Challenges of Glucose Control in Postoperative Patients

John H. MacIndoe, MD
Department of Endocrinology, HealthPartners Medical Group
Associate Chairman for Inpatient Glycemia Management, Regions Hospital
Adjunct Professor of Medicine, Univ. of Minnesota

The hospital is a dangerous place

for a diabetic patient

.

Agenda

- Is glucose management important in the inpatient setting?
- How common is perioperative hyperglycemia?
- Which patients are most at risk for complications?
- Does improving glycemic control improve outcomes?
- What is “optimal” inpatient glucose control?
- What are the common barriers to achieving good control?
- How can we achieve safe and effective transitions to home?

Is inpatient glucose management important?

- Until 8 years ago, glycemic control was not considered to be a major goal of inpatient care.
- Since then, multiple studies have clearly demonstrated that both hypoglycemia and short term hyperglycemia in a hospital setting are linked to bad outcomes

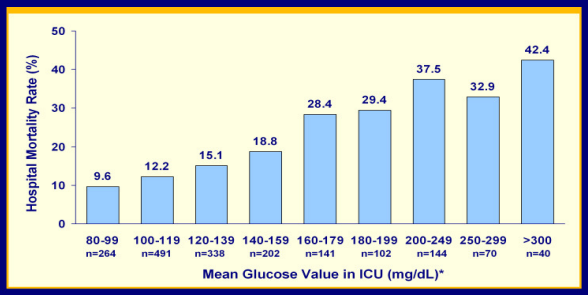
- Severe Hypoglycemia (glucose ≤ 40mg/dl)
  - Independent marker for in house mortality
- Recent data suggests even BG's 70-80 associated with higher ICU mortality rates
  - Death occurs at a time distant from episodes
  - Likely both a *biomarker and a mediator*

1. *JCEM 2002 87:978*
2. *J Par Enteral Nutr 1994 18;398; Mayo Clinic Proc 1989 64;443; Diabetes Care1998 21;246*

- Hyperglycemia linked to increased
  - Morbidity
  - Mortality
  - Hospital and patient costs

1. *JCEM 2002 87:978*
2. *J Par Enteral Nutr 1994 18;398; Mayo Clinic Proc 1989 64;443; Diabetes Care1998 21;246*

Hyperglycemia and Poor Hospital Outcomes: Mortality in Critically Ill Patients With DM



*P<0.001 for trend.
Adapted from Krinsley JS. *Mayo Clin Proc.* 2003;78:1471-1478.

Early studies

Early Postoperative Hyperglycemia

- BG >220 sensitive but relatively non-specific indicator of postop nosocomial infection
- Compared to pt's having all POD-1 BGs <220, those with 1 or more BG's >220 during the same time had
  - A 2.7 times higher total infection rate and
  - A 5.7 times higher serious infection rate

Pomposelli JJ *et al.* **Journal of Parental and Enteral Nutrition** 22:77 1997

Early Studies

Cardiac surgery patients:

- Greater mortality
- More deep wound infections
- Glucose >200 mg/dl
  - @ 36 hrs. is an independent predictor of short term infection risk. (Golden, et al, 1999)
  - @ 24-48 hrs. post open heart surgery predicts deep sternal wound infection (Zerr, et al. Ann Thorac Surg 63:356, 1997)
- Multiple outcomes complications with BG >200 (Furnary, et al. Circulation 100:I-591,1999)

Early studies

Patients with acute MI

- 15 study meta analysis: FBS >126; random >200
  - CHF and mortality increased with glucose >110
  - With and without a prior dx of DM

Capes, et al :Lancet 355:773,2000 and a 336 pt. prospective study (Bolk, et al: Int J Cardiol 79:207,2001

Early Studies

General medical and surgical pts:
(Umpierrez , et al, J Clin Endocrinol Metab 87:978, 2002)

- 18-fold increase in in-house mortality
- Longer length of stay (9 vs. 4.5 days)
- More subsequent nursing care
- Greater risk of infection

How Common is Inpatient Hyperglycemia?

- 30-40% of all admissions ·hospital wide
  - 2/3 known DM
  - 1/3 newly dx'ed hyperglycemia
    - Undiagnosed DM
    - "Stress" hyperglycemia

1. *JCEM 2002 87:978*
2. *J Par Enteral Nutr 1994 18;398; Mayo Clinic Proc 1989 64;443; Diabetes Care1998 21;246*

How Common is Perioperative Hyperglycemia?

