Management Tips – Insulin Regulation

CDA Diabetes Educator Section
Calgary DES Chapter
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Disclosure
- Book sales – all pump companies
- Instructor – J&J Diabetes Institute
- Advisory Board Member – Agamatrix, Medingo, Tandem Diabetes, Unomedical
- Royalties – Roche, Abbott
- Consultant – Bayer, Roche, Tandem Diabetes
- Speakers Bureau – Smiths Medical, Tandem Diabetes
- Sub-Investigator – Glaxo Smith Kline, Animus, Sanofi-Aventis, Bayer, Biodel, Dexcom, Novo Nordisk
- Web Advertising – Sanofi-Aventis, Sooil, Medtronic, Animas, Accu-Chek, Abbott, etc.

Outline
- Insulin Overview
- Insulin Dosing
- Find TDD, Basals, Boluses
- Change Doses Carefully
- Insulin Tips

Terms To Know
- TDD – total daily dose of insulin (all basals and boluses)
- Basal – background insulin released slowly through the day
- Bolus – a quick release of insulin
  - Carb bolus – covers carbs
  - Correction bolus – lowers high readings that arise from deficits in basal rates or carb boluses
- Bolus On Board (BOB) – bolus insulin still active from recent boluses, aka Unused Insulin Rule for MDI
- Duration of Insulin Action (DIA) – time that a bolus will lower the BG – used to measure BOB

What Insulin Does
- Aids glucose entry into cells for energy storage & heat product.
- Enhances protein synthesis and cell growth
- Enhances fat storage and reduces fat mobilization
- Inhibits glucose release from liver and from glycogen stores in muscle
- Inhibits glucose formation from amino acids

Impact Of Insulin Deficit
- Glucose elevation from decreased cell uptake (loss of energy)
- Glucose loss in urine (weight loss)
- Excess glucose produced by liver & released from muscle glycogen (increased urination and thirst)
- Muscle used for energy (weight loss)
- Excess fat used for energy --> ketones (DKA)
- Complications (multiple mechanisms)
Who Needs Insulin?
- All Type 1s
- Type 2s not in control with meds, diet, exercise
- Women with gestational diabetes if MNT or oral agents don’t work
- With parenteral nutrition
- Acute MI (keep BG under 110mg/dl)
- SI/P pancreatitis, pancreatectomy, or other loss of beta-cell function

Insulin Varieties – Injection

Rapid / Short
- Apidra, Humalog, Novolog / Regular
  - Covers meal intake
  - Used for elevated BG

Intermediate / Long acting
- NPH / Lantus, Levemir
  - Used for basal insulin needs
  - Not intended to cover meals

Even Long-Acting Insulins Peak
- NPH has a pronounced peak that can be useful for a Dawn Phenomenon, etc.
- Lantus has an action time of 18 to 26 hours – those with shorter action times get more peaking
- Lantus and Levemir may not sustain activity for full 24 hrs

Somoygi Phenomenon
Body’s counter-regulatory response to hypo causes a followup high
- Too little insulin at bedtime
- Excess food at bedtime
- Skipping evening LA insulin

Take Home: the more injections the flatter the action

Dawn Phenomenon
Growth hormone rises in early morning and causes high fasting BGs
- Too little insulin at bedtime
- Excess food at bedtime
- Skipped evening LA insulin

Treatment:
- Increase or don’t forget night dose
- Less bedtime snack or low GI food
- Give NPH before supper

Insulin Varieties – Injection

Mixed – rapid and intermediate insulins
- 50:50 (50% NPH and 50% insulin Lyspro)
- 75:25 (75% NPH and 25% insulin Lyspro)
- 70:30 mixtures (70% NPH, 30% insulin aspart)
- 70:30 (70% NPH, 30% Regular)
Insulin Pens

- Convenience, flexibility, accuracy
- Used for over 90% of insulin delivery in most European countries and Japan
- Rising use in U.S. but still only about 20%

Mixed Insulin Pens

Best for:
- Older person with regular meal and activity patterns
- Diminished vision
- Trouble with dexterity
- Just starting insulin therapy

Mixed insulin pens
- 50/50
- 70/30

Insulin Varieties – Pumps

Uses only Rapid (Novolog, Humalog, Apidra) or Short (U100 or U500 Regular) insulin

