Advances in Diabetes Care Technologies

1979

Puzzling Ailment
Hope for juvenile diabetics

Placing insulin-pump needle under skin

2015

THRESH SUSPEND
Introduction

- Roughly 20% to 30% of patients with T1DM and fewer than 1% of insulin-treated patients with T2DM use an insulin pump.
- In 2007, the U.S. FDA estimated that the number of patients with T1DM using CSII was ~375,000.
- By 2050, up to one-third of U.S. residents may have T2DM; many of these individuals will be insulin-requiring.
- Therefore, more clinicians must develop a comprehensive understanding of insulin pumps and other diabetes medical devices.

T1DM = type 1 diabetes mellitus
T2DM = type 2 diabetes mellitus
FDA = U.S. Food and Drug Administration
CSII = continuous subcutaneous insulin infusion
Why We Do It
Better Control Reduces Complications

76% Risk Reduction
59% Risk Reduction
39% Risk Reduction
54% Risk Reduction
64% Risk Reduction

- 55.0
- 29.8
- 23.9
- 5.1
- 13.4

13.0
29.8
23.9
16.4
5.0

Retinopathy Progression
Laser Rx¹
Micro-albuminuria²
Albuminuria²
Clinical Neuropathy³

Cumulative Incidence (%)

2. DCCT Research Group, Kidney Int. 1995;47:1703-1720
Insulin Pumps Reduce Incidence of Diabetic Retinopathy vs MDI in Patients with Similar A1C Levels

- Study followed incidence of DR in 1604 adolescents with T1DM ages 12-20 over 20 years
- Incidence of DR declined by 38% as more patients were transitioned to MDI and CSII vs twice-daily injections
- A1Cs were identical in all cohorts, suggesting that reduction in GV influenced progression towards DR

CSII = continuous subcutaneous insulin infusion; DR = diabetic retinopathy; GV = glycemic variability; MDI = multiple daily injection; T1DM = type 1 diabetes mellitus; T2DM = type 2 diabetes mellitus.

Downie et al. Diabetes Care. 2011;34:2368-73
Improved Control: Decreased Hypoglycemia


CSII = continuous subcutaneous insulin infusion
Type 1 Diabetes

• A 2010 Cochrane review compared the use of CSII vs. MDI insulin regimens
  – 23 randomized studies involving 976 patients with T1DM
  – A significant difference was documented in A1C response, favoring CSII
  – CSII users showed greater improvements in quality of life measures
  – Severe hypoglycemia appeared to be reduced in CSII users

CSII = continuous subcutaneous insulin infusion; MDI = multiple daily injection; T1DM = type 1 diabetes mellitus

Basal Bolus Regimen with Glargine and Lispro

Insulin Effect

- Lispro
- Glargine

B L S HS B
Continuous Subcutaneous Insulin Infusion

Insulin Effect

Bolus
Basal

B L S HS B
Pharmacokinetics of CSII vs MDI

• Uses only immediate acting insulin
  – More predictable absorption

• Uses one injection site
  – Reduces variations in absorption

• Eliminates most of the subcutaneous insulin depot

• Closest match with physiologic needs
Advantages of Pump Therapy

• Improved blood glucose control
  – Improved A1C levels
  – Decreased hypoglycemia and hyperglycemia
  – Delay in incidence and progression of complications

• Precise dosage delivery

• Improved control for pre-conception and pregnancy

• Management of dawn phenomenon

• Increased flexibility in lifestyle

• Improved control during exercise

• Improved gastroparesis management

AACE/ACE Insulin Pump Management Task Force Consensus Statement. 2014
# Insulin Pumps on the Market

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<tbody>
<tr>
<td>Roche Health Solutions</td>
<td>Medtronic MiniMed</td>
<td>Medtronic MiniMed</td>
<td>Medtronic MiniMed</td>
<td>Animas</td>
<td>Dexcom</td>
<td>Valeritas, Inc.</td>
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</table>
Indications and Contraindications for CSII

