Dilemmas in Diabetes Management

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Disclosure

Michael McDermott MD

No Conflict of Interest to Disclose

Inpatient Hyperglycemia Management

Current Issues - 2016

- Admission A1C Interpretation
- Inpatient Glucose Goals
- Medications to Use and Avoid
- Enteral and Parenteral Feedings
- Glucocorticoid Use
Inpatient Hyperglycemia
Why Glucose Levels May Increase

Stress Hormones
- Growth Hormone
- Cortisol
- Catecholamines
- Glucagon

↑ Glucose
↑ Gluconeogenesis
↑ Glycogenolysis
↑ Insulin Resistance

Enteral / Parenteral Nutrition
Glucocorticoid Administration

Inpatient Hyperglycemia
Why Hyperglycemia Impacts Outcomes

- Impaired Immunity / Infection Risk
- Impaired Protein Synthesis / Healing
- Dehydration / Electrolyte Disorders
- Impaired Myocardial Metabolism
- Circulating Inflammatory Cytokines

Moghissi E, Diabetes Care 2009; 32:1119
Umpierrez G, J Clin Endocrinol Metab 2012; 97:16

Inpatient Hyperglycemia
Increased Morbidity and Mortality

Myocardial Infarction
Renal Transplant
Stroke
Community Acquired Pneumonia
Trauma
Cardiothoracic Surgery
Orthopedic Surgery

Moghissi E, Diabetes Care 2009; 32:1119
Umpierrez G, J Clin Endocrinol Metab 2012; 97:16
Inpatient Hyperglycemia
Why Glucose Levels May Decrease

- NPO Status
- Medication Errors
- Liver Dysfunction
- Renal Dysfunction
- Diet Different than Home Diet
- Anorexia from Illness/Medications

Inpatient Hyperglycemia
Why Hypoglycemia Impacts Outcomes

↑ Catecholamines
Cardiac Rhythm Disorders
Myocardial Dysfunction

Moghissi S, Diabetes Care 2009; 32:1119
Umpierrez G, J Clin Endocrinol Metab 2012; 97:16

Dilemma # 1

Admission A1C Interpretation
Case History
55 year old woman admitted with urosepsis. Past history remarkable only for rheumatoid arthritis. Random blood glucose is 220 mg/dl. A1C is 5.5%.

How do you interpret her A1C and random glucose?
1. Stress hyperglycemia without pre-existing diabetes
2. Stress hyperglycemia and pre-diabetes
3. Diabetes with illness-related exacerbation
4. Uncontrolled diabetes with illness exacerbation
5. Blood drawn from arm during D5 infusion

Inpatient Hyperglycemia
Admission A1C: Interpretation
A1C < 5.7% and Inpatient BG High
  • Stress Hyperglycemia
A1C 6.5-8.0% and Inpatient BG High
  • DM2 Adequately Controlled + Stress Hyperglycemia
A1C > 8.0% and Inpatient BG High
  • DM2 Poorly Controlled + Stress Hyperglycemia

High A1C on Admission Indicates Need for Adjustment of Outpatient Regimen At Discharge

Dilemma # 2
Inpatient Glucose Targets
**Case History**

63 year old woman on the medicine for pneumonia. She has DM2 treated outpatient with Metformin and Glipizide. Admission A1C is 9.2%. Inpatient BG values are all > 200 mg/dl.

What are evidence based blood glucose goals for her?
1. Pre-meal BG < 110, Random BG < 140
2. Pre-meal BG < 120, Random BG < 150
3. Pre-meal BG < 140, Random BG < 180
4. Pre-meal BG < 150, Random BG < 200
5. Goals are for soccer players; avoid hypoglycemia

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**Inpatient Hyperglycemia**

**Glucose Targets**

<table>
<thead>
<tr>
<th>Illness Severity</th>
<th>Glucose Targets (mg/dl)</th>
<th>Insulin Initiation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Critically Ill</td>
<td>Pre-Meal BG 90-140</td>
<td>&gt; 180 mg/dl</td>
</tr>
<tr>
<td></td>
<td>All BG &lt; 180</td>
<td>&gt; 180 mg/dl</td>
</tr>
<tr>
<td>Critically Ill</td>
<td>BG 140-180</td>
<td>&gt; 180 mg/dl</td>
</tr>
</tbody>
</table>

Evidence Supporting These Targets is Sparse

Moghissi E, Diabetes Care 2009; 32:1119
Umpierrez G, J Clin Endocrinol Metab 2012; 97:16

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**Dilemma # 3**

**Medications to Use and to Avoid**
Case History

A 63 year old woman is on the medicine ward being treated for pneumonia. She has DM2 treated with Metformin and Glipizide. A1C is 9.2%. BG values are all > 200 mg/dl.

