Challenges of Inpatient Glycemic Control

ACPE UAN 107-000-11-005-L01-P 0.2 CEU/2.0 Hr

Activity Type: Knowledge-Based

Program Objectives for Pharmacists: Upon completion of this program, participants should be able to:
1. Identify current glycemic control goals for inpatients, both in the critical care and non-critical care areas.
2. Organize an inpatient glycemic control committee dedicated to improving the institutions’ glycemic control.
3. Develop protocols addressing which diabetes medications are and are not appropriate for utilization in the inpatient setting.
4. Institute physiologically based intravenous and subcutaneous insulin protocols for utilization within the institution.
5. Remove sliding scale approaches to insulin from the institution.

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Speaker Disclosure: Mary Starry reports she has no actual or potential conflicts of interest in relation to this program. The speaker has indicated that off-label use of medications will not be discussed during this presentation.
Challenges of Inpatient Glycemic Control
Mary J Starry BS Pharm, PharmD, CDE

Provide Tools For You To.....
- Appropriately handle hyperglycemia in the hospital by:
  - Leading an inpatient glycemic control committee.
  - Identifying inpatients with risk for hyperglycemia.
  - Determining goals for inpatient glycemic control.
  - Removing sliding scale regimens.
  - Developing protocols for non-insulin diabetes medications.
  - Instituting IV and SQ insulin protocols.
  - Transferring from IV to SQ and discharge to home.

Resources
resources.aace.com/
- American Association of Clinical Endocrinologists
- Inpatient Glycemic Control Resource Center

AACE-ADA Consensus Statement on Inpatient Glycemic Control

Patient Scenario
- TM is 62 y/o Caucasian male, 5'11", 203lb admitted with community acquired pneumonia
- Hx of hypertension and hyperlipidemia. 90 pack year smoking, 14 to 21 beers/week.
- Home meds of lisinopril 40mg QD, HCTZ 50mg QD, atorvastatin 80mg QD
- Nurse reports glucose of 189mg/dl at 4PM on day of admit. Pt denies any intake besides water in past 6.5 hours.
- Should this glucose level be of concern?

Questions to Raise?
- Is hyperglycemia in a patient without diabetes a concern?
  1. Yes
  2. No

- Should hyperglycemia caused by medications or stress be treated the same as that due to diabetes?
  1. Yes
  2. No
Successful Strategies for Implementation

- Champion(s)
- Administrative support
- Multidisciplinary steering committee to drive the development of initiatives
  - Medical staff, nursing and case management, pharmacy, nutrition services, dietary, laboratory, quality improvement, information systems, administration
- Assessment of current processes, quality of care, and barriers to practice change

A Champion is Needed to Lead the Development of the...

- Standardized order sets
- Protocols, algorithms
- Policies
- Educational programs (physicians and nurses)
- Metrics for evaluation
  - A system to track hospital glucose data in an ongoing basis
  - Assess the quality of care delivered
  - Continuous improvement of processes and protocols

Administration Support

- Education on:
  - Patient Benefits
  - Financial Benefits
  - Financial support needed

Cost Analysis of Stamford Trial

- Based on the 1600-patient before-and-after study published in Mayo Clinic Proceedings, August 2004
- Coauthor: Richard Jones, CFO; Stamford Hospital
- Attempted to quantify the major components of the total cost of care

Components of the Cost of Care

- Number of ICU hours: 17.2% reduction
- Number of ventilator hours: 19.0% reduction
- Lab costs: 24.3% reduction
- PHARMACY COSTS: 16.7% reduction
- Imaging costs: 5.0% reduction
- Median number of days in hospital after ICU discharge decreased from 5 to 4
Annualized cost savings = $1,340,000
Savings per patient = $1560
Mean LOS = 3.4 days; median LOS = 1.7 days


Administration Support Essential to...
- Obtain key personnel on your committee
- Move protocols and policies through committees
- Provide initial hospital-wide education
- Provide ongoing education
- To address and overcome hurdles
  - Staffing issues
  - Timing issues
- To maintain emphasis long-term

Who will be the most important member of your working team?
1. Administrator
2. Physician
3. Pharmacist
4. Diabetes educator
5. Dietitian
6. Staff nurse

Diabetes Champion for each unit...
- Nurse with special interest in diabetes
- Special recognition for the champions
- Regular meetings with champions
- Provide ongoing education for them to share at unit meetings
- Learn what is happening on the units from people who deal with the obstacles daily
- Likely already organized and in place through your diabetes education department

Core Knowledge for Physicians
- Impact of BG on hospital outcomes
- Institutional targets for BG
- Terminology: basal/nutritional/correction
- Insulin product knowledge
- Hypoglycemia prevention and treatment

Core Competencies for Nurses
- Bedside glucose monitoring technique
- Critical and target BG values
- Insulin administration technique
- Optimum timing of subcutaneous insulin shots
- Hypoglycemia prevention and treatment
- BG and insulin dose documentation
- Basic patient education (ability to teach patient "survival skills")
Education on Impact of Hyperglycemia

Hyperglycemia: A Common Comorbidity in Medical-Surgical Patients in a Community Hospital

Hyperglycemia is Linked to Mortality Regardless of Diabetes Status

Mortality in Inpatients with “New Hyperglycemia”

