Managing Insulin Therapy

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Disclosures

- Stuart T. Haines, PharmD, BCPS, BCACP declares that he has been an educational consultant to Sanofi US.
- Joshua J. Neumiller, PharmD, CDE, FASCP declares that he has received research grant support from Amylin, Eli Lilly, Johnson & Johnson, Merck, and Novo Nordisk, and he is an advisor to Janssen Pharmaceuticals and Sanofi US.
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A Little About Us

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- Clinical pharmacy specialist in diabetes management clinic at VAMC with an expanded scope of practice
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Joshua J. Neumiller, PharmD, CDE, FASCP
- Investigator in an academic diabetes research clinic and consultant pharmacist in the home care setting
- Editor-in-Chief of Diabetes Spectrum – a journal of the American Diabetes Association

A Little About You

Do you see a lot of people with diabetes in your practice?

a) Yes, essentially everyone in my practice has diabetes
b) Yes, quite a few
c) No, not recently
d) Not sure … I’d rather not know

Target Audience: Pharmacists
ACPE#: 0202–0000–14–088–H01–P
Activity Type: Application–based
A Little About You

How confident are you in your knowledge and skills related to insulin therapy management?

a) Very confident – I do this stuff every day
b) Confident – but I know my skills could always use some brushing up
c) Not very confident – I could really use more practice
d) Not at all confident – I would need assistance

Learning Objectives

At the completion of this activity, the participant will be able to:

1. Determine when insulin therapy is indicated.
2. Develop a plan to initiate and titrate insulin therapy to achieve a desired goal.
3. Recommend strategies to mitigate the weight gain associated with insulin therapy for a patient who is overweight or obese.
4. Recommend strategies to reduce the risk of severe hypoglycemia for a patient with autonomic failure.

Program Format

› Case–based discussion
  ◦ Authentic cases that are commonly seen in practice
› Audience participation
  ◦ Audience response questions related to decisions you’ll face when managing insulin therapy
  ◦ Post your comments in the chat box

Case #1

SS is a 27–year–old female patient with DM type 1
CC: “I’ve had a few lows, but I’m determined to lower my A1C.”

HPI: Symptoms:
› Frequent low blood glucose (BG) readings
› Reports hypoglycemic symptoms when BG reaches the 30s or 40s
› 2 recent hypoglycemic episodes have required assistance

PMHx:
DM type 1 (1999)

Current Medications:
› Insulin aspart 4 units prior to breakfast and lunch and 6 units prior to dinner
› Insulin detemir 21 units BID
**Insulin Action Profiles**

![Graph showing insulin action profiles: Regular 6-8 hours, NPH 12-20 hours, Insulin glargine; insulin detemir 18-24 hours.]

**Case #1**

**Social and Family Hx:**
- Lives with husband; married 9 months
- No children
- Works 12-hour shifts in a call center – eats meals when call volumes are low
- Occasionally misses mealtime insulin while at work
- Reports financial hardship with insulin prescriptions due to large copays
- Drinks 2–3 alcoholic beverages on occasion

**Vital Signs:**
- BP = 116/70 mm Hg
- Pulse = 70 bpm, regular
- Weight = 139 lb
- Height = 5' 6"
- BMI = 22.4

**Labs (fasting):**
- Glucose = 72 mg/dL
- A1C = 8.1%
- eCrCl = 95 mL/min
- TCHO = 159 mg/dL
- LDL = 90 mg/dL
- HDL = 52 mg/dL
- TG = 86 mg/dL

**Type 1DM: Insulin Initiation**
- Recommended to start conservatively at approx. 0.5 units/kg/day (Range: 0.4–1.0 units/kg/day)

**Audience Response Question**

Given SS’s chief complaint and SMBG data, which of the following would be the most appropriate first step?

- a) Implement insulin:CHO ratio for mealtime insulin dose
- b) Implement correction factor 1 unit of insulin: 50 > 100 mg/dL
- c) Simplify her insulin detemir regimen to 44 units QD
- d) Decrease her insulin detemir dose

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Optimizing Basal – Bolus Strategy

- Must adequately address both basal and prandial needs
- Titrate insulin to individualized needs
- Many factors to consider:
  - Self-care abilities
  - Motivation
  - Preferences
- Careful assessment of basal doses, insulin:CHO ratio, and correction factor (sensitivity)
  - Based on SMBG, CHO intake, and other pertinent considerations

American Diabetes Association. Medical Management of Type 1 Diabetes, 6th Ed.

Audience Response Question

Given SS’s presentation, chief complaint, and history, which of the following would be the best insulin delivery system for her?

