Optimizing Glycemic Control and Avoiding Hypoglycemia in Older Adults with Type 2 Diabetes

WORKSHOP LEADER:
Charmaine D. Rochester, PharmD, CDE, BCPS
Associate Professor of Pharmacy
University of Maryland, School of Pharmacy
Department of Pharmacy Practice and Science
Baltimore, MD

Faculty Disclosure

• Dr. Rochester discloses that she receives research support from sanofi aventis.

Agenda

• 8:00-8:10: Introduction and Setting the Stage
• 8:10-8:20: Cases: Group Discussions
• 8:20-8:50: Group Presentations/Discussions
• 8:50-9:00: Summarizing Key Points/Q&A
• 9:00: Adjourn
Objectives
Upon completion of this educational activity, the participant should be able to:

• Outline strategies to prevent hypoglycemia in older adults with type 2 diabetes.
• Recommend treatment adjustments for older adults with type 2 diabetes experiencing hypoglycemia.
• Outline strategies to overcome suboptimal glycemic control in older adults with type 2 diabetes.
• Adjust treatment regimens for patients with type 2 diabetes to minimize adverse events.

Type 2 Diabetes Mellitus (T2DM)
• Centers for Disease Control and Prevention
  – 26 million (~8.3% population have DM), estimated 39 million by 2020; >90% have T2DM
  – Particular concern among aging
    • Nearly 1 in 4 >60 years of age have DM
    • 7th leading cause of death in 2006
    • $218 billion (total costs in 2007)
    • Significant impact on macrovascular and microvascular diseases

Key Topics
• How do we help our elderly patients attain optimal glycemic control and goal A1c?
• When do we consider intensifying therapy?
• How to prevent or treat hypoglycemia?
Case 1: JT – A 75-year-old Female in Long-Term Care (LTC)

History of Present Illness
- JT is a 75-year-old woman in a LTC facility.
- She is ambulatory.
- She skipped breakfast this morning and was found in her room confused and disoriented at 9:10 am.
- A fasting finger stick blood glucose (FSBG) was taken, which revealed a reading of 50 mg/dL.
- A repeat FSBG revealed a reading of 48 mg/dL.
- Over the past 2 months, staff at the LTC have been noticing JT’s mood as sad and withdrawn; and she is now uninvolved with social activities.

Medications
- Glyburide 10 mg bid
- Metformin 1000 mg bid
- HCTZ 25 mg daily
- Toprol XL 100 mg daily (recent increase from 50 mg)
- Atorvastatin 40 mg daily
- Acetaminophen ES 500 mg q 4-6 hrs prn for pain
- Ranitidine 150 mg bid
- ASA 81 mg daily
- Naproxen sodium 500 mg bid prn for pain
Case 1: JT

Past Medical History
- Type 2 diabetes
- Dyslipidemia
- Osteoarthritis

Allergies
- ACE Inhibitors (cough)

Vital Signs
- BP: 90/50 mmHg (sitting)
- Pulse: 50
- Resp: 22
- Height: 5’4”
- Weight: 140 lbs

Case 1: Laboratory Results

<table>
<thead>
<tr>
<th>Lab Values</th>
<th>Lab Values</th>
<th>Lab Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na 139 mg/dL</td>
<td>K 4.6 mg/dL</td>
<td>Total chol 166 mg/dL</td>
</tr>
<tr>
<td>Cl 99 mg/dL</td>
<td>CO2 23 mg/dL</td>
<td>HDL 39 mg/dL</td>
</tr>
<tr>
<td>BUN 18 mg/dL</td>
<td>TSH 1.26 mIU/L</td>
<td>LDL 92 mg/dL</td>
</tr>
<tr>
<td>Scr 1.4 mg/dL</td>
<td>ALT 26 U/L</td>
<td>TG 177 mg/dL</td>
</tr>
<tr>
<td>Gluc 190 mg/dl</td>
<td>AST 26 U/L</td>
<td>A1c 8.4%</td>
</tr>
</tbody>
</table>

Case 1: Blood Glucose Logs

<table>
<thead>
<tr>
<th>Dates</th>
<th>Breakfast (8 am)</th>
<th>Pre Lunch</th>
<th>Pre Dinner (6 pm)</th>
<th>Dinner (2 hours post-prandial)</th>
<th>Bedtime (12 midnight)</th>
</tr>
</thead>
<tbody>
<tr>
<td>11/8/12</td>
<td>50 mg/dL &amp; 48 mg/dL</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11/7/12</td>
<td>98 mg/dl</td>
<td>205 mg/dL</td>
<td>180 mg/dL</td>
<td>250 mg/dL</td>
<td>110 mg/dL</td>
</tr>
<tr>
<td>11/6/12</td>
<td>80 mg/dL</td>
<td>166 mg/dL</td>
<td>200 mg/dL</td>
<td>242 mg/dL</td>
<td>108 mg/dl</td>
</tr>
<tr>
<td>11/5/12</td>
<td>90 mg/dl</td>
<td>185 mg/dL</td>
<td>190 mg/dL</td>
<td>290 mg/dl</td>
<td>120 mg/dL</td>
</tr>
</tbody>
</table>
Case 2: MB – A 79-year-old Female Living Independently

History of Present Illness
- MB is a 79-year-old female who is ambulatory and lives independently.
- Her family members live out of state.
- At her last clinic appointment, the physician was considering initiating insulin therapy, but the patient refused stating that she will try lifestyle strategies.
- She states “my mother died when she was put on insulin.”
- The physician is also concerned about hypoglycemia since she lives alone.

Medications
- Glipizide 10 mg bid
- Metformin 1000 mg bid
- Pioglitazone 45 mg daily
- Sitagliptin 100 mg daily
- Lisinopril HCT 20-25 mg daily
- Metoprolol 100 mg daily
- Atorvastatin 80 mg daily
- ASA 81 mg daily
Case 2: MB

**Patient Medical History**
- Type 2 diabetes
- HTN
- Dyslipidemia
- Diabetic neuropathy
- Obesity

**Vital Signs**
- BP: 190/94 mmHg (sitting)
- Pulse: 80
- Resp: 30

**Allergies:** NKDA

**Diet:** McDonald meals; Subway sandwiches; Mom and pop’s “all you can eat” buffet at least 3 days/week

**Insurance:** Self-pay

**Education:** Completed high school

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**Case 2: Laboratory Results**

<table>
<thead>
<tr>
<th>Labs</th>
<th>Values</th>
<th>Labs</th>
<th>Values</th>
<th>Labs</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na</td>
<td>139 mg/dL</td>
<td>K</td>
<td>4.4 mg/dL</td>
<td>Total Chol</td>
<td>166 mg/dL</td>
</tr>
<tr>
<td>CI</td>
<td>99 mg/dL</td>
<td>CO2</td>
<td>23 mg/dL</td>
<td>HDL</td>
<td>39 mg/dL</td>
</tr>
<tr>
<td>BUN</td>
<td>18 mg/dL</td>
<td>TSH</td>
<td>3.26 mIU/L</td>
<td>LDL</td>
<td>92 mg/dL</td>
</tr>
<tr>
<td>SCr</td>
<td>1.2 mg/dL</td>
<td>ALT</td>
<td>26 U/L</td>
<td>TG</td>
<td>177 mg/dL</td>
</tr>
<tr>
<td>Gluc</td>
<td>290 mg/dL</td>
<td>AST</td>
<td>26 U/L</td>
<td>A1c</td>
<td>11.4%</td>
</tr>
</tbody>
</table>

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**Case 2: Blood Glucose Logs**