- Basal: delivered all day to cover the normal needs of the body when not eating
- Carb Bolus: On demand insulin to cover food
- Correction Bolus: extra insulin to cover hyperglycemia

Goals For Insulin Use

Clinical:
- Eliminate hyperglycemia and ketosis
- Prevent chronic complications

Control:
- HbA1c < 6.5% or 7%
- Pre-meal BG 80-120 mg/dl (4.4-6.7 mmol/L)
- 2 hr PP < 160 mg/dl (8.9 mmol/L)
- Bed time SMBG 100-140 mg/dl (5.6-7.8 mmol/L)
- Mean blood glucose level 120-160 mg/dl (6.7-8.9 mmol/L)

Other:
- Maintain desirable weight
- Maintain normal growth and sexual development
- Maintain mental and social well-being

Goals For Insulin Use

Set Clear Goals For Self-Management

- Set glucose and A1c targets
- Bring records to clinic
- Look for patterns
- Adjust basals and boluses from glucose patterns

Thanks Bill King!
Insulin Education
- Address fears and myths
- Review insulin action
- Demonstrate insulin administration
- Site rotation
- Storage
- Needle disposal
- Glucose monitoring
- Handling hyper and hypoglycemia
- Referrals

Barriers To Insulin Use
DAWN Study by NovoNordisk and International Diabetes Federation sought psychosocial issues related to poor outcomes.

Results:
- 50% report insulin use means they failed to manage their disease
- Only 27% believe insulin would help them better manage their DM
- 43% of MDs postpone meds and insulin until absolutely essential


Other Barriers
- Fear of needles
- Fear of the unknown
- Cost
- Inconvenience
- Weight gain
- Using insulin, especially multiple injections, means you have “bad” diabetes and it’s getting worse

Type 2 Is Progressive
- Type 2 diabetes is progressive with a gradual loss of insulin production
- Insulin is usually required for treatment
- Progression is obvious even in clinical trials focused on control, like the UKPDS.


Why Insulin Causes Weight Gain
- Less glycosuria with improved control
  - Reduce calorie intake at start if avg BG > 10 mmol
- Anabolic effect of insulin
- Over–treatment of hypoglycemia
  - Avoid lows with accurate dosing
- Defensive eating to avoid hypoglycemia
  - Avoid lows with accurate dosing
- Consider metformin, Symlin, GLP-1 agonist

How To Avoid Weight Gain
- If starting average BG is above 180 mg/dl, current diet intake needs to be reduced to avoid gaining weight
- Avoid foods that raise the glucose
- Set and test insulin doses to avoid hypoglycemia and the need to overeat
- Advise that only 15 to 20 grams of carb are usually needed for lows and it takes 20 minutes to feel better
- Treat lows with glucose tabs or other fast carbs
Insulin Dosing

Starting Insulin – Type 2

Dose timing for start depends on whether highest readings occur fasting or after meals

High fasting BGs
- Start with once daily long-acting insulin and continue oral agents (except sulfonylureas)

High postmeal BGs
- Start with meal coverage for largest meal of day and continue oral agents (except sulfonylureas)

Insulin Dose – How Much?

Consider weight, age, level of insulin resistance, and lifestyle

- Starting dose (adults):
  - Starting dose: 0.5-1.0 units/kg/day
  - Average dose 0.8-1.2 u/kg

- Starting dose (children):
  - Starting pre-puberty 0.2-1.0 u/kg
  - Average dose 0.5-1.0 u/kg
  - Starting puberty 0.3-1.2 u/kg
  - Average dose 0.8-1.5 u/kg

Insulin Dose – How Much?

Determine glucose target range

Start with small dose based on weight

Gradually learn to adjust both rapid and long insulin doses from glucose readings

Individualize

Realize that gradual increase in doses is normal due to gradual loss of beta cells

