Glycemic Control in the ICU

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A 45-year-old male patient was admitted to hospital with cough, breathlessness, dizziness, and fever for the past 5 days. He was hypoxemic (SpO_2 88% on a nonrebreathing mask) and hypotensive (blood pressure 82/34 mmHg after 2 L of IV fluid). He was intubated and started on mechanical ventilation. His blood glucose was 350 mg/dL on the glucometer.

Hyperglycemia is commonly seen in both diabetic and nondiabetic patients in ICUs. Hyperglycemia is also an independent risk factor for mortality and morbidity in medical and surgical ICU patients. Various factors contribute to hyperglycemia in the ICU. These include increased counterregulatory hormones (glucagon and cortisol), hepatic insulin resistance, glucocorticoid therapy, dextrose-containing solutions, and high-calorie enteral and parenteral nutrition.

Step 1: Check Blood Glucose

- Check Capillary glucose by point of care properly calibrated glucometer
- Caution is required in interpreting results of point-of-care glucose meters in patients with anemia, polycythemia, hypoperfusion, or use of medications that can interfere with glucose measurements.
- Arterial glucose (in patients with arterial line) or venous glucose measured in laboratory glucose analyser may be more accurate in patients with shock on vasopressors or hypoxia or anaemia.
- Treatment for the underlying disease should not be withheld while one is waiting for a laboratory glucose value.

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Step 2: Assess Glycemic Risk

- Patients should be asked about history of diabetes, current treatment and recent blood sugar levels
- Check for HbA1c to assess control of blood glucose.
- Check comorbidities such as hypertension, renal disease, liