Tried and True Tips and
New Advances in Diabetes
San Diego Pump Club, Oct 10, 2016
John Walsh PA, CDTC

Tried and True Tips

How Basal Rate Change Affects BG

<table>
<thead>
<tr>
<th>Change in Basal Rate</th>
<th>Total units over 6 hrs</th>
<th>Total units over 8 hrs</th>
<th>Total units over 24 hrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>+/- 0.025 u/hr</td>
<td>+/- 0.15 u</td>
<td>+/- 0.2 u</td>
<td>+/- 0.6 u</td>
</tr>
<tr>
<td>+/- 0.05 u/hr</td>
<td>0.3 u</td>
<td>0.4 u</td>
<td>1.2 u</td>
</tr>
<tr>
<td>+/- 0.1 u/hr</td>
<td>0.6 u</td>
<td>0.8 u</td>
<td>2.4 u</td>
</tr>
</tbody>
</table>

Basal adjustments of 0.025 and 0.1 u/hr equal 0.6 and 2.4 units over the entire day. For a glucose that falls or rises slightly during a basal test, a basal change of 0.025 or 0.05 u/hr (or 0.2 and 0.4 units over 8 hours) may fix this.

Avg. rise or fall in BG/hr = Change in Basal x CorrF

Example:
+/- 0.05 x 40 mg/dL/unit = 2 mg/dL average rise or fall in BG per hour

Plus a small additive effect over longer time periods.

Common BG Patterns & Fixes

A) most common pattern (raise afternoon & evening basal, lower supper CarbF),
B) frequent lows (lower TDD by 5-10% & find new settings),
C) high and flat most of the time (raise basal rates),
D) frequent highs with post-meal rise (raise basal rates & lower CarbF/ICR),
E) highs or lows at particular times of the day (raise or lower prior basal rate or CarbF in previous meal),
F) post-meal spiking (bolus earlier, lower CarbF),
G) over-correction of highs (do not increase recommended bolus, raise the CorrF/ISF, set DIA to 4.5 hrs or longer),
H) over-treatment of lows (stop lows, don’t overtreat). Several patterns often coexist. Adjust basals or boluses most responsible.

The Right Number of Carbs for a Low

Treat lows with:

Grams of carb = Wt(lbs)/10 + (BOB* x CarbF)

Example: Amy’s BG = 52 mg/dL, with 2u of BOB (CarbF = 10 g/u)
- 120 lbs, she needs 12 grams for the low glucose
- Plus 2u BOB x 10 gram/u = 20 grams to cover her BOB
- Amy needs 12 g + 20 g = 32 grams for this low

* DIA time must be accurate
Don’t shorten DIA to “fix” control problems!

Glucose Levels Before and After Infusion Set Changes

Average glucose levels for 6-hour intervals before and after infusion set change in 398 pumps (>20 set changes/pump).

Can We Extend Infusion Set Use?

Most pump wearers use an infusion set for 2-3 days.

BD Flowsmart for Silent Occlusions

- BD researchers suspected infusion pressure might increase with a new intradermal sets, but not with standard sets.
- Silent occlusions were seen in both.
- Silent occlusions lasting >30 min. were more common during first 4 hours of set use.
- FlowSmart dual port set may eliminate some unexplained hypoglycemia.

Steel versus Teflon Sets

Steel:
- No kinking
- Fewer silent occlusions
- Manual insertion
- Less failure
- Better biocompatibility, less back pressure
- Easier to train
- 28-30 gauge

Teflon:
- More selections
- Straight or slanted
- Manual or automatic insertion
- Less needle phobia
- 25 gauge (27-gauge introducer needle)
- FlowSmart: 28 gauge (30-gauge introducer)

Safe Site Setup

Steel sets have a flatter profile and can be secured as shown.

Alternate setup would be to place IV300 or Tegaderm adhesive over needle and line, and remove adhesive from connector to let it dangle.

Super Bolus = Faster Action

Use temp basal reduction to shift part of the next 2 to 3.5 hrs of basal insulin into a bolus.

Better readings and low risk of lows.

Done by user, not the pump.

Will Hypoglycemia Soon Disappear?