Begin Self-Management Right Away

<table>
<thead>
<tr>
<th>Rapid Insulin Adjustments</th>
<th>Current Units</th>
<th>Loses at next meal</th>
<th>Highs at next meal</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 10u / meal</td>
<td>- 1u</td>
<td>+ 1u</td>
<td></td>
</tr>
<tr>
<td>11-19u / meal</td>
<td>- 2u</td>
<td>+ 2u</td>
<td></td>
</tr>
<tr>
<td>&gt; 20u / meal</td>
<td>- 3u</td>
<td>+ 3u</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Long Acting Insulin Adjustments</th>
<th>Avg FBG</th>
<th>Add</th>
<th>Every</th>
<th>Till Below</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 180 mg/dl</td>
<td>+ 4u</td>
<td>3 days</td>
<td>180 mg/dl x 2 days</td>
<td></td>
</tr>
<tr>
<td>&gt; 140 mg/dl</td>
<td>+ 2 u</td>
<td>3 days</td>
<td>140 mg/dl x 2 days</td>
<td></td>
</tr>
<tr>
<td>&gt; 90 mg/dl</td>
<td>+ 1 u</td>
<td>3 days</td>
<td>90 mg/dl x 2 days</td>
<td></td>
</tr>
</tbody>
</table>

Lantus / Levemir

- Are clear solutions
- Don’t confuse with rapid insulin !!!
- Don’t use in pump
- Don’t give IV (it precipitates)
- Don’t mix with a rapid insulin (pH rises and changes absorption)
Long-Acting (LA) Insulin Tips
- Flatten LA insulin action (& avoid insulin gaps)
  - Give NPH (mixed) TID
  - Give Lantus or Levimir BID
- Best measures of LA insulin dose
  - Breakfast BG
  - Presence of lows 4 or less hrs before breakfast

Causes For Lows
- "Stacking" insulin
- Eating fewer carbs than expected
- Insulin-to-carbohydrate ratio number is too low
- Excessive basal insulin
- Delayed eating after taking mealtime insulin
- Increased activity or exercise
- Delayed stomach (gastric) emptying
- Fear of complications
- Taking the wrong insulin by mistake
- Drinking alcohol
- Increased insulin sensitivity
- "Covering" snacks for exercise or lows with insulin
- Use of an incretin based therapy or an amylin analog

Causes For Highs
- Incorrect carb counting
- "Out-eating" the insulin
- Insufficient insulin for carbs
- Needle phobia
- Inadequate insulin dose
- Inactivity
- Rebound from low glucose
- Weight gain
- Delayed stomach (gastric) emptying
- Increased in stress hormones
- Under-insulinization
- Bad (spoiled) insulin
- Incorrect insulin injection technique
  - because of fear of lows
  - Not checking glucose levels

Prevent Progression Of Type 2
- GLP-1s
- Glitazones
- Insulin

See Dr. Ralph D’Fronzo’s presentation at the 2008 ADA meeting.

Beta Cell Preservation
In Type 2 diabetes, MANY studies show long-term benefit after short-term use of insulin pumps to normalize glucose levels. Benefits may arise from:
- Decreased glucose toxicity
- Decreased oxidative damage
- Increase in 1st phase insulin release

In new onset Type 1 diabetes, the honeymoon phase also appears to be extended with early and aggressive insulin use.


The Elephant In The Room
"The elephant in the room, cannot be seen or acknowledged."

Insulin
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Insulin
Behaviors That Lower The A1c

Approximate A1c lowering effect:
- Carb counting – 0.6%
- Bolusing on accurate carb count – 0.3%
- Record BGs, carbs, doses, & activity – 0.5%
  - Especially when BG records are used to adjust doses
- Frequent monitoring – 0.5-2.0%
- Continuous monitoring – 0.6%
- Frequent bolusing – 0.5-2.0%

Records Help

- Immediate feedback
- Speeds corrections
- Lowers A1c ~ 0.5%
- Gives “big picture” that speeds problem identification and correction

Steps To Insulin Start

1. Find an optimal TDD
2. Set and test basal rates/doses
3. Set and test carb boluses/doses
4. Set and test correction boluses/doses
5. Enjoy good control, or return to #1

Find An Optimal TDD

Find the current TDD

1. Lower it: Is the TDD too low or too high?
   - For frequent lows
   - For highs AND lows IF lows come first
2. Raise it:
   - For a high A1c
   - For a high average BG on meter

Keep basal and carb bolus totals balanced

Reset TDD For Major Problems

- Lower the TDD for frequent lows
- Raise the TDD for high A1c or meter average

Chase BG with TDD.