<table>
<thead>
<tr>
<th>Dates</th>
<th>Breakfast (8 am)</th>
<th>Pre Lunch (6 pm)</th>
<th>Pre Dinner (6 hours post prandial)</th>
<th>Dinner (2 hours post prandial)</th>
<th>Bedtime (12 midnight)</th>
</tr>
</thead>
<tbody>
<tr>
<td>11/8/12</td>
<td>290 mg/dL</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
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<td>11/7/12</td>
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<td>205 mg/dL</td>
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<td>250 mg/dl</td>
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<td>212 mg/dL</td>
<td>196 mg/dL</td>
<td>200 mg/dl</td>
<td>242 mg/dl</td>
<td>178 mg/dl</td>
</tr>
<tr>
<td>11/5/12</td>
<td>210 mg/dL</td>
<td>185 mg/dL</td>
<td>190 mg/dl</td>
<td>290 mg/dl</td>
<td>200 mg/dl</td>
</tr>
</tbody>
</table>
Discuss Cases at Your Table for 10 Minutes

Group 1: Case 1
Group 2: Case 2

Case 1: Question 1

List the potential risk factors that could be responsible for producing this patient's hypoglycemic symptoms.

Risk Factors for Hypoglycemia

- Variable Appetite
- Comorbid Medical Conditions
- Longer Duration of Disease
- Renal Insufficiency
- Polypharmacy
- Extremely Tight Control
- Poor Cognition
- Memory Deficits
- Visual Impairments
- Decline in Counter-regulatory Responses
- Depression
- Exercise or Strenuous Activities
JT’s Risk Factors for Hypoglycemia

- **Drug Therapy**
  - Contraindication/precautions: Metformin, Glyburide, Salicylates/NSAIDS, HCTZ
  - Beta Blocker (Metoprolol): Blunting of hypoglycemic symptoms
- **Self-Monitoring Blood Glucose (SMBG) and Pattern Management**
  - Early morning BG at a low-normal

JT’s Risk Factors for Hypoglycemia

- **Renal Dysfunction (Clcr <30 ml/min)**
  - Reduced excretion of Glyburide, Metformin, NSAIDS
- **Diet and Nutrition**: Inconsistent diet
- **Possible Depression**
- **Autonomic neuropathy with longstanding disease leading to decreased counter regulation**

**Case 1: Question 2**

Recommend treatment strategies for this patient’s acute hypoglycemia episode.
Treatment of Hypoglycemia

• 15:15 Rule
  – Glucose tablets 4 grams – 4 tablets OR
  – Glucose tablets 5 grams – 3 tablets OR
  – Glucose gel 15-30 grams as needed OR
  – 4 ounces of orange or apple juice OR hard candy
  – Recheck BG in 15 minutes
  – At goal >70 mg/dL (immediately provide the patient with a meal); if still low (<70 mg/dL), treat with 15 grams carbohydrates and recheck BG.

• CHECK  TREAT  CHECK  EAT

Case 1: Question 3

The physician wishes to introduce a sliding scale for this patient.

• Would you support this recommendation?

• Why or why not?

Sliding Scale Insulin

• Neither efficient nor effective.
• Historical artifact dating to the days of urine testing.
• Responsive not proactive to hyperglycemia.
• Based on the premise that insulin sensitivity is uniform among all patients.
• Risk factor for hypoglycemia.

Case 1: Question 4

What pharmacologic and non-pharmacological recommendations should the pharmacist make to prevent/minimize further hypoglycemic episodes?

Please include drug therapy monitoring plans.

