Observational Study

Insulin in critical care settings

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Inpatient hyperglycemia is common and is associated with an increased risk of hospital complications, higher costs, and higher in-hospital morbidity & mortality rates. Appropriate glycemic control strategies can reduce these risks, although hypoglycemia is a concern. In critically ill patients, intravenous (IV) insulin is most appropriate, with a starting threshold no higher than 180 mg/dL. Once IV insulin is started, the glucose level should be maintained between 140 and 180 mg/dL.

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Insulin administration is the preferred way to control hyperglycemia in hospitalized patients. In critically ill patients, such as those with hypotension requiring pressor support, hyperglycemic crises, sepsis, or shock, insulin is best given via continuous intravenous (IV) infusion. It is well established that mortality, morbidity, and length of hospital stay increases when Blood Glucose (BG) levels increase greater than 180 to 200 mg/dL in critically ill patients[1].

Hypoglycemia in critically patients is also associated with increased mortality. It is, therefore, important to use insulin that both acts as well as clears rapidly in order to quickly correct and prevent hyperglycemia and hypoglycemia.

IV insulin infusions are the standard of care in critically ill patients. When regular insulin is injected by IV versus SC routes, peak serum levels are reached within 2minutes by IV route versus 60minutes by SC route resulting in peak glucose lowering at 15 minutes by IV route versus 180 minutes by SC route. Rapid glucose lowering by IV insulin coupled with rapid insulin clearance allows BG levels to return to baseline 30 minutes after injection if the insulin infusion is stopped.The short half-life of IV insulin (<15 minutes) allows fl exibility in adjusting the infusion rate[1].

Target Blood Glucose Range :

The current BG recommendations for critically ill patients by the ADA in conjunction with the AACE and separately by the Society of Critical Care Medicine are listed in Table 1[2].

The Leuven trial in 2001 was a single-center trial that compared the BG target of 80 to 110 mg/dL versus 180 to 200 mg/dL in the surgical ICU[3]. It showed 42% reduction in mortality and 34% reduction in length of stay. The Leuven group repeated their study in the medical ICU but were not able to show similar reduction in mortality[4]. In fact, there was a trend toward increase mortality that was found to be strongly associated with hypoglycemia. The efficacy and safety of volume insulin therapy in severe sepsis (VISEP) study compared the 2 target BG range groups defined by the Leuven trials[5]. The study reported a significant increase in adverse events (11% *versus* 5%) in the 80 to 110 mg/dL group versus the 180 to 200 mg/ dL group, and the study was stopped early because of the significantly increased rate of hypoglycemia (17% *versus* 4%) in the tightly controlled group. The NICE-SUGAR study, a large, multinational study, compared a target range of 81 to 108 mg/dL with 140 to 180 mg/dL in both surgical and medical ICUs[6]. The trial showed significant increase in 90-day mortality. This increased mortality was shown to be associated with hypoglycemia, although no causal relationship was established. Of note, this was the only study that had a comparison group with BG levels less than 180 mg/dL, which is well below the 200 mg/dL threshold that prior studies had shown to increase morbidity and mortality. It is worth noting that the safety of BG levels between 110 mg/dL and 140 mg/dL is still unanswered.

- **Poor outcome and cost of therapy in critically ill patients with BGs > 180 mg%.**
- **Short or rapid acting IV insulin through infusion pump is preferred.**
- **Hypoglycemia is a concern. Safety of insulin infusion protocols is followed.**
- **Appropriate glycemic targets, monitoring and education are necessary.**

Table 1 — *Glucose targets in critically ill patients with and without diabetes*

Established diabetes	No diabetes • After cardiac surgery or • After ischemic cardiac or neurological event
140–180 mg/dL	100–150 mg/dL

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For patients who have had cardiac surgery, the Society of Critical Care Medicine recommends a target range of 100 to 150 mg/dL . However, tight control (100-140 mg/dL) on IV insulin infusion in patients who have had cardiac surgery has shown to lower adverse outcomes for patients without diabetes. Patients with diabetes have no increased complications in the 140 to 180 mg/dL target group when compared with the 100 to 140 mg/dL target group[2].

Selecting an Insulin Infusion Protocol :

Successful implementation of an insulin infusion protocol requires multidisciplinary interaction and ongoing staff education to ensure optimal patient outcomes. An ideal protocol achieves the desired target blood glucose quickly (within 3-12 hours in published protocols) and maintains blood glucose in the target range. Effective insulin infusion protocols must use dynamic as opposed to static algorithms that use both the last BG, the rate of change in BG, as well as the current insulin infusion rate when recommending the new insulin infusion rate. This practice will help prevent hyperglycemia if the rate of correction is too slow and prevent hypoglycemia if the rate of correction is too fast. Hourly glucose measurements until stable glycemic control is established, followed by point-of-care testing every 1 to 2 hours, is needed to assess response to therapy and prevent hypoglycemia[7].

