

Glycemic Control in Ambulatory Surgery

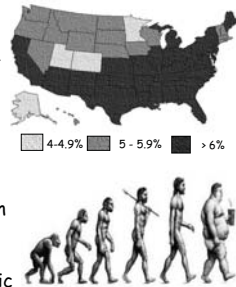
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Outline

- Review effects of surgical stress on blood glucose levels
- Examine the rationale for 'tight' perioperative blood glucose control
- Discuss the current literature on 'tight' perioperative blood glucose control
- Present a clinical pathway for blood glucose control in patients undergoing ambulatory surgery

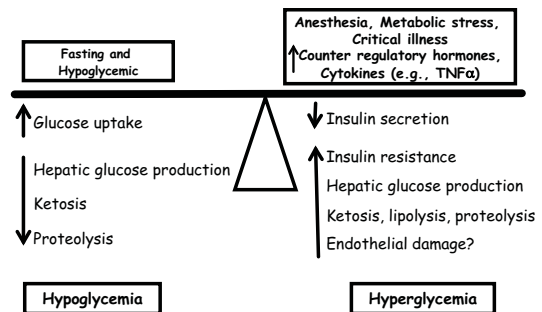
Worldwide Prevalence of Diabetes Expected to Increase

- ~ 20 million in the US have DM
- ~ 50% do not know they have it
- Prevalence of diabetes will increase due to obesity, aging population, changing lifestyle and diet as well as liberalization of definitions of diabetes
- Diabetes considered an epidemic



World Health Organization. Available at http://www.who.int/diabetes/facts/world_figures/en/print.html
Chan JM et al: Diabetes Care 1994; 17: 961-9; Colditz GA et al: Ann Intern Med 1995; 122: 48

Perioperative Glucose Homeostasis



Hyperglycemia and Perioperative Outcome



- Hyperglycemia is an independent risk factor for poor outcome, even in non-diabetic patients
- Increased morbidity including infections, pressure ulcers, delayed wound healing
- Increased sepsis and multi-organ failure
- Hyperglycemia, ketoacidosis, hyperosmolar states
 - Osmotic diuresis, volume depletion, hypotension
 - Acidemia, hypophosphatemia, hyperkalemia

Shilling Am, Raphael J: Best Prac Res Clin Anaesthesiol 2008; 22: 519-35

'Tight' Blood Glucose Control

Intensive Insulin Therapy in Critically Ill

- Prospective study in surgical ICU patients (n = 1548, 13% DM) randomized to
 - Intensive insulin therapy (infusion started if BG >110 mg/dL, goal 80-110 mg/dL)
 - Conventional therapy (mandated starting insulin infusion only if BG >215 mg/dL, goal 180-225 mg/dL)

Van Den Berghe et al: N Eng J Med 2001; 345: 1359-67

Intensive Insulin Therapy in Critically Ill

- Tight control reduced sepsis, ARF, transfusions, polyneuropathy, reduced mortality but only in patients with >5 day ICU stay
- Beneficial effects predominantly in cardiac surgical patients (62% of study population) who were received a glucose load (200-300 gm/24-h)

Van Den Berghe et al: N Eng J Med 2001; 345: 1359-67

Intensive Insulin Therapy in Critically Ill

- Prospective study in Medical ICU patients (n = 1200, 15-16% DM)
 - Intensive insulin therapy (infusion started if BG >110 mg/dL, goal 80-110 mg/dL)
 - Conventional therapy (insulin infusion only if BG >215 mg/dL (target 180-225 mg/dL)

Van Den Berghe et al: N Eng J Med 2006; 354: 449-61

Intensive Insulin Therapy in Critically Ill

- No difference in mortality, but reduced mortality in a sub-group with MICU stay ≥ 3 days (43% vs. 52%)
 - Reduced renal injury, ventilation duration, ICU and hospital duration
- Incidence of hypoglycemia (BG <40 mg/dL) was 6-fold higher in the insulin group 18.7% vs. 3.1%
- Higher mortality in patients with hypoglycemia

Van Den Berghe et al: N Eng J Med 2006; 354: 449-61

Perioperative Blood Glucose Control

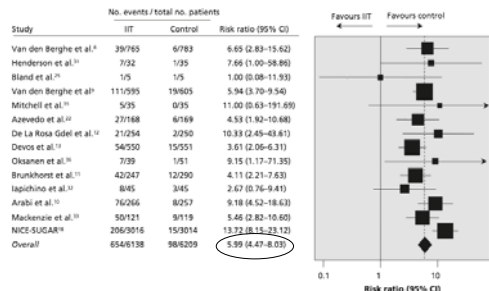
- Several professional organizations have recommended 'tight' blood glucose control in critically ill (e.g., acute MI, CVA, closed head injury, surgical patients)
- Some have recommended 'tight' blood glucose control in all hospitalized patients as well as all surgical patients including those undergoing ambulatory surgery

