Hyperglycemia

Jacob Aaron
Med-Peds PGY-2
University Hospitals Cleveland Medical Center
Learning Objectives

- Know acute and chronic effects of hyperglycemia
- Be able to order insulin appropriately for an inpatient in various situations
- Know the different types of insulins and how they are used
- Understand the diagnostic criteria and basic pathophysiology of DKA
- Understand how to manage hyperglycemia in the inpatient setting
Case 1

55-year old female with PMH DM2 (Last HbA1C 9, 1 month ago) was admitted by orthopedic surgery at UH for emergent hip arthroplasty after a fracture. She had an uncomplicated post-operative course and is now POD2, but orthopedic surgery noticed that her blood glucose level has persistently been in the 400’s and is now consulting internal medicine for assistance with BG control. On admission, she was placed on a moderate sliding scale with insulin lispro and her home diabetes meds were discontinued.
Why do we care about high blood glucose in the hospital?
# Complications of Hyperglycemia

<table>
<thead>
<tr>
<th>Short term</th>
<th>Long Term</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NEURO:</strong> Neuron apoptosis 2/2 oxidative damage</td>
<td><strong>NEURO:</strong> Stroke, peripheral neuropathy</td>
</tr>
<tr>
<td><strong>CV:</strong> Increased atherosclerosis</td>
<td><strong>CV:</strong> MI, PAD</td>
</tr>
<tr>
<td><strong>PULM:</strong> ?????????????</td>
<td><strong>PULM:</strong> Increased risk of ARDS and PNA and higher morbidity and mortality from PNA</td>
</tr>
<tr>
<td><strong>GI:</strong> Reduced gastric emptying and gallbladder contractility</td>
<td><strong>GI:</strong> Gastroparesis</td>
</tr>
<tr>
<td><strong>MSK/DERM:</strong> Poor wound healing</td>
<td><strong>MSK/DERM:</strong> Impaired wound healing, foot ulcers</td>
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<tr>
<td><strong>HEME:</strong> Increased platelet activation</td>
<td><strong>HEME:</strong> Hemoglobin glycosylation</td>
</tr>
<tr>
<td><strong>RENAL:</strong> Osmotic diuresis/dehydration</td>
<td><strong>RENAL:</strong> ESRD, diabetic nephropathy</td>
</tr>
<tr>
<td><strong>IMM/ID:</strong> Increased infection rates, impaired neutrophil function</td>
<td><strong>IMM/ID:</strong> Immunocompromise, infection with mucor</td>
</tr>
</tbody>
</table>
Case 1

**PMHx:** DM, obesity, HLD, HTN

**Home Meds:** Metformin 500 mg BID, insulin glargine 20 units qHS, insulin lispro 8 units TID AC, aspirin 81, atorvastatin 80, lisinopril 10, ibuprofen 400 PRN, reports adherence to all medications at home

**Allergies:** NKDA

**Past Surgeries:** Cholecystectomy

**Family History:** DM2, stroke

**Social History:** No history of tobacco, alcohol, or drug use
What do you notice?

**PMHx:** DM, obesity, HLD, HTN

**Home Meds:** Metformin 500 mg BID, insulin glargine 30 units qHS, insulin lispro 8 units TID AC, aspirin 81, atorvastatin 80, lisinopril 10, ibuprofen 400 PRN, reports adherence to all medications at home

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**Social History:** No history of tobacco, alcohol, or drug use
So many types of insulin!