What medication changes do you recommend?
1. Continue metformin and glipizide
2. Stop metformin; increase glipizide dose
3. Stop oral medications; start basal and CF insulin
4. Start an IV Insulin infusion
5. Consult an Endocrinologist

Type 1 Diabetes: Inpatient Hyperglycemia
Insulin Only

**Basal Bolus Insulin Regimen**

**Basal Insulin at All Times**
- Home Dose: 75-100%, depending on -
  - Home control (A1C)
  - Eating or NPO status
  - Usually 0.1-0.2 U/kg; ~50% of total daily dose

**Bolus Insulin for Meals and High BG Corrections**
- Nutritional Component (before or right after meal)
  - Home mealtime dose or C:I ratio of 15:1
- Correction Component (with nutrition dose or alone)
  - Home correction dose or CF of 50:1 to Target BG 150 mg/dl

**Basal Bolus Insulin Therapy**

Moghissi E, Diabetes Care 2009; 32:1119
Umpierrez G, J Clin Endocrinol Metab 2012; 97:16
Type 2 Diabetes: Inpatient Hyperglycemia

Recommendations

- Insulin is preferred agent for achieving glucose control in hyperglycemic hospitalized patients
- Non-insulin therapies should be discontinued in most hospitalized patients with Type 2 Diabetes

Endocrine Society, ADA, AACE Recommendations

Moghissi S, Diabetes Care 2009; 32:1119
Umpierrez G, J Clin Endocrinol Metab 2012; 97:16

Type 2 Diabetes: Inpatient Hyperglycemia

Non-Insulin Medications

<table>
<thead>
<tr>
<th>Medication</th>
<th>Recommendation</th>
<th>May Continue (+/-) If</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulfonylurea</td>
<td>Stop almost always</td>
<td>No chance of missed meals</td>
</tr>
<tr>
<td>Meglitinides</td>
<td>Stop almost always</td>
<td>No chance of missed meals</td>
</tr>
<tr>
<td>Metformin</td>
<td>Stop usually</td>
<td>No chance of AKI and eGFR &gt; 45</td>
</tr>
<tr>
<td>GLP-1 Analogs</td>
<td>Stop usually</td>
<td>No nausea, vomiting, pancreatitis</td>
</tr>
<tr>
<td>DPP4 Inhibitor</td>
<td>Stop usually</td>
<td>No angioedema, pancreatitis</td>
</tr>
<tr>
<td>SGLT2 Inhibitor</td>
<td>Stop usually</td>
<td>No volume depletion, ketosis, UTI</td>
</tr>
<tr>
<td>Thiazolidinediones</td>
<td>Stop usually</td>
<td>No CHF or edema</td>
</tr>
</tbody>
</table>

Type 2 Diabetes: Inpatient Hyperglycemia

Management

Home: Lifestyle Measures Only – Controlled (A1C)

Glucose Testing (POC) QID for 24-48 Hours

Correction Insulin for BG ≥ 180 mg/dl

- Aspart, Glulisine, Lispro, Regular
  - Correction Factor 50:1 to Target 150 mg/dl

Basal Insulin if Multiple Correction Doses Needed

- Detemir, Glargine, NPH
  - Dose 8.2-8.3 U/kg/day

Mealtime Insulin if Post-Meal BG Remains ≥ 180 mg/dl

- Aspart, Glulisine, Lispro, Regular
  - C/I Ratio 15:1
### Type 2 Diabetes: Inpatient Hyperglycemia Management

**Home: Lifestyle or Non-Insulin Rx**

**Glucose Testing (POC) QID for 24-48 Hours**

<table>
<thead>
<tr>
<th>Basal Insulin - Start</th>
<th></th>
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<tbody>
<tr>
<td>Detemir, Glargine, NPH</td>
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<td>C:I Ratio 10:1</td>
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### Type 2 Diabetes: Inpatient Hyperglycemia Management

**Home: Basal Insulin and Non-Insulin Rx**

**Glucose Testing (POC) QID for 24-48 Hours**

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<th>Basal Insulin - Start</th>
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<td>Detemir, Glargine, NPH</td>
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<td>Home Dose: 75-100% depending on:</td>
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<td>C:I Ratio 10:1</td>
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### Type 2 Diabetes: Inpatient Hyperglycemia Management

