Reducing Hypoglycemic Risk in Diabetes Care

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Disclosure Statement

• Dr. Timothy Gieseke, MD, CMD has no relevant financial relationship with commercial interests to disclose.
Learning Objectives

• Recognize the subtle presentations of hypoglycemia in seniors
• Set individualized targets for glycemic control
• Minimize care plans that are high risk for hypoglycemia
• Know why and when to add a trial of GLP 1 receptor agonists to the care plan

Diabetes in NHs

• Independent predictor of placement
• In a 2012 study:
  – Prevalence ~32%
  – Cost of care 19.6 billion
• ~90% are Type II diabetics (elevated C-peptide), but we do see Type 1s
• Prediabetes confers 2x > risk of CVDz
• Complications of DM ~ triple cost of care
Why Focus on Diabetes?

- Readmission Penalties (adjusted payments) as of January 1, 2019
- The CMS “SNF Readmission Measure (SNF-RM)” has been tracked and reported since Oct 2016 (2% withhold began then)
- SNF-RM is for all-cause SNF Readmissions the first 30 days after discharge from the Acute Hospital.
- Payments are adjusted based on SNF-RM relative to other SNFs.
- Hypo- & Hyperglycemia are major causes for readmissions.

Readmission Rate > in Diabetes

- CMS (data April 2016–March 2017) found persons on diabetic medications had readmission rate:
  - 22.75% vs. 18.8% for all persons.
- Serious hypoglycemia was a common cause for these readmissions
Case of Duncan Mills

• 86 y/o long stay resident with old right CVA, Stage 3B CKD, HBP, MCI, and Type II IDDM. His FS BG is ~ 140 before breakfast & ~ 180 before dinner. He receives: Metformin LA 1500 mg daily & NPH 70/30 a.c. bid. Lately, he has been mentally slow in the morning though his FS BG has increased to 160. His CNA notices at 2:00 am that he is moaning and restless.

• If you were his nurse, what would you be thinking?

Check FBG = 50 mg/dl

• Somogyi effect—when nocturnal hypoglycemia occurs and isn’t recognized, Norepinephrine and Glucagon are released raising glucose levels so hours later, the FBG is 160

• NPH at dinner has peak effect at 2-3 a.m.

• NPH should only be given a.c breakfast or HS(peak effect at bkft)

• NPH has higher-risk for hypoglycemia then other basal insulins
Hypoglycemia in the Elderly is Often Subtle

• May not have robust alarm symptoms (tremors, anxiety, sweating, hunger, lightheadedness or rapid palpitations)
• CNS Dysfunction common
  – Confusion, agitation, fatigue, or reduced LOC
  – Weakness & falls
  – If severe: Seizures, MI, CVA, Brain Injury, or Death
• Definition:
  – Mild if < 70 mg/dl or higher (if typical symptoms)
  – Severe if:
    • < 55
    • Hypoglycemia requiring bystander resuscitation

Approach to Setting A1C Goal

ADA Glycemic Targets for Older Adults

<table>
<thead>
<tr>
<th>Patient Characteristics/Health Status</th>
<th>Rationale</th>
<th>Reasonable A1C Goal</th>
<th>Fasting or Preprandial Glucose</th>
<th>Bedtime Glucose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy (few coexisting chronic illnesses, intact cognitive and functional status)</td>
<td>Longer remaining life expectancy.</td>
<td>&lt;7.5%</td>
<td>90–130 mg/dl</td>
<td>90–150 mg/dl</td>
</tr>
<tr>
<td>Complex/Intermediate (multiple coexisting illnesses or 2+ instrumental ADL$^1$ impairments or mild-to-moderate cognitive impairment)</td>
<td>Intermediate remaining life expectancy, high treatment burden, hypoglycemia vulnerability, fall risk.</td>
<td>&lt;8.0%</td>
<td>90–150 mg/dl</td>
<td>100–180 mg/dl</td>
</tr>
<tr>
<td>Very complex/Poor health (LTC$^2$ or end-stage chronic illnesses or moderate-to-severe cognitive impairment or 2+ ADL dependencies)</td>
<td>Limited remaining life expectancy makes benefit uncertain. Avoid hyperglycemia to prevent dehydration, electrolyte abnormalities, urinary incontinence, dizziness, falls, hyperglycemic crisis.</td>
<td>&lt;8.5%</td>
<td>100–180 mg/dl</td>
<td>110–200 mg/dl</td>
</tr>
</tbody>
</table>