Treatment

- Non-Pharmacological Recommendations
  - Depression screening ASAP
  - Diabetes self-management education
  - Evaluate patient’s diet and ensure consistency
  - Involve family and friend’s support

- Monitoring Parameters
  - SMBG daily especially in the early AM (Goal 90-130 mg/dL)
  - Evaluate for depression daily
  - A1c – quarterly
  - Evaluate for confusion and disorientation daily
  - Evaluate pain scores daily

Medication Options

<table>
<thead>
<tr>
<th>Biguanides (metformin)</th>
<th>500 mg BID w/meals (increase by 500 mg every 1-3 wks)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Most effective dose 2000 mg QD, max. 2550 mg QD</td>
</tr>
<tr>
<td></td>
<td>Long-acting: XR (500 mg QD, max. 2000 mg QD)</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>TZDs</th>
<th>Peglitazone: 15-45 mg QD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rosiglitazone: 2-4 mg QD**</td>
</tr>
<tr>
<td></td>
<td>** available only with special exemption</td>
</tr>
</tbody>
</table>

| Sulfonylurcencs | 1-2 times a day (Once daily with XL) |

<table>
<thead>
<tr>
<th>Alpha-glucosidase inhibitors</th>
<th>Acarbose: 25 - 300 mg. Every 4 hrs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Miglitol: 25 - 200 mg. Every 4 hrs</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>DPP4 Inhibitors</th>
<th>Sitagliptin: 50 -100 mg QD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Saxagliptin: 5 - 5 mg QD</td>
</tr>
<tr>
<td></td>
<td>Linagliptin: 5 mg QD</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Incretin Mimetics</th>
<th>Exenatide: 5-10 mcg BID SQ (once weekly now avail.)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Liraglutide: 0.6-1.8 mg QD SQ</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Meglitinides</th>
<th>Repaglinide: 16 mg QD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Nateglinide: 360 mg QD</td>
</tr>
</tbody>
</table>
**Treatment**

- Therapy Discontinuation
  - Beta blocker to be discontinued or dose lowered (25 mg)
  - Glyburide to be discontinued
  - Metformin to be discontinued
  - NSAIDS to be discontinued

- Therapy Initiation
  - Initiate Glargine or Detemir 10 units at bedtime
  - Increase by 2 units every 3 days and monitor AM fasting BG readings

**Case 2: Question 1**

List the potential barriers that could be responsible for this patient’s lack of glycemic control.

**Potential Barriers to Glycemic Control**

- Physician barriers
- Patient barriers
  - Educational
  - Psychological
  - Psychosocial
  - Economic
  - Physical
Case 2: Question 2
What strategies would you implement to reduce some of these barriers and encourage the patient to be participatory in her care?

Motivational Interviewing
• Open-ended Questions
  – “Tell me what you like about your current control.”
  – “What makes you think it might be time for a change?”
  – “What was that like for you?”
• Reflective Listening
  – “It sounds like you are saying…”
  – “What I hear you saying is…”
  – “I get the sense that…”

Motivational Interviewing
• Normalizing
  – “A lot of people are concerned about changing their…”
  – “Many people report feeling like you do.”
• Affirmation, Advice, and Feedback
  – “You showed a lot of courage by coming today…”
  – “Do you mind if we spend a few minutes talking about…”

Improving Adherence

• Health Care Clinicians
  – Show interest in the patient’s health and understand the diagnosis.
  – Find ways to fit medication regimen into his/her daily routine.
  – Believe that the patient can carry out the treatment plan.

• Patient
  – Understand the potential impact of the diagnosis.
  – Believe that the prescribed treatment will help.
  – Know exactly how to take the medication and the duration of therapy.
  – Value the outcome of treatment more than the cost of treatment.
  – Believe that the health care clinicians involved truly care about you as a person, rather than as a disease to be treated.


Improving Adherence

• Levine (1998) demonstrated that the following steps increase adherence:
  – Assessing the person’s understanding of the disease and the treatment regimen and then providing information where knowledge gaps exist.
  – Tying the medication-taking process to other daily routines.
  – Using adherence aids, such as medication organizers/charts.
  – Simplifying medication regimens.
  – Providing human support within the health care team.
  – Recognizing difficulty in coping and other sociobehavioral issues that may affect the person’s ability to follow the treatment regimen.