<table>
<thead>
<tr>
<th>Type</th>
<th>Examples</th>
<th>Pharmacokinetics</th>
<th>Typical Dosing</th>
<th>Uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid-acting</td>
<td>lispro (Humalog), aspart (Novolog), glulisine (Apidra)</td>
<td>Onset 15 min</td>
<td>qAC/HS (eating) q4h (NPO/ continuous feeds)</td>
<td>sliding scale, mealtime coverage, used in pumps</td>
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<tr>
<td></td>
<td></td>
<td>Peak 1 hr</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lasts 2-4 hrs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short-acting</td>
<td>regular insulin</td>
<td>Onset 30 min</td>
<td>qAC (eating) q6h (NPO / continuous feeds)</td>
<td>sliding scale, mealtime coverage, for IV drips</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Peaks 2-4 hrs</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lasts 5-8 hrs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intermediate -</td>
<td>NPH, detemir</td>
<td>Onset 2 hrs</td>
<td>BID</td>
<td>basal</td>
</tr>
<tr>
<td>acting</td>
<td></td>
<td>Peaks 3-12 hrs</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lasts 6-28 hrs</td>
<td></td>
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</tr>
<tr>
<td>Long-acting</td>
<td>glargine (Lantus), degludec (Tresiba)</td>
<td>Onset 2 hrs</td>
<td>Daily (occasionally BID)</td>
<td>basal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NO Peak</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lasts &gt;20 hrs</td>
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</table>

Slide courtesy of Erika Lundgren, MD
Daily blood glucose in non-diabetics
Insulin vs. blood glucose

Case 1 – Blood glucose trends and insulin administration over last 24 hours

- Pre-breakfast: 420 => 10 units lispro
- Pre-lunch: 439 => 10 units lispro
- Pre-dinner: 451 => 10 units lispro

Total: 30 units of insulin lispro, 0 units of insulin glargine, and persistent hyperglycemia (with post-prandial highs)!
What should we do?

• Consensus: pre-prandial glucose levels should be < 180 in noncritically ill patients

• Disagreement:
  • Endocrine society: Pre-prandial glucose levels should be < 140 in non-critically ill patients
  • ADA: Pre-prandial glucose levels should be between 140-180 in non-critically ill patients
So how should we manage this patient’s hyperglycemia?

• Basal-bolus method
• Look at total insulin requirement for the day as an estimate – in this patient, 30 units
• Split 50/50 into basal (long-acting) delivered qHS and bolus (short-acting) split into three portions and given at meals
• Insulin sliding scale to correct for high blood glucose
• Repeat this calculation each day to ensure adequate dosing
• So for this patient:
  • 30 units/2 = 15 units lispro/3 meals = 5 units lispro TID
  • 30 units/2 = 15 units insulin glargine qHS
  • Insulin sliding scale (moderate) to correct for inadequate dosing qACHS
Case 1

• The patient is put on her new in-house insulin regimen, and her blood glucoses the next day (POD3) are in the 200’s.

• You readjust her insulin doses the next day based on the amount of insulin she required from her sliding scale, and her blood glucoses on POD4 are all between 160-180.

• The patient is ultimately discharged home on POD6 on her home insulin regimen.
Case 1 – How should the team have initially dosed this patient’s insulin?

1. Calculate total daily dose (TDD) of home insulin.
   -Glargine 20 units+ lispro 8 units TID = 44 units
2. Use approximately ½ to 2/3 of this TDD, split into about ½ long acting insulin and ½ pre-prandial insulin.
   -44 units /2 = 22 units total.
   -Final dosing: 11 units lantus qHS and 4 units lispro TID AC

3. Order a corrective scale to account for unexpected highs
4. Recalculate total daily dose based on corrective scale use daily until blood glucose is controlled

Question: Why not use the patient’s entire home TDD of insulin?

Answer: Avoid hypoglycemia; patients often don’t eat as well in the hospital (We restrict them!) which can lead to reduced insulin requirements.
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   - **Final dosing: 11 units lantus qHS and 4 units lispro TID AC**

3. Order a corrective scale to account for unexpected highs

4. Recalculate total daily dose based on corrective scale use

Question: What would we do if this patient were NPO?

Answer: Hold mealtime insulin, continue lantus at ½ home dose, and order corrective scale q4h (if lispro or aspart) or q6h (if regular insulin)
Case 1 – How should the team have initially dosed this patient’s insulin?

