A Call to Action: Addressing Diabetes Medication Safety

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Endocrine News

Highs & Lows

HYPOGLYCEMIA IN ELDERLY PATIENTS

- Why is hypoglycemia so misunderstood by both patients and healthcare providers?
- How can medications make matters worse?
- Elderly patients face an entirely different series of risks.
- What is the Endocrine Society doing to raise awareness about this confusing condition?

PRACTICAL APPROACHES:
CGM trend arrows and how to interpret them

DIABETES & UROLOGY:
A look at a team approach to treating diabetes & urologic issues
FDA Launches CE for Healthcare Providers to Reduce Hypoglycemic Events

The U.S. Food and Drug Administration (FDA) is making available a free, one-hour continuing education (CE) lecture for healthcare providers on Leveraging Health Literacy and Patient Preferences to Reduce Hypoglycemic Events in Patients with Type 2 Diabetes. With hypoglycemia from anti-diabetic medications, such as insulin, being the second most common adverse drug event implicated in emergency department visits, it is critical for healthcare providers to recognize risk factors, such as low health literacy and numeracy, cognitive decline, and food insecurity, and know how to mitigate these risks to improve patient outcomes. The course introduces and provides healthcare providers with printable tools that they can use with their patients and will be available on the CDERLearn website (under Continuing Education Courses) until October 31, 2020.

Reducing ED visits for insulin induced hypoglycemia is a Healthy People 2020 goal!
Scope of the Problem

- 9.3% of the US population has DM (>90% type2)
- 7th leading cause of death
- 14 million emergency department visits annually
- In 2011, there were 4,841 practicing endocrinologists or 1/6,000 patients with Diabetes
ED Visits for Adverse Drug Events

• 2013-2014: 4 ED visits/1000 persons for ADE
• 27% of these resulted in hospital admission
• 34.5% of ER visits for ADE occurred in seniors (age >65)
• 5 Diabetes medications account (Insulin, metformin, glipizide, glyburide, glimepiride) were among the 15 most common causes of ED visits for ADEs

How did we get here?

• Jean Pirart, 1978 Diabetes Care volume 1!
  Reported his personal observations of 4400 patients over years and correlated complications with his perceptions of glycemic control
  Before that there was no consensus on causality of complications
How did We get Here?

– Finger stick glucose monitoring
– HbA1c measurement
– New delivery systems- pumps and pens
– New and improved medications
  • Heavy pharma engagement
How did We get Here?

• Great science- 2 landmark studies
  – DCCT- 1993
  – UKPDS
The Effect of Intensive Treatment of Diabetes on the Development and Progression of Long-Term Complications in Insulin-Dependent Diabetes Mellitus

The Diabetes Control and Complications Trial Research Group

Median HbA1c concentrations during DCCT, the “training” period between DCCT and EDIC, and EDIC. P < 0.001 for INT vs.

David M. Nathan, and for the DCCT/EDIC Research Group Dia Care 2014;37:9-16
Implications of the United Kingdom Prospective Diabetes Study

American Diabetes Association
How did We get Here?

• DCCT- proved that microvascular complications correlated with A1c in Type 1
• UKPDS- demonstrated similar findings in Type 2
• How low is low enough?
Relationship of A1C to Risk of Microvascular Complications

Diabetes Control and Complications Trial (DCCT)

Relative Risk (%)

HbA1c (%)

ADA Goal

Risk of Progression of Complications: DCCT Study

DCCT = Diabetes Control and Complications Trial.
From: Intensive Treatment and Severe Hypoglycemia Among Adults With Type 2 Diabetes

Rates of Estimated Hospital Admissions for Hyperglycemia and Hypoglycemia Among Medicare Beneficiaries With Diabetes Mellitus, 1999 to 2010

The circles and diamonds indicate observed values; the lines represent the smoothed trend over time.
Kaplan-Meier Curves for the Primary Outcome and Death from Any Cause

Hazard Ratios for the Primary Outcome and Death from Any Cause in Prespecified Subgroups

Addition of a Second Line Drug Before it’s Time

- Metformin is the most important oral agent in the treatment of Type 2 Diabetes
- Every patient with Type 2 DM should be on metformin on the maximal tolerated dose consistent with compliance
- Use of metformin is safe if eGFR is >30 and in the absence of advanced CHF, or COPD
- A recent study demonstrated that only 8.25 (1875/52544) had evidence of recommended use of metformin before beginning a second line agent¹
- This is a huge problem- rapid up-migration to medications with high hypoglycemia risk!