Intensive Insulin Therapy Increases Risk of Hypoglycemia-Related Adverse Events

- VISEP (Efficacy of Volume Substitute and Insulin Therapy in Severe Sepsis), multi-center (488 patients in 17 German Centers) study to evaluate the role of intensive insulin therapy (BG = 80-110) in ICU patients with sepsis
- Trial stopped early for safety reasons
- Rate of severe hypoglycemia (BG <40) higher in the intensive therapy group (17% vs 4.1%)
- Rate of serious adverse events related to hypoglycemia higher (10.9% vs. 5.2%)

Brunkhorst et al: N Engl J Med 2008; 358: 125-39

Systematic Review Tight Glucose Vs. Conventional Control: Hypoglycemia



Griesdale et al: CMAJ 2009

Metaanalysis of Clinical Trials of "Tight Control"

- "Our findings do not support the guidelines of organizations such as the American Diabetes Association, the American Association of Clinical Endocrinologists, and other organizations, including the Surviving Sepsis Campaign..."
- "We are not aware of any other trial of sufficient size to affect these results, thus we suggest that policy-makers reconsider recommendations promoting the use of intensive insulin therapy in all critically ill patients."

Griesdale et al: CMAJ 2009

Tight Glycemic Control as a Pay For Performance Metric

THE WALL STREET JOURNAL

COMPASSION | APRIL 8, 2008, 12:18 A.M. ET

Why 'Quality' Care Is Dangerous

The growing number of rigid protocols meant to guide doctors have perverse consequences.

By JEROME GROOPMAN and PAMELA HARTZBARD

- Clinical guidelines and 'metrics' developed for complex diseases
- Rigid and punitive rules to broadly standardize care for all patients
- Quality metrics coerce physicians into rigid and ill-advised therapy
- Tight BG control in ICU, physicians not complying have to attend 're-education sessions'

Tight Glucose Control in ICU Increases Mortality and Hypoglycemia

- Cohort study of > 10,000 critically ill adult patients
- Trend toward increased mortality with increasing use of tight glucose control after adjustment for disease severity
- High rate of hypoglycemia (30-40%)
 - Serious neurologic events ranging from seizures to coma

Treggiari et al: Crit Care 2008; 12: R29

Hyperglycemia and Perioperative Outcome



- Hyperglycemia may merely reflect the severity of underlying illness and surgical stress
- Adverse outcome primarily due to end organ dysfunction, rather than blood glucose level
- Association between hyperglycemia and adverse outcome does not prove causality

Lipshutz AKM, Gropper MA: Anesthesiology 2009; 110: 408-21

Detrimental Effects of Insulin

- Insulin dose was an independent negative predictor for acute renal failure (1548 ICU patients)
 - Van den Bergh et al: Crit Care Med 2003; 61: 359-66
- Increased administration of insulin associated with increased death, regardless of BG levels (531 ICU patients)
 - Finney et al: JAMA 2003; 290: 2041-7
- Insulin dose greater than 100 units per day was associated with greater odds for hospital death (7285 ICU patients)
 - Rady et al: Mayo Clin Proc 2005; 80: 1558-67

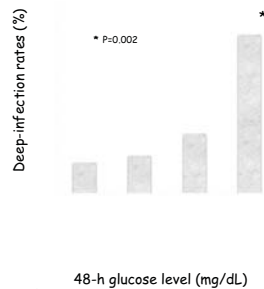
What is the optimal blood glucose level in the perioperative period?