1. Activities of daily living (ADL)
2. Long term care (LTC)

Monitoring Glycemic Control

- **FBG**
  - Frequency depends on desired control, risk of hypoglycemia, and patient preference
  - Before meals and bedtime until stable
  - 2 or 3 a.m. if identify risk for nocturnal hypoglycemia
  - Values > 400 mg% may not be accurate & could be considerably higher

- **A1C**
  - Assumes RBC half life of 3 months
  - Falsely low if < 3 mo. RBC half life as in CKD, HCT < 30
  - When A1C does not correlate with FBG measurements, rely on FBGs

1. Post acute/long term care (PA/LTC)
2. Red blood cell count (RBC)
3. Hematocrit (Hct)
Block FBG Testing for Stable DM

- Test 1 time a day (a.c tid + h.s) over the course of a week, to assess control over the whole day. Eg.
  - Monday (Bkft), Tuesday (Lunch), Weds(Dinner), Thurs(h.s.), Friday (Bkft), Sat (Lunch), Sunday (Dinner)
  - May only do this for 1-2 weeks prior to next visit and not test at other times unless becomes unstable.
- FBG testing is expensive and wearing on the fingers and patient

Rule of 15 for Rx Hypoglycemia

- When fasting (FS) glucose is <70 mg/dl, give 15 grams carbohydrate
- Carbohydrate sources (15–20 g) for treating hypoglycemia
  - ½ cup fruit juice or non-diet soda or 3-4 lifesavers
  - 1 cup milk (no fat or low fat works faster)
  - If unable to take PO, give glucose gel or glucagon and call MD
- Wait 15 minutes and recheck FS BG
  - If glucose is still <70 mg/dl, repeat 15 grams carb p.o
  - Wait additional 15 minutes and recheck.
  - If still low, repeat treatment and call MD
- Once FBG returns to normal, the individual should consume a meal or snack to prevent recurrence of hypoglycemia
- Inform physician or NP, so that regimen can be assessed and future low can be prevented

1. PO=by mouth
ADA & EASD Consensus Report on Rx Type 2 DM
• Diabetes Care October 4, 2018
  – http://care.diabetesjournals.org/content/early/2018/09/27/dci18-0033
• For patients with CVDz or high risk of CVDz, SGL2s or Incretin RAs are next drugs of choice if Metformin inadequate, not tolerated, or contraindicated.
• Incretin RAs are generally recommended as the first injectable medicine
• Updates: Lifestyle, Diabetes Self-management, Medications, Obesity, & Surgical interventions

Glucose Management for Patients With Type 2 Diabetes

<table>
<thead>
<tr>
<th>HbA1c</th>
<th>5.7%</th>
<th>Diabetes education on self-management, lifestyle interventions 3%-5% weight loss 150 min/wk exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.5%</td>
<td></td>
<td>Add metformin</td>
</tr>
<tr>
<td>&gt;9.0%</td>
<td></td>
<td>Add a second antihyperglycemic drug</td>
</tr>
<tr>
<td>HbA1c</td>
<td></td>
<td>Dio</td>
</tr>
<tr>
<td>Weight</td>
<td></td>
<td>↑</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>No effect</td>
<td>No effect</td>
</tr>
<tr>
<td>MACE</td>
<td>No effect</td>
<td>No effect</td>
</tr>
<tr>
<td>HF</td>
<td>↑</td>
<td>No effect</td>
</tr>
</tbody>
</table>

a. Indicates a higher-cost drug.  1. Major adverse cardiac event (MACE)

Metformin is First Line Rx

- First line drug therapy as long as renal function is adequate (ok to use EGFR)
  - EGFR 30-45 ml/min can use sub-max. dose (500 BID), but avoid new start in this range.
  - Metformin ER 1500 mg daily may be safer
  - Don’t use if EGFR < 30 ml/min (Lactic Acidosis).