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3. Order a corrective scale to account for unexpected highs

4. Recalculate total daily dose based on corrective scale use

Question: What should I do for patients who don’t take insulin at home?
Answer: Hold oral hyperglycemics. Order a corrective scale. After day 1, calculate daily requirements and follow the same steps.
Case 2

You are the intern on UH NF and you get a call at 22:30 from a nurse stating that your patient has a blood of 423. The nurse asks for advice on what to do to correct this blood glucose.

What do you do?
Case 2

You smartly ask the nurse if you can have 5 minutes to look over the patient’s history and decide to take a look at the signout the day intern prepared for you. The patient is a 25 year old male with PMH DM1 admitted to the hospital today for nausea and vomiting due to acute viral gastroenteritis complicated by dehydration s/p 1 L IV NS bolus in ED.

PMH: DM1, obesity

Home Meds: Insulin glargine 40 units qHS, Insulin lispro carbohydrate coverage 1unit : 6g carbs, insulin lispro correction 1unit: every 20 > 140
Case 2

Before you hang up the phone, you ask the nurse to get a set of vitals. As you finish taking a look at the chart, the nurse pages you the following vitals:

- T 37.2
- HR 120
- BP 110/72
- RR 24
- O2 sat 99% on RA
Sick or Not Sick?

T 37.2
HR 120
BP 110/72
RR 24
O2 sat 99% on RA
Case

You also noticed that the team ordered PM labs: CBC, RFP, HFP, UA for nighttime that have just resulted!

<table>
<thead>
<tr>
<th></th>
<th>13</th>
<th>13.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>13</td>
<td>40</td>
</tr>
<tr>
<td>Hb</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HCT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Na</td>
<td>145</td>
<td>4.2</td>
</tr>
<tr>
<td>K</td>
<td>110</td>
<td>15</td>
</tr>
<tr>
<td>Cl</td>
<td>15</td>
<td>27</td>
</tr>
<tr>
<td>CO2</td>
<td>2.7</td>
<td>1.2</td>
</tr>
<tr>
<td>BUN</td>
<td>451</td>
<td>4.5</td>
</tr>
<tr>
<td>Cr</td>
<td>100</td>
<td>1</td>
</tr>
<tr>
<td>Glu</td>
<td>1</td>
<td>0.3</td>
</tr>
</tbody>
</table>

UA:
- Glucose: 4+
- Ketones: 3+
- Bacteria: -
- Nitrites: -
- Leukocyte esterase: -+

SICK OR NOT SICK?
What is your presumptive diagnosis?

DKA
**INSULIN**

- **↑ Fat storage**
- **↓ Fat utilization**
- **↑ Glucose use**
- **↓ Blood Glucose**
- **↑ Protein synthesis**
- **↓ Proteolysis**
- **↓ Gluconeogenesis**

**KETONES**

**↓ Glucose use**
**↓ Blood Glucose**

**HYPERGLYCEMIA**
**OSMOTIC DIURESIS**

**HYPERGLYCEMIA**
**OSMOTIC DIURESIS**
Case 2

What other study do you need to confirm the diagnosis?
### Case 2

<table>
<thead>
<tr>
<th>DKA – Diagnostic Criteria</th>
<th>Our patient has . . .</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood glucose &gt; 250 mg/dL</td>
<td>451</td>
</tr>
<tr>
<td>Ketonuria OR Ketonemia</td>
<td>Ketonuria</td>
</tr>
<tr>
<td>Serum bicarbonate &lt; 19</td>
<td>15</td>
</tr>
<tr>
<td>Anion gap &gt; 10</td>
<td>AG 20</td>
</tr>
<tr>
<td>Serum pH &lt; 7.3</td>
<td>pPPP7?22</td>
</tr>
</tbody>
</table>