Benefits of Tight Glycemic Control: Observational Studies and Early Intervention Trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Setting</th>
<th>Population</th>
<th>Clinical Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Furnary, 1999</td>
<td>ICU</td>
<td>DM undergoing open heart surgery</td>
<td>65% ↓ infection</td>
</tr>
<tr>
<td>Furnary, 2003</td>
<td>ICU</td>
<td>OR undergoing CABG</td>
<td>57% ↓ mortality</td>
</tr>
<tr>
<td>Krinsley, 2004</td>
<td>Medical/Surgical ICU</td>
<td>Mixed, no Cardiac</td>
<td>29% ↓ mortality</td>
</tr>
<tr>
<td>Malmberg, 1995</td>
<td>CCU</td>
<td>Mixed</td>
<td>28% ↓ mortality After 1 year</td>
</tr>
<tr>
<td>Van den Benye, 2001*</td>
<td>Surgical ICU</td>
<td>Mixed, with CABG</td>
<td>42% ↓ mortality</td>
</tr>
<tr>
<td>Lazar, 2004</td>
<td>OR and ICU</td>
<td>CABG and DM</td>
<td>60% ↓ Fib post op survival 2 yr</td>
</tr>
</tbody>
</table>

*RCT: randomized clinical trial

### Intensive Glucose Management in RCTs Showing No Benefit

<table>
<thead>
<tr>
<th>Trial</th>
<th>N</th>
<th>Setting</th>
<th>Primary Outcome</th>
<th>ARR</th>
<th>RRR</th>
<th>Odds Ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Van den Berghe 2006</td>
<td>1200</td>
<td>ICU</td>
<td>Hospital mortality</td>
<td>2.7%</td>
<td>7.0%</td>
<td>0.94* (0.84-1.06)</td>
<td>N.S.</td>
</tr>
<tr>
<td>HI-S 2006</td>
<td>240</td>
<td>CCU AMI</td>
<td>6-mo mortality</td>
<td>-1.8%*</td>
<td>-30%*</td>
<td>NR</td>
<td>N.S.</td>
</tr>
<tr>
<td>Glucosta 2007</td>
<td>1001</td>
<td>ICU</td>
<td>ICU mortality</td>
<td>-3.5%</td>
<td>-10%</td>
<td>1.10* (0.84-1.44)</td>
<td>N.S.</td>
</tr>
<tr>
<td>VISEP 2008</td>
<td>537</td>
<td>ICU</td>
<td>28-d mortality</td>
<td>1.3%</td>
<td>5.0%</td>
<td>0.89* (0.59-1.38)</td>
<td>N.S.</td>
</tr>
<tr>
<td>De La Rosa 2008</td>
<td>504</td>
<td>ICU</td>
<td>28-d mortality</td>
<td>-4.2%*</td>
<td>-13%*</td>
<td>NR</td>
<td>N.S.</td>
</tr>
<tr>
<td>NICE-SUGAR 2009</td>
<td>604</td>
<td>ICU</td>
<td>3-mo mortality</td>
<td>-2.6%</td>
<td>-10.6</td>
<td>1.14 (1.00-3.28)</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>

* not significant

### What Should We Take Away from These Trials?

- Good glucose control, as opposed to near-normal control, is likely sufficient to improve clinical outcomes in the ICU setting.
- Hyperglycemia and hypoglycemia are markers of poor outcome in critically and non-critically ill patients.
- Importantly, the recent studies do not endorse a *laissez-faire* attitude toward inpatient hyperglycemia that was prevalent a decade ago.

### Education on Impact of Hypoglycemia

Severe hypoglycemia (<40 mg/dL) was associated with an increased risk of mortality (OR, 2.28; 95% CI, 1.41-3.70; P=0.008)

### 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

### Hypoglycemia Also Increases Cytokines

Unpublished work.

References:

AACE/ ADA Recommended Target Glucose Levels in ICU Patients

- ICU setting:
  - 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
  - Targets <110 mg/dL or >180 mg/dL are not recommended

<table>
<thead>
<tr>
<th>Not recommended</th>
<th>Acceptable</th>
<th>Recommended</th>
<th>Not recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;110</td>
<td>110-140</td>
<td>140-180</td>
<td>&gt;180</td>
</tr>
</tbody>
</table>

Back to TM...

- TM is a non-ICU patient.
- Your goals for BG control for TM are:
  1. Below 200 mg/dL
  2. 140 to 180 mg/dL
  3. 100 to 140 mg/dL
  4. 70 to 110 mg/dL

AACE/ADA Target Glucose Levels in Non-ICU Patients

- Non-ICU setting:
  - Premeal 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 and/or above these cut-points

- Hypoglycemia = BG <70 mg/dL
- Severe hypoglycemia = BG <40 mg/dL

Education on Glucose Variability—Why Are Ups and Downs Bad?

- Smoothing out the roller coaster!

What We Know So Far.....

- In cell culture, alternating from low to high glucose results in inflammatory activation, oxidative stress, and cell death.\(^1\)
- In large retrospective studies, glycemic variability is associated with poor outcomes including death.\(^2,3\)
- This suggests that glucose fluctuation may be involved in the development of oxidative stress and vascular injury

Glucose Fluctuations May be Involved in the Pathogenesis of Vascular Diabetic Complications

- Cell death of human umbilical vein endothelial cells
- "Variability in glycemic control may be more deleterious than a constant high concentration of glucose"
How to measure...

- Glycemic variability
  - Mean Amplitude of Glycemic Excursions (MAGE)
    - Measures both the UPS and the DOWNS of glucose control
  - Standard deviation on SMBG meter download

So What Is The Significance of the Understanding of Glucose Variability?

- "...it suggests that different therapeutic strategies now in use should be evaluated for their potential to minimize glycemic excursion, as well as their ability to lower A1C."
- "...wider use of real-time continuous glucose monitoring in clinical practice would provide the required monitoring tool to minimize glycemic variability and superoxide overproduction."

And What Is the Greatest Single Reason for Oxidative Stress in Most Hospitals?

**Sliding Scale Insulin!**

Does Sliding Scale Insulin Work?

- N = 171 (mostly T2DM) administered sliding scale insulin X 4d
- No improvement in glycemia during hospitalization
- 40% with at least one BG > 300 mg/dL
- 23% with at least one BG < 60 mg/dL

"...sliding scale insulin regimens provide no benefit..."

