Recent Advances in the Management of Diabetes

Raja Hanania, R.Ph, CDM, CDE, LDE, BCPS
Clinical Pharmacy Specialist
IU Health Bloomington Hospital
Bloomington, Indiana

Indiana Pharmacists Alliance Annual Convention

September 27th, 2018
Disclosure

• Novonordisk Speakers Bureau
Objectives

• Identify at least two medication options and strategies to manage patients with diabetes in the inpatient setting
• Describe at least two strategies for successful transition of care for patients with diabetes from the inpatient setting to the outpatient setting
• Review medication options and outline at least two strategies to manage patients with diabetes in the outpatient setting
National Diabetes Estimates

- 30.3 million Americans
  - 7.2 million undiagnosed
  - 84.1 million at high risk (pre-diabetes)
- 1-in-3 American adults will have diabetes by 2050
- The 7th leading cause of death in the US
  - The leading cause of blindness, renal failure and non-traumatic amputations
- Cost burden in U.S. of $327 billion in 2017,
  - $245 billion in 2012
  - $218 billion in 2007
  - $132 billion in 2002

Every 6 seconds a person dies from diabetes!

Pathogenesis of Type 2 Diabetes

- Impaired insulin secretion
- Decreased incretin effect
- Increased lipolysis
- Increased glucagon secretion
- Increased hepatic glucose production
- Neurotransmitter dysfunction
- Decreased glucose uptake

Medications sites of action

Audience Response Question 1

Which of the following does not carry the diagnosis of diabetes according to ADA standards 2018?

1. A patient with fasting BG levels of 127 and 131 on two separate days
2. A patient with an A1c of 6.9% and fasting BG of 128
3. A patient with a random BG of 202 and symptoms of polydipsia, polyuria and polyphagia
4. All carry the diagnosis of diabetes
Criteria for the Diagnosis of Diabetes

<table>
<thead>
<tr>
<th>Criteria for the Diagnosis of Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>FPG $\geq 126$ mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h.*</td>
</tr>
</tbody>
</table>

**OR**

| 2-h PG $\geq 200$ mg/dL (11.1 mmol/L) during OGTT. The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75-g anhydrous glucose dissolved in water.* |

**OR**

| A1C $\geq 6.5\%$ (48 mmol/mol). The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.* |

**OR**

| In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose $\geq 200$ mg/dL (11.1 mmol/L). |

*In the absence of unequivocal hyperglycemia, result should be confirmed by repeat testing.*
Diabetes in Hospitalized Patients

- Prevalence 13-26%
  - 30-50% in acute MI acute stroke patients
- In 2017, 14 million visits to the ED with diabetes as the primary diagnosis
- Up to 38% of hospitalized patients experience hyperglycemia
- Inpatient hyperglycemia is associated with
  - Longer hospital stays
  - Higher admission rates to intensive care
  - More patients requiring transitional or nursing home care
- Up to 36% of patients with diabetes are first diagnosed in hospital

Additional Hospital Management Needs: A1c orders

• Causes of inpatient hyperglycemia
  • Stress induced hyperglycemia
  • Previously undiagnosed diabetes
  • History of poorly controlled diabetes
  • Medications

• Be aware of recent blood transfusions or hemoglobinopathies (blood disorders) which may affect A1c interpretation

• Assessing the A1c may help increase early diagnosis!!

# Glycemic Control During Hospitalization…. Why ??

<table>
<thead>
<tr>
<th>Reference</th>
<th>Patient Population Studied</th>
<th>Significant Hyperglycemic-Related Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omar AS, et al(^1)</td>
<td>Cardiac surgery</td>
<td>Increased: surgery time, length of stay in both ICU and hospital, ventilation time, wound infection</td>
</tr>
<tr>
<td>Pasquel FJ et al(^2)</td>
<td>Total parenteral nutrition</td>
<td>Increased: mortality risk, pneumonia risk, acute renal failure</td>
</tr>
<tr>
<td>Bochicchio GV et al(^3)</td>
<td>Critically injured trauma patients</td>
<td>Increased: length of stay, mortality risk, ventilation time, infection</td>
</tr>
<tr>
<td>Firsch A et al(^4)</td>
<td>Non-cardiac surgery</td>
<td>Increased: length of stay, mortality risk, hospital complications</td>
</tr>
</tbody>
</table>

Effect of A1C on Total Hospitalization Cost

AACE/ADA Recommendations for Managing Patients With Diabetes in the Hospital Setting

ADA Position on Noninsulin Therapies in Inpatient Use

• Area of active research

• Dipeptidyl peptidase 4 inhibitor (DPP-4)
  – Similar glucose control and hypoglycemia frequency (compared to basal-bolus)

• Glucagon-like peptide 1 agonist (GLP-1)
  – Show promise for inpatient use
  – Await proof of safety and efficacy

• Sodium/Glucose cotransporter 2 inhibitor (SGLT-2)
  – Not recommended (lack of data)
Physiologic Components of Insulin Therapy