- a) Continue insulin vials and syringes
- b) Insulin pens
- c) Insulin infusion device (insulin pump)
- d) Insulin infusion device (insulin pump) and a continuous glucose monitor (CGM)

Insulin Delivery Systems: Pros and Cons

<table>
<thead>
<tr>
<th></th>
<th>Pros</th>
<th>Cons</th>
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<tbody>
<tr>
<td>Vial and Syringe</td>
<td>• Cost</td>
<td>• Time</td>
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<tr>
<td></td>
<td></td>
<td>• Potential for dosing errors</td>
</tr>
<tr>
<td>Insulin Pens</td>
<td>• Convenience</td>
<td>• Cost</td>
</tr>
<tr>
<td></td>
<td>• Portability</td>
<td></td>
</tr>
<tr>
<td>Insulin Pumps</td>
<td>• Improved control</td>
<td>• Educational needs</td>
</tr>
<tr>
<td></td>
<td>• Ease of prandial dose calculations</td>
<td>• Constant wear</td>
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<tr>
<td></td>
<td></td>
<td>• Cost</td>
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Managing Hypoglycemia

- **First priority is avoidance!**
- Those at risk for hypoglycemia should be asked about symptomatic and asymptomatic hypoglycemia at each encounter
- Glucose (15–20 g) is the preferred treatment for a conscious individual
- Once a patient recovers from an episode, the individual should consume a meal or snack to avoid a recurrence
- Glucagon should be prescribed for all people at significant risk of severe hypoglycemia

Hypoglycemia–Associated Autonomic Failure (HAAF)

- HAAF can severely compromise glycemic control, safety, and quality of life
  - Repeated hypoglycemic events lead to:
    - Deficient counter-regulatory hormone release
    - Deficient autonomic response (tachycardia, etc.)
- Several weeks of hypoglycemia avoidance can help to improve hypoglycemic awareness
- ADA states patients with ≥1 episode of severe hypoglycemia may benefit from short-term relaxation of glycemic targets

The Case of SS – 3 Months Later

- SS’s basal insulin was initially decreased by 25%
- SS was asked to complete a 3-day glucose, diet, and insulin log
- Via weekly titrations, SS was stabilized on:
  - Insulin aspart 1 unit/10 g CHO + 1 unit/40 > 100 mg/dl (approx. 20 units/day)
  - Insulin detemir 12 units BID
- No severe hypoglycemic events; A1C = 6.9%

Case #2

MH is a 57-year-old male patient with DM type 2 (dx 1 year ago)
CC: “I just can’t get my diabetes under control. I’m really trying to lose weight.”

HPI: Symptoms:
- Admits to nocturia 3–5 times per night
- Occasional blurred vision

Case #2

PMHx:
Current Medications:
- Glimepiride 4 mg – 2 tablets PO daily
- Atorvastatin 40 mg – 1 tablet PO daily
- Lisinopril 20 / HCTZ 12.5 mg – 1 tablet PO daily
- Amlodipine 5 mg – 1 tablet PO daily
- EC Aspirin 81 mg – 1 tablet PO daily
- Allopurinol 100 mg – 2 tablets PO daily

Social and Family Hx:
- Lives with wife; married 35 years
- Had leadership position but semi-retired now
- 3 grown children who live some distance away
- Travels a lot and eats meals at haphazard times
- Has adequate health insurance and tiered copay for prescription medications
- Able to afford medications
Case #2

<table>
<thead>
<tr>
<th>AM (Fasting)</th>
<th>Pre-Dinner</th>
<th>Bedtime</th>
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<tbody>
<tr>
<td>Monday</td>
<td>163</td>
<td>211</td>
</tr>
<tr>
<td>Tuesday</td>
<td>181</td>
<td></td>
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<tr>
<td>Wednesday</td>
<td>179</td>
<td>234*</td>
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<tr>
<td>Thursday</td>
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<td>173</td>
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<tr>
<td>Friday</td>
<td>199</td>
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<tr>
<td>Saturday</td>
<td>207</td>
<td></td>
</tr>
<tr>
<td>Sunday</td>
<td>186</td>
<td>267</td>
</tr>
<tr>
<td>Monday</td>
<td>186</td>
<td>232</td>
</tr>
</tbody>
</table>

* Forgot to take morning pills

Vital Signs:
BP = 136/64 mm Hg  Pulse = 84 bpm, regular
Weight = 241 lb  Height = 5'11"  BMI = 33.6

Labs (fasting):
Glucose = 193 mg/dL  A1C = 9.6%
eCrCl = 82 ml/min
TCHO = 185 mg/dL  LDL = 97 mg/dL
HDL = 34 mg/dL  TG = 271 mg/dL

Therapeutic Considerations in DM Type 2

- Combination therapies that make sense
  - Complementary mechanisms of action
  - Address both fasting and post-prandial BG
- Patient-related variables to consider
  - Risk of hypoglycemia
  - Comorbidities (CVD, renal dysfunction) and weight
  - Age and life expectancy
  - Duration of disease and degree of hyperglycemia
  - Patient attitudes, expectations, support systems
    - Women of childbearing potential / pregnancy

Initiating Insulin in DM Type 2

- Basal vs. basal–bolus strategies
  - If fasting BG is elevated and A1C is ≥9%, basal strategy is good starting place
  - If A1c ≥10%, basal–bolus strategy is likely needed
- Initial dose
  - Basal only: 0.1–0.2 units/kg single evening dose
  - Basal–bolus: 0.3–0.4 units/kg divided in 2 or 3 doses with 50% given as basal
- Choice of insulin (glargine vs. detemir vs. NPH)
- Oral agents – which to continue and stop?

Audience Response Question

When starting basal insulin therapy, which of the following would be the best approach in the case of MH?

a) NPH insulin 5 units at bedtime and schedule follow-up visit in 1 month
b) Insulin glargine 10 units at bedtime and call in 2 weeks to review SMBG results
c) Insulin detemir 10 units at bedtime and call patient in 1 week to review SMBG results
d) NPH insulin 15 units at bedtime and have patient titrate dose by 2–6 units every 2 days based on morning SMBG results

Treat to Target Strategies

“Classic” strategy – start with 10 units at bedtime:

<table>
<thead>
<tr>
<th>Mean of SMBG from preceding 2 days</th>
<th>Increase insulin dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥180 mg/dL</td>
<td>8 units</td>
</tr>
<tr>
<td>140–180 mg/dL</td>
<td>6 units</td>
</tr>
<tr>
<td>120–140 mg/dL</td>
<td>4 units</td>
</tr>
<tr>
<td>100–120 mg/dL</td>
<td>2 units</td>
</tr>
<tr>
<td>&lt;100</td>
<td>0 units</td>
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Target fasting BG ≤ 100mg/dL. This may be too aggressive for many patients.


Hamaty M. Cleveland Clinic J Med. 2011;78:332-42.

Many protocols have been formally tested

The fasting target BG is typically <100 mg/dL or 100–120 mg/dL

Titration increments are 2–10 units every 2–7 days over 8–12 weeks

Clinician vs. patient self-titration; degree of clinic oversight

Mean insulin dose (28–90 units)

Mean achieved A1c <7.5%

Titration increments are 2–10 units every 2–7 days over 8–12 weeks

Clinician vs. patient self-titration; degree of clinic oversight

Mean insulin dose (28–90 units)

Mean achieved A1c <7.5%

Which of the following would be the most appropriate strategy to address MH’s concerns about weight gain?

a) Switch NPH to insulin glargine at 8:00 am
b) Switch NPH to insulin detemir at 10:00 pm
c) Discontinue glimepiride, use NPH insulin with metformin (titrate to 1000 mg BID)
d) Tell him to exercise 30–45 minutes every day at moderate intensity (HR = 130–140 bpm)

MH started metformin and the dose was titrated to 1000 mg BID. He self-titrated NPH insulin over 6 weeks to 54 units at bedtime. His FBG readings have been consistently <120mg/dL.

MH states that he’s been walking 2–3 miles most days. His weight has remained stable. His A1C is now 7.4%.

Which of the following is the most appropriate action now in the case of MH?

a) Continue metformin and NPH; wait another 3 months before making any changes
b) Switch NPH insulin to insulin glargine and titrate to achieve target FBG <100mg/dL
c) Initiate basal–bolus regimen with a single dose of rapid acting insulin prior to largest meal
d) Add dipeptidyl peptidase–4 (DPP–4) inhibitor to current regimen

Basal–Plus One
- Adding a single dose of rapid–acting insulin prior to largest meal of the day
- Start 3–4 units and self-titrate dose by 1–2 units every 2–7 days based on pre–meal/bedtime BG
- Basal insulin plus GLP–1 agonist
- Exenatide or liraglutide or lixisenatide
- Several small studies have shown significant A1C (0.5–1.7%) and weight (1.8–12.8 kg)

Diet and exercise
- Medication choices
  - Insulin choice (NPH vs. glargine vs. detemir)
  - GLP-1 agonists
  - SGLT2
  - Metformin
  - DPP-4 Inhibitors
  - Sulfonylureas
  - Thiazolidinediones (Avoid with insulin)
- Weight loss meds?
Key Points

- Insulin therapy is physiologic. All patients with DM type 1 require insulin and most patients with DM type 2 will (eventually) need it.
- The initial insulin regimen should be guided by:
  - Type of diabetes
  - Patient’s weight
  - Current level of glycemic control
- Patient self-management of insulin therapy highly desirable (but not always achievable)
- Hypoglycemia and weight gain are common adverse effects that must be proactively addressed