Inpatient Glycemic Control: Consensus Conference on Patient Safety 2005

- There is a high incidence of injurious medical errors world-wide
- Errors in diabetes care are an important cause of poor outcomes
- Errors in insulin administration are a common cause of injurious errors
- Sliding scale insulin is ineffective and sometimes dangerous but still remains in wide usage

Problem: Managing DM with Sliding Scale Insulin Only

<table>
<thead>
<tr>
<th>Problems</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reactive, not proactive</td>
<td>Dosing based on inadequacy of previous dose</td>
</tr>
<tr>
<td>Goal is hyperglycemia</td>
<td>Starts at 200mg/dL</td>
</tr>
<tr>
<td>Does not account for previous regimen</td>
<td>“one size fits all”</td>
</tr>
<tr>
<td>Rarely reevaluated</td>
<td>Pt’s glucose control is rarely reevaluated</td>
</tr>
<tr>
<td>Little to no clinical thinking</td>
<td>Without clinical basis, endpoints, lack critical thinking</td>
</tr>
<tr>
<td>No basal insulin</td>
<td>Fasting, postprandial, nocturnal, and inter-meal glucose control</td>
</tr>
</tbody>
</table>
TM is started on sliding scale......

- **Scale:**
  - 200 – 250: 5 Units
  - 250 – 300: 8 Units
  - > 300: 10 Units
- TM receives no insulin for his 189mg/dl, eats supper and is 302mg/dl at 10PM, when he receives 10 Units.
- At 6AM TM has a BG reading of 166mg/dl and receives no insulin. He has 60grams CHO for breakfast.
- What do you think TM's pre-lunch BG reading will be?
  1. Below 200mg/dl?
  2. 250 – 300 mg/dl?
  3. > 300 mg/dl?

A Typical Meal Tray in the Hospital Will Raise Blood Glucose by About 200 mg/dL

- Breakfast-2 slices toast, 1/2 banana, 4 oz. Juice, eggs & sausage
- Lunch-sandwich, 8 oz. Milk, 1 small cookie
- Dinner-roll, 1/4 cup fruit, 2/3 cup rice, 8 oz. Milk, Pork-chop

Return to Patient Scenario.......

- TM is 62 y/o Caucasian male, 5'11", 203lb with pneumonia, hypertension and hyperlipidemia
- 90 pack year smoking hx, 14 to 21 beers/week.
- Home meds of lisinopril 40mg QD, HCTZ 50mg QD, atorvastatin 80mg QD
- Nurse reports glucose of 189mg/dl at 4PM on day of admit. Pt denies any intake besides water in past 6.5 hours.
- What would be appropriate therapy?

Questions to Raise?

- Is his hyperglycemia of new onset or did he have undiagnosed diabetes?
- What was his glucose control prior to his admittance?
  - Routine orders for A1c levels for all patients with hyperglycemia and no A1c level within past 2 mths
  - Routine orders for A1c levels for all patients with diagnosis of diabetes and no A1c within past 2 mths

Questions to Raise?

- How should we treat his hyperglycemia?
  1. Secretagogue
  2. Insulin sensitizer
  3. Incretin mimetic agents
  4. Amylin analog
  5. Insulin

Medications for Hyperglycemia

- **Oral Agents**
  - Sulfonylureas (Glyburide, Glipizide, Glimiperide)
  - Meglitinides (Repaglinide, Nateglinide)
  - Alpha Glucosidase Inhibitors (Acarbose, Miglitol)
  - Biguanides (Metformin)
  - Thiazolidinediones (Rosiglitazone, Pioglitazone)
- **Incretin Mimetic Agents**
  - Exenatide (Byetta) - subcutaneous
  - Sitagliptin (Januvia) - oral
- **Amylin Analogs**
  - Pramlintide (Symlin) - subcutaneous
- **Exogenous Insulin**
Considerations with Non-insulin therapies in the hospital

- Sulfonylureas are a major cause of prolonged hypoglycemia
- Metformin is contraindicated in patients with decrease renal function, use of iodinated contrast dye, and any state associated with poor tissue perfusion (CHF, sepsis)
- Thiazolidinediones associated with edema and CHF
- α glucosidase inhibitors are weak glucose lowering agents
- Amylin and GLP1 agonists can cause nausea and exert a greater effect on postprandial glucose
- Time action profiles of oral agents can result in delayed achievement of target glucose ranges in hospitalized patients

ACE/ADA: Standardize Insulin Therapy to Reduce Errors

- Single Insulin Infusion Concentration
- Single Insulin Infusion Protocol
- SC Insulin order set
- Hypoglycemia Protocol
- Guidelines for Transitions
  - IV to SC
  - Back to ambulatory regimen
- Guidelines for Special Situations
  - Enteral Nutrition
  - Parenteral Nutrition

Indications for Intravenous Insulin Therapy

- Diabetic ketoacidosis
- Nonketotic hyperosmolar state
- Critical care illness (surgical, medical)
- Postcardiac surgery
- Myocardial infarction or cardiogenic shock
- NPO status in type 1 diabetes
- Labor and delivery
- Glucose exacerbated by high-dose glucocorticoid therapy
- Perioperative period
- After organ transplant
- Total parenteral nutrition therapy

Questions to Raise?

- Why type of insulin regimen should TM be started on?
  1. Insulin drip
  2. Subcutaneous regimen
  3. Sliding scale regimen

Subcutaneous Insulin Therapy
Insulin Requirements in Health & Illness

Relative proportion of insulin requirement (%)*

- Estimations for illustrative purposes: requirements may vary widely.