Many different paper-based and computerbased dynamic algorithms are available, and no single protocol or algorithm has been established as the most effective for achieving and maintaining glucose targets or achieving lowest hypoglycemia rates. It is important that the hospital's chosen protocol is validated and has demonstrated safety and efficacy. Key elements of an IV insulin infusion protocol are listed in Table 2. In the event of abrupt TPN/peripheral parenteral nutrition (PPN) or steroid or vasopressor discontinuation, the infusion rate should be reduced by 50%, with resumption of BG checks once every hour until BGs are stable[8].

Hypoglycemia Prevention and Treatment :

Minimizing the risk of hypoglycemia with any insulin infusion protocol requires ongoing evaluation of hypoglycemia episodes and the contributing factors such that the protocol can be revised to address and minimize the rsik. Some hypoglycemia protocols temporarily stop the insulin infusion for hypoglycemia and restart it at a lower rate once hypoglycemia has resolved. However, failure to restart the infusion can result in profound hyperglycemia and ultimately diabetic ketoacidosis (DKA) in patients with type 1 diabetes. Thus, some hypoglycemia protocols do not stop the infusion, but significantly reduce the rate[8].

An embedded hypoglycemia treatment protocol is imperative for the safety of insulin infusion therapy. A hypoglycemia protocol allows bedside nurses to immediately implement treatment without additional orders. Key components of a hypoglycemia protocol include specific instructions regarding temporarily turning off or reducing the infusion rate, treating with dextrose or other glucose sources, and monitoring more frequently, as well as when the insulin infusion, if temporarily stopped, should be restarted and at what rate.

Table 2 — *Components of a Safe and Effective Insulin Infusion Protocol*

• Includes clear glycemic targets
• Identifies threshold for implementation
• Easy to implement
• Good coordination between attending nurse and treating doctor
• Provides clear, specific instructions for blood glucose monitoring and titration
• Includes titration based on both current blood glucose level and rate of change*
• Is safe: carries a low risk for hypoglycemia and includes an embedded protocol for treatment of hypoglycemia should it occur
• Is effective: gets patients to target quickly and maintains blood glucose within the target range with minimal titration
• Includes a plan for transition to subcutaneous insulin
• *Rate of change is calculated based on the slope of the blood glucose trend line and is incorporated into protocols by movement to a more aggressive algorithm if blood glucose is not declining by ~ 40–75 mg/dl or to a less aggressive algorithm if blood glucose is declining rapidly.*

Conclusion :

Extremes of blood glucose lead to poor outcomes . Continuous IV Insulin infusionprotocols are the preferred treatment modality for glycemic control in the critical care setting. Insulin infusion can be an effective treatment modality in acute care settings with appropriate glycemic targets, monitoring, and education. The safety of insulin infusion protocols depends on appropriate blood glucose monitoring and titra¬tion.

References

1 Lansang MC, Umpierrez GE — Inpatient hyperglycemia management: A practical review for primary medical and surgical teams. *Cleve Clin J Med* 2016; **83:** S34-43.

2 Khazai NB, Hamdy O — Inpatient Diabetes Management in the Twenty-First Century. *Endocrinol Metab Clin North Am* 2016; **45:** 875-94.

3 Van den Berghe G, Wouters P, Weekers F — Intensive insulin therapy in critically ill patients. *N Engl J Med* 2001; 345: 1359-67.

4 Van den Berghe G, Wilmer A, Hermans G — Intensive insulin therapy in the medical ICU. *N Engl J Med* 2006; **354:** 449-61

5 Brunkhorst FM, Engel C, Bloos F — Intensive insulin therapy and pentastarch resuscitation in severe sepsis. *N Engl J Med* 2008; **358:** 125-39.

6 Investigators N-SS, Finfer S, Chittock DR, — Intensive versus conventional glucose control in critically ill patients. *N Engl J Med* 2009; **360:** 1283-97.

7 Jacobi J, Bircher N, Krinsley J — Guidelines for the use of an insulin infusion for the management of hyperglycemia in critically ill patients. *Crit Care Med* 2012; **40:** 3251-76.

8 Kelly JL — Continuous Insulin Infusion: When, Where, and How? *Diabetes Spectr* 2014; **27:** 218-23.