- Hypo-Minimizer pumps (now available).
- CGMs can predict BG (hypo or hyper events) 30 min. ahead (but don’t yet inform wearers).
- Soon-to-arrive insulins peak faster and don’t stick around as long: FIAsp and Biochaperone® Inspro.
- Hypo-Manager software that recommends a bolus or the exact carbs needed for each glucose.
A Thing of the Past?

Trendline vs Trend Arrow and BOB

79 mg/dL (4.4 mmol/L) with down arrow and trend line

79 mg/dL with down arrow and BOB – A CGM screen with BOB gives more information!!

Should Predicted BG Replace Trend Arrow?

- Recommended dose adjustments vs actual adjustments in survey of 222 pumpers for a 220 mg/dL glucose
- WIDE VARIATION in individual adjustments
- Trend arrows are imprecise and a poor guide for dosing
- A 30 min predicted BG would be a far better guide

New – Faster Insulin Aspart (FIAsp)

New insulin is slightly faster than Novolog with avg BG 13 mg/dL lower at 1 hr, 22 mg/dL lower at 2 hrs, with A1c reduction of 0.15%.

New – Biochaperone-lispro

A protein molecule is added to lispro (Humalog), to speed up insulin action.

Remote Software Upgrades

Tandem t:slim X2 received FDA approval to upgrade software remotely, similar to phones and PCs.
Lets existing hardware be rapidly upgraded for artificial pancreas and other features.
Get a new pump in seconds, not years! Available Oct, 2016

www.tandemdiabetes.com
Connectivity – the Next Big Wave

- Bluetooth LE connects to:
  - Pumps, smart insulin pens, meters, CGMs, activity monitors (FitBit, JawBone, MotoActv, BodyMedia)
  - Cell phones
  - Integrates data from different devices
  - Tidepool, Glooko, MySugr DiaSend
  - Telecommunication companies and the FDA are on board!
- BLE-4 range = 150 ft
- BLE-5 range = 500 ft

Bolus Calculators

BCs – How Many and How Good?

- A review of 42 BC apps that existed in 2014 showed that only one fulfilled all the desired criteria and less than one third showed how they calculated a bolus recommendation
- Only 8 BCs are FDA approved in insulin pumps (5), BG meters (2), and a Bluetooth insulin pen
- Today, over 84 BC apps exist

Analysis of 42 Phone Apps

- “The majority of insulin dose calculator apps provide no protection against, and may actively contribute to, incorrect or inappropriate recommendations that put current users at risk of both catastrophic overdose and more subtle harms resulting from suboptimal glucose control.”
- It is time to standardize BCs for safety.

Bolus Calculator Settings

- Pump Settings Often Wrong
  - Only 40% of CarbFs in 400 pumps had an expected value
  - People prefer “magic” numbers – 5, 10, 15, and 20 g/unit.
  - Formulas provide accurate settings – far better than WAG!

Carb Factors Found in 400 Pumps

- Don’t use “magic” numbers!

Case Study – Decision Support Software

JD is a 20 yo DM1 college student referred to clinic. WI 180 lb (84 kg), TDD = 80 u, avg BG = 194 mg/dL (10.8 mmol/L).

- Basal rate: 1.8 u/hr
- CarbF 10 gr
- CorrF 45 mg/dL (2.5 mmol/L)
- DIA 4 hrs
- A1c 8.4%

Decision Support for Settings

Enter Your Information:

Settings For Target BG

From adjusted TDD to reach target
- TDD: 85.5 u/day
- Avg Basal: 1.708 u/hr
- Carb Factor: 0.5 grs per unit
- Correction Factor: 22.9 mg/dL per unit
- Relative Insulin Sensitivity: 51%

Results of Decision Support

Suggestions

JD’s Pump Settings:

<table>
<thead>
<tr>
<th>Original</th>
<th>New</th>
</tr>
</thead>
<tbody>
<tr>
<td>TDD</td>
<td>85 u</td>
</tr>
<tr>
<td>Basal rate:</td>
<td>1.8 u/hr</td>
</tr>
<tr>
<td>CarbF</td>
<td>10</td>
</tr>
<tr>
<td>CorrF</td>
<td>45</td>
</tr>
<tr>
<td>DIA</td>
<td>4 hr</td>
</tr>
<tr>
<td>A1c</td>
<td>8.4%</td>
</tr>
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</table>

www.opensourcediabetes.org

CGM Advances

DIAMOND Study – Do CGMs Work?