Sick/Eating

Healthy

Sick/ NPO

Illness-Related

Correction

Nutritional

Prandial

Basal

Maintaining Physiologic Insulin Delivery in the Hospital

Subcutaneous Insulin Options

- Basal Insulin – controls blood glucose in the fasting state
- Prandial or Nutritional Insulin – blunts the rise in blood glucose following nutritional intake
- Correction Insulin – corrects hyperglycemia due to mismatch of nutritional intake and/or illness related factors and scheduled insulin administration

Insulin Analogs

Recombinant DNA Technology

Altered Absorption Characteristics

PRANDIAL

- Lispro (Humalog®)
- Aspart (Novolog®)
- Glulisine (Apidra®)

BASAL

- Glargine (Lantus ®)
- Detemir (Levemir ®)

Options for Basal Insulin

Controls BG in fasting state

NPH

Glargine

Detemir

Basal Insulin: Pharmacokinetics

<table>
<thead>
<tr>
<th>Insulin Type</th>
<th>Onset</th>
<th>Peak</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>NPH</td>
<td>2 hr</td>
<td>4-6hrs</td>
<td>8-12 hrs</td>
</tr>
<tr>
<td>Glargine</td>
<td>1-2 hrs</td>
<td>relatively peakless</td>
<td>up to 24 hrs*</td>
</tr>
<tr>
<td>Detemir</td>
<td>2-4 hrs</td>
<td>relatively peakless</td>
<td>up to 24 hrs*</td>
</tr>
</tbody>
</table>

*Dose dependent
Options for Nutritional Insulin

Food or Bolus Insulin

- Regular
- Lispro
- Aspart
- Glulisine

Nutritional Insulin: Pharmacokinetics

<table>
<thead>
<tr>
<th>Insulin Type</th>
<th>Onset</th>
<th>Peak</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regular</td>
<td>30-60 min</td>
<td>3-4 hrs</td>
<td>6-8 hrs</td>
</tr>
<tr>
<td>Lispro</td>
<td>5-15 min</td>
<td>1 hr</td>
<td>4 hrs</td>
</tr>
<tr>
<td>Aspart</td>
<td>5-15 min</td>
<td>1 hr</td>
<td>4 hrs</td>
</tr>
<tr>
<td>Glulisine</td>
<td>20 min</td>
<td>1.5 hr</td>
<td>5 hrs</td>
</tr>
</tbody>
</table>

RAA = Rapid Acting Analog (Lispro/Aspart/Glulisine)
Subcutaneous Correction
Insulin Algorithms

- Do NOT replace schedule insulin
- Correction for changing needs
- Based on the insulin sensitivity of the patient
  - Total daily insulin requirement
  - Weight/BMI
- Utilize rapid acting analogs
  - Need rapid onset and short duration of action

Subcutaneous Insulin Order Form

- BG Monitoring: 4 ac & hs
- Goal Range Premeal BG = 100-150 mg/dl
- Goal Range Bedtime BG = 100-180 mg/dl

Components of Ideal
Subcutaneous Insulin Order Forms

- Specific instructions regarding blood glucose monitoring
- Goal blood glucose ranges
- Clear definition of hypoglycemia and treatment for it
- Unambiguous insulin orders
  - Amount and type of insulin to be administered
  - Time insulin is to be administered (basal)

Subcutaneous Correction Algorithms

- Low-Dose Algorithm
  - For pts requiring < 40 units of insulin/day
- Medium-Dose Algorithm
  - For pts requiring 40-80 units of insulin/day

Selection of Formulary Insulin

- Safety
- Efficacy
- Cost
- VALUE
Value of Rapid Acting Insulin Analogs

- Better matches the absorption of carbohydrate from typical hospital meals
- Fast onset and short duration is key for correction insulin algorithms
- Convenience
  - No need for lag time (can be given after meal if concern about how much will be eaten)
  - Easier to coordinate insulin administration with food intake

Less hypoglycemia

Initiating Insulin Therapy in the Hospital

Obtain patient weight in kg

Calculate total daily dose (TDD) as 0.2-0.4 units per kg/day

Choose the dosing schedule
- Give 50-60% of TDD as basal insulin
- Give 40-50% of TDD as bolus (premeal or nutritional) insulin
- Use Correction Insulin for BG above goal range

Adjust according to results of BSGM
- Adjust dose for NPO status or changes in clinical status

Changing Insulin Therapy in the Hospital

Determine total amount of insulin patient takes daily on average.
This is the:
- Total Daily Dose (TDD)

Choose the dosing schedule
- Give 50-60% of TDD as basal insulin
- Give 40-50% of TDD as bolus (premeal or nutritional) insulin
- Use Correction Insulin for BG above goal range

Adjust according to results of BSGM
- Adjust dose for NPO status or changes in clinical status

Starting Insulin Therapy in the Hospital

Obtain patient weight in kg

Calculate total daily dose (TDD) as 0.2-0.4 units per kg/day

Choose the dosing schedule
- Give 50-60% of TDD as basal insulin
- Give 40-50% of TDD as bolus (premeal or nutritional) insulin
- Use Correction Insulin for BG above goal range

Adjust according to results of BSGM
- Adjust dose for NPO status or changes in clinical status

Starting MDI in 100-kg Person with Moderate Insulin Resistance

- Starting dose = 0.5 x wt in kg
  - 0.5 x 100 kg = 50 U
- Basal dose = 40%-50% of starting dose at bedtime
  - 50% of 50 U = 25 U at hs
- Total bolus dose = 50%-60% of starting dose evenly distributed 1/3 at each meal
  - 25 U ÷ by 3 meals = 8 U before meals (tid)
- Give after meals as rapid-acting analog if food intake is in doubt
- Do not skip correction dose even if no food eaten
- Adjust upwards daily by adding 50% of correction doses to basal and bolus doses

Bolus Insulin Calculations

- Based on total daily dose (TDD) of insulin needed.
- Prandial needs calculated with Rule of 500
  - 500/ TDD = Amount of carbohydrates covered by 1 Unit of prandial or bolus insulin
- Supplement or correction needs calculated with Rule of 1700 (1500 or 1800 often used as well)
  - 1700/TDD = Amount of glucose in mg/dl that 1 Unit of bolus insulin should lower

Are starting points!!! Be prepared to adjust!