Case 2: Question 3

What would be your A1c goal for this patient?
**Targets for Glycemic Control**

- **ADA: A1c <7%**
  - Bedtime glucose: 100-140 mg/dL
  - Postprandial target: 100-180 mg/dL
  - Preprandial or fasting target: 70-130 mg/dL

- **AACE: A1c ≤6.5%**
  - Bedtime glucose: 100-140 mg/dL
  - Postprandial target: <140 mg/dL
  - Preprandial or fasting target: <110 mg/dL

*Achieve the lowest possible A1c without unacceptable hypoglycemia*

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**A1c Goal: Key Concepts in Setting Glycemic Goals**

- **ADA Goal: <7% vs AACE Goal: ≤6.5%**
  - Goals should be individualized.
  - Certain populations such as the elderly require special considerations.
  - Less intensive goals may be appropriate in those with a history of significant hypoglycemia or hypoglycemia unawareness.
  - More stringent goals (i.e., a normal A1c of <6%) may further reduce the risk of microvascular complications at the cost of increased risk of hypoglycemia.

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**Case 2: Question 4**

What pharmacologic and non-pharmacologic recommendations should the pharmacist make to optimize goal glycemic control?

Please include drug therapy monitoring plans.
## Clinical Trials – Regarding Tight Glycemic Control

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Trial</th>
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<tbody>
<tr>
<td>ACCORD</td>
<td>Action to Control Cardiovascular Risk in Diabetes Trial</td>
</tr>
<tr>
<td>ADVANCE</td>
<td>Action in Diabetes and Vascular Disease: Prexar and Diamon Modified Release Controlled Evaluation</td>
</tr>
<tr>
<td>VADT</td>
<td>Veterans Administration Diabetes Trial</td>
</tr>
</tbody>
</table>

## Study Designs

<table>
<thead>
<tr>
<th></th>
<th>ACCORD</th>
<th>ADVANCE</th>
<th>VADT</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>10,251</td>
<td>11,140</td>
<td>1,791</td>
</tr>
<tr>
<td>Primary Outcomes</td>
<td>Death from CV disease Nonfatal MI Nonfatal stroke</td>
<td>Death from CV disease Nonfatal MI Nonfatal stroke Major microvascular events</td>
<td>Death from CV disease MI; stroke; CHF Surgery for vascular disease; amputation for ischemic gangrene</td>
</tr>
<tr>
<td>Study Groups: Intensive (I) vs Standard (S)</td>
<td>Subjects received BP control fenofibrate vs placebo</td>
<td>Subjects received perindopril indamine vs placebo</td>
<td>Subjects received antihypertensives and lipid treatment</td>
</tr>
<tr>
<td>A1c goals (I vs S)</td>
<td>&lt;6.0% vs 7.0%-7.9%</td>
<td>≥6.5% vs based on local guidelines</td>
<td>&lt;6.0% (action if &gt;6.5%) vs planned separation of 1.5%</td>
</tr>
</tbody>
</table>

## Results Summary

<table>
<thead>
<tr>
<th></th>
<th>ACCORD</th>
<th>ADVANCE</th>
<th>VADT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median A1c</td>
<td>6.4% vs 7.5% *</td>
<td>6.4% vs 7.0% *</td>
<td>6.9% vs 8.4% *</td>
</tr>
<tr>
<td>Nonfatal Stroke</td>
<td>1.3% vs 1.2%</td>
<td>3.8 vs 3.8%</td>
<td>-</td>
</tr>
<tr>
<td>Nonfatal MI (%)</td>
<td>3.6% vs 4.6% *</td>
<td>2.7% vs 2.8%</td>
<td>6.3% vs 6.1%</td>
</tr>
<tr>
<td>CV Death (%)</td>
<td>2.6% vs 1.8% *</td>
<td>4.5% vs 5.2%</td>
<td>2.1% vs 1.7%</td>
</tr>
<tr>
<td>Death (any cause)</td>
<td>5% vs 4% *</td>
<td>8.9% vs 9.6%</td>
<td>-</td>
</tr>
<tr>
<td>Summary</td>
<td>MI risk but risk of deaths in intensive group</td>
<td>(-) improvement with CV events</td>
<td>(-) improvement with CV events</td>
</tr>
</tbody>
</table>