**Indications:**
- Failure to achieve targeted A1C with MDI
- Hypoglycemia unawareness
- Athletes and patients who incorporate exercise into daily routines
- Persistent fasting hyperglycemia ("Dawn phenomena")
- Pregnancy
- Frequent travel
- Shift workers
- Poorly adherent, DKA-prone adolescent patients
- Insulin-resistant patients
- Females in whom glycemic control is lost during menstruation

**Contraindications:**
- Uncontrolled psychiatric disorders (until corrected or stabilized)
- History of lack of adherence to prescribed treatment regimen (pumps do NOT cure diabetes)
  - However, some insulin is better than no insulin. Some non-adherent patients may do better on a pump than MDI
- Lack of financial ability to pay for pump and supplies

DKA = diabetic ketoacidosis; MDI = multiple daily injection

Unger J. Diabetes Management in Primary Care. 2nd Ed. Lippincott. 2012.
Vintage Blood Glucose Meters

DextroStix (Ames), 1965

Reflomat (Boehringer-Mannheim), 1974
Traditional Glucose Meters on the Market
Mobile Phone-based Glucose Testing

- Some systems allow glucose-checking and data management generated directly from a phone.

- Other systems pair glucose meter with a mobile phone for a data sync.
Glucose Meters for the Blind

Glucose meters that have:

- Speech output
- Capillary traction
- No need for test strip coding
Glucose Monitoring Apps

Several apps for both Android and iOS are available to facilitate data tracking, trending, and communication with providers.

- BG Monitor
- BlueLoop
- OnTrack Diabetes

- Some studies suggest positive results using mobile phone-based interventions for diabetes control
- Apps specific for the needs of minorities with diabetes are needed
Are There Needle-free Glucose Meters?

- **Glucowatch Biographer:**
  - Released in 2002
  - Needed 3 hour ‘warm-up period’
  - Skin irritation
  - Discontinued by manufacturer

**In development:**
- **Temporary sensor “tattoo”**
  - Tested in 7 patients at UCSD
- **“Smart” Contact Lens Project**
When Finger-stick Testing Is More Reliable Than A1C Measurement

• Several anemias due to low Hb values (eg, sickle cell, hemolytic)
• CKD on erythropoetin-analogue therapies
• Pregnancy
• Splenectomy
• Some ethnic groups

CKD=chronic kidney disease

Accuracy of Glucose Meters

- **FDA guidance (non-binding):**
  - +/- 15% for OTC self-monitoring devices
  - +/- 10% for clinical use meters

  **Acceptable to measure only as low as 50mg/dL for self-monitoring devices**

- **2013 ISO Standards:**
  95% of blood glucose results
  - Below 100 mg/dL need to be within 15 mg/dL of reference
  - Above 100 mg/dL need to be within 15% of reference

  **At least 30% of glucose meters do not meet ISO 2013 standards!**
Does Monitoring Lead To Better Outcomes?

• SMBG provides treatment guidance and feedback to patients with type 1 and 2 diabetes
• Several studies suggest a relationship between more frequent monitoring and improved glucose control
• Increased frequency of monitoring reduces hypoglycemia in patients with type 1 and 2 diabetes
• There are ongoing trials on the effect of SMBG on provider and patient outcomes in non-insulin patients with type 2 diabetes

SMBG = Self-Monitoring of Blood Glucose

What is Continuous Glucose Monitoring?

- CGM consists of a sensor inserted through the skin that measures interstitial glucose levels every 5 minutes
  - Average 8- to 10 minute lag behind BG values
  - MARD between CGM sensor glucose readings and venous plasma BG measurements averages at about 10%-12%, but can vary by up to 20%

- Useful for identifying BG trends

- As yet not a replacement for SMBG
  - Currently available personal systems still require 2-4 BG checks daily
  - Should not use the values to calculate insulin dosing

BG = blood glucose; CGM = continuous glucose monitoring; MARD = mean absolute relative difference; SMBG = self-monitoring of blood glucose

Continuous Sensors Currently Available in the U.S.
Continuous Sensors Currently Available in the U.S. (continued)

Coming Soon...
(Spring 2017)
Types of CGM

• **Professional**
  – Masked, retrospective
  – Reviewed in clinic typically by physician; can also be reviewed by ARNP, PA

• **Personal**
  – Monitor shows real-time glucose levels with trends

ARNP = advanced registered nurse practitioner; PA = physician assistant.