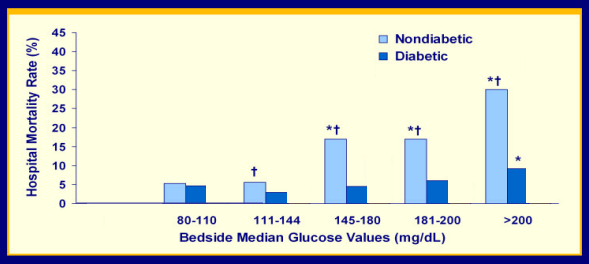
- SCIP patients
  - Pre-operative fasting BG's:
    - 1/3 are >126 mg/dL (overtly diabetic)
    - 1/3 are 100-125 mg/dl ('pre-diabetic')
    - 1/3 are ≤ 99 mg/dL (normal)
  - Post operative:
    - All cardiac surgeries >150 mg/dL
    - Other surgeries: 10- 70% >150 mg/dL

Which hyperglycemic pts are most at risk for bad outcomes?

- Any inpatient with high blood sugar,
  - Diabetic or not
    - In fact…patients with newly discovered / "stress" hyperglycemia have worse prognosis than those with established diabetes

1. *JCEM 2002 87:978*
2. *J Par Enteral Nutr 1994 18;398; Mayo Clinic Proc 1989 64;443; Diabetes Care1998 21;246*

Hyperglycemia and Poor Hospital Outcomes: Mortality in the ICU With and Without DM



*P<0.001 for differences among 3 subgroups; †P<0.001 for diabetic vs nondiabetic patients.
ICU indicates intensive care unit; Nondiabetic, patients without diabetes who received insulin for glycemic control; Diabetic, patients with a history of diabetes; Control, patients who did not receive insulin.
Adapted from Rady MY et al. *Mayo Clin Proc.* 2005;80:1558-1567.

Who is at risk ?

- Any inpatient with high blood sugar
  - Diabetic or not
  - Regardless of the inpatient setting

1. *JCEM 2002 87:978*
2. *J Par Enteral Nutr 1994 18;398; Mayo Clinic Proc 1989 64;443; Diabetes Care1998 21;246*

- Bottom Line
  - Poor glucose control is an important risk factor for all hyperglycemic inpatients

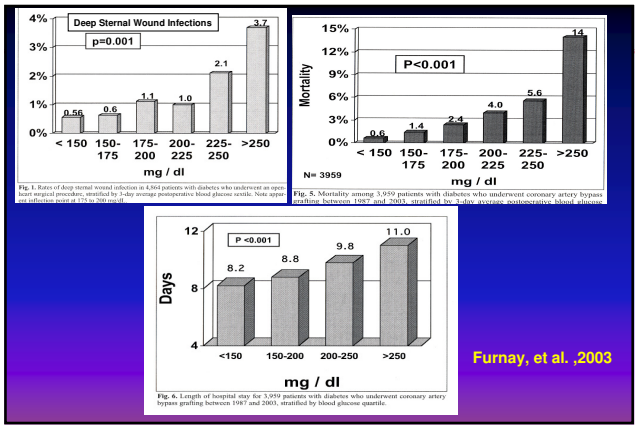
Does improving glycemic control improve outcomes?

- Yes – in almost all inpatient settings
  - Labor and delivery
  - Cardiac Surgery
  - SICU; CVICU, MICU, Burn Unit
  - General surgery floors
- No data yet
  - General medicine units
  - Inpatient psychiatry units

What Is Optimal Inpatient Glucose Control?

- Goal:
  Minimize risk of hyperglycemia without any hypoglycemia
- Achieving BG <220 important for proper immune function and phagocytosis

  BUT…
- The *optimal* targets for BG control have been subject to ongoing controversy