**VBG:** pH 7.22 CO2 35
<table>
<thead>
<tr>
<th></th>
<th>DKA</th>
<th>HHS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Moderate (plasma glucose &gt;250 mg/dL)</td>
<td>Severe (plasma glucose &gt;250 mg/dL)</td>
</tr>
<tr>
<td>Arterial pH</td>
<td>7.25–7.30</td>
<td>7.00 to &lt;7.24</td>
</tr>
<tr>
<td>Serum bicarbonate (mEq/L)</td>
<td>15–18</td>
<td>10 to &lt;15</td>
</tr>
<tr>
<td>Urine ketone*</td>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td>Serum ketone*</td>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td>Effective serum osmolality†</td>
<td>Variable</td>
<td>Variable</td>
</tr>
<tr>
<td>Anion gap‡</td>
<td>&gt;10</td>
<td>&gt;12</td>
</tr>
<tr>
<td>Mental status</td>
<td>Alert</td>
<td>Alert/drowsy</td>
</tr>
</tbody>
</table>
Question: Can a patient with normal blood glucose still be in DKA?

Answer: Yes! Many patients at home will notice their blood sugar is high and immediately correct their blood sugar with insulin before seeking medical care. These patients should be treated using the same protocol!
You walk to the room to examine the patient.

Gen: Patient is visibly uncomfortable, clutching his stomach. 
Resp: Tachypneic, clear breath sounds bilaterally, no retractions or paradoxical breathing
CV: Regular rhythm, tachycardia, no murmurs appreciated, peripheral pulses 2+, extremities warm and well perfused
Abd: Soft, moderately tender to palpation, nondistended, no rigidity or guarding
Neuro: AOx4, grossly intact, fluent speech
Case 2

What do we do now?
Case 2

Complete initial evaluation. Check capillary glucose and serum/urine ketones to confirm hyperglycemia and ketonemia/ketonuria. Obtain blood for metabolic profile. Start IV fluids: 1.0 L of 0.9% NaCl per hour.1

- **IV Fluids**
  - Determine hydration status
  - Severe hypovolemia
  - Administer 0.9% NaCl (1.0 L/hr)
  - Evaluate corrected serum Na++
  - Serum Na+ high: 0.45% NaCl (250-500 mEq/l) depending on hydration state
  - Serum Na+ normal: 0.9% NaCl (250-500 mEq/l) depending on hydration state
  - Serum Na+ low: 0.45% NaCl (250-500 mEq/l) depending on hydration state

- **Bicarbonate**
  - pH ≥ 6.9
  - pHe < 6.9
  - No HCO3-
  - Cardiogenic shock
  - Hemodynamic monitoring/pressors

- **Insulin: Regular**
  - IV Route (DKA and HHS)
    - 0.1 U/kg/B.Wt. as IV bolus
    - 0.14 U/kg Bwt/hr as IV continuous insulin infusion
  - IV Route (DKA and HHS)
    - 0.1 U/kg/h IV continuous insulin infusion
  - 0.14 U/kg Bwt/hr IV continuous insulin infusion
  - If serum glucose does not fall by at least 10% in first hour, give 0.14 U/kg as IV bolus, then continue previous Rx

- **DKA**
  - When serum glucose reaches 200 mg/dl, reduce regular insulin infusion to 0.02 - 0.05 U/kg/hr IV, or give rapid-acting insulin at 0.1 U/kg SC every 2 hrs. Keep serum glucose between 150 and 200 mg/dl until resolution of DKA.

- **HHS**
  - When serum glucose reaches 300 mg/dl, reduce regular insulin infusion to 0.02 - 0.05 U/kg/hr IV. Keep serum glucose between 200 and 300 mg/dl until patient is mentally alert.

- **Potassium**
  - Establish adequate renal function (urine output ~ 50 ml/hr)
  - K+ <3.3 mEq/L
  - Hold insulin and give 20 - 30 mEq/hr Until K+ > 3.3 mEq/L
  - K+ >5.2 mEq/L
  - Do not give K+, but check serum K+ every 2 hrs.