- **Basal insulin**
  Amount of insulin necessary to regulate glucose level between meals and overnight

- **Nutritional insulin (prandial)**
  Amount of insulin required to cover meals, IV dextrose, enteral nutrition, TPN or other nutritional supplements

- **Correctional insulin**
  Supplemental doses of insulin given to correct hyperglycemia that occurs despite use of basal & nutritional insulin. **Not recommended as monotherapy for >24-48h. NEVER appropriate as monotherapy in type 1 DM**

The Dark Side of The Sliding Scale

• Problems:
  – Omits basal insulin requirements
  – Insulin does not work retroactively (treating hyperglycemia after it occurs instead of preventing it)
  – Does not account for mealtime calories
  – Grossly underestimates insulin requirements

• Benefits:
  – Very popular but hazards exceed the advantages of its convenience
## Example of a Sliding Scale Protocol

<table>
<thead>
<tr>
<th>Glucose</th>
<th>□ A</th>
<th>□ B</th>
<th>□ C</th>
<th>□ D</th>
</tr>
</thead>
<tbody>
<tr>
<td>mg/dL</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;110</td>
<td>none</td>
<td>none</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>110-140</td>
<td>none</td>
<td>none</td>
<td></td>
<td></td>
</tr>
<tr>
<td>141-180</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>181-220</td>
<td>1</td>
<td>2</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>221-260</td>
<td>2</td>
<td>4</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>261-300</td>
<td>3</td>
<td>6</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>301-340</td>
<td>4</td>
<td>7</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>341-380</td>
<td>5</td>
<td>8</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>381-420</td>
<td>6</td>
<td>9</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>421-460</td>
<td>7</td>
<td>10</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>&gt;460</td>
<td>8</td>
<td>12</td>
<td>18</td>
<td></td>
</tr>
</tbody>
</table>
## Characteristics of Insulin

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Name</th>
<th>Onset</th>
<th>Peak</th>
<th>Duration</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bolus</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rapid Acting Analogs</td>
<td>Aspart (Fiasp)</td>
<td>2.5 min</td>
<td>45-60 min</td>
<td>3-5 hrs</td>
<td>Prandial and Correction</td>
</tr>
<tr>
<td>Rapid Acting Analogs</td>
<td>Aspart (Novolog)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rapid Acting Analogs</td>
<td>Lispro (Humalog), Admelog</td>
<td>5-15 min</td>
<td>30-60 min</td>
<td>3-5 hrs</td>
<td></td>
</tr>
<tr>
<td>Rapid Acting Analogs</td>
<td>Glulisine (Apidra)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short Acting (Human)</td>
<td>Regular (Novolin R, Humulin R)</td>
<td>30-60 min</td>
<td>2-3 hrs</td>
<td>5-8 hrs</td>
<td></td>
</tr>
<tr>
<td><strong>Basal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intermediate</td>
<td>NPH</td>
<td>2-4 hrs</td>
<td>4-10 hrs</td>
<td>10-16 hrs</td>
<td>Controls fasting and between meals</td>
</tr>
<tr>
<td>Long Acting</td>
<td>Detemir (Levemir)</td>
<td>2-4 hrs</td>
<td>No peak</td>
<td>UP TO 24 HRS</td>
<td></td>
</tr>
<tr>
<td>Long Acting</td>
<td>Glargine (Lantus/Basaglar/Toujeo)</td>
<td>2-4 hrs</td>
<td>No peak</td>
<td>Up to 24 hrs</td>
<td></td>
</tr>
<tr>
<td>Long Acting</td>
<td>Degludec (Tresiba)</td>
<td>1 hr</td>
<td>No peak</td>
<td>&gt; 42 hrs</td>
<td></td>
</tr>
<tr>
<td><strong>Basal &amp; Bolus</strong></td>
<td>Combination of NPH &amp; Regular</td>
<td></td>
<td>Dual Peaks</td>
<td>10-16 hrs</td>
<td>Usually dosed twice daily</td>
</tr>
<tr>
<td>Intermediate &amp; Short</td>
<td>70/30 (NPH/Regular)</td>
<td>30-60 min</td>
<td>Dual Peaks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intermediate &amp; Short</td>
<td>50/50 (NPH/Regular)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intermediate &amp; Rapid</td>
<td>Novolog Mix 70/30</td>
<td>5-15 min</td>
<td></td>
<td>10-16 hrs</td>
<td></td>
</tr>
<tr>
<td>Intermediate &amp; Rapid</td>
<td>Humalog mix 75/25 (or 50/50)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intermediate &amp; Rapid</td>
<td>Ryzodeg Mix 70/30 (degludec/aspart)</td>
<td></td>
<td></td>
<td>24 hrs</td>
<td></td>
</tr>
</tbody>
</table>

Pharmacological Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes-2018;41:S73-S85
AACE-ADA Consensus Statement on Inpatient Glycemic Control