* significant
Results Summary (Cont’d)

- **ACCORD**
  - No clear explanation for increased mortality.
  - Mortality was 22% higher in the intensive group (study halted).
  - Hypoglycemia
  - Weight gain
  - Rapid lowering of A1c level
  - Medication interaction

- **ADVANCE**
  - Intensive glucose therapy had no impact on CV events.
  - Decreased RR of nephropathy ↓ 21% of intensive vs standard.
  - Decreased RR of retinopathy ↓ 5% of intensive vs standard.

- **VADT**
  - Intensive glucose therapy had no impact on CV events.

Kahn SE. JAMA. 2009;301(5):1590-1592

Take Home Message From Trials

- Intensive therapy for diabetes does not improve or reduce CV events.
- There is no excess risk of cardiovascular events with the use of rosiglitazone (TZD used).
- Intensive therapy resulted in hypoglycemia and increased weight.
- Trials confirm intensive therapy improved microvascular disease (nephropathy, retinopathy).

Case 2: Pharmacologic Therapy Recommendations

- Discontinue glipizide, sitagliptin.
- Continue metformin (possibly pioglitazone).
- Initiate glargine or detemir 20 units at bedtime. Use insulin pens. Titrate to goal.
- Initiate aspart protamine and insulin aspart (70/30) or other rapid acting insulin with meals.
- Consideration of other drug classes?
- Monitor parameters.
Glucose Monitoring

- **Self-monitoring**
  - TID or more for patients on multiple daily injections or insulin pump therapy.
  - In patient using less frequent insulin therapy, noninsulin therapies, or medical nutritional therapies, SMBG can be a useful measure of success.
  - Postprandial.
- **A1c**
  - Twice yearly in patients meeting treatment goals/stable glucose.
  - Quarterly in patients requiring change in treatment or those not meeting glycemic goals.
  - Point-of-care testing when timely decisions are needed.
- **Continuous glucose monitoring (CGM)** is a useful tool in patients on intensive insulin therapy.

Other Non-Pharmacologic Strategies

- Disease specific and medication regimen education
  - Why medication is needed
  - What to do if doses are missed or delayed
  - Common adverse effects that might occur
  - Serious adverse effects that should be monitored
- “Teach back” – ask patient to repeat instructions
- Involve social support network
  - Disease and medication education for spouse/family
- Team approach to diabetes management
  - Make patient a part of the team decisions
- Set realistic goals

Hypertension Management

- **Non-pharmacologic Management**
  - BP 130-139/80-89 mmHg: manage with 3 months of lifestyle changes, then if remains high —pharmacologic treatment
  - BP >140/>90 should receive pharmacologic therapy and lifestyle changes
- **Pharmacologic management**
  - ARB/ACE
  - Add thiazide diuretic if GFR >30 mL/min
  - Add loop diuretic if GFR <30 mL/min
  - 2-3 agents may be necessary to meet goals

GFR: glomerular filtration rate
Lipid Management

- Check lipid profile at least annually
- **Lifestyle modification**
  - Reduction of saturated fat, trans fat and cholesterol
  - Increase of omega-3 fatty acids
  - Viscous fiber and plant stanols/sterols
  - Weight loss
  - Physical activity
- **Add statin therapy to ALL patients with diabetes:**
  - With CVD
  - Without CVD if >40 + one or more risk factors for CVD


Summary

- Pharmacist should help patients attain optimal A1c and glycemic control but without hypoglycemia.
- Provide comprehensive drug therapy management to identify any potential hypoglycemia and minimize risks.
- Utilize a team approach to educate patients and providers.
- Assist in the development of protocols and clinical pathways to prevent and treat hypoglycemia.