- B12 deficiency possible with long term use

SGLT2 Inhibitors (Empagliflozin, Cana-, Dapa-)

- Block sodium glucose cotransporter in the proximal renal tubule, enhancing excretion of glucose and sodium.
- Must have adequate renal function (eGFR > 45 ml/min).
- Expect: Weight loss & lower Systolic/diastolic BP
- Empagliflozin reduced mortality 32% within 3.1 yrs (CV Mortality 38%, Heart Failure 35% in NEJM Nov 2015).
  - FDA indication for reducing MACE
- May reduce progression CKD
- Concerns: Genital mycotic infections, UTI’s, High Cost, Euglycemic DKA, PVD Amputations (Canagliflozin)
Injectable Therapies – Start with GLP-1 RAs

- **GLP-1 Receptor Agonists (Liraglutide, Dulaglutide, Bydureon)**
  - Act like supra-physiologic levels of *incretins*:
    - Enhance glucose stimulated insulin secretion and glucagon suppression
    - Post-prandial hyperglycemia improved
    - Slows gastric emptying & promotes early satiety @ CNS\(^1\) level
  - **Potent**, low risk of hypoglycemia, promote weight loss, modest decrease in BP
  - **Liraglutide**: decreased mortality and reduced MACE w/in 3.8 years, but not heart failure (NEJM July 2016)
    - **FDA indication** for reducing MACE
  - **Concerns**: risk of pancreatitis?, GI side effects (nausea, vomiting, diarrhea), C-cell hyperplasia and MTC\(^2\) in rodents, **Cost high**

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Basal Insulin (NPH, Glargine, Levemir, Degludec)

- Activate insulin receptor to enhance postprandial glucose disposal and suppress hepatic glucose production
- Universally effective
- Degludec has lower risk hypoglycemia
- **Concerns** (for all insulins): serious hypoglycemia, weight gain, training requirement,
- **High Cost**: Only 3 companies produce insulin analogs
  - Doubled price 2012-2016

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1. Central nervous system (CNS)
2. Medullary thyroid carcinoma (MTC)
Rapid Acting Insulins

- **Highest risk** for inducing serious hypoglycemia
- Regular insulin greater risk than analogs
- Give immediately a.c meals (even regular insulin)
- May give analogs immediately p.c. if eating not predictable
- Minimize bedtime use to reduce risk nocturnal hypoglycemia (eg. SSI a.c. tid – not h.s.)

Why Not Just Use Sliding Scale Insulin?

- Dose is not individualized
- Insulin is reactive, rather than proactive to what will happen
  - Giving insulin to cover when the BG is already high, rather than preventing the hyperglycemia
  - Leads to wide fluctuations in glucose levels
  - “brittle diabetes” is commonly iatrogenic
- Does not provide basal insulinization (needed by insulin deficient diabetics) nor consider nutritional coverage
- If used w/o basal insulin, Calif. facilities have received **IJ citation**
  1. Immediate jeopardy (IJ)

Some of the Variability of FBG May be Due to Injection Errors

- Diabetes Care in the UK, “FIT UK Forum for Injection Technique UK”
- Free
- Only 1 pen/patient
- Wrong angle of injection
- Wrong size needle
- Injection time errors
- Failure to rotate injection sites in predictable pattern to minimize tissue injury
- Wrong injection site
- Injecting into site of lipodystrophy or hypertrophy

Case of Laura C.

- 80-year-old with HBP, chronic atrial fibrillation, diastolic heart failure, overweight, and prediabetes.
- She is hospitalized with acute abdomen due to perforated diverticulitis with SIRS.
- She requires emergency laparotomy, colostomy, ICU level care, antibiotics, SSI insulin in the ICU on the ward.
- She had complicating *C. diff* for which she is now on oral Vancomycin.
- She is starting to eat, but still has FBG in 200–330 range.
- She is transferred to you on SSI Novalog AC TID + HS.
- How would you manage her diabetes?

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1. High blood pressure (HBP)
2. Systemic inflammatory response syndrome (SIRS)
3. Intensive care unit (ICU)
4. TID=3x/day
Adjust Orders to Reduce Hypoglycemic Risk

- Medically complex and sick
  - A1C target 8.0–8.5%
  - FBG 100–180 on AC TID + HS
  - Check 2–3 a.m. FBG 2x/wk
- Add basal insulin in the morning with goal of morning FBG 100–140 range
- Cancel SSI at bedtime
- Add 3 units of RA analog insulin with or after each meal with hold if doesn’t eat
- Continue corrective SSI
- RA analog added to scheduled meal insulin
- Reassess in 2–3 days

Case of Shirley M.

- 50+ year-old women with Type II IDDM with class 3 obesity, severe OSA (BiPAP\textsuperscript{1}-dependent HS), and persistent flaccid left hemiparesis after a large CVA.
- Her glycemic control remains poor with FBG in 150–350 range before meals and bedtime despite Lantus 80 units a.m./40 units HS and Novalog 30 units AC TID.
- She attempts to restrict calories, but is commonly hungry.
- What might you do to improve her glycemic control and health?