Furnay, et al. ,2003

BG Goals: A Moving Target

- 2003 Furnary (Portland Protocol)
  - Post-op CABG: < 150mg/dL

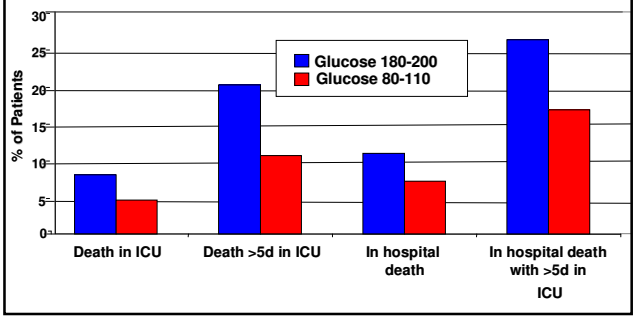
Glucose Control and In-House Outcomes

2001 SICU Patient Study

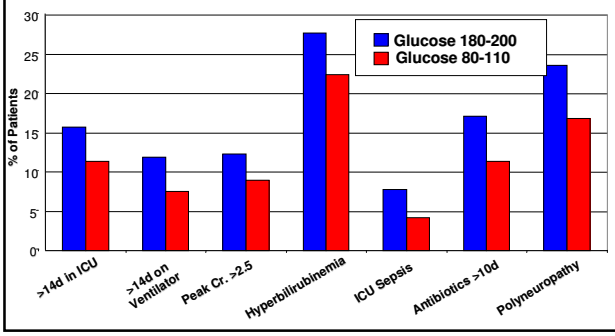
- 1548 SICU pts on mechanical ventilation [1.]
  - Most post CABG
- Protocol
  - 783: IV insulin with goal sugars 180-200
  - 765 : IV insulin with goal sugars 80-110

Van den Berghe, et al., NEJM 2001 19:1359

Van den Berghe Mortality Data



Van den Berghe Morbidity Data



BG Goals: A Moving Target

- 2003 Furnary (Portland Protocol)
  - Post-op CABG: < 150mg/dL
- 2004 Van Den Berghe
  - SICU : 80-120 better than 180-200
- 2004-2009:
  - VdB protocol produces frequent severe hypoglycemia
  - Hypoglycemia : independent risk factor for inpatient mortality
- 2009: NICE SUGAR

The NICE-SUGAR Study

- NICE-SUGAR study: NEJM 360:1283-1297, March 26,2009
  - Multicenter medical and surgical ICU
  - 6104 patients
    - ½: intensive control BG target 81-108 mg/dL
    - ½: conventional control: BG target 140-180 mg/dL
  - Primary end point: death within 90 days of admission
  - Secondary endpoints: ICU LOS; Hospital LOS; days of mechanical ventilation; days of dialysis

NICE-SUGAR : NEJM 360:1283-1297, March 26,2009

	Median BG	Mortality	Hypoglycemia (<40 mg/dL)
Intensive	115±18	27.5%	6.8%
Conventional	144±23	24.9%	0.5%
p value		0.02	<0.001

No difference in secondary end points
ICU or Hospital LOS
days of mechanical ventilation
days of dialysis

NICE-SUGAR

Conclusion:

In surgical and medical ICU patients…

- BG target range of 140-180 (median=147 mg/dL) is superior to euglycemia (80-110; median=112 mg/dL)
  - Equally positive outcomes
  - Much less hypoglycemia, lower mortality

Glucose Metrics at Regions

- Blood glucose targets
  - ICU: 80-180 mg/dl (IV drip targeted 80-160)
  - Other floors:
    - FBS and pre-meal: 70-140 mg/dL
    - Postprandial or random: 70-180 mg/dL
- Current metrics
  - Hyperglycemia:
    % of pts with a median BG >150 mg/dL
  - Hypoglycemia
    - Any: # BG <70 mg/dL
    - Severe: # of BG's <50 mg/dL

What are the keys to achieving good control in surgical patients?

1. Identify all patients with hyperglycemia
2. Use insulin to manage hyperglycemia during acute phase

Identify all patients with hyperglycemia (treat BG>150)

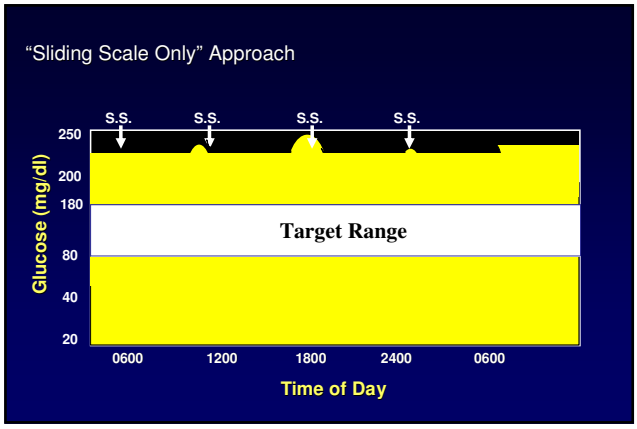
- Pre-op:
  - Fasting blood sugar (FBS) on all patients
- Post op
  - FSG on admission to PACU
    - FSG AC and HS x 24h after transfer to general surgery floor
  - FSG q4h x 24h after admission to SICU
  - D/C BG checks for those <150 mg/dL x 24h
- Get HbA1c (important for discharge planning)
  - All diabetic pts without a value in the past 30 days
  - Any patient who needs insulin supplementation 2 or more time during the first 24h

