VUMC Surgical Critical Care Platform Guideline

Maintenance of Normoglycemia in Critically Ill Surgical Patients

I. BACKGROUND:

For some time the presence of diabetes and hyperglycemia has been known to be a risk factor for infectious complications in surgical patients. Recently, **Latham R, et al. (***Infect **Control Hosp Epidemiol*** 2001; 22:607-612) evaluated 1000 consecutive cardiac surgery patients (including non-diabetic) for incidence of infections complications. Overall, 3% developed surgical site infections. In regression analysis, perioperative glucose values significantly predicted the risk of infection with one or more perioperative glucose value of $\geq$ 200 mg/dl doubling the infection rate. The risk increased with higher glucose levels.

Glucose	Odds Ratio
200-249	2.54
250-299	2.97
$\geq$300	3.32

This study did not evaluate treatment or control of hyperglycemia and its effect on infectious outcomes.

A landmark study was published by **Van den Berghe G, et al.** (*NEJM* 2001; 345:1359-67) in 2001 and set a new standard of care for glucose control in critically ill and injured surgical patients. The authors performed a randomized trail of 1548 consecutive patients (total population 1562, 14 excluded) admitted to a surgical ICU and who were mechanically ventilated. Patients were randomized to receive IV insulin infusion to maintain serum glucose levels at either:

180 – 200 mg/dl (control group)

80 – 110 mg/dl (treatment group)

On day one of admission all patients received intravenous glucose and were subsequently changed to some form of nutritional support by day 2, either TPN or TEN. Patients with glucose values above the randomization range received continuous infusion intravenous insulin titrated at one hour intervals to reach their target levels. Once glucose control had stabilized, glucose analysis intervals were lengthened to Q2 to Q4 hours.

"Tight" glucose control resulted in a <u>significant reduction in mortality</u> for the group overall, but particularly the population with prolonged ICU stays (>5 days). Tight glucose control resulted in a 32% adjusted risk reduction for mortality. (See table below.)

Variable (%)	Control Group	Treatment Group	P value
IV insulin Rx	**39**	**99**	**< 0.001**
hypoglycemia	**<1**	**5**	**NS**
In-hosp. Mort			
All patients	**10.9**	**7.2**	**0.01**
ICU > 5d	**26.3**	**16.8**	**0.01**

For the total population, inclusion in the treatment arm resulted in fewer deaths due to sepsis but not deaths due to other causes. This group also demonstrated fewer overall infections, less requirement for dialysis, and less critical illness polyneuropathy.

Less than 110 appears to be better than less than 150: Subsequent published analysis of the data demonstrates that glucose control to mean values of 80-110 mg/dL was associated with statistically improved mortality than those with mean values of 110-150 mg/dL Glucose control and not insulin dosing is associated with favorable outcomes (Van den Berghe, G, et al, *Crit Care Med* 2003; 31:359-66).

Study applies to cardiac, general, trauma surgical populations: While the entire study population was weighted towards cardiac surgical patients (~62%), only ~30% of the patients staying >5 days were cardiac in origin. Sub-group analysis of various patient populations demonstrates improved outcomes for nearly all with adequate power. Non-cardiac patients (n=578) also demonstrated a significant reduction in mortality in the treatment arm. 122 thoracic surgery patients admitted to the ICU for post-operative sepsis demonstrated a significant reduction in subsequent bacteremia for those patients with in the treatment arm. 63 patients with isolated brain injury were included in the study. Those head injured patients in the treatment arm had a lower incidence of diabetes insipidus, lower mean intracranial pressures, and a similar mean cerebral perfusion pressures with lower norepinephrine use.

Physiologic mechanisms: Research into possible physiologic mechanisms for the observed improvement in outcome with maintenance of normoglycemia has demonstrated numerous candidate alterations at the cellular level. Increased glucose uptake by muscle cells, prevention of a rise in triglycerides and HDL/LDL ratio that occurs with elevated glucose, reduction of changes in mitochondrial function noted with hyperglycemia, and improved phagocytic function all have been shown to occur.

II. GUIDELINE FOR MAINTANANCE OF EUGLYCEMIA: SURGICAL CRITICAL CARE PLATFORM

All patients being admitted to surgical or trauma ICU should undergo accu-check of glucose on admission to the ICU. The majority of critically ill patients will require initiation of continuous insulin VGR protocol in WIZ. Category 2 (see below) patients with accu-checks above target range should have this protocol initiated either upon admission or subsequently.

Protocol:

1. **Accu-check on admission:**
    a. Blood glucose **≤ 60 mg/dl**?
        i. Administer ½ ampoule iv Dextrose (50%)
        ii. Contact ICU Resident
        iii. Re-check accucheck Q 15 min after iv dextrose therapy and reassess
        iv. Review home medications and premorbid conditions that predispose hypoglycemia; correct cause if possible
    b. Blood glucose **61 – 79 mg/dl**?
        i. Re-check accucheck Q 1h x 2 to confirm stable blood glucose
        ii. If stable, blood glucose monitoring (per accucheck) Q 4h until stable x2 then interval accuchecks may be decreased to Q6h.
    c. Blood glucose **80 – 110 mg/dl**?
        i. Blood glucose monitoring (per accucheck) Q 4h until stable x2 then interval accuchecks may be decreased to Q6h.
        ii. RN may d/c accuchecks if normoglycemia (61 – 110 mg/dl) is maintained x 24 hrs
    d. Blood glucose **> 111 mg/dl**?
        i. Yes – choose patient **Category** below and continue

Category 2 – Critically Ill:
Critically ill patient

Category 1 – Non-critically Ill
Non-critically ill patients

(acute resuscitative, inotropic support, acute organ dysfunction)

Mechanically ventilated	Not mechanically ventilated
Intravenous steroid therapy	No active steroid use
Known or suspected active infection	No active infection
Premorbid history of diabetes mellitus	No hx of diabetes

Critically Ill Patients - Category 2:

2. **Begin continuous infusion insulin using SCC platform WIZ-VGR**
3. **Consider changing to Subcutaneous regimen at Q 4hr intervals if:**
   - Insulin requirements are stable
   - Critical illness resolved, subcutaneous absorption appropriate, and without new clinical deterioration
   - Minimal insulin requirements for 24 hours

Non-critically Ill patients - Category 1:

2. Blood glucose > **250 mg/dl**, begin **Continuous Insulin Infusion Therapy**
   - Initiate and titrate as per guideline for Category 2 above

3. Blood glucose **111 – 250 mg/dl**, begin **Subcutaneous Insulin Therapy**
   - Q 4 hr accuchecks and dosing
   - Subcutaneous Insulin dose (units of regular insulin) calculated as:

$$\frac{\{[\text{blood glucose (mg/dl)}] - 90\}}{10}$$

   - Adjust insulin dosing (number divided by) as needed to reach target of 80 – 110 mg/dl
   - Notify ICU resident if questions

4. Consider initiating home antihyperglycemic regimen if adequate oral intake and mobility is present; contact MD for orders

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