**Home: Basal Bolus Insulin Therapy**

**Glucose Testing (POC) QID for 24-48 Hours**

<table>
<thead>
<tr>
<th>Basal Insulin at All Times</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Home Dose: 75-100% depending on:</td>
<td></td>
</tr>
<tr>
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<td></td>
</tr>
<tr>
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<th>Bolus Insulin for Meals and High BG Corrections</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Nutritional Component (before or right after meal)</td>
<td></td>
</tr>
<tr>
<td>Home mealtime dose or C:I ratio of 10:1</td>
<td></td>
</tr>
<tr>
<td>Correction Component (with nutrition dose or alone)</td>
<td></td>
</tr>
<tr>
<td>Home correction dose or CF of 25:1 to Target 150 mg/dl</td>
<td></td>
</tr>
</tbody>
</table>
Dilemma # 4

Enteral and Parenteral Nutrition

Case History
64 y.o. woman with DM2 is on ward having daily continuous tube feedings. BG > 200 all day.

What would you recommend to control her BG?
1. Correction rapid acting insulin Q 4-6 hr
2. Glargine at the beginning of each cycle with correction rapid acting insulin Q 4-6 hr
3. NPH at the beginning of each cycle with correction rapid acting insulin Q 4-6 hrs
4. Human Mix 70/30 (NPH/Reg) Insulin TID with correction rapid acting insulin Q 4-6 hr
5. Regular insulin Q 6 hr during feeds

Inpatient Hyperglycemia
Enteral and Parenteral Nutrition

- BG Testing Q 4-6 hr for 24-48 hr in All Patients on EN/PN
- Start Scheduled Insulin if BG > 140 mg/dl and persistent correction insulin requirement w/wo History of Diabetes

Use Insulin With Duration of Action Consistent With Duration of Nutrition Administration

Moghissi E, Diabetes Care 2009; 32:1119
Umpierrez G, J Clin Endocrinol Metab 2012; 97:16
### Insulin Preparations

<table>
<thead>
<tr>
<th>Generic</th>
<th>Name</th>
<th>Peak</th>
<th>Duration</th>
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</thead>
<tbody>
<tr>
<td>Aspart</td>
<td>Novolog</td>
<td>1-2 hr</td>
<td>3-5 hr</td>
</tr>
<tr>
<td>Glulisine</td>
<td>Apidra</td>
<td>1-2 hr</td>
<td>3-5 hr</td>
</tr>
<tr>
<td>Lispro</td>
<td>Humalog</td>
<td>1-2 hr</td>
<td>3-5 hr</td>
</tr>
<tr>
<td>Detemir</td>
<td>Levemir</td>
<td>Minimal</td>
<td>20-24 hr</td>
</tr>
<tr>
<td>Glargine</td>
<td>Lantus</td>
<td>Minimal</td>
<td>22-24 hr</td>
</tr>
<tr>
<td>Glargine U300</td>
<td>Toujeo</td>
<td>Minimal</td>
<td>24-26 hr</td>
</tr>
<tr>
<td>Degludec</td>
<td>Tresiba</td>
<td>None</td>
<td>36 hr</td>
</tr>
<tr>
<td>NPH</td>
<td>Humulin-N</td>
<td>8-12 hr</td>
<td>12-20 hr</td>
</tr>
<tr>
<td>Regular</td>
<td>Humulin-R</td>
<td>2-4 hr</td>
<td>6-8 hr</td>
</tr>
<tr>
<td>U500</td>
<td>Humulin-R U500</td>
<td>8-12 hr</td>
<td>12-16 hr</td>
</tr>
</tbody>
</table>

### Inpatient Hyperglycemia

#### Enteral Nutrition

**Bolus Tube Feeding**

**Nutrition Coverage**
- Insulin: Rapid / Short Acting at Bolus Start
  - Aspart, Glulisine, Lispro, Regular
- Dose: C:I Ratio 15:1 (DM) or 25:1 (non-DM)

**Correction Doses Q6H**
- Insulin: Rapid / Short Acting
  - Aspart, Glulisine, Lispro, Regular
- Dose: CF 50:1 to Target BG 150 mg/dl

**Continuous Tube Feeding**

**Nutrition Coverage**
- Insulin: Long / Intermediate Acting at Bolus
  - 70/30 (NPH/Reg) BID/TID or NPH BID/TID or
  - Detemir, Glargine QD
- Dose: C:I Ratio 15:1 (DM) or 25:1 (non-DM)

**Correction Doses Q6H**
- Insulin: Rapid / Short Acting
  - Aspart, Glulisine, Lispro, Regular
- Dose: CF 50:1 to Target BG 150 mg/dl
Insulin Treatment of Tube Feedings
Retrospective Study: Patients on Tube Feeding – 3 Regimens