*Diabetes Care.* 2009;32:1119-31
ADA/AACE Target Glucose Levels in ICU Patients

• ICU setting:
  – Insulin infusion should be used to control hyperglycemia
  – Starting threshold of no higher than 180 mg/dl
  – Once IV insulin is started, the glucose level should be maintained between 140 and 180 mg/dl
  – Lower glucose targets (110-140 mg/dl) may be appropriate in selected patients
ADA/AACE Target Glucose Levels in Non-ICU Patients

• Non-ICU setting:
  – Pre-meal glucose targets <140 mg/dL
  – Random BG <180 mg/dL
  – To avoid hypoglycemia, reassess insulin regimen if BG levels fall below 100 mg/dL
  – Occasional patients may be maintained with a glucose range below or above these cut-points

_Hypoglycemia_ = $BG < 70$ mg/dl
_Severe hypoglycemia_ = $BG < 40$ mg/dl
## Classification of Hypoglycemia

<table>
<thead>
<tr>
<th>Level</th>
<th>Glycemic criteria</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoglycemia alert value (level 1)</td>
<td>$\leq 70 \text{ mg/dL (3.9 mmol/L)}$</td>
<td>Sufficiently low for treatment with fast-acting carbohydrate and dose adjustment of glucose-lowering therapy</td>
</tr>
<tr>
<td>Clinically significant hypoglycemia (level 2)</td>
<td>$&lt;54 \text{ mg/dL (3.0 mmol/L)}$</td>
<td>Sufficiently low to indicate serious, clinically important hypoglycemia</td>
</tr>
<tr>
<td>Severe hypoglycemia (level 3)</td>
<td>No specific glucose threshold</td>
<td>Hypoglycemia associated with severe cognitive impairment requiring external assistance for recovery</td>
</tr>
</tbody>
</table>

Risk of Hypoglycemia

- May increase in the following conditions:
  - Lack of coordination between dietary and nursing leads to mistiming of insulin dosage with respect to food
  - Sudden NPO status or reduction in oral intake
  - Enteral feeding discontinued
  - TPN or IV dextrose infusion discontinued
  - Premal insulin given and meal not ingested
  - Reduction in corticosteroid dose
  - Patients on sulfonylureas and meglitinides
  - Patients on intensive insulin therapy

Hypoglycemia is Associated with Cardiovascular Complications

- Tachycardia and high blood pressure

- Myocardial ischemia
  - Silent ischemia, angina, infarction

- Cardiac arrhythmias
  - Transiently prolonged corrected QT interval,
  - Increased QT dispersion

- Sudden death

Wright RJ, Frier BM. *Diabetes Metab Res Rev* 2008; 24:353-363
Example of an Inpatient Hypoglycemia Protocol

• **Patients with IV access:**
  – Dextrose 50%, 4 ml for every 10 mg/dL under 100 mg/dL IV push for BG ≤ 70 mg/dL (60 mg/ dL for pregnant women)

• **Patients with no IV access, NPO or non responsive:**
  – Glucagon 1 mg (0.5 mg for patients < 100 lbs) SubQ for BG ≤ 70 mg/dL (60 mg/ dL for pregnant women)

• **Patients with no IV access and responsive:**
  – Apple juice 30 ml for every 10 mg/dL under 100 mg/dL for BG ≤ 70 mg/dL (60 mg/ dL for pregnant women)
Example of an Inpatient Hypoglycemia Protocol (Cont.)

- Continue the process of observing for 15 min, rechecking and treating if necessary until glucose > 70 mg/dl (or >60 mg/dL if pregnant)

- Notify physician

- Some hospitals recheck BG 90 minutes after resolution of hypoglycemia

- If an unplanned interruption in feeding occurs for patients on continuous tube feeds or total parenteral nutrition, use Dextrose 10% as a rescue measure to prevent hypoglycemia
## Approach to ordering Insulin in the Inpatient Setting

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>For patients on basal /bolus insulin at home</strong></td>
<td>Order home regimen but consider reducing dose by 20% (unless home BG high). Omit prandial dose if patient is NPO.</td>
</tr>
</tbody>
</table>
| **For patients on premixed insulin at home**  | Order 50-60% TDD as long acting insulin  
Order 40-50% TDD as nutritional insulin  
Divided into 3 pre meal doses (if patient eating)  
Consider reducing TDD by 20% unless home BG high                                                                                       |
| **For patients not previously on insulin**    | Order sliding scale with prandial insulin for the first 24 hours. Don’t react to just one BG  
If BG > 180 x 2, add 10 units or 0.1-0.2 units/kg of basal insulin (as a start) to prandial and sliding scale                                          |

How to Adjust Insulin in Hospitalized Patients

- If most BG 140-180, make no change
- If BG <100 mg/dl, decrease TDD by 10-20%
- If BG >180 mg/dl AND none <100 mg/dl, increase TDD by 10-20% OR add 50-100% of previous 24h correction insulin to TDD
- If fasting BG consistently out of range, adjust basal insulin
- If premeal or bedtime BG consistently out of range, adjust or add nutritional insulin to preceding meal