- **Hyponatremia**
  - Serum Na+ low: 0.45% NaCl (250-500 mEq/l) depending on hydration state
  - 0.45% NaCl (250-500 mEq/l) depending on hydration state

- **Hypernatremia**
  - Serum Na+ high: 0.45% NaCl (250-500 mEq/l) depending on hydration state
  - 0.45% NaCl (250-500 mEq/l) depending on hydration state

- **Check** electrolytes, BUN, venous pH, creatinine and glucose every 2 - 4 hrs until stable. After resolution of DKA or HHS and when patient is able to eat, initiate SC multidose insulin regimen. To transfer from IV to SC, continue IV insulin infusion for 1 - 2 hr after SC insulin begun to ensure adequate plasma insulin levels. In insulin naïve patients, start at 0.5 U/kg to 0.8 U/kg body weight per day and adjust insulin as needed. Look for precipitating cause(s).
Case 2

**Fluids:**

- Start 0.45 % NS @ 250-500 mL/hr

**Bicarbonate:**

- None. pH > 6.9

**Insulin:**

- Bolus insulin 0.1 Units/kg insulin
- Start insulin GTT @ 0.1 units/kg/hr

**Potassium:**

- 30 mEQ in IVF

**BG checks:**

- Q 1 hour

**Labs:**

- STAT RFP q4h

**Communication:**

- Touch base with nurse, patient
Case 2

One hour later . . .

The nurse for the patient calls and tells you the patient’s blood glucose is 430.

What do you do?

Bolus insulin regular 0.14 units/kg IV, continue infusion
Case 2

One hour Later . . .

The nurse for the patient calls and tells you the patient’s blood glucose is 360.

What do you do?

Continue insulin infusion
Case 2

One hour Later . . .

The nurse for the patient calls and tells you the patient’s blood glucose is 250.

What do you do?

Continue insulin infusion
Case 2

One hour Later . . .

The nurse for the patient calls and tells you the patient’s blood glucose is 192.

What do you do?

Switch IVF to D5 0.45%NS @ 150-250 mL/hr
Switch insulin GTT to 0.02-0.05 units/kg/hr
Case 2

Your RFP returns!

What now?

- Restart home insulin regimen! Make sure patient gets insulin glargine!
- Continue insulin GTT
IMPORTANT!!!

• DO NOT DISCONTINUE YOUR INSULIN GTT RIGHT AFTER GIVING SUBCUTANEOUS INSULIN!

• The patient is still at risk of going back into DKA!
Case 2

One hour Later . . .

The nurse for the patient calls and tells you the patient’s blood glucose is 70.

What do you do?

Switch IVF to D10 0.45%NS @ 150-250 mL/hr
CONTINUE INSULIN GTT
Case 2

One hour Later . . .

The nurse for the patient calls and tells you the patient’s blood glucose is 110.

What do you do?

Discontinue Insulin GTT
Subcutaneous insulin per patient’s home schedule
1-2 extra q1hr dsticks to ensure patient’s BG remains normal
Change IVF to maintenance fluids without glucose and without potassium
Case 2 - End

- After you treat the patient’s DKA, you sign out to the day team. Whew! You did it!
Take-home points

• In almost all cases, inpatients with diabetes who take insulin at home should have three insulin orders – a long-acting insulin, a short-acting insulin with meals, and a pre-meal sliding scale for correction UNLESS the patient is NPO.
• ½ to 2/3 of a patient’s home insulin should be split into 50/50 long acting and short-acting pre-prandial doses in house.
• Insulin administered from an ISS order should be considered in the next day’s insulin needs and the orders readjusted daily
• DKA is diagnosed by serum pH <7.3, BG > 250, ketonuria or ketonemia, anion gap >10, and serum HCO3 < 19, but keep alternative presentations in mind.
• Use UH’s DKA protocol for treatment of DKA, and consider transfer to ICU if patient is in shock or unstable
• DO NOT START SUBCUTANEOUS INSULIN UNTIL THE ANION GAP CLOSES! DO NOT STOP THE INSULIN DRIP UNTIL 2 HOURS AFTER YOU START YOUR SUBCUTANEOUS INSULIN!
• Involve a senior resident if you are unsure of your next steps!
THANK YOU!
REFERENCES