Benefits of Continuous Glucose Monitoring?

- **A1C lowering with less hypoglycemia**
  - 0.5% to 0.8% for adults with type 1 diabetes

- **Hypoglycemia warning for individuals with hypoglycemia unawareness**

Drawbacks To CGM

• Can be overwhelming for some patients
• Alarms can be annoying, lead to discontinuation
• Cost—not covered by Medicaid or Medicare
• Comfort
• Accuracy
• Frustration—the analog insulin we call “fast” can be slow to kick in!

Who Can Benefit From Continuous Glucose Monitoring?

• **Patients with type 1 diabetes**
  – With A1C <7.0% to maintain control with lower risk of hypoglycemia
  – With A1C above goal, if used on a daily basis
  – Severe hypoglycemia unawareness

• **Intermittent, retrospective CGM useful in certain situations**
  – Concern for nocturnal hypoglycemia
  – Dawn phenomena
  – Post-prandial hyperglycemia

AACE/ACE Consensus Statement on Continuous Glucose Monitoring. 2016.;
Continuous Glucose Monitor Use in Clinical Practice – Real-world Experience

- Retrospective review of university-based clinical practice patient base
- Review of 30 months of clinical encounters
- Severe hypoglycemia defined as needing assistance to treat
- Continuous CGM use vs intermittent (defined as <2/3 of time)
- All patients on pump therapy

# Real-world Experience: Reductions in Hypoglycemia

## Results of CGM Use

<table>
<thead>
<tr>
<th></th>
<th>Baseline A1C</th>
<th>A1C on CGM</th>
<th>Rate of Severe Hypoglycemia at Baseline*</th>
<th>Rate of Severe Hypoglycemia on CGM*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Continuous Users</strong></td>
<td>7.5%</td>
<td>7.2% (P&lt;0.05)</td>
<td>66.4</td>
<td>22.3 (OR 0.34; CI 0.19-0.59)</td>
</tr>
<tr>
<td><strong>Intermittent Users</strong></td>
<td>7.7%</td>
<td>7.3% (P&lt;0.05)</td>
<td>44.8</td>
<td>29.0 (OR 0.65; CI 0.24-1.78)</td>
</tr>
<tr>
<td><strong>All Users</strong></td>
<td>7.6%</td>
<td>7.2% (P&lt;0.05)</td>
<td>58.9</td>
<td>23.6 (OR 0.40; CI 0.24-0.65)</td>
</tr>
</tbody>
</table>

* Per 100 patient-years

CGM = continuous glucose monitoring; CI = confidence interval; OR = odds ratio

Continuous Glucose Monitoring Data

Overall 24-hour blood glucose patterns over multiple days are displayed:

- Look for overlap patterns at same time of day
- Look for hypoglycemia – frequency, time of day
- Check timing of insulin injections, meal choice effect
- Check for effect of increased physical activity

Interpret the Data To...

• **Look for patterns**
  – Highs and lows occurring at the same time each day

• **Fix lows first**

• **Basal insulin**
  – Start overnight, then progress through the day

• **Bolus insulin**
  – Look at glucose response to meals and to correction doses

• **Now practice!**
Sensor Linked To Pump

- Glucose trends visible on pump or PDA
- Pump suspend feature available (one system)
- Integration of insulin delivery and real-time glucose trends

PDA = personal digital assistant
Pump + CGM patterns

- Adds information regarding blood glucose trends between checks, after boluses, and overnight

CGM = continuous glucose monitoring