<table>
<thead>
<tr>
<th>Nutritional Condition</th>
<th>Necessary Insulin Components</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eating meals</td>
<td>Basal: 50% of TDD. Nutritional: 50% of TDD divided equally before each meal.</td>
</tr>
<tr>
<td>NPO (or clear liquids)</td>
<td>Basal: 50% of TDD. Nutritional: none</td>
</tr>
<tr>
<td>Bolus tube feeds</td>
<td>Basal: 40% of TDD. Nutritional: 60% of TDD divided equally each bolus feed</td>
</tr>
<tr>
<td>Continuous tube feeds</td>
<td>Basal: 40% of TDD. Nutritional: 60% of TDD in divided doses.</td>
</tr>
<tr>
<td>Parenteral nutrition (TPN)</td>
<td>Insulin usually given parentally with the nutrition</td>
</tr>
</tbody>
</table>

Maynard G et al *J Hosp Med.* 2008; 3(suppl 5); S29-S41.
Diabetic Ketoacidosis (DKA)

- Life threatening medical condition caused by insulin deficiency, either relative or absolute

- In most cases, DKA happens to people with Type I diabetes who fail to take insulin

- Usual presentation includes hyperglycemia, dehydration and thirst, acidosis, rapid deep respiration (kussmaul), hyperosmolality, Urine/serum ketones & electrolyte imbalance.

- Other possible findings include elevated BUN/Creatinine and WBC, abdominal pain/vomiting, hypertension, hyperlipidemia, altered mental status and ultimately coma.

Diabetic Ketoacidosis (DKA) cont.

- Type 2 diabetics may experience a different serious condition known as “Hyperosmolar Hyperglycemic Non-ketotic Syndrome (HHNS)

- The most common precipitating factor in DKA & HHNS patients is infection but may also be caused by acute stress and may be drug induced (steroids, thiazides and sympathomimetic agents)

First choice for treatment of patients with Diabetes Ketoacidosis (DKA)

1. IV fluids
2. Insulin
3. Electrolytes replacement
4. Sodium Bicarbonate
Treatment of Adult DKA/HHNS

- Fluid therapy to correct dehydration
- **Do not start Insulin until K>3.3 mEq/L!!!**
- Insulin Therapy (insulin drip unless mild DKA). Drip should be started at 0.1 unit/kg/hr
  - Most common rates needed are 0.1, 0.15 or 0.05 unit/kg/hr depending on how fast BG is dropping.
- Include D5 in IV fluids once glucose level < 300 mg/dL

Treatment of Adult DKA/HHNS

• DKA resolves when BG < 200 mg/dL and two of the following: anion gap is ≤12; HCO3 is ≥15; or pH is > 7.3

• HHNS resolves when mental status returns to baseline and electrolytes are balanced (Anion gap may be variable)

• Give first dose of basal subq insulin 2-4 hours prior to stopping IV insulin

• Add Potassium to maintenance fluids if potassium < 5.3

• Correction of electrolytes and lab values mainly Potassium, correction of Bicarbonate and Phosphate (controversial)

• Key to successful treatment is identification of precipitating events and above all frequent patient monitoring

Patient Discharge
Diabetes at Discharge

- 23% of all discharges have diabetes diagnosis
- 8 – 9 million patients with diabetes discharged each year
- $1 out of every $3 Medicare dollars spent on diabetes care
- 1.7 – 1.9 million will return as an early readmission

According to ADA standards what steps are needed to reduce hospital readmissions?

1. Medication reconciliation
2. Diabetes self-care education
3. Follow-up care planning
4. All of the above
Preventing Readmission

- ADA Standards of Care
  - Discharge planning should begin upon admission and tailored to the individual patient at discharge
    - Medication reconciliation
    - Structured plan of care
    - Diabetes self-care education
    - Follow-up care planning
  - Individualize therapy

- Must provide comprehensive discharge planning via care coordination

Transitioning from Inpatient Stay

- Preparation from inpatient setting should begin at the time of admission
- Clear communication with outpatient providers is crucial
- Collaboration across the entire spectrum of the interdisciplinary team is critical for successful management

Key Patient Education Points Prior to Discharge

- How, when and what to expect from medications/insulin
- How and when to test blood glucose and target ranges to shoot for
- Basics of meal planning
- How to treat hypoglycemia
- Sick-day management plan
- Date/time of follow-up visits
- When and who to call if needed

Example of Diabetes Home Instructions

<table>
<thead>
<tr>
<th>Type of Med</th>
<th>Name</th>
<th>Dose</th>
<th>Time</th>
<th>Test Blood Glucose at these times</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral Agents</td>
<td></td>
<td></td>
<td></td>
<td>Test before breakfast and at bedtime, at least three days a week</td>
</tr>
<tr>
<td>Long Acting Insulin</td>
<td></td>
<td></td>
<td></td>
<td>Test before breakfast and at bedtime everyday</td>
</tr>
<tr>
<td>Rapid Acting Insulin</td>
<td></td>
<td></td>
<td></td>
<td>Test before each meal and at bedtime everyday</td>
</tr>
</tbody>
</table>

