Type 2 Diabetes Mellitus
Insulin Therapy
2012

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Insulin Preparations

<table>
<thead>
<tr>
<th>Insulin</th>
<th>Onset</th>
<th>Peak</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lispro</td>
<td>5-15 min</td>
<td>1-2 hr</td>
<td>3-5 hr</td>
</tr>
<tr>
<td>Aspart</td>
<td>10-20 min</td>
<td>1-3 hr</td>
<td>3-5 hr</td>
</tr>
<tr>
<td>Glulisine 5-20 min</td>
<td>1-3 hr</td>
<td>3-5 hr</td>
<td></td>
</tr>
<tr>
<td>Glargine</td>
<td>1-4 hr</td>
<td>none</td>
<td>22-24 hr</td>
</tr>
<tr>
<td>Detemir</td>
<td>1-4 hr</td>
<td>none</td>
<td>20-24 hr</td>
</tr>
<tr>
<td>Regular   30-60 min</td>
<td>2-4 hr</td>
<td>6-8 hr</td>
<td></td>
</tr>
<tr>
<td>NPH</td>
<td>1-4 hr</td>
<td>8-12 hr</td>
<td>12-20 hr</td>
</tr>
</tbody>
</table>

Insulin Pharmacokinetics

- Lispro / Aspart / Glulisine
- Glargine / Detemir
- Regular
- NPH

Insulin Injection
- 4-5 hr
- 6-8 hr
- 12-16 hr
- 24 hr
- 1-2 hr
- 2-4 hr
- 8-12 hr
- +/- 24 hr
- +/- Peakless
HPI: 56 y.o. woman returns for DM2 management.
PMH: DM2 x 10 yr
DM Meds: Metformin 2000 mg, Pioglitazone 45 mg, Sitagliptin 100 mg
PE: Ht 5’8” Wt 248 lb BP 124/80 P 80
Lab: FBG 192-218 A1C 9.2%
Lifestyle modification is again emphasized.
What therapy would you now recommend?
A. Add a Sulfonylurea
B. Add a GLP-1 Agonist/Analog
C. Start Basal Insulin Therapy
D. Start Basal Bolus Insulin Therapy
E. Bariatric Surgery

Case History
- A1C > 11%
- FBG > 250 mg/dl
- Random BG > 300 mg/dl
- Ketonuria / Ketonemia
- Weight Loss, Polydipsia, Polyuria
- A1C > 7% on 1-3 Oral Agents

Basal Insulin Therapy
Indications
- A1C > 11%
- FBG > 250 mg/dl
- Random BG > 300 mg/dl
- Ketonuria / Ketonemia
- Weight Loss, Polydipsia, Polyuria
- A1C > 7% on 1-3 Oral Agents

Basal Insulin Therapy
Background Insulin to Control Fasting Glucose
- Glargine / Detemir / NPH HS

Mean Total Daily Dose (DM2): 0.4-0.5 U/kg or 0.25 U/lb
Discontinue Thiazolidinediones
Continue Metformin (+/-)
Continue Postprandial BG Agents
**Case History**

HPI: 56 y.o. woman returns for DM2 management.
PMH: DM2 x 10 yr
DM Meds: Metformin 2000 mg, Pioglitazone 45 mg, Sitagliptin 100 mg
PE: Ht 5’8” Wt 248 lb BP 124/80 P 80
Lab: FBG 192-218 A1C 9.2%

A decision is made to start basal Insulin. What starting dose do you recommend?
A. 10 units (0.1 U/kg)
B. 20 units (0.2 U/kg)
C. 30 units (0.3 U/kg)
D. 40 units (0.4 U/kg)
E. Other

**Basal Insulin Therapy**

Initiate and Titrate

Agents: Glargine / Detemir / NPH HS

Start: 10-25 U Daily (0.4-0.5 U/kg Mean Requirement)