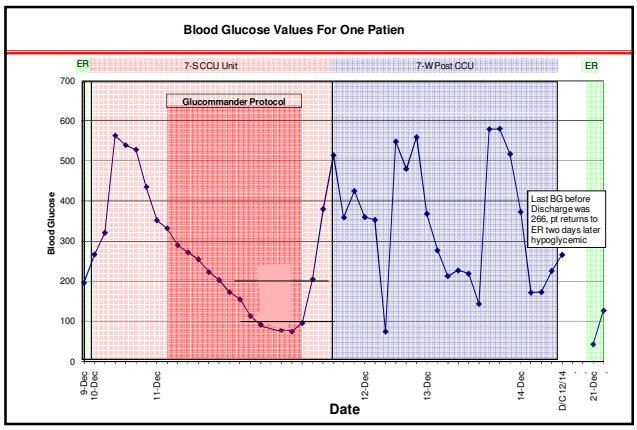
Use INSULIN to manage hyperglycemia during acute phase

- Achieving any BG target requires the routine use of *physiologic* regimens
  - 'Sliding scale only' treatment
    - acceptable for short term use
    - it is NOT an option for continuous glycemic management

Typical 'Sliding Scale' Order

- Check FSG AC and HS
  - If BG <70: initiate hypoglycemia protocol
  - If BG 70-150: no additional insulin
  - If BG 150-200: give 2 units of Novolog insulin
  - If BG 201-250: give 4 units Novolog insulin
  - If BG 250-300: give 6 units of Novolog insulin
  - If BG ≥ 301: give 8 units of Novolog and call provider for further instructions

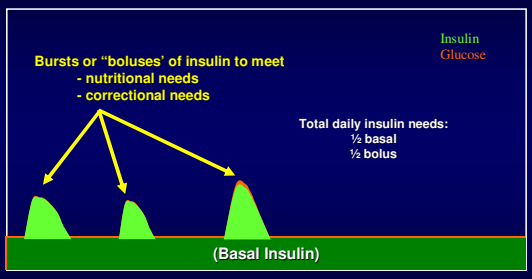




Use INSULIN to manage hyperglycemia during acute phase

- Achieving any BG target requires the routine use of *physiologic* regimens
  - 'Sliding scale only' not an option
  - SC "basal / bolus" regimens or
  - IV insulin with subsequent transition to SC basal / bolus
- What is "basal/bolus" insulin management?

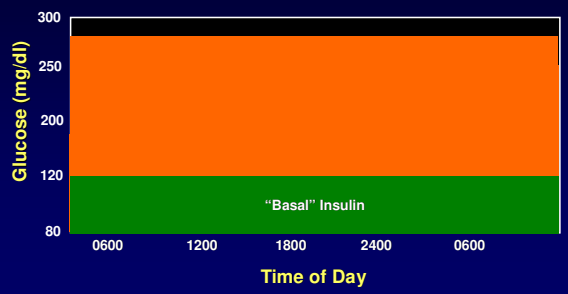
Normal Pancreatic Function



Basal/Bolus Therapy: Truly Physiologic Insulin Replacement

- Basal insulin: long acting insulin to cover 'liver sugar'
  - cuts the work in half without hypoglycemia

Using Basal / Bolus Therapy



Basal Insulin

Everyone on daily insulin needs some basal

Regardless of past diabetes history

Regardless of nutrition plan

Meals

Tube feedings

TPN

NPO

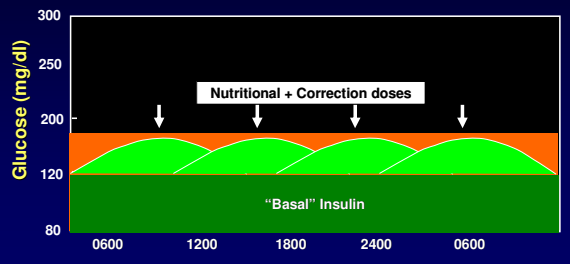
Basal Insulin Choices

- Glargine (Lantus ®) once daily
- Detemir (Levemir ®) twice daily (q 12h)
- NPH three times daily (q8h)