Target Intraoperative Blood Glucose

Trial	Target BG Levels in Study Group	Target BG Levels in Control Group
WISEP (study stopped)	80-110	180-200
GLUCONTROL (study stopped)	80-110	140-180
NICE-SUGAR	80-110	140-180

Perioperative Glycemic Control and Risk of Infection in Diabetes

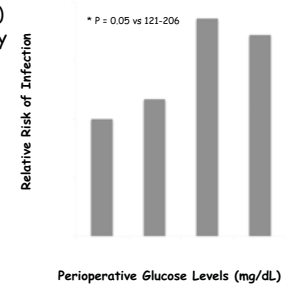
- Prospective, observational study in patients (n= 1585) undergoing cardiac surgery
- Deep wound infections (chest and leg), n=33 (2.1%)
- Multivariate analysis: 48-h blood glucose >200 mg/dL predicted risk of infection (P<0.005)



Zerr KJ et al: Ann Thorac Surg 1997; 63: 356

Perioperative Glycemic Control and Risk of Infections

- Retrospective study (chart review) of patients (n=411) undergoing cardiac surgery
- Major outcomes: leg and chest wound infections, pneumonia, urinary tract infections
- Mean postop BG levels (6 tests during 36-h postop period) divided into four quartiles



Golden et al: Diabetes Care 1999; 22: 1408

Perioperative Blood Glucose As Performance Indicator

- Joint Commission recommends morning BGL on postoperative days 1 and 2 in cardiac surgery patients ≤ 200 mg/dL
- Surgical Quality Improvement Program (SQIP) recommends BGL maintained <180 mg/dL in surgical patients

www.jointcommission.org/PerformanceMeasurement/Current+NHQM+Manual.htm

American Association of Clinical Endocrinologists and American Diabetes Association Consensus Statement on Inpatient Glycemic Control

- Critically ill patients
 - Blood glucose 140-180 mg/dL using insulin infusion
- Non-critically ill patients
 - Blood glucose 140-180 mg/L using SubQ insulin
- Safety issues
 - Frequent monitoring

Moghissi et al: Diabetes Care 2009; 32: 1119-31

How do we achieve the optimal blood glucose level in the intraoperative period?

Perioperative Insulin Therapy: IV Vs. SubQ

- Intravenous insulin ensures a more controlled and effective tissue delivery, particularly when the subQ compartment is suboptimally perfused (e.g., hypothermia, hypotension)
- Half-life of IV Insulin is short (<10 min), therefore, intermittent dosing may require large doses (50-100 U/h regular insulin) for adequate BG control

Preoperative Management of Antidiabetic Therapy

Preoperative Glucose Control and Postoperative Glycemic Control

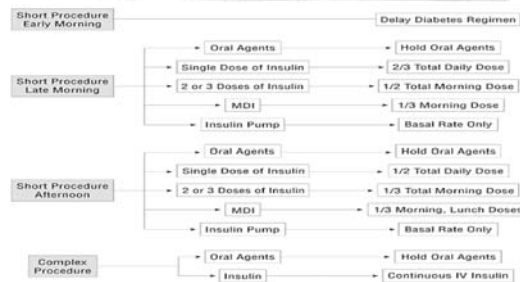
- Preoperative blood glucose control (HbA1c levels) may imply better general health and improved metabolic milieu
- Preoperative control of glucose may allow better intra- and postoperative glucose control
- Preoperative management of antidiabetic therapy critical in intra- and postoperative glucose control

Latham et al. Infection Control and Hospital Epidemiology 2001; 22: 607-612. 34; Dronge et al. Arch Surg 2006; 141: 375-80

Preoperative Management

- Is there a preoperative blood glucose level (or HbA1c) above which one should postpone elective surgery?
 - No study!
 - Determine patients' baseline control (HbA1c and fasting blood glucose)
 - Presence of dehydration, ketosis
 - Previous use of insulin
 - Type of surgical procedure

Perioperative Drug Management



MDI indicates multiple doses of short-acting insulin
Anticipated start time, invasiveness and duration of the procedure, and type of anesthesia

Antidiabetic Drug Therapy

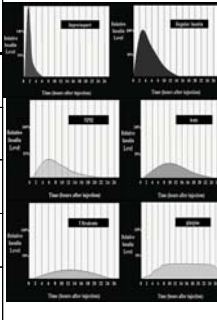
- Basal insulin therapy: control blood glucose level during fasting
 - Oral antidiabetics
 - Insulin: peakless (glargine) or long-acting (NPH, lente, ultralente)
- Control blood glucose after meals
 - Mealtime bolus doses of rapid-acting insulin

Oral Anti-Diabetic Medications

- Stimulate endogenous insulin secretion from pancreas
 - **Sulfonylureas:** Chlorpropamide (Diabinese), Glyburide (Micronase), Glipizide (Glucotrol)
 - **Meglitinides:** Repaglinide (Prandin), Nateglinide (Starlix)
- Increase insulin sensitivity (increase glucose utilization)
 - **Biguanides:** Metformin (Glucophage)
 - **Thiazolidinediones:** Rosiglitazone (Avandia), Pioglitazone (Actos)
- Decrease GI glucose absorption
 - **α -Glucosidase Inhibitors:** Acarbose (Precose), Miglitol (Glyset)
- Combinations: Metformin/Glyburide (Glucovance)