**Case History**

HPI: 56 y.o. woman returns for DM2 management.
PMH: DM2 x 10 yr
DM Meds: Metformin 2000 mg, Pioglitazone 45 mg, Sitagliptin 100 mg
PE: Ht 5’8” Wt 248 lb BP 124/80 P 80
Lab: FBG 192-218 A1C 9.2%

She is started on 20 units of basal Insulin. How do you recommend that she adjust her insulin?
A. Stay on the current dose and return in 1 month
B. Call the office for a weekly adjustment by staff
C. Increase by 1 U daily until FBG is at goal
D. Increase by 3 U every 3 days until FBG is at goal
E. Other
### Basal Insulin Therapy

**Initiate and Titrate**

**Agents:** Glargine / Detemir / NPH HS  
**Start:** 10-25 U Daily (0.4-0.5 U/kg Mean Requirement)  
**Titrate:** FBG x 3 Days, Calculate Mean FBG

<table>
<thead>
<tr>
<th>3-0-3 Protocol: Mean FBG</th>
<th>Insulin Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 130</td>
<td>↑ 3 U</td>
</tr>
<tr>
<td>80-130</td>
<td>No Δ</td>
</tr>
<tr>
<td>&lt; 80</td>
<td>↓ 3 U</td>
</tr>
</tbody>
</table>

**Summary:** ↑ by 3 U every 3 days until FBG < 130 mg/dl

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### Case History

HPI: 52 y.o. man returns for DM2 management.  
PMH: DM2 x 6 yr  
DM Meds: Metformin 2000 mg, Glipizide 10 mg, Glargine 48 U QAM  
PE: Ht 6'1”  Wt 235 lb  BP 131/78  P 84  
Lab: FBG 96-133  PPBG 194-243  A1C 8.7%  

Lifestyle modification is again emphasized.  
What therapy would you now recommend?  
A. Start Bolus Insulin Therapy  
B. Add a GLP-1 Agonist/Analog  
C. Add a DPP4 Inhibitor  
D. Add Pioglitazone  
E. Start a Very Low Carbohydrate Diet

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### Mealtime Insulin Therapy

**Indications**

- FBG at Goal - but A1C > 7%  
- FBG at Goal - but PPBG > 180 mg/dl
Case History
HPI: 52 y.o. man returns for DM2 management.
PMH: DM2 x 6 yr
DM Meds: Metformin 2000 mg, Glipizide 10 mg,
Glargine 48 U QAM
PE: Ht 6’1” Wt 235 lb BP 131/78 P 84
Lab: FBG 96-133 PPBG 194-243 A1C 8.7%
A decision is made to start bolus Insulin.
What regimen do you recommend?
A. Add Bolus at Largest Meal; Titrate to PPBG Goal
B. Add Bolus at All 3 Meals; Titrate to PPBG Goal
C. Change to Insulin Mix at Breakfast and Dinner
D. Take Insulin After Meals if PPBG is High
E. Start Insulin Pump

Basal Plus Insulin
Basal Insulin Plus Bolus at Largest Meal

- Glargine / Detemir / Pump
- Lispro / Aspart / Glulisine

Start:
4-5 U at Largest Meal

Titrate:
Check Pre-Meal BG and HS BG Daily

↑ 2-3 U Every 2-3 days Until:
2 Hour PPBG < 180 mg/dl or
BG before next meal < 130 mg/dl

Then: Add Bolus at Next Largest Meal if Needed
Then: Add Bolus at Third Meal if Needed
Basal Small Bolus Insulin
Basal Insulin Plus Small Bolus at Each Meal

- Basal Insulin ~ 75%
- Bolus Insulin ~ 25%

Glargine / Detemir / Pump
Lispro / Aspart / Glulisine

Start:
4-5 U at All 3 Meals

Titrate:
Check Pre-Meal BG and HS BG Daily
- 2-3 U Every 2-3 days Until:
  2 Hour PPBG < 180 mg/dl or
  BG before next meal < 130 mg/dl