Which Regimen for TM?

- TM’s weight is 203 lbs. His estimated total daily dose would be 0.4 to 0.5 Units per kg.
- Which insulin regimen would you start TM on?
  1. 20 Units Lantus q AM and 7 Units Humalog at each meal.
  2. 20 Units Lantus q HS and 1 Unit Apridra for each 8 grams of carbohydrate.
Randomized Study of Basal-Bolus Insulin Therapy in the Inpatient Management of Patients With Type 2 Diabetes (RABBIT 2 Trial)

Adjusting scheduled insulin regimen
If fasting and premeal BG >140 mg/dl, dose of glargine increased by 20%

For BG <70 mg/dl, glargine reduced by 20%

Back to TM......

- TM's pneumonia is not improving and his BG has been > 200mg/dl his last two tests. His nurse institutes an insulin infusion per protocol.....
- What is the goal glucose range for TM now that he is on an insulin infusion?
  1. < 200 mg/dl
  2. 140 to 180 mg/dl
  3. 100 to 140mg/dl
  4. 70 to 110mg/dl

Components of IV Insulin Therapy

- Concentrations should be standardized throughout the hospital
  - Regular insulin in concentrations of 1 U/mL or 0.5 U/mL
  - Infusion controller adjustable in 0.1-U doses
- Accurate bedside blood glucose monitoring done hourly (and if stable, every 2 hours)
- Potassium should be monitored and given if necessary

Selection of Insulin Infusion Protocol

Features of the ideal protocol include:
- Based not only on current blood glucose, but also on the rate of change, and insulin sensitivity of the patient.
- Easy to implement and use
  - Paper vs. Computer
- Clear and specific directions for titration
- Specific directions for blood glucose monitoring
- Clear definition of hypoglycemia and treatment

Go with a validated protocol!
Various IV Insulin Protocols Exist

- Yale protocol
- Markovitz protocol
- Leuven protocol
- Portland protocol
- DIGAMI
- University of Washington
- Luther Midelfort Mayo Health System
- Brigham and Women’s Hospital insulin protocol

An Optimal IV Insulin Protocol

- Easily ordered (signature only)
- Effective (gets to goal quickly)
- Maintains BG within a defined target range
- Includes an algorithm for making temporary corrective increments or decrements of insulin infusion rate
- Safe (minimal risk of hypoglycemia)
- Easily implemented
- Can be executed by nursing staff in response to a single physician order

Example: Yale Insulin Infusion Protocol

**Insulin infusion:** Mix 1 U regular human insulin per 1 mL 0.9% NaCl. Administer via infusion pump in increments of 0.5 U/h.

**Bolus and initial infusion rate:**

Divide initial BG by 100, round to nearest 0.5 U for bolus and initial infusion rates

**Example:** Initial BG = 325 mg/dL; 325/100 = 3.25, round up to 3.5. IV bolus = 3.5 uU + start infusion at 3.5 U/h.

**Subsequent rate adjustments:**

Changes in infusion rate are determined by the current infusion rate and the hourly rate of change from the prior BG level; see table for instructions.

Indications for Bedside Glucose Monitoring

- Strong quality-control program essential
- Specific situations rendering capillary tests inaccurate
  - Shock, hypoxia, dehydration
  - Extremes in hematocrit
  - Elevated bilirubin, triglycerides
  - Drugs (acetaminophen, dopamine, salicylates)
- **Point-of-care measurement**
  - Most practical and actionable for guiding treatment
  - But need to consider limitations in accuracy

Education is Key to Success

- Education
- Education
- Education

Needs to be provided on a regular basis and can be given through a variety of approaches

- Lectures
- Presence on rounds
- Online (available 24/7)
- Pocket tools for house staff (laminated cards)

What rate do I start at?

- Algorithm 1. Start here for most patients
- Algorithm 2. For patients not controlled with Algorithm 1, or start here if no CAGD, sicca, solid organ transplant, or transplant rejection, up-regulating, or patient with diabetes (not hyperglycemia or hypoglycemia) or no verbal communication
- Algorithm 3. For patients not controlled on Algorithm 2, NO PATIENTS START FEEDING WITHOUT INSTRUCTING FROM THE MEDICAL SERVICE
- Algorithm 4. For patients not controlled on Algorithm 3. NO PATIENTS START FEEDING WITHOUT INSTRUCTING FROM THE MEDICAL SERVICE

<table>
<thead>
<tr>
<th>Algorithm 1</th>
<th>Algorithm 2</th>
<th>Algorithm 3</th>
<th>Algorithm 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>BG U/L</td>
<td>U/L</td>
<td>U/L</td>
<td>U/L</td>
</tr>
<tr>
<td>70-100</td>
<td>0.5</td>
<td>0.75</td>
<td>0.75</td>
</tr>
<tr>
<td>110-150</td>
<td>1</td>
<td>1.25</td>
<td>1.5</td>
</tr>
<tr>
<td>150-200</td>
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<td>1.75</td>
<td>2</td>
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<tr>
<td>200-250</td>
<td>2</td>
<td>2.25</td>
<td>2.5</td>
</tr>
<tr>
<td>250-300</td>
<td>2.5</td>
<td>2.75</td>
<td>3</td>
</tr>
<tr>
<td>300-350</td>
<td>3</td>
<td>3.25</td>
<td>3.5</td>
</tr>
<tr>
<td>350-400</td>
<td>3.5</td>
<td>3.75</td>
<td>4</td>
</tr>
<tr>
<td>400-450</td>
<td>4</td>
<td>4.25</td>
<td>4.5</td>
</tr>
</tbody>
</table>

U/L = Units per hour
Frequency of Monitoring……

Monitoring:
- Check blood glucose hourly and adjust insulin infusion per chart below.
- Can reduce checks in every other hour if ALL of the criteria are met. If any criteria are not met, resume hourly checks.
- < 70 mg/dL in 2 hours and ≤ 140 mg/dL in 4 hours.
- ≤ 2 mmol/L change between 14 and 16.
- ≤ 3 mmol/L change in admission ≤ 16 mmol/L change.
- Physician, nurse, or medical facility therapy are started, stopped, or changed.