The Optimal TDD Table

If frequent highs are main problem, increase current TDD based on A1c or 14-day meter average as shown in table

If frequent lows are main problem, lower current TDD by 5%, 10%, or so
Get Basals & Boluses From TDD

To dose insulin well:
- Select starting basal rate and correction factor from Optimal TDD
- Select starting carb factor from Optimal TDD and weight

To get a fresh start for major control problems, do this over again

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Easy Basal Rates & Correction Factors

<table>
<thead>
<tr>
<th>Starting TDD</th>
<th>Optimal Basal</th>
<th>Average Basal</th>
<th>Correlation Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>10 mg/dl</td>
<td>20 mg/dl</td>
<td>50 mg/dl</td>
</tr>
<tr>
<td>Medium</td>
<td>20 mg/dl</td>
<td>40 mg/dl</td>
<td>100 mg/dl</td>
</tr>
<tr>
<td>High</td>
<td>40 mg/dl</td>
<td>80 mg/dl</td>
<td>200 mg/dl</td>
</tr>
</tbody>
</table>

Corr. Factor = 2000/TDD*

*The better the control, the higher the correction factor

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Easy (Safe) Basal Adjustments

<table>
<thead>
<tr>
<th>Basal Adjustment</th>
<th>Value (per lb)</th>
<th>Value (per kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 lbs</td>
<td>-0.5 x TDD</td>
<td>-0.5 x TDD</td>
</tr>
<tr>
<td>10 lbs</td>
<td>-1.0 x TDD</td>
<td>-1.0 x TDD</td>
</tr>
<tr>
<td>15 lbs</td>
<td>-1.5 x TDD</td>
<td>-1.5 x TDD</td>
</tr>
</tbody>
</table>

These basal adjustments provide about 1/3 to 1/2 of the full basal adjustment that may be required.

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Easy And Accurate Carb Factors

| Carb Factor = 10.4 g/u x Wt (kgs) x TDD x 1.8
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>130</td>
<td>3.5</td>
</tr>
<tr>
<td>120</td>
<td>3.3</td>
</tr>
<tr>
<td>110</td>
<td>3.1</td>
</tr>
<tr>
<td>100</td>
<td>2.9</td>
</tr>
<tr>
<td>90</td>
<td>2.7</td>
</tr>
<tr>
<td>80</td>
<td>2.5</td>
</tr>
<tr>
<td>70</td>
<td>2.3</td>
</tr>
<tr>
<td>60</td>
<td>2.1</td>
</tr>
<tr>
<td>50</td>
<td>1.9</td>
</tr>
<tr>
<td>40</td>
<td>1.7</td>
</tr>
<tr>
<td>30</td>
<td>1.5</td>
</tr>
</tbody>
</table>

Carb factor = an average carb factor times the individual's insulin sensitivity

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Carb Factors Found In Pumps

Carb factors in 183 complaint-free pumps from US and Canada user in good control (avg BG 145 mg/dl, 4.45 tests/day over 73.9 days)*

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Carb Factors Actually Used For Meals

Pump users in good control adapt despite incorrect Carb Factors in pump*

Unfortunately, to do this, they must change carb count or ignore the bolus recommendation from their pump*
Verify Carb & Correction Factors

Carb factor = avg. carb factor times insulin sensitivity:

Carb Factor = \( \frac{10.4 \text{ g/u}}{\text{TDD}} \times \text{Weight (lb)} \)

Check: Does result match current Carb Factor?

Correction factor closely estimated with the 2000 Rule:

Correction Factor = \( \frac{2000}{\text{TDD}} \)

Check: Does Corr Factor \( \times \) TDD = 1800 to 2400?

Change Doses Carefully

Know BG Impact Before Changing Doses

How a dose change affects glucose:

- A 5% change in the TDD changes the glucose about 25 mg/dl through the day.
- 5% TDD increase (i.e., from 40 to 42 u/day) = fall in avg BG from 175 to 150 mg/dl.
- A 5% change in the carb factor changes the glucose about 20 mg/dl* per meal.
- 5% = an increase from 10 to 10.5 g/u or 6 to 6.3 g/u, for a postprandial BG fall from 160 to 140 mg/dl.

