

## Superiority of Tight Control of Hyperglycemia to Moderate Control?

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## Hyperglycemia

- occurs frequently in hospitalized patients and affects patient outcomes
  - Mortality
  - Inpatient Complications
  - Length Of Stay
  - Overall Hospital Costs.

## Treatment

### Tight Glycemic control

- A decreased release of insulin, increased release of hormones with effects countering insulin, and increased insulin resistance combine to produce stress hyperglycemia in many critically ill patients.
- Hyperglycemia diminishes the ability of neutrophils and macrophages to combat infections. Also insulin possesses antiapoptotic effects.
- A large, single-center, randomized trial of more than 1500 critically ill patients demonstrated that, maintaining serum glucose levels between 80 and 110 mg/dL (mean morning glucose of 103 mg/dL) through the use of a continuous insulin infusion decreased mortality (4.6% vs 8%;  $P < 0.04$ ), development of renal failure ( $P = 0.04$ ), and episodes of septicemia ( $P = 0.003$ ), compared with conventional treatment (mean morning glucose of 183 mg/dL).
- Physicians liberalize their insulin treatment to keep blood glucose levels less than 150 mg/dL due to concerns of hypoglycemia.
- Studies are needed to determine whether less tight control of blood glucose — for example, a blood glucose level of 120 to 160 mg per deciliter (6.7 to 8.9 mmol per liter) — provides similar benefits.

Sept: Pathophysiology and Treatment, Talash Abdala, Apr 25, 2006

## Insulin

- Insulin is first-line therapy for hyperglycemia
- It is adaptable to the changing patient physiology over the course of hospitalization.
- Critically ill patients should receive intravenous (IV) insulin infusion
- All non-critically ill patients with hyperglycemia should be managed using a subcutaneous (SC) insulin algorithm with basal, nutritional, and correctional dose components.

## Euglycemic State

- The limiting factor to achieving a near euglycemic state is hypoglycemia.
- Similar to hyperglycemia, hypoglycemia is an independent risk factor for poor outcomes in the hospitalized patient.

## Safe Insulin Use

Institutions can increase safe insulin use by :

- Utilizing insulin algorithms
- Pre-printed order sets
- Hypoglycemia protocols
- Patient and health care provider education

### Target Range

- Various degrees of glycemic control have been studied and a recent consensus statement from American Diabetes Association (ADA)/American Association of Clinical Endocrinologists (AACE) recommends a target glucose range of 140–180 mg/dL in most hospitalized patients.

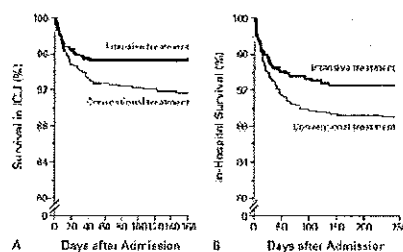
### Question #1

- A 64 y/o man (BMI = 32) is admitted to the ICU after a left sigmoid colectomy for perforated diverticulitis. The patient's past medical history is significant for type 2 diabetes mellitus, treated with metformin.
- While he is in the ICU, the patient's blood glucose concentration should be:
  - Maintained between 80-110 mg/dL with IV insulin as needed
  - Maintained between 140-180 mg/dL with IV insulin as needed
  - Maintained less than 220 mg/dL with IV insulin as needed
  - Controlled with oral metformin

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Van den Berghe G et al. Intensive insulin therapy in critically ill patients. *N Engl J Med* 2001; 345:1359-1367



Intensive : blood [glucose] = 80-110 mg/dL  
Conventional: blood [glucose] = 180-200 mg/dL

Association of Tight Glucose Control vs Usual Care With Hospital Mortality, Stratified by ICU Setting and Glucose Goal in Tight Control Group

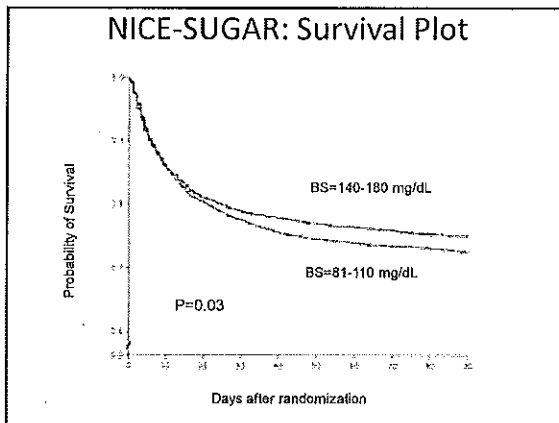
Study	Intensive (n)	Conventional (n)	Relative Risk (95% CI)
<b>All patients</b>	1000	1000	0.85 (0.75-0.96)
<b>ICU</b>	500	500	0.80 (0.70-0.91)
<b>Non-ICU</b>	500	500	0.90 (0.80-1.00)
<b>Glucose goal &lt; 110 mg/dL</b>	500	500	0.75 (0.65-0.85)
<b>Glucose goal 110-140 mg/dL</b>	500	500	0.90 (0.80-1.00)

Wenger, R.S. et al. *JAMA* 2008;300:933-941

JAMA

The NICE-SUGAR Study Investigators. Intensive versus conventional glucose control in critically ill patients. *N Engl J Med* 2009; 360:1283-97

- Within 24 h after admission to an ICU, adults who were expected to require treatment in the ICU on 3 or more consecutive days were randomly assigned to undergo either intensive glucose control (target blood glucose concentration = 81 to 108 mg/dL) or conventional glucose control (target = 140-180 mg/dL).
- Primary end point was death from any cause within 90 days after randomization.



Why is it so hard to get physicians to modify their practice based on the best available evidence ?

Practice	% Compliance PHI/UPMC	% Compliance UCLA	Barrier to more complete adoption
Handwashing	65%	?	Forgetfulness, laziness
1 dose of peri-operative ABX	<10%	<10%	Counter-intuitive data, lack of familiarity with literature, no obvious downside with non-compliance
{Hgb} = 7 g/dL transfusion trigger	~20%	<10%	Counter-intuitive data, no obvious downside with non-compliance
S-barrier precautions	>90%, except in OR	?	Laziness, perceived "time pressure"

- ### Summary
- Insulin is the preferred therapy for treating all hospitalized patients with hyperglycemia, independent of their diabetes status.
  - We have transitioned from the era of "tight" glycemic control to one of "less-tight" glycemic control.

- Focusing intensely on the safety and efficacy optimal target glucose ranges remain controversial.
- Consensus is that glycemic control is important and hospitals should continue to manage blood sugars with insulin.
- Choose glycemic targets to balance the risk of hypoglycemic events and ensure patient safety.

- ### Improvement in Glycemic Control
- Physician education
  - Ordering of appropriate insulin and medication regimens
  - Nursing coordination on the timing of insulin administration and treatment of hypoglycemia
  - Measuring capillary glucose and communicating results promptly
  - Dietary coordination of meals & insulin administration

### Bibliography

- **Management of Inpatient Hyperglycemia**, Lowell R. Schmelz, MD, *Assistant Professor, Oakland University William Beaumont School of Medicine; Chief of Endocrinology, Detroit Medical Center Huron Valley-Sinai Hospital; Associated Endocrinologists, PC and Endocrine Hospital Consultants, PC, West Bloomfield, MI*
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