Agents:
Lispro / Aspart / Glulisine
Basal Small Bolus Insulin
Initiate and Titrate

Progress:
Learn Carbohydrate Counting
Establish: C:I Ratio and Correction Factor (CF)

Basal Bolus Insulin
Basal Insulin Plus Full Bolus with Each Meal

- Basal Insulin ~ 50%
- Bolus Insulin ~ 50%

Glargine / Detemir / Pump
Lispro / Aspart / Glulisine

Mean Total Daily Dose (DM2): 0.8-1.0 U/kg or 0.4 U/lb

Discontinue Metformin (+/-)
Postprandial BG Agents
**Basal Bolus Insulin**
Initiate and Titrate

**Agents:** Lispro / Aspart / Glulisine

**Start:** Calculate TDD
- Add 10% if A1C > 8%
- Add 20% if A1C > 10%
- Divide new TDD into 50% / 50% Basal/Bolus

**Progress:** Learn Carbohydrate Counting
**Establish:** C:I Ratio and Correction Factor (CF)

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**Case History**

**HPI:** 50 y.o. woman returns for DM2 management.

**PMH:** DM2 x 12 yr
**DM Meds:** Metformin 2000 mg, Glargine 26 U QAM, Aspart 8 U TID AC

**PE:** Ht 5’3” Wt 211 lb BP 136/72 P 76

**Lab:** FBG 86-127 PPBG 116-212 A1C 7.2%

PPBG values show significant variability.

What do you now recommend?

A. Eat More Consistent Meals
B. Exercise after Meals if BG High
C. Take Insulin After Meals if PPBG is High
D. Start Insulin Pump
E. Carbohydrate Counting; Use C:I Ratio + CF

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**Basal Bolus Insulin**
Basal Insulin Plus Bolus with Each Meal

<table>
<thead>
<tr>
<th>Basal Insulin – 50%</th>
<th>Glargine / Detemir / Pump</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bolus Insulin – 50%</td>
<td>Lispro / Aspart / Glulisine</td>
</tr>
</tbody>
</table>

Mean Total Daily Dose (DM2): 0.8-1.0 U/kg or 0.4 U/lb

**Bolus Doses Determine By Meal**
Carbohydrate Content and Pre-Meal BG
Flexible Mealtime Bolus Insulin

Bolus Components

C:I Ratio: Gm of Carb covered by 1U Insulin.

CF: Expected BG drop from 1U Insulin.

Add to bolus if pre-meal BG high.

Starting Calculations at UCH (DM2)

C:I = 500/TDD (~10:1)  CF = 1650/TDD (~30:1)

Dose Adjustment Goal

PPBG < 180 mg/dl  or

Next Pre-meal BG < 130 mg/dl  or

PPBG 30-50 mg/dl above pre-meal BG

Case History

HPI: 59 y.o. man returns for DM management. Would like to change to a more reliable insulin regimen.

PMH: DM2 x 14 years

DM Meds: NPH 30 U BID, Reg 15 U BID

PE: Ht 6'0''  Wt 220 lb  BP 132/78  P 80

Lab: FBG 82-213  6 PM 88-283  A1C 7.8%

A decision is made to change to Basal Bolus Insulin.

What starting dose do you recommend?

A. Basal 20 U, Bolus 7 U TID AC

B. Basal 30 U, Bolus 10 U TID AC

C. Basal 45 U, Bolus 15 U TID AC

D. Basal 60 U, Bolus 20 U TID AC

Switching to Basal Bolus Therapy

Total Daily Dose: Current Dose

Wt: 220 lb (100 kg)

<table>
<thead>
<tr>
<th>TDD</th>
<th>Basal Dose ½ TDD</th>
<th>Bolus Dose ½ TDD</th>
</tr>
</thead>
<tbody>
<tr>
<td>CF ~ 1650/TDD</td>
<td>Split Equally TID</td>
<td></td>
</tr>
<tr>
<td>Breakfast Dose 1/6 TDD + CF</td>
<td>Lunch Dose 1/6 TDD + CF</td>
<td>Dinner Dose 1/6 TDD + CF</td>
</tr>
</tbody>
</table>
HPI: 83 y.o. woman returns for DM2 management. Gets confused about types of insulin and misses shots. Lives at home; has predictable meal content and timing.