- Glargine QD + Lispro CF
- Human 70/30 Premix BID
- Human 70/30 Premix TID

Adapted from Hsia E, Nutr Clin Pract 2011; 26:714-7

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Insulin Treatment of Tube Feedings
Retrospective Study: Patients on Tube Feeding – 3 Regimens

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Inpatient Hyperglycemia
Enteral Nutrition
Carbohydrate Contents of EN Formulas (g/L)

- Peptamen AF: 107
- Peptamen 1.5: 188
- Promote: 130
- Nutren 2.0: 196
- Osmolite: 144
- Ensure Plus: 211
- Nepro: 167
- 2 Cal HN: 219
- Jevity 1.2: 169
**Inpatient Hyperglycemia**

**Enteral Nutrition**

Example from UCH

- 62 year old man with pre-existing DM2 in SICU receiving continuous tube feeding with Nutren 20 (196 g CHO/L) at 60 cc/hr (282 g CHO/day).
- Insulin needed for C:I ratio 15:1 = 18 units/day
- Ordered: 70/30 (NPH/Reg) 6 units TID

**Inpatient Hyperglycemia**

**Parenteral Nutrition**

**Total Parenteral Nutrition**

Nutrition Coverage

- Insulin: Short Acting in TPN Fluid
  - Regular Human Insulin
- Dose: C:I Ratio 15:1 (DM) or 25:1 (non-DM)

Correction Doses Q6H (SQ)

- Insulin: Rapid / Short Acting
  - Aspart, Glulisine, Lispro, Regular
- Dose: CF 50:1 to Target BG 150 mg/dl

**Inpatient Hyperglycemia**

**Enteral or Parenteral Nutrition Stopped**

EN/TPN Stopped or Interrupted

- Give D10 or D5 Infusion (with same COOH Concentration) as EN/PN for the Remaining Active Insulin Time
Inpatient Hyperglycemia
Enteral or Parenteral Nutrition Stopped
Adapted from: Low Wang C, Hosp Pract 2013; 41:45-53

<table>
<thead>
<tr>
<th>Blood Glucose (mg/dl)</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
<th>13</th>
<th>14</th>
<th>15</th>
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</thead>
<tbody>
<tr>
<td>Time (Hours)</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
<td>8</td>
<td>9</td>
<td>10</td>
<td>11</td>
<td>12</td>
<td>13</td>
<td>14</td>
<td>15</td>
</tr>
<tr>
<td>Enteral or Parenteral Nutrition</td>
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</tr>
<tr>
<td>D10 Infusion</td>
<td></td>
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<tr>
<td>Long Acting Insulin</td>
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<tr>
<td>No D10 Infusion</td>
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</tbody>
</table>

Dilemma # 5

Glucocorticoid Administration

Case History
A 45 year old woman with lupus nephritis. Prednisone 40 mg QAM and Cyclophosphamide are started.
BG levels: AM 80-130  Noon 120-160
PM 195-245  HS 165-205

What do you recommend to treat her hyperglycemia?
1. Sliding scale regular insulin Q 6 hr
2. Correction rapid acting insulin Q 4-6 hr
3. AM NPH + correction rapid acting insulin
4. AM glargine + correction rapid acting insulin
5. IV regular insulin infusion
Inpatient Hyperglycemia
Glucocorticoid Administration

- BG Testing Q 6 hr for 24-48 hr in All Patients started on Glucocorticoid Therapy w/wo History of Diabetes
- Correction Insulin (Rapid/Short Acting) Q6H
  - CF 25:1 to Target BG 150 mg/dl
  - Start Scheduled Insulin if BG > 140 mg/dl and persistent correction insulin requirement

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Umpierrez G, J Clin Endocrinol Metab 2012; 97:16
Inpatient Hyperglycemia
Glucocorticoid Administration

Prednisone or Methylprednisolone:
Glucose Maximal Rise 6-12 hr after Administration
- NPH: QD/BID for QD/BID Prednisone / Methylprednisolone
  Alone or add-on to existing insulin regimen.
- Dose: NPH 10 U (sensitive) or 20 U (resistant) per 40 mg
  Prednisone or Methylprednisolone
- Correction Doses: Rapid Acting Insulin Q6H, CF 25:1
- Taper: as Steroid Dose is Tapered

Dexamethasone or Multi-dose Steroid Regimen
- Long Acting Insulin Plus Correction Rapid Acting Insulin


Thank You