Impact on BG per meal*

<table>
<thead>
<tr>
<th>Carbohydrate</th>
<th>Carbohydrate/meal</th>
<th>Carb/day</th>
<th>Carb/unit</th>
<th>Impact on BG per meal</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/10 to 1/9</td>
<td>160 to 190 (≈40 u)</td>
<td>220 g</td>
<td>73 g</td>
<td>+ 1.44 u (CorrF = 60)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- 73.3 mg/dl</td>
</tr>
<tr>
<td>1/7 to 1/6</td>
<td>240 to 280 (≈100 u)</td>
<td>330 g</td>
<td>110 g</td>
<td>+ 3.62 u (CorrF = 20)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- 72.4 mg/dl</td>
</tr>
</tbody>
</table>

* Varies by weight and insulin sensitivity

How Change In Carb Factor Affects BG

Table shows avg fall in glucose after each meal when carb factor is reduced from 10 to 9 g/u and from 5 to 4 g/u (for approx. wt & TDD).

Remember

Raise the carb factor for frequent postmeal lows
Lower the carb factor for frequent postmeal highs

AFTER checking basal / carb bolus balance

Insulin Tips
Most TDDs Need To Rise

The average glucose on a pump is 196 mg/dl*
Most pump users need a higher TDD

Roughly 75% of Type 1s and 50% of Type 2s are above loose BG target goal of less than 7%

* Cozmo Data Analysis 2 Study (CDA2)

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Stop Lows First
Better control, less variability

- Release of stress hormones raises glucose for hours
- Avoids overtreatment and skipped boluses
- Preventing lows improves accuracy of all doses
- Lows may be treated with no test (NO RECORD! – ASK!)

Lower the TDD!!!

* Low overtreated? Count the wrappers and bolus right away for excess carbs

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Control Guides

TDD (nl insulin sensitivity) = \( \frac{\text{Wt (kg)}}{1.8} \)

Individual’s Insulin Resistance = \( \frac{\text{TDD} \times 1.8}{\text{Wt (kg)}} \)

1 g Carb raises BG = \(~8 \text{ mg/dl} \) \(~4 \text{ mg/dl} \) \(~2 \text{ mg/dl} \)

Max allowable carbs in a meal\(^1\) = \( \text{Wt (lb)} \times 0.38 \)


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Sweet Spots For Control

- Night basal – BGs middle of the night to breakfast
- Day basal – start with average of night basals
- Carb bolus doses – premeal to premeal BGs
- Correction bolus doses
  - Should bring high BG to target 4-5 hrs later with no lows
  - If highs are frequent, raise basal or carb bolus doses
  - % of TDD devoted to correction boluses should be less than 8%

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Questions That Guide Treatment

Look at recent glucose results for trends and patterns:

- Does the blood sugar fall or rise overnight? (basal)
- Is the blood sugar controlled after most meals? (carb factor/bolus)
- When a high blood sugar is treated, does the blood sugar end up at target 4-5 hours later without going low? (correction factor/bolus)
- Are lows often followed by highs? (overtreatment)
- What percent of TDD is used for corrections?
Bolus Early – Stop PP Spikes

Figure shows rapid insulin injected 0, 30, or 60 min before a meal.
Normal glucose and insulin profiles shown in the shaded areas.
Best glucose profile when bolus given 60 min ahead, but this is too risky to recommend!!!

Evaluate Glucose Exposure And Variability

Exposure or Average = A1C avg. BG from meter

Variability or Swing = Standard deviation or GlycoMark test

One day – BG checks every 30-60 min.

Insulin / Carb Bolus Balance

When the glucose goes high or low, a quick insulin analysis helps determine the cause.

If BG 4-5 hrs later is:

High

Low

Starting BG

In Target

High, low, normal

Well balanced

Too Little Insulin **

Too Many Carbs **

Too Much Insulin **

Too Few Carbs **

** Pump can show exact insulin and carb excess or deficit

Check The 5 Hour Insulin Window

When a low or high reading occurs, check:

- how much basal and
- how much bolus
- was active over the previous 5 hours

Lows – usually caused by the larger insulin amount
Highs – usually caused by the smaller insulin amount

Assume that boluses work for 5 hours!

Examples – 5 Hour Window

# 1
BG = 54 mg/dl (3 mmol)
at 1:00 am
In previous 5 hours:

Boluses = 9.2 u
Basal = 4.6 u

# 2
BG = 252 mg/dl (14 mmol)
at 4:30 pm
In previous 5 hours:

Boluses = 6.5 u
Basal = 2.4 u

For Answers To Your Questions

Available at www.diabetesnet.com or 800-988-4772