\textsuperscript{1} Bi-level positive airway pressure (BiPAP)
Options

- Reduce basal insulin if TDD$^1$ of insulin > 1 unit/kg/day
  - Reduce Glargine and see if hunger, xs PO intake, and FBG improve
- Add a GLP-1 RA
  - Liraglutide .6 mg SQ x 1 wk, then 1.2 mg SQ x 1 wk, then 1.8 mg SQ thereafter
  - She tolerated this well, lost ~5 kg, took less insulin, and had FBG most of the time in the low 100 range and no documented lows

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Case of Phil M.

- 60+ year-old with developmental delay, long standing schizophrenia, over-weight, and Type 2 NIDDM for about 10 year managed with Metformin
- Hospitalized for poorly controlled DM with dehydration, glucose 650, and A1C 10.9
- He received IV fluids and insulin, but is transferred to SNF for rehab only on Metformin because DPOA$^1$ is concerned that he will lose his independent living, if his care is too complex
- What do you do?

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1. Total daily dose (TDD)
2. Durable power of attorney (DPOA)
Many Concerns

- Was he taking his Metformin?
- Was his supervision adequate?—delayed crisis recognition
- **Glucotoxicity**
  - High glucose levels worsen insulin resistance
  - Using insulin to control hyperglycemia, resistance improves reducing need for supplemental insulin
- Lantus 15 units daily initially
- Decided to try Liraglutide because it is once a day with much lower risk of hypoglycemia
- Able to stop Lantus and achieve near normal FBG w/o lows
- TAR¹ for Dulaglutide (SQ weekly)

¹. Treatment authorization request (TAR)

Evidence Based Consensus Guidelines for Managing Type 2 DM

- Consensus statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the comprehensive type 2 diabetes management algorithm – 2019 executive summary
Resources for Clinicians

1. ADA 2019 Standards of Care—Abridged Version for PCPs
   http://clinical.diabetesjournals.org/content/diaclin/early/2018/12/16/cd18-0105.full.pdf
2. ADA 2019 Standards of Care—Abridged Version for PCPs
   http://clinical.diabetesjournals.org/content/diaclin/early/2018/12/16/cd18-0105.full.pdf
3. American Association of Clinical Endocrinologists (AACE) 2018 Comprehensive Type 2 Diabetes Management Algorithm—free
   b. Evidence based, but more expert opinion
   c. Free slide presentation
4. AMDA, The Society of Post Acute and Long Term Care Medicine
   a. https://paltc.org/ (Resources, Clinical Products, Product type, Clinical Practice Guidelines (CPGs), Diabetes CPG)
   b. Clinical Practice guideline for Diabetes Care in PA/LTC updated 2016
   c. Hard copy and electronic version ($39 for members)

Resources for Clinicians

- HSAG Readmission California Tools and Worksheets
  - https://www.hsag.com/care-coord-ca-tools
- HSAG Readmission California Tools and Worksheets
  - https://www.hsag.com/care-coord-ca-tools
- Yale Monograph Newsletter list serve—Free
  - https://visitor.r20.constantcontact.com/manage/optin?v=001TYH5ba1NOYXIMLoSFlimmerUFVVvBwFAQ7-5IPWBG9d91yDf2baDSH-MY0J1vQYH1urG7sAwC3vbNqQY24vFLE9ICVr6CyM0dJ7/o-y2bL.DauNFwTzPVRz6R9vypW-xhFVX1d0sS7mbsbFnu7UupRpsPVKebo6s
  - Concise daily 5–6 page review of ADA (June), and European Association for the Study of Diabetes (EASD) (September), annual meetings
  - Quick way to keep up on current clinical developments in diabetes care
- Epocrates Online—commercial for PC, tablets, and smart phones
  - https://online.epocrates.com/
  - Quick and practical resource I use multiple times daily
Resources for Patient Ed

- Diabetes Self-Management Education and Support (DSME and DSMS)
  - Knowledge is power and power
  - A 24/7 disorder that is complex and can quickly change
  - Diabetes educator(s) in your community extremely valuable
- Internet based free patient education:
  - UpToDate for Patients: https://www.uptodate.com/contents/table-of-contents/patient-information