Insulins

Insulin type	Onset of action	Time to peak effect	Duration of action
Rapid Acting: Lispro, Aspart, Glulisine	5-15 min	45-75 min	2-4 h
Short-acting: Regular	30 min	2-4 h	5-8 h
Intermediate-acting: NPH, lente	2 h	6-10 h	18-24 h
Long-acting, Peakless: Glargine	2 h	No peak	20-24 h
Short-acting, Peakless: Detemir	2 h	No peak	6-24 h

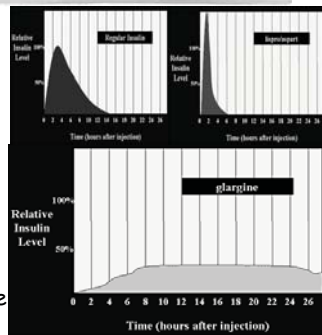


Preoperative Advice to Patients

- How do we manage preoperative oral antidiabetic therapy?
- How do we manage preoperative insulin therapy?

Perioperative Insulin Therapy

- Insulin pump: maintain basal rate
- Peakless (glargine) single dosing \pm short acting insulin: 80-100% evening dose based on fasting blood glucose

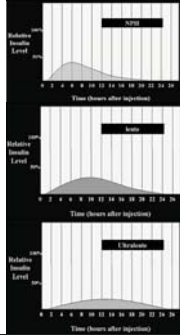


Preoperative Insulin Glargine: Strategies For Evening Before Surgery

- Patients (n=401) randomized to
 - 80% current insulin glargine dose
 - Call physician for insulin glargine dose
 - Dosing table
 - Patient on glargine alone: 50% of current dose if usual morning BGL is <150 and 80% if BGL \geq 150
 - Patient on glargine and rapid-acting insulin: 80% of current dose if usual morning BGL is <150 and 100% if BGL \geq 150
 - Target (100-179 mg/dL) achieved in 58.6%, 61.2%, 67.9% in respective groups
 - 5.5% patients had blood glucose <80 and 6% >249
- Ramsdell et al: Anesthesiology 2009; A1081

Perioperative Insulin Therapy

- Multiple dose peakless or long-acting insulins
 - Hold morning dose for early case
 - Give a 50% of dose based on time to first meal or next dose for late cases
- Fixed combination long and short-acting (70:30) insulin
 - Calculate amount of long-acting insulin and dose as for multiple dose



Blood Glucose Monitoring in Diabetics

- Upon admission to facility
- Every 1-2 h, intraoperatively
- Upon admission to the PACU
- Approximately, 30 min after insulin administration

Considerations in Diabetic Outpatients

- Perform procedure early in the day
- Avoid periop dehydration: encourage water intake until 2 h preop, intraop crystalloids
- Administer preoperative antibiotic therapy
- Aggressive perioperative antiemetic therapy, limit postoperative opioids
- Early postoperative oral intake

Intraoperative Blood Glucose Control For Outpatients

- What is the optimal intraoperative blood glucose?
 - No outcome data for ambulatory surgery patients
 - Recommendation blood glucose 140-180 mg/dL or at patient's baseline
- How do we maintain optimal blood glucose level?
 - Insulin administered SubQ (not IV)
 - Consider ultra-rapid acting insulin (lispro or aspart)
- Should we use insulin in a patient on oral antidiabetics who has never received insulin?
 - No data!

Postoperative Management

- What is the optimal blood glucose level in PACU and phase II unit?
 - No Study!
 - Possibility of resumption of oral intake and subsequent routine DM therapy
- What advice should we give to patients for glucose control after discharge home?
 - No Study!
 - Resume routine insulin therapy after oral intake
 - Frequent postop blood glucose monitoring

Summary

- No conclusive evidence that 'tight' intraop blood glucose control improves perioperative outcome
- 'Tight' control increases hypoglycemia that may be even more dangerous in outpatients
- Preoperative antidiabetic therapy is crucial
- Set clear goals for perioperative monitoring and control of blood glucose levels

• "The progress of science is strewn,
like an ancient desert trail, with the
bleached skeletons of discarded
theories which once seemed to
possess eternal life."

Arthur Koestler