Changing infusion rates……

<table>
<thead>
<tr>
<th>Blood Glucose</th>
<th>&lt; 60</th>
<th>60-80</th>
<th>80-100</th>
<th>100-120</th>
<th>&gt; 120</th>
</tr>
</thead>
<tbody>
<tr>
<td>UHC/HR</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>UHC/4HR</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>UHC/16HR</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>UHC/64HR</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Changing columns……

Changing columns:
- More one column to the right only if ALL of the criteria are met:
  - Plasma glucose < 80 mg/dL for 2 consecutive hours while in the same column.
  - Plasma glucose < 80 mg/dL for 2 consecutive hours while in the same column.
  - Plasma glucose ≤ 120 mg/dL for 2 consecutive hours while in the same column.
  - Plasma glucose ≤ 160 mg/dL for 2 consecutive hours while in the same column.

Handling hypoglycemia……

Treatment of Hypoglycemia: See hypoglycemia protocol for treatment of blood glucose below 80 mg/dL.

Handling meals……

Mealtime Coverage:
- If patient is at least 50% of goal (60 mmol/L or less), they receive an IV bolus based on the column they are in. See chart below.
- Set pump for bolus by subtracting mg/dL bolus factor on IV pump, but the volume to be infused at the bolus should be less than 50 mL/50 mg/hour.
- Bolus with a pump and IV bolus and purge return to patient.

Clinical Situations Associated with Inpatient Hyperglycemia

- Enteral or parenteral nutrition
- Glucocorticoid therapy
Glycemic Management of the Patient Receiving Enteral Nutrition

Continuous enteral nutrition (EN)
Basal: 40-50% of TDD as long or intermediate acting insulin given once twice a day
Short acting 50-60% of TDD given q6h

Cycled enteral nutrition
Intermediate acting insulin given together with a rapid or short acting insulin with start of TF
Rapid or short acting insulin administered q4 to 6 hours for duration of EN administration
Correctional insulin given for BG above goal range

Bolus enteral nutrition
Rapid acting analog or short acting insulin given prior to each bolus

Recommendations for Patients Receiving Parenteral and Enteral Nutrition

- Initiate bedside capillary blood glucose (CBG) monitoring for all patients receiving enteral nutrition (EN).
- Continue glucose monitoring during upward (or downward) titrations of enteral nutrition
- Initiate correctional insulin for any patient with CBG levels > 140 mg/dL during EN.
- Consider use diabetes-specific formulas in patients with pre-existing diabetes.
- Consider use of Diabetes-specific formulas in patients with new onset or difficult to control hyperglycemia.

Glycemic Management of the Patient Receiving Enteral Nutrition

Patients who already have an underlying diagnosis of diabetes are likely to experience further elevations in blood glucose levels with the initiation of enteral nutrition.
Patients receiving EN often have a higher severity of illness that those who do not.

Unanticipated dislodgement of a feeding tube, temporary discontinuation of the feedings, or changes in the rate of administration can result in hypoglycemia.

Protocols for avoidance and early treatment of hypoglycemia are recommended in case of abrupt discontinuation of EN.

For example: Keep order in place to start dextrose-containing IVFs in event of abrupt discontinuation of EN.

Glycemic Management of the Patient Receiving TPN

Usual method
Adding incremental doses of insulin to TPN based on previous days requirement of correctional (sliding scale insulin)

Other (preferred?)
Use of a separate IV insulin infusion titrated according to bedside glucose levels

There are no controlled trials examining different strategies for achieving glycemic control in this group of patients

Suggested
In patients with known type 2 diabetes, add 1 unit for each 10 Grams of carbohydrate in the solution
Initiate Correctional Insulin Scale for BG > 140 mg/dL
Add 60 to 100% of previous days correctional insulin dose to next day’s TPN solution

Consider
Add basal long or intermediate acting insulin at a dose of 0.2 to 0.4 units per kg per day

Frequency of hyperglycemia in patients receiving high dose steroids

- 1 BG > 200 mg/dL
- 2 BG > 200 mg/dL

<table>
<thead>
<tr>
<th>%</th>
<th>All</th>
<th>No Hx DM</th>
<th>Hx DM</th>
</tr>
</thead>
<tbody>
<tr>
<td>90</td>
<td>64</td>
<td>52</td>
<td>81</td>
</tr>
<tr>
<td>60</td>
<td>52</td>
<td>56</td>
<td>75</td>
</tr>
<tr>
<td>30</td>
<td>41</td>
<td>41</td>
<td>75</td>
</tr>
</tbody>
</table>
Risk for New Onset Diabetes with Glucocorticoid Therapy

- **Reference**
  - Goldblatt et al. (2006)
  - Gravina et al. (2004)
  - Cooper et al. (1994)
  - Blackman et al. (2002)

- **Population**
  - United Kingdom Audit Improvement Network
  - New Jersey Medicaid Database
  - Multi-centric study
  - Ontario Drug Benefit Database

- **Odds ratio**
  - 1.36 (1.09-1.69)
  - 2.22 (1.20-2.39)
  - 1.71 (1.12-2.63)
  - 3.51 (2.11-5.64)