Randomized Trial of 158 adult MDI users with T1D
- Randomly assigned to CGM (Dexcom™ G4 Platinum CGM System® with software 305) or Usual Care
- Mean baseline HbA1c 8.6% in both groups
- Primary outcome HbA1c at 24 weeks completed by 98%
- CGM usage in month 6: >6 days/wk in 93%

Results

CGMs
- Reduced HbA1c by 0.6% compared with control group
  - consistent reduction in sub-groups: baseline HbA1c, age, education
  - Increased Time-in-Range
  - Reduced Biochemical Hypoglycemia
  - Reduced Glycemic Variability

HbA1c Treatment Group Differences

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 24</th>
</tr>
</thead>
<tbody>
<tr>
<td>CGM</td>
<td>8.6%</td>
<td>7.4%</td>
</tr>
<tr>
<td>Usual care</td>
<td>8.2%</td>
<td>7.6%</td>
</tr>
</tbody>
</table>

Adjusted mean difference (95% CI) -0.5% (-0.7% to -0.3%) -0.4% (-0.6% to -0.3%)
HbA1c Secondary Outcomes – Week 24

Percentage of Time Glucose Levels <60 mg/dL

Inplanted Sensionics CGM
- Implanted fluorescent CGM
- Lasts up to 90 days
- Implanted in doctor's office
- MARD ~11.4%
- Vibe alerts when low or high
- Adhesive base for transmitter replaced daily
- Bluetooth LE communication to cell phone
- Rechargeable battery

Inplanted Glysense CGM
- Implanted dual-enzyme CGM
- Lasts 12 mos or more
- Implanted in surgeon's office
- MARD?
- Vibe alerts when low or high
- Proprietary receiver
- Rechargeable battery

glysens.com

Artificial Pancreas Projects

The AP Pathway
- Basal Threshold Suspend
- Reactive
- Predictive
- Control to Range
- Control to Target
- Bi-hormonal

fda.gov/GuidanceDocuments/UCM259305.pdf
Steps to a Better Artificial Pancreas

- More accurate CGM devices
- More rapid insulins
- Further refinements in control algorithm (exercise, stress, illness, etc)
- Improved user interface and connectivity
- More reliable longer-lasting infusion sets
- Stable glucagon
- Dual-hormone systems

Early AP System Approved

- Medtronic 670G
- Available April or May 2017
- Treat to target, proportional integral derivative
- Enlite 3 MARD: 10.3%
- No Bluetooth
- For meal boluses:
  - Manually bolus well before eating
  - Eat mostly low-GI foods
  - Or give larger meal bolus (risk reduced, essentially a Super Bolus)

670G Pivitol Study

- A1c lowered by 0.5% from 7.4% to 6.9% in 124 people
- 44% reduction in time under 70 mg/dl
- 40% decline in time under 50 mg/dl
- 11% decline over 180 mg/dl with 8% more time-in-range (71-180 mg/dl)

Bigfoot Biomedical

Asante pump + Dexcom CGM + Smart Phone
Milpitas, CA; available late 2017 or 2018
www.bigfootbiomedical.com

Univ of Virginia Type Zero

Univ of Virginia Diabetes Assist.
Tandem Diabetes or CellNovo pump,
Dexcom G5 or G6
$12.7 mil NIH study
To market late 2017 or 2018
Treat to target, model predictive control

Bionic Pancreas

Developed at Boston Univ.
by Ed Damiano, PhD.
Insulin only – late 2017
Insulin + glucagon -2018
Treat to target, model predictive control
Crowdsource funding at wefunder.com/betabionics/ or sites.bu.edu/bionicpancreas/donate/

http://www.artificialpancreas.org/
Do It Yourself with OpenAPS

Visit www.openAPS.org – Assembly is required!!!
www.nightscoutfoundation.org

Viacyte Encapsulated Pancreas

Full pancreas response – insulin, glucagon, somatostatin.

- Pec-Direct – Direct vascularization of cells, immune suppression required.

www.viacyte.com

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