Bolus Insulin Therapy

- Bolus insulin: short acting insulin with 2 roles
  - Nutritional coverage
    - meals (given AC)
    - TPN, continuous tube feedings
  - Correction (catch up) :"supplemental" or "sliding scale" doses
    - Added to nutritional doses for meals, TPN, tube feedings
    - Given q4h for patients who are NPO

Using Basal/ Bolus Therapy



Choosing a 'Bolus' Insulin

Regular insulin

- Onset 20-40 min
- Peak 2-4h
- Duration: 6h
- Consider using it only for IV drips

Rapid Acting Analog ("RAA")

- Lispro (Humalog®)
  Aspart (Novolog®)
  Glulisine (Apidra®)
- Onset: 10-15 min
- Peak: 60-90 min
- Duration: 3-4h
- Consider using for all SC bolus doses

Perioperative Glucose Management: General Guidelines

- Known diabetic patients
  - Discontinue any non-insulin anti-glycemic meds (oral agents) after midnight before surgery
  - Long acting insulin is ordered by PCP for the night before or the morning of surgery based upon pt.'s usual insulin regimen
    - Pre-op hyperglycemia:
      - Cover with supplemental ('sliding scale' bolus)
    - Intra-op hyperglycemia :
      - IV insulin drip or IV bolus
    - Post op hyperglycemia :
      - 'Sliding scale' in PACU; IV insulin drip in SICU
      - Begin basal/bolus insulin after transfer to general surgical floor

Perioperative Glucose Management: General Guidelines

- Newly Diagnosed Hyperglycemia
  - Pre-op hyperglycemia:
    - Cover with 'sliding scale' bolus PRN
  - Intra-op hyperglycemia:
    - IV insulin drip or IV bolus (anesthesiology)
  - Post op hyperglycemia:
    - PRN 'sliding scale' coverage in PACU
      - If supplemental insulin needed 2 or more times in the first 24h following transfer to general surgical service, begin basal/bolus insulin
    - SICU: FSG q4h x 24h; cover with PRN 'sliding scale'
      - Begin IV insulin drip or SC basal/bolus if insulin needed 2 or more times during that time

Starting Basal/Bolus Therapy

- Patients eating meals
  - Order a constant carbohydrate (not "ADA diabetic") diet
  - FSG checks AC and HS
  - Basal insulin
    - Type: glargine
    - Frequency and timing: once daily (I like at noon)
    - Starting Dose: 0.3 units x weight in Kg.
  - Note:
    Do not hold glargine without specific OK from provider
    (common management error)

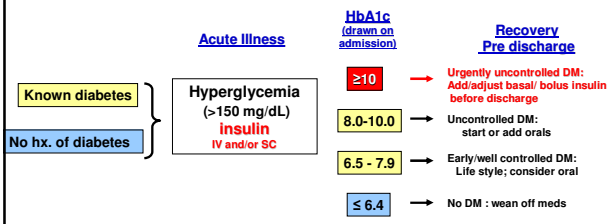
Starting Basal/Bolus Therapy (Patients eating meals)

- Bolus insulin
  - Type: RAA (Apidra ®, Humalog ®, Novolog ®)
  - Timing: With meal
  - Dose:
    - nutritional: 0.1unit x wt in Kg plus
    - 'sliding scale' for BG>150 mg/dl
  - Note:
    - Hold nutritional component if patient unlikely to eat
      BUT…
    - Always give 'sliding scale' component if BG >150 mg/dL
      (common management error)

Achieving safe and effective transitions to home

- The admission HbA1c to indicate the patient's glycemic status *before they became ill*
  - ≤ 5.7 = normal glucose metabolism
  - 5.7 - 6.4 = 'pre-diabetes'(high risk for DM)
  - ≥ 6.5 = diabetes
  - ≥ 8.0 = poorly controlled diabetes

Inpatient Hyperglycemia Management Flow



Summary

- Poor peri-operative glucose control (both hypo- and hyperglycemia) linked to preventable morbidity, mortality and costs of care in surgical patients.
- The currently acceptable range for inpatient glucose values is 70-180 mg/dL with a median BG of <150 mg/dl for at least the first 3 days post op.
- Until prospective data are available to indicate otherwise, this control shhould be maintained for at least the first 72h postoperatively.

Summary

- These goals are most readily achieved using a basal/bolus SC insulin regimen that employs the newer analog insulins
- Initiating and maintaining these measures represents a culture change for most hospitals and usually requires
  - a dedicated leadership team
  - a strong ' no blame' educational environment