**MEALS ONLY**

**Correction Scale of Rapid Acting Insulin**

<table>
<thead>
<tr>
<th>If Blood Glucose is (mg/dL)</th>
<th>Then Give</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 70</td>
<td>Units</td>
</tr>
<tr>
<td>70 - 110</td>
<td>Units</td>
</tr>
<tr>
<td>111 - 150</td>
<td>Units</td>
</tr>
<tr>
<td>151 - 200</td>
<td>Units</td>
</tr>
<tr>
<td>201 - 250</td>
<td>Units</td>
</tr>
<tr>
<td>251 - 300</td>
<td>Units</td>
</tr>
<tr>
<td>301 - 350</td>
<td>Units</td>
</tr>
<tr>
<td>More than 350</td>
<td>and call Physician</td>
</tr>
</tbody>
</table>

**Home Blood Glucose Monitoring Targets**

- Before Meals 90 - 130 mg/dL
- After Meals less than 180 mg/dL
- Call Doctor if your Glucose Level is Less than 70 mg/dL or More than 300 mg/dL on 2 consecutive tests.

(You may need a medication adjustment.) If BG < 50 mg/dL with diminished consciousness call EMS.

To help prevent complications please follow up with your medical provider for the following exams: Hgb A1c every 3 months; Blood pressure with each doctors appointment; Fasting Lipid panel; Urine Albumin; Serum creatinine; Diabetic Foot Exam; and Dilated Eye exam yearly.

**Low Blood Glucose Treatment:**

- If blood glucose is less than 70 mg/dL, eat 4 glucose tablets or 15 grams of carbohydrate (½ cup juice, or regular soda or 1 cup of milk). Wait 10 to 15 minutes and recheck blood glucose. If still less than 70, repeat treatment. Call EMS if blood glucose continues to drop.

**Sick Day Guidelines:** (Sick day includes fever over 100.5°F, diarrhea or nausea)

- Never stop taking your long acting insulin. If eating meals take your insulin, as usual.
- Drink adequate fluids. If you have kidney or heart problems, consult your doctor, otherwise drink 1 cup of liquid every hour. Include liquids with carbohydrates if you are unable to eat solid food.
- Test your blood glucose every 2 to 4 hours. Call your doctor promptly if you are nauseated and vomit more than once, if you have stomach pain or fever over 100.5°F, if your blood glucose is over 240 mg/dL (with moderate ketones for type I), or if your illness lasts over 24 hours.

Hanania, et al. AADE 2017 Poster Presentation. Indianapolis, IN
Revised Discharge Insulin Algorithm

Choosing a Discharge Regimen

A1C < 8%
Restart outpatient treatment regimen (oral agents and/or insulin)

A1C 8%-10%
Restart outpatient oral agents and keep basal at 50% of hospital dose

A1C >10%
Discharge on basal/bolus at same hospital dose.
Alternative: Restart oral agents, keep basal at 80% of hospital dose

Algorithm shown to decrease average A1C from 8.67% to 7.26% in 12 weeks (224 patients)

Diabetes in the Outpatient Setting

ARE YOU A BOX OF BD PEN NEEDLES?

BECAUSE YOU ARE ULTRA-FINE
Diabetes Prevention:
Use of Metformin in Prediabetes

• Should be considered for patients with prediabetes
  – with BMI ≥35
  – under 60 years old
  – women with history of gestational diabetes

• Potential for vitamin B12 deficiency with long-term metformin use

ADA Glycemic Targets for Non-Pregnant Adults

<table>
<thead>
<tr>
<th>Patient / Disease Features</th>
<th>More stringent</th>
<th>A1C 7%</th>
<th>Less stringent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risks potentially associated with hypoglycemia and other drug adverse effects</td>
<td>low</td>
<td>A1C 7%</td>
<td>high</td>
</tr>
<tr>
<td>Disease duration</td>
<td>newly diagnosed</td>
<td>A1C 7%</td>
<td>long-standing</td>
</tr>
<tr>
<td>Life expectancy</td>
<td>long</td>
<td>A1C 7%</td>
<td>short</td>
</tr>
<tr>
<td>Important comorbidities</td>
<td>absent</td>
<td>A1C 7%</td>
<td>few / mild</td>
</tr>
<tr>
<td>Established vascular complications</td>
<td>absent</td>
<td>A1C 7%</td>
<td>severe</td>
</tr>
<tr>
<td>Patient attitude and expected treatment efforts</td>
<td>highly motivated, excellent self-care capabilities</td>
<td>A1C 7%</td>
<td>less motivated, poor self-care capabilities</td>
</tr>
<tr>
<td>Resources and support system</td>
<td>readily available</td>
<td>A1C 7%</td>
<td>limited</td>
</tr>
</tbody>
</table>

Audience Response Question 4

Which of the following medications have the highest chance to cause hypoglycemia?