---

One Suggested Approach for Treatment of Hyperglycemia in Patients Receiving Glucocorticoid Therapy

<table>
<thead>
<tr>
<th>Prednisone (mg/day)</th>
<th>NPH (units/kg/day)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 40</td>
<td>0.4</td>
</tr>
<tr>
<td>30</td>
<td>0.3</td>
</tr>
<tr>
<td>20</td>
<td>0.2</td>
</tr>
<tr>
<td>10</td>
<td>0.1</td>
</tr>
</tbody>
</table>

*Administered in AM at time of prednisone administration
- Glargine preferred if dexamethasone used or Prednisone given twice a day

Steroid Therapy and Glycemic Control General Guidelines

- The majority of patients (but not all) receiving high dose glucocorticoid therapy will experience elevations in blood glucose
- For patients without prior DM or hyperglycemia or those with diabetes controlled with oral agents:
  - Institute glucose monitoring with low dose correction insulin scale administered prior to meals
- For patients previously treated with insulin:
  - Increase total daily dose by 20 to 40% with start of high dose steroid therapy
  - Increase correctional insulin by one step (low to moderate dose)
  - Adjust insulin as needed to maintain glycemic control

Glucocorticoid Therapy

- **Suggested approach:**
  - Institute glucose monitoring for at least 48 hours in all patients
  - Prescribe insulin therapy as needed according to results of bedside BG monitoring
  - During initiation and taper of steroid therapy, proactive adjustment of insulin therapy can help avoid uncontrolled hyperglycemia and hypoglycemia.

Nursing Education as Key Factor
Hyperglycemia

• What is the goal for the bedside nurse?
  • Notify the physician when blood glucose levels are out of control
  • Implement the orders and notify the physician when indicated to avoid hyperglycemia and hypoglycemia
  • Correctly interpret and dose insulin per insulin order sets

Interventions for Hyperglycemia

• Blood glucose >140 mg/dL
  • Call the physician if:
    • Blood glucose is >200 mg/dl on admission
    • The first time BG is 200 mg/dl if not previously reported
    • Written in the physician orders, “call for blood sugar remains out of control despite therapy or per orders”
  • Administer insulin per physician’s order
  • Hydrate the patient as indicated by physician’s order

Factors Increasing Risk of Hypoglycemia in an Inpatient Setting

➤ Lack of coordination between dietary and nursing leads to mistiming of insulin dosage with respect to food
➤ Inadequate glucose monitoring
➤ Inadequate insulin dose adjustment
➤ Lack of coordination between transportation and nursing
➤ Unsafe work environment
➤ Indecipherable orders

Role of Timing in Good Glycemic Control

• Appropriate timing of point of care testing / insulin administration and meal delivery
  • Coordination required!!
    • Document capillary blood glucose and the time
    • Document insulin dose and the time given
    • Document % of the carbohydrate eaten
  • For NPO, BG and insulin must be coordinated
  • Requires co-operation between pharmacy, dietary and nursing departments!!

Blood Glucose Check – Too Early

• The blood glucose is checked at 0610, and the patient requires regular insulin coverage. The insulin is given at 0620. Breakfast arrives at 0800
• This could potentially lead to hypoglycemia
• Ideally the regular insulin should be given ½ hour before or if needs be-with the meal but not greater than ½ hour before the meal

Hypoglycemia Is Serious But Treatable

• Be aware of, or institute a “Hypoglycemia Order Set”, “Hypoglycemia Protocol”
• Know the “peak time” of the different types of insulin
• Remember that more activity (energy output) or less carbohydrate (energy intake) can cause hypoglycemia
The 15-15 Rule

• The 15-15 Rule of hypoglycemia means to give 15 grams of fast-acting carbohydrate & wait 15 minutes, recheck a blood glucose & then give another dose of 15 grams of fast-acting carbohydrate, if necessary.

Question

• Is it ok to add a packet of sugar to ½ cup of orange juice to treat a BG of 61mg/dl?

1. Yes
2. No

15 Grams of Carbohydrate Raises Blood Glucose by 30-50 mg/dL!

• 1 tube oral glucose gel
• 3-4 glucose tablets*
• ½ cup juice
• 1 tablespoon sugar, honey or jelly
• 8 oz. Milk

*Glucose tablets may contain 4 or 5 Gm of glucose

Transition from IV To SQ Insulin

➢ Continue IV insulin until patient is able to tolerate solid food intake
➢ Continue IV insulin at least 2 hr after the first SC insulin injection is given
   • Can even start basal the night before you plan to DC
➢ Don’t use only basal insulin in patients with an A1C greater than 8.5% on 2 or more oral agents
➢ Don’t switch to only oral agents from IV insulin in patients with type 2 diabetes
➢ Arrange for outpatient follow-up of patients placed on insulin in the hospital
Therapeutic Options to Consider When Converting to SC Insulin

- Resumption of prior insulin regimens
- Initiation of basal insulin
- Initiation of basal/bolus MDI
- Initiation of premixed insulin

Recommendations for Converting IV to SC Insulin: Basal or MDI

- Establish 24 h insulin requirement
  - Extrapolate from average over last 4-8 h if stable
  - Calculate TDD as 80 to 100% of above
- Give 1/2 amount as basal
- Give ac boluses
  - Based on CHO intake (1 U of insulin for x grams of CHO)
  - Remaining 50% given 1/3 before each meal
- Monitor ac, tid, hs, and 3 AM
- Correction bolus for all BG >140 mg/dL

