Insulins

Dr. Roland Halil, PharmD, ACPR, BScPharm, BSc(Hon)
Clinical Pharmacist, Bruyère Academic Family Health Team
Assistant Professor, Dept of Family Medicine, Uottawa
rhalil@bruyere.org
Twitter: @RolandHalil

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<table>
<thead>
<tr>
<th>Insulin Product*</th>
<th>Administration</th>
<th>Onset†</th>
<th>Peak†</th>
<th>Duration†</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rapid-acting analogues</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Humalog (insulin lispro)</td>
<td>0-15 minutes before meals (ideally); may be given up to 20 minutes after start of meals</td>
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<td>5-10 minutes before meals</td>
<td>10-15 min</td>
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</tr>
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<td><strong>Short-acting</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Humulin R Novolin ge Toronto Hypurin Regular (pork)</td>
<td>30-45 minutes before meals</td>
<td>0.5-1 h</td>
<td>2-4 h</td>
<td>5-8 h</td>
</tr>
<tr>
<td><strong>Intermediate-acting</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Humulin N Novolin ge NPH Hypurin NPH (pork)</td>
<td>Usually once or twice daily</td>
<td>1-3 h</td>
<td>5-8 h</td>
<td>Up to 18 h</td>
</tr>
<tr>
<td><strong>Long-acting analogues</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lantus (insulin glargine)</td>
<td>Once daily (usually at bedtime)</td>
<td>1.5 h</td>
<td>None</td>
<td>24 h</td>
</tr>
<tr>
<td>Levenir (insulin detemir)</td>
<td>Once or twice daily</td>
<td>1-2 h</td>
<td>6-8 h</td>
<td>Up to 24 h</td>
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<td><strong>Premixed</strong></td>
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* Humulin L, Humulin U, Iletin Regular, Iletin NPH, Iletin Lente, Novolin ge Lente, and Novolin ge Ultralente have been discontinued.
† Onset, peak and duration values are estimates only.
Insulins

• **Long = Basal**
  – NPH (Humulin N®/Novolin NPH®)
  – Glargine
    • 100u/mL – Lantus®
    • 100u/mL - Basaglar® (biosimilar)
    • 300u/mL - Toujeo®
  – Detemir (Levemir®)
  – Degludec (Trusiba®)

• **Short = Prandial**
  – Short
    • Regular (Humulin R)
    • Novolin ge Toronto
  – Rapid
    • Lispro (Humalog®)
    • Aspart (NovoRapid®)
    • Glulisine (Apidra®)

• **Premixed**
  • 30/70 (and 10/90, 20/80, 40/60, 50/50)
  • Humalog Mix-25, NovoMix-30 etc

Which to choose?
Clinical Priorities
Basic Concepts

- Hyperglycemia = Chronic Hypoglycemia = Acute
  - So, go after **Hypo’s** first!

- Fed: 6h/24h = 25%
- Fasting: 18h/24h = 75%
  - So, go after **Fastings** first!

- AM affects PM & HS
  - So, go after **AM** first!

1. ?Any hypo’s?- fix ‘em!
then,
2. FBS AM
3. FBS Noon
4. FBS PM
5. FBS HS
then,
6. 2h PPG AM
7. 2h PPG Noon
8. 2h PPG PM
## Insulins

### Long – Basal
- NPH / Humulin N
- Glargine (Lantus/Basaglar® & Toujeo®)
  - (Basaglar® = a Lantus® biosimilar)
- Detemir (Levemir®)
- Degludec (Trusiba®)

### Short – Prandial
- Short
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### Premixed
- 30/70 (and 10/90, 20/80, 40/60, 50/50)  (R + NPH)
- Humalog Mix-25, NovoMix-30  (Rapid + NPH)

Now, which to choose?
Rational Prescribing

• Four priorities of Rational Prescribing:

  1. Benefit
  2. Harm
  3. Cost
  4. Convenience
Long – Basal Insulins

**Benefit:**
- NPH = glargine = detemir = degludec = NPH
- Equivalent
  - Morbidity benefits, A1c lowering effect
- Despite the marketing:
  - Kinetics don’t affect overall **efficacy**:
    - Slowest absorption: Thigh (best for basal insulins)
    - Fastest absorption: Abdomen (best for prandial insulins)
- *Lots* of glargine is injected BID
- NPH *can* be used QHS for many (esp. CKD)
Long – Basal Insulins

**Harm:**
- All: Hypoglycemia
- NPH:
  - Peak effect at ~ 8hrs (4-10hrs)
    - Greater risk of hypoglycemia vs glargine
    - Small difference
- Insulin analogues:
  - Glargine / Detemir:
    - Increased breast cancer risk?
      » Glargine: 1.4 fold higher risk vs NPH
      » Detemir – more research needed
  - Degludec: too new - unknown

Long – Basal Insulins

• **Cost:**
  – **All:** covered under ODB
    • **N.B.** No Rx *required* for any insulins – all Schedule II (behind the counter)
  – NPH: ~ $59
  – Glargine (Lantus®: ~ $114) (Basaglar®: ~ $87)
  – Detemir (Levemir®): ~ $114
  – Degludec ~ $155

• **Convenience:**
  – All sc injections, via penfills
  – All QD – BID

Prices from Rxfiles.ca Feb 2019
Bottom Line – **Basal Insulins**

- All equivalent
- Choose therapy based on cost (NPH)
  - For the very small proportion suffering from hypoglycemia due to the peak effect of NPH or lamenting BID dosing, consider glargine or detemir.
Starting Basal Insulin

• **Fancy Way:**
  – calculate unit/kg dose = 0.1 - 0.2u/kg/day sc
    • Risk hypoglycemia on first dose – lose your patient’s buy-in forever.