PMH: DM2 x 24 yr
DM Meds: Glargine 24 U QAM, Lispro 6 U TID AC
PE: Ht 5’7” Wt 154 lb BP 144/88 P 84
Lab: FBG 78-198 PPBG 113-265 Cr 2.3 A1C 8.8%

What therapy would you now recommend?
A. Stop Insulin; Use Only Oral Agents
B. Add Sitagliptin; Reduce Mealtime Insulin
C. Change to Insulin Pump
D. Change to Insulin Mix BID
E. Use Basal Insulin Only

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**Case History**

**70/30 Novolog Mix**
70% Protamine Aspart 30% Aspart

Aspart (30%)

Protamine Aspart (70%)

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**75/25 Humalog Mix**
75% Protamine Lispro 25% Lispro

Lispro (25%)

Protamine Lispro (75%)
**Analog Mix (70/30 or 75/25)**

**Starting Dose if Not on Insulin**
10-12 U (AM) and 8-10 U (PM)

**Starting Dose if Already on Insulin**
90-100% of current Total Daily Dose (TDD)
Give 50-67% TDD (AM) and 33-50% TDD (PM)

**Adjust 1-2 x Weekly:**
- If most BG < 80: ↓ 2 U
- If most BG 80-110: No Change
- If most BG 110-140: ↑ 2 U
- If most BG 140-180: ↑ 4 U
- If most BG > 180: ↑ 6 U

Adjust AM dose to control pre-lunch BG + pre-dinner BG
Adjust PM dose to control HS BG + pre-breakfast BG

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**50/50 Humalog Mix**

50% Protamine Lispro  50% Lispro

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**Case History**

HPI: 49 y.o. man returns for DM2 management.
PMH: DM2 x 13 yr
DM Meds: Detemir 90 U BID, Aspart 60 U TID
PE: Ht 5’9”  Wt 254 lb  BP 144/88  P 84
Lab: FBG 195-305  PPBG 245-410  Cr 2.0  A1C 9.0%

Lifestyle modification is again emphasized.

What therapy would you now recommend?
A. Add Metformin
B. Add a GLP-1 Agonist/Analog
C. Change to U-500 Insulin
D. Add Pioglitazone
E. Bariatric Surgery
HPI: 61 y.o. woman returns for DM2 management. She notes significant lipoatrophy at injection sites.

PMH: DM2 x 11 yr
DM Meds: NPH 20 U BID, Reg 10 U BID
PE: Ht 5’2”  Wt 184 lb  BP 124/70  P 74
Lab: FBG 90-127  PPBG 133-192  A1C 7.2%

What would you advise for her lipoatrophy?
A. Change to Analog Insulin
B. Add Small Amount of Steroid to Insulin
C. Topical Cromolyn
D. Short Course of Systemic Steroids
E. Oral Pentoxifylline

Case History

U-500 Insulin

Less than 200U of insulin prescribed per day
U-100 insulin therapy (NPH, regular, fortis, lente, glargine, exenatide)

200U or greater of insulin

U-500 Insulin

200U-500/day
Twice daily
(Pre-breakfast & pre-dinner)

300U-750U/day
Three times a day
(Pre-breakfast, pre-lunch, pre-dinner)

>1000U/day
Four times a day
(Pre-breakfast, pre-lunch, pre-dinner, bedtime dose: 1/4 less than pre-dinner dose)

>3000U/day
Consider delivery of U-500 Via insulin pump

Insulin Induced Lipoatrophy

- Mast Cell Mediated
- Responds to Topical Cromolyn

Lopez X, Diabetes Care 2008; 31:442-4
Thank You