Bode: Transition from Intravenous Insulin Infusion to Subcutaneous Therapy

Example
- Patient has received an average of 2 U/h IV during previous 6 h.
  - Recommended doses are as follows:
    - SC TDD is 80% of 24-h insulin requirement:
      - 80% of (2 U/h x 24) = 38 U
    - Basal dose is 50% of SC TDD:
      - 50% of 38 U = 19 U of long-acting analogue
    - Bolus total dose is 50% of SC TDD:
      - 50% of 38 U = 19 U of total prandial rapid-acting analogue or ~6 U with each meal
    - Correction dose is actual BG minus target BG divided by CF
      - CF = 1,700 ÷ TDD
      - Correction dose = (BG – 100) ÷ CF

Moving TM from IV back to SubQ Insulin

- Establish 24 h insulin requirement
  - Stable blood glucose for past 2 days of 153 mg/dl
- Rate of 4 Units/hr for past 6 hours
- What diabetes regimen would you start TM on?
  1. Metformin 1000mg BID plus glipizide 10mg BID
  2. Lantus 70 Units HS
  3. NPH 15 Units TID plus Regular 15 Units TID AC plus Regular for correction
  4. Levemir 40 Units q AM plus Novolog 1 Unit per 8 grams CHO plus Levemir 1 Unit per 20 mg/dl above 140 mg/dl

Discharge Considerations

- What are your discharge plans for this patient?
- Will they be discharged on insulin therapy?
- When and where will follow-up take place?
- What education do they need prior to discharge?
Effective Discharge Planning for Continuity of Care

- A1C on admission for all diabetic patients, as well as patients experiencing hyperglycemia prior to discharge
- Timely Referral to Inpatient Diabetes Educator if applicable
- Post Hospital Plan of Care discussed with Patients during Hospital stay - Nursing to reinforce
- Reconciliation of medications - If new to insulin, regime discussed with patient prior to discharge. Insulin Instruction Sheet given to patient to take home
- DME supplies – meter, syringes, lancet, needles etc.
- Referral for OP diabetes Self management If appropriate
- Follow-up care with PCP within 15-30 days, or if new to insulin within 7-14 days

A1C is Helpful in Determining Post Discharge Treatment

In these-situation previously-diagnosed diabetes and an A1C level of:

- 6.5% or higher: Indicates the likelihood of diabetes and referral to inpatient Diabetes Educator is essential to begin self-management education prior to discharge
- 6.7 - 6.9%: Indicates a category of increased risk for diabetes. Lifestyle interventions that promote weight loss and increased activity should be addressed prior to discharge

Patients Previously Diagnosed with Diabetes Prior to Hospitalization:

- A1C <7%  
  - Return to Previous Therapy

- A1C >7%  
  - Opportunity to Intensify Therapy

Recommended Treatment Strategies for the Discharging Patient

In those with previously diagnosed diabetes and an elevated A1C level:

- If HbA1C 7-8%: Increase dose of home oral agents, add third agent or add basal insulin at bedtime
- HbA1C > 8%: If already on two oral agents, add once daily basal insulin at bedtime
- If HbA1C 9-10%: Patient should be discharged home on basal and bolus insulin regime. Use the amount of basal insulin required in the hospital as once daily glargine/detemir or bid NPH dose. Continue multiple daily dose as started in the hospital if appropriate.
- Twice daily premixed insulin should be considered for less complex insulin regimens particularly in elderly patients.

Recommended Treatment Strategies for the Discharging Patient

In those with previously diagnosed diabetes and an elevated A1C level:

- HbA1C > 7% and no new contraindication to prior outpatient therapy, resume home medication at discharge
Discharge Considerations for Patients with Known Diabetes

- Home regimen prior to admission
- Admission reason: hypoglycemia?, acute MI?, related to hyperglycemia? (DKA, HHS, etc.)
- Readmission for diabetes within 30 days
- New co-morbidities that may limit prior oral therapy
- Treatment goals
- Depression?

DKA = diabetic ketoacidosis; HHS = hyperosmolar, hyperglycemia state

Continuum of Care

- If new to insulin
  1. Referral to an outpatient diabetes education program shortly after discharge to discuss ongoing diabetes control
  2. Discharge Information on when to check BG and timing of insulin administration. Information should also include parameters for when to call PCP
  3. Communication to patients PCP regarding changes made to patients treatment regime during hospitalization and a complete medication list
  4. An assessment of the need for home health care

Caution: Possible Insulin Medical Error Ahead

- Transition from Inpatient to the Outpatient setting represents a crucial break in care
- Nearly one half of patients may experience a medical error after hospital discharge.
- Elderly patients with recent hospital discharge are at high risk of developing serious hypoglycemia

Timely Discharge Information Required by the Receiving PCP

- Primary and secondary diagnoses; and Diagnostic findings
- Dates of hospitalization, treatment provided and a summary of hospital course
- Discharge Medications
- Patient or family counseling
- Tests pending at discharge
- Details of follow-up arrangements
- The name and contact information of the responsible hospital physician

Metrics for Evaluation

- A system to track hospital glucose data on an ongoing basis can be used to
  - Assess the quality of care delivered
  - Allow for continuous improvement of processes and protocols
  - Provide momentum
Graphic Display of Glucometrics Data

Metrics Traditionally Used in the Inpatient Glucose Literature

- Raw blood glucose (BG) average
- % of BGs within a pre-specified range (80-110, 100-150, <180, <200 mg/dl)
- % of patients with a certain % of BGs within a pre-specified range
- Hypoglycemia rates (<40, <50, <60, <70 mg/dl)
  - % of BGs
  - % of patients
- Hyperglycemic excursions (>180, >200, >300 mg/dl)
  - % of BGs
  - % of patients

Methods: Units of Analysis

- "Ward" n = 1,552
- "Patient Stay" n = 118 [13.2 BGs / stay]
- "Patient Day" n = 467 [3.3 BGs / day]

Overcoming the Barriers to Optimal Glycemic Control in the Hospital

Achievable Goals

Optimal Glycemic Control

Teamwork

We Can Do It!
Our Patients Are Counting on Us!