to thrive
  - Hepatomegaly
  - Severe fasting hypoglycemia
  - Hyperlipidemia
  - Hyperuricemia
  - Kasapkara, Demir, Hasanoglu, & Turner (2013)
Gastric Surgery

- Dumping syndrome as a complication of fundoplication surgery is characterized by severe post prandial hypoglycemia (PPH).
- PPH
  - occurs 1-3 hours after meal
  - Occurred in 24%
  

ACTH & GH Deficiency

- “Impaired synthesis and release of ACTH from the pituitary gland, or impaired release or action of hypothalamic corticotropin-releasing factor, eventually leading to blunted cortisol secretion”.

  Cambiaso, Schiaffini, Postrillo, Carnes, Ubertini, Crea & Cappa (2013)

Kidney Transplant

- New-onset diabetes after transplantation (NODAT) and impaired glucose tolerance (IGT) are common complications following solid organ transplant.
- Incidence/prevalence
  - Occurs in 2-53% of all solid organ transplants
  - Incidence 3 yrs post transplant 7.1%
  - Prevalence of 13% in children

  Pasti, Andrea, Prokid, Memenza, Polo, Delporte, Bajey, Reznik, (2013)
Kidney Transplant

- Causes for glucose issues:
  - Increased insulin resistance
  - Increased insulin clearance
  - Deficient insulin production

- Risk factors:
  - Age > 10 years
  - Steroid use
  - Obesity
  - Diseased donor graft
  - Use of tacrolimus
  - Cytomegalovirus

USE OF CGM IN ASSESSING GLYCEMIC VARIABILITY

- Sensor composed of microelectrode coated with glucose oxidase beneath biocompatible membrane, which converts glucose in the interstitial fluid into an electronic signal proportional to amount of glucose present.
- Provides BG readings every 5 minutes (288 readings/day)
- Lag time = 5 minutes
- Requires finger stick BG at least q12 hours for calibration
- Accurate for BG 40-400mg/dL

What is CGM?
CGM at a Glance

- GlucoWatch – 1999
- Current devices
  - DexCom G4 Platinum
  - Medtronic Guardian REAL-Time
  - MiniMed Paradigm REAL-Time
  - MiniMed 530G with Enlite
  - FreeStyle Libre Pro
- Two categories:
  - Professional: Medtronic iPro2, FreeStyle Libre or DexCom G4 Platinum Professional
  - Personal

CGM Categories and Devices

- Receiver:
  - Displays sensor BG readings (range up to 6 meters)
- Sensor:
  - Measures glucose levels q 5 minutes
- Transmitter:
  - Wirelessly sends BG readings to receiver

DexCom G4
Medtronic ipro2

Libre Pro Sensor

Site Selection and Size of Transmitter
Detection of hyper/hypoglycemia

CGM provides a "movie" of BG readings as opposed to a "snapshot". (Grunberger, 2015)

**Benefits of CGM** (DiaMonD Study, ADA 2016)

<table>
<thead>
<tr>
<th>Results</th>
<th>CGM</th>
<th>Preglucose</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1C Reduction</td>
<td>0.09% improvement</td>
<td>0.4% improvement</td>
</tr>
<tr>
<td>Time spent &lt; 70 mg/dL</td>
<td>36% improvement in 23 minutes per day</td>
<td>22% improvement in 10 minutes per day</td>
</tr>
<tr>
<td>Time spent 70-180 mg/dL</td>
<td>56% improvement in 1-11 minutes per day</td>
<td>23% improvement in 7 minutes per day</td>
</tr>
<tr>
<td>Time spent &gt;=180 mg/dL</td>
<td>50% improvement in 0-6 minutes per day</td>
<td>2% worse in 1-5 minutes per day</td>
</tr>
<tr>
<td>Glycemic variability</td>
<td>4% reduction</td>
<td>No change</td>
</tr>
</tbody>
</table>

**RESULTS FROM RECENT STUDIES**

**USE OF CGM FOR NON-DIABETES GLYCEMIC VARIABILITY MANAGEMENT**
Hypoglycemia in Glycogen Storage Disease

- Aim: determine magnitude & significance of hypoglycemia and evaluate efficacy of revised dietary treatment
- Subjects: 16 children with GSD, mean age 7.59 +/- 4.12 years
- Results: significant hypoglycemia detected & duration of events as well as liver size were reduced
- Conclusions: CGM is a useful tool for assessment and long term management of hypoglycemia in GSD

Post prandial Hypoglycemia after Gastric Surgery

- Aim: to evaluate pathogenesis of PPH by examining post meal BG & insulin responses
- Subjects: 6 children with known PPH age 6-18 years
- Results: No significant hypoglycemia detected
- Conclusion:

Nocturnal Hypoglycemia in ACTH & GH Deficiency

- Aim: to evaluate use of CGM to identify nocturnal hypoglycemia and optimize hydrocortisone therapy.
- Subjects: 11 patients with ACTH & GH deficiency, mean age 5.3 years
- Results: hypoglycemia lasting 30-155 minutes was detected
- Conclusions: CGM is useful in detecting nocturnal asymptomatic hypoglycemia and assisting in dosing of hydrocortisone.
**Glucose Variability Following Kidney Transplant**

- **Aim:** to monitor BG levels following renal transplant using CGM
- **Subjects:** 20 patients, mean age 16 years
- **Results:** 5% w/NODAT and 30% w/IGT
- **Conclusions:** IGT has prevalence of approximately 30% in renal transplant patients. CGM may be useful in detecting post-transplant hyperglycemia.

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**BENEFITS AND CHALLENGES OF CGM USE**

**Benefits**
- Ability to detect impending hypoglycemia
- More BG information with fewer finger sticks
- Ability to remotely monitor (overnight, daycare, preschool, etc.)

**Challenges**
- Limited body surface for sensor placement
- Difficulty with adherence
- Pain with insertion

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**Parent/Caregiver Perspective (Young Children)**

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- Ability to detect impending hypoglycemia
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- Pain with insertion
Patient Perspective (Adolescents)

Benefits
• Increased/constant availability of readings
• Increased self-care

Challenges
• Overwhelming amount of data
• Unwilling to have parents follow remotely

Forlenza, Argento & Laffel, 2017

Take Home Message

• CGM can be useful in assessing glycemic variability beyond diabetes management

• CGM use in the pediatric population is safe and efficacious

References

THANK YOU!!