• **Primary Care Method:**
  – Initiate 5u or 10u qhs sc
  – Titrate by **1-2u q3-4d until AM FBS = 4 - 7 mmol/L**
    • 10% titrations
      – If dose = 30’s – increase by 3 units
      – If dose = 40’s – increase by 4 units etc.
    • Alternative: 1 unit every day till AM FBS = 4-7 mmol/L
Rx

1. NPH
   - Sig: 10u qhs sc or ud
   - M: 1 box penfills
   - Repeat x 12

2. Needle tips – 28G - 6mm
   - Sig: ud
   - M: 1 box
   - r x 12

• N.B. (Please teach pt pen technique)
## Insulins

### Long = Basal
- NPH / Humulin N
- Glargine (Lantus/Basaglar® & Toujeo®)
- Detemir (Levemir®)
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- Short
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### Premixed
- 30/70 (and 10/90, 20/80, 40/60, 50/50)  (R + NPH)
- Humalog Mix-25, NovoMix-30  (Rapid + NPH)
Short – Prandial Insulins

- **Efficacy**
  - Equivalent reduction in morbidity, HgbA1c

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Short – Prandial Insulins

- **Toxicity**
  - Hypoglycemia
  - Rapid insulins better reflect physiological effect of pancreatic insulin (vs Regular insulin)

- More important in CKD (=longer insulin t½)
Short – Prandial Insulins

• **Cost**
  – All covered under ODB
    • Regular (R) / Toronto ~ $40
    • NovoRapid (aspart) ~ $56
    • Humalog (lispro) ~ $55
    • Apidra (glulisine) ~ $48

• **Convenience**
  – All injected with meals
  – Regular insulin injected 30-45 min **before** meal
  – Rapid insulin can be **with** meal
    • Reduced risk of hypo if patient injects, then forgets to eat
    • Easier / more intuitive Carb Counting
Bottom Line – Prandial Insulins

• All equivalent
• Choose therapy based on cost / familiarity
  – Rapid insulins reflect pancreatic insulin release better than [R]/Toronto.
  – The worse the CrCL, the more important this fact becomes.
Starting Prandial Insulin

• **Fancy Way:**
  – Total dose: 0.5u/kg
  – 40% of total dose - basal insulin qHS
  – 20% of total dose TID with meals (60%) – prandial insulin 15-30 min before meals
    • Eg. 80kg pt – 0.5u/kg = 16u basal (40%); 8u TID (20% x 3 = 60%)

• **Primary Care Method:**
  – Start 5u sc with meals
    • Titrate AM to HS to target
      – Monitor 2h PPG
    • Start injection TID or only single meal as required
      – If poor control: inj TID sc; If mediocre control: inj qAM sc
    • Still aim for ~ 2/3rds split (40% basal / 60% prandial)
Insulins

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Pre-mixed Insulins

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<th>Efficacy</th>
<th>Toxicity</th>
<th>Cost (Rapids)</th>
<th>Cost (Regular 30/70)</th>
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- **NovoMix-30 = Humalog Mix25 (equivalent)**
- **Efficacy**
  - All ~ 30% short / 70% long
- **Toxicity**
  - Hypoglycemia (less with Rapid vs Regular insulin as CrCL drops)
- **Cost:** ~$53 (Rapids) ~$40 (Regular 30/70)
- **Convenience** ~ Rapids can be injected with/after meal
Starting Pre-mixed Insulins

- **Fancy Way:**
  - Estimate total starting daily dose
    - (0.3-0.6 units/kg)
  - Divide daily dose:
    - 2/3 before breakfast; 1/3 before supper

- **Primary Care Method:**
  - From scratch: Start 5-10u QD-BID and titrate
  - From other insulins: Calculate approximate amount of basal and prandial units and divide 2/3rd - 1/3rd AM and PM
Pearls

• Insulin is 2\textsuperscript{nd} line after metformin when a1c is far from target (No need to save it for last!)
• Better than adding a 3\textsuperscript{rd} PO drug
  – Better efficacy, lower toxicity, better studied
• Improve buy-in from patient:
  – “Natural” supplement
  – Only BID glucochecking at alternating times required:
    1. Pre-Breakfast + Post-Breakfast,
    2. Pre-Breakfast + Pre-Lunch,
    3. Pre-Breakfast + Post-Lunch,
    4. Pre-Breakfast + Pre-Supper,
    5. Pre-Breakfast + Post-Supper,
    6. Pre-Breakfast + Pre-Bedtime
    7. Repeat
Pearls (cont’d)

• D/C secretagogues after starting insulin to reduce risk of hypo’s.
  – Eg. Sulfonylureas, meglitinides
  – Black box warning against combo with glitizones! (Actos, Avandia)
Glucose monitoring

NPH 45u QHS
Glucose monitoring

NPH 33u BID
Glucose monitoring

NPH 40u QHS + Glulisine 12u TID cf
Glucose monitoring

Novomix30 – 20u BID
Questions?

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