Table 4. Number of Cases and Estimates of Precipitating Factors Identified in ED Visits for IHEs (United States, 2007-2011)*

<table>
<thead>
<tr>
<th>Precipitating Factor</th>
<th>ED Visits for IHEs</th>
<th>Annual National Estimate, % (95% CI)</th>
<th>Illustrative Cases(^b)</th>
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</table>
| Meol-related misadventure | 952 | 45.9 (38.2-53.6) | • Unrestrained 19-year-old female driver hit tree and brick wall. Blood glucose was 24. Took insulin 2 hours ago, but no time to eat. Diagnosis: scalp abrasion, hypoglycemia.
• 75-year-old male is an insulin-dependent diabetic, had a syncopal episode at home, found with blood glucose in the 20s by paramedics. EMS gave patient an ampule of D50 (dextrose 50%) intravenously. Per wife, patient has been having low blood glucose and it has been difficult to keep elevated. She feels it is due to chemotherapy, possibly not eating enough. Diagnosis: hypoglycemia. |
| Unintentionally took wrong insulin product | 332 | 22.1 (17.2-26.9) | • 51-year-old male, per spouse she injected patient with 50 units of NovoLog instead of 50 units of Lantus, blood glucose 33 at time of arrival. Diagnosis: hypoglycemia.
| Unintentionally took wrong dose/confused units | 205 | 12.2 (9.2-15.2) | • Patient started new insulin regimen, 30-35 units of Lantus, 3-6 units of NovoLog; patient took 35 units of NovoLog accidentally; blood glucose 40. Diagnosis: insulin overdose.
• 62-year-old male given 40 units of regular insulin instead of 4, finger-stick blood glucose 47. Diagnosis: insulin overdose, hypoglycemia. |
| Intentionally took "additional" dose | 113 | 6.0 (4.4-7.6) | • 69-year-old male hypoglycemic—patient’s blood glucose was over 400; took 12 units insulin in addition to his insulin pump; blood glucose dropped to 38; found unresponsive by wife. Diagnosis: insulin shock. |
| Pump-related misadventure | 38 | 1.5 (0.7-2.2) | • 33-year-old female accidentally gave self bolus of 36 units regular insulin while changing insulin pump. Diagnosis: overdose, accidental.
• 27-year-old male is an insulin-dependent diabetic on insulin pump, had a witnessed tonic-clonic seizure. EMS found blood glucose of 20. Patient admitted that he had eaten dinner but his pump had run out so he gave himself an injection and feels he may have overcompensated. Diagnosis: hypoglycemia, seizure. |
| Other misadventure\(^c\) | 211 | 13.4 (10.4-16.4) | • 76-year-old male with syncopal episode after mowing lawn for 3 hours; took usual insulin at noon rather than in the morning—passed out. Diagnosis: hypoglycemic reaction. |
Diabetes in Seniors

- 25% of those over 65 have Diabetes
- Multiple co-morbidities
- High rate of cognitive impairment
- Polypharmacy
- Seniors over 80 have twice the risk of ED visits for hypoglycemia and 5x risk of hospital admission
Consequences of Hypoglycemia

- Increased risk of dementia
- Falls
- Fall-related fractures
- C-V events
- Diminished QOL
- Increased mortality
ADA HbA1c Targets- 2017

- Non-pregnant adults- <7%
- Selected patients, or those treated by lifestyle modification or metformin only <6.5%
- For patients with severe hypoglycemia or advanced complications <8%
- For many seniors, relax targets to prevent symptomatic hypoglycemia
Using Admission A1c to Guide Discharge Planning

- A1c<8%- No meds-begin metformin. On meds, continue current regimen
- A1c 8-9- No meds-begin metformin. On meds, increase meds, add another agent or consider basal insulin at 50% of hospital dose
- A1c>9 no symptoms- No meds-begin metformin and 2nd agent. On meds-increase doses and consider addition of basal insulin at 80% of inpatient level
- A1c>9 with symptoms- Consider metformin and add basal/bolus therapy
Summary

• Hypoglycemia has surpassed hyperglycemia as a cause of ER visits and hospitalization
• A1c targets might have been overly aggressive in many patients
• Patient and prescriber errors are major contributors
• Hypoglycemia risk is exaggerated in the elderly- and consequences may be severe