1. Metformin
2. Glyburide
3. Pioglitazone
4. Exenatide
# Oral Diabetes Medications

<table>
<thead>
<tr>
<th>Class/Main Action</th>
<th>Name(s)</th>
<th>Daily Dose Range</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Biguanides</strong></td>
<td>metformin (Glucophage)</td>
<td>500 - 2500 mg (usually BID w/ meal)</td>
<td>Side effects: nausea, bloating, diarrhea, B12 deficiency. To minimize GI Side effects, use XR and take w/ meals. Obtain GFR before starting.</td>
</tr>
<tr>
<td></td>
<td>Riomet (liquid metformin)</td>
<td>500 - 2500mg 500mg/5mL</td>
<td>• If GFR &lt;30, do not use.</td>
</tr>
<tr>
<td></td>
<td>Extended Release-XR (Glucophage XR)</td>
<td>(1x daily w/dinner)</td>
<td>• If GFR &lt;45, don’t start Metformin</td>
</tr>
<tr>
<td></td>
<td>(Glumetza)</td>
<td>500 – 2000 mg 500 – 2000 mg</td>
<td>• If pt on Metformin and GFR falls to 30-45, eval risk vs. benefit; consider decreasing dose.</td>
</tr>
<tr>
<td></td>
<td>(Fortamet)</td>
<td>500 – 2500 mg</td>
<td>For dye study, if GFR &lt;60, liver disease, alcoholism or heart failure, restart metformin after 48 hours if renal function stable.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Benefits: lowers cholesterol, no hypo or weight gain, cheap. Approved for pediatrics, 10 yrs + Lowers A1c 1.0%-2.0%.</td>
</tr>
<tr>
<td><strong>Sulfonylureas</strong></td>
<td>glyburide: (Diabeta)</td>
<td>1.25 – 20 mg 0.75 – 12 mg</td>
<td>Can take once or twice daily before meals. Low cost generic.</td>
</tr>
<tr>
<td></td>
<td>(Glynase PresTabs)</td>
<td></td>
<td>Side effects: hypoglycemia and weight gain. Eliminated via kidney.</td>
</tr>
<tr>
<td></td>
<td>glipizide: (Glucotrol)</td>
<td>2.5 – 40 mg 2.5 – 20 mg</td>
<td>Caution: Glyburide most likely to cause hypoglycemia.</td>
</tr>
<tr>
<td></td>
<td>(Glucotrol XL)</td>
<td></td>
<td>Lowers A1c 1.0% – 2.0%.</td>
</tr>
<tr>
<td></td>
<td>glimepiride (Amaryl)</td>
<td>1.0 – 8 mg</td>
<td></td>
</tr>
</tbody>
</table>
# Oral Diabetes Medications (cont.)

<table>
<thead>
<tr>
<th>Class/Main Action</th>
<th>Name(s)</th>
<th>Daily Dose Range</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SGLT2 Inhibitors</strong></td>
<td></td>
<td></td>
<td><strong>Side effects:</strong> hypotension, UTIs, increased urination, genital infections, ketoacidosis. Monitor GFR and other considerations: See package insert for dosing adjustment based on GFR. - Canagliflozin increases risk of amputation. - Dapagliflozin, don’t use in pts w/ bladder cancer. - Empagliflozin &amp; canagliflozin decrease risk of death from CV disease. <strong>Benefits:</strong> no hypo or weight gain. Lowers A1c 1.0%-2.0%. Lowers wt 1-3 lbs.</td>
</tr>
<tr>
<td>“Glucoretic”</td>
<td>Canagliflozin (Invokana)</td>
<td>100 - 300 mg 1x daily Don’t start if GFR &lt;45. 5 - 10 mg 1x daily Don’t start if GFR&lt;60. 10 - 25 mg 1x daily Don’t start if GFR &lt;45. 5 – 15 mg 1x daily Don’t start if GFR &lt;60.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dapagliflozin (Farxiga)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Empagliflozin (Jardiance)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ertugliflozin (Steglatro)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>DPP – 4 Inhibitors</strong></td>
<td>sitagliptin (Januvia)</td>
<td>25 - 100 mg daily – eliminated via kidney*</td>
<td>* If creat elevated, see med insert for dosing. Side effects: headache and flu-like symptoms. Can cause severe, disabling joint pain. Contact MD, stop med. Report signs of pancreatitis. + Saxagliptin and alogliptin can increase risk of heart failure. Notify MD for shortness of breath, edema, weakness, etc. No wt gain or hypoglycemia. Lowers A1c 0.6%-0.8%.</td>
</tr>
<tr>
<td>“Incretin Enhancers”</td>
<td>saxagliptin (Onglyza)†</td>
<td>2.5 - 5 mg daily – eliminated via kidney*, feces</td>
<td></td>
</tr>
<tr>
<td></td>
<td>linagliptin (Tradjenta)</td>
<td>5 mg daily – eliminated via feces</td>
<td></td>
</tr>
<tr>
<td></td>
<td>alogliptin (Nesina)†</td>
<td>6.25 - 25 mg daily – eliminated via kidney*</td>
<td></td>
</tr>
</tbody>
</table>
## Oral Diabetes Medications (Cont.)

<table>
<thead>
<tr>
<th>Class/Main Action</th>
<th>Name(s)</th>
<th>Daily Dose Range</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Thiazolidinediones “TZDs”</strong></td>
<td>pioglitazone (Actos)</td>
<td>15 – 45 mg daily</td>
<td>Black Box Warning: TZDs may cause or worsen CHF. Monitor for edema and weight gain. Increased peripheral fracture risk. Actos may increase risk of bladder cancer. Lowers A1c 0.5% – 1.0%</td>
</tr>
<tr>
<td></td>
<td>rosiglitazone (Avandia)</td>
<td>4 – 8 mg daily</td>
<td></td>
</tr>
<tr>
<td><strong>Glucosidase Inhibitors</strong></td>
<td>acarbose (Precose)</td>
<td>25 – 100 mg w/meals; 300 mg max daily dose</td>
<td>Start low dose, increase at 4-8 wk intervals to decrease GI effects. Caution with liver or kidney problems. In case of hypo, treat w/ glucose tabs. Lowers A1c 0.5– 1.0%.</td>
</tr>
<tr>
<td></td>
<td>miglitol (Glyset)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Meglitinides</strong></td>
<td>repaglinide (Prandin)</td>
<td>0.5 – 4 mg w/meals (metabolized in liver)</td>
<td>Take before meals. Side effects may include hypoglycemia and weight gain. Lowers A1c 1.0% – 2.0%.</td>
</tr>
<tr>
<td></td>
<td>nateglinide (Starlix)</td>
<td>60 – 120 mg w/meals (eliminated via kidney)</td>
<td></td>
</tr>
<tr>
<td><strong>Dopamine Receptor Agonists</strong></td>
<td>bromocriptine mesylate—Quick Release “QR” (Cycloset)</td>
<td>1.6 to 4.8 mg a day (each tab 0.8 mg)</td>
<td>Take within 2 hrs of waking. Side effects: nausea, headache, fatigue, hypotension, syncope, somnolence. Lowers A1c 0.6% – 0.9%.</td>
</tr>
<tr>
<td><strong>Bile Acid Sequestrants</strong></td>
<td>Colesevelam HCL (Welchol)</td>
<td>Up to six (6) 625 mg pills (3 tabs am, 3 tabs pm) 3.75gm packet in 4-8 ounces of fluid</td>
<td>Do not use if history of bowel obstruction, triglycerides &gt;500, or pancreatitis. Can decrease absorption of certain meds, soluble vitamins. Lowers LDL by 15-30%. Side effects GI in nature. Lowers A1c 0.5%</td>
</tr>
</tbody>
</table>
Human Insulin Inhalation Powder

• Rapid acting, meal time inhaled insulin for type 1 and 2
• Prior to administration, assess lung function including spirometry (FEV1) in all patients
• Afrezza® is contraindicated in patients with chronic lung disease (eg asthma or COPD); risk of acute bronchospasm
According to ADA algorithm for treatment of type 2 diabetes, which agent(s) could be considered as a second additive to metformin in patients with cardiovascular disease?

1. Glipizide
2. Liraglutide
3. Empagliflozin
4. Answers 2 & 3
Antihyperglycemic Therapy in Adults with Type 2 Diabetes

American Diabetes Association. 8. Pharmacologic approached to glycemic treatment: Standards of Medical Care in Diabetes 2018; Diabetes Care 2018; 41 (Suppl. 1) S73-S85.
# Injectable Diabetes Medications (Non Insulin)

<table>
<thead>
<tr>
<th>Class/Main Action</th>
<th>Name</th>
<th>Dose Range</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GLP-1 Receptor Agonist (GLP-1 RA)</strong></td>
<td>exenatide (Byetta)</td>
<td>5 and 10 mcg BID</td>
<td>Side effects for all: Nausea, vomiting, weight loss, injection site reaction. Report signs of acute pancreatitis (severe abdominal pain, vomiting), stop med. Renally excreted.</td>
</tr>
<tr>
<td></td>
<td>exenatide XR (Bydureon)</td>
<td>2mg 1x a week Pen injector - Bydureon BCise</td>
<td></td>
</tr>
<tr>
<td>“Incretin Mimetic”</td>
<td>liraglutide (Victoza)*</td>
<td>0.6, 1.2 and 1.8 mg daily</td>
<td>Black box warning: Thyroid C-cell tumor warning for exenatide XR, liraglutide, dulaglutide, and semaglutide (avoid if family history of medullary thyroid tumor). * Victoza significantly reduces risk of CV death, heart attack, and stroke. Lowers A1c 0.5 – 1.6% Weight loss of 1.6 to 6.0kg†</td>
</tr>
<tr>
<td></td>
<td>dulaglutide (Trulicity)</td>
<td>0.75 and 1.5 mg 1x a week pen injector</td>
<td></td>
</tr>
<tr>
<td></td>
<td>semaglutide (Ozempic)†</td>
<td>0.5 and 1.0 mg 1x a week pen injector</td>
<td></td>
</tr>
<tr>
<td></td>
<td>lixisenatide (Adlyxin)</td>
<td>(Only available in combo with glargine, iGlarLixi, see below)</td>
<td></td>
</tr>
<tr>
<td><strong>Amylin Mimetic</strong></td>
<td>pramlintide (Symlin)</td>
<td>Type 1: 15 - 60 mcg; Type 2: 60 - 120 mcg immediately before major meals</td>
<td>For Type 1 or 2 on insulin. Black box warning: severe hypoglycemic risk 3 hrs post injection. Prevent hypoglycemia, decrease insulin dose when starting pramlintide. Side effects: nausea, weight loss. Lowers A1c 0.5 – 1%</td>
</tr>
</tbody>
</table>

*Remind patients to build meals around their injections.*

---

*For a full list of injectable diabetes medications, visit the Lexi-Comp database.*

---

*Lexi-Comp 2018*
# Insulin/Injectable Combos

<table>
<thead>
<tr>
<th>Name</th>
<th>Combines</th>
<th>Considerations</th>
</tr>
</thead>
</table>
| **IDegLira**   | Insulin degludec (IDeg or Tresiba) Ultra long insulin + Liraglutide (Victoza) GLP-1 Receptor Agonist (GLP-1 RA) | **Xultophy 100/3.6 pre-filled pen** = 100 units IDeg / 3.6 mg liraglutide per mL  
Once daily injection – Dose range 10 to 50 = 10 – 50 units IDeg + 0.36 - 1.8 mg liraglutide  
**Recommended starting dose:**  
• 16 IDegLira (= 16 units IDeg + 0.58 mg liraglutide)  
Titrato dose up or down by 2 units every 3-4 days to reach target.  
Supplied in package of five single-use 3mL pens.  
Once opened, good for 21 days. |
| **iGlarLixi**  | Insulin glargine (Lantus) Basal Insulin + Lixisenatide (Adlyxin) GLP-1 Receptor Agonist | **Soliqua 100/33 Solostar Pen** = 100 units glargine / 33 μg lixisenatide per mL  
Once daily injection an hour prior to first meal of day.  
Dose range 15 – 60 = 15-60 units glargine + 5 – 20μg lixisenatide  
**Recommended starting dose:**  
• 15 units for pts not controlled on 30 units basal insulin or GLP-1 RA  
• 30 units for pts not controlled on 30 - 60 units basal insulin or GLP-1 RA  
Titrato dose up or down by 2-4 units every week to reach target.  
Supplied in package of five single-use 3mL pens.  
Once opened, good for 14 days. |

*Discontinue basal insulin /GLP-1 RA therapy before starting. If dose missed, resume with next usual scheduled dose.*
Considerations with Common Non-Insulin Diabetes Medications

- **Metformin**
  - Inexpensive, initial for most, no hypoglycemia, positive long term data, GI and renal considerations, weight neutral

- **Sulfonylureas (SU)**
  - Inexpensive, potent, weight gain, hypoglycemia, renal considerations

- **Thiazolidinediones (TZD)**
  - Weight gain, CHF, edema, no hypoglycemia

- **Dipeptidyl peptidase (DPP)-4 inhibitors (gliptins)**
  - Weight neutral, no hypoglycemia, renal considerations for some, CHF signal with saxagliptin and alogliptin

- **Sodium glucose co-transporter (SGLT)-2 inhibitors**
  - Potent, weight loss, no hypoglycemia, renal considerations, UTI/yeast infection risk, lower BP (watch for orthostasis), positive CVD benefit with empagliflozin and canagliflozin, amputation risk with canagliflozin, Normoglycemic DKA, flesh-eating bacterial infection of the genitals (Fournier’s gangrene)

- **Glucagon-like peptide (GLP)-1 agonists**
  - Injectable, potent, weight loss, pancreatitis risk, thyroid C-cell tumor risk, no hypoglycemia, positive CVD benefit with liraglutide and semaglutide

Antihyperglycemic Therapy in Adults with Type 2 Diabetes: After Basal Insulin

Summary

- Hyperglycemia is frequent in hospitalized patients with and without history of diabetes and imposes a huge economic burden and health care risks
- Insulin is the most effective agent to treat hyperglycemia in the hospital setting
- Standards continue to focus on individualization of therapy for both glycemic control and comorbidities of diabetes
- Successful transition of care is very critical to ensure continuity of care and prevent early readmission of patients with diabetes
- Hypoglycemia can be very dangerous and should be avoided
- Pharmacy teams in all settings have a huge role to play in the proper management of patients with diabetes
Recent Advances in the Management of Diabetes

Raja Hanania, R.Ph, CDM, CDE, LDE, BCPS
Clinical Pharmacy Specialist
IU Health Bloomington Hospital
Bloomington, Indiana

Rhanania1@iuhealth.org

Indiana Pharmacists Alliance
Annual Convention

September 27th, 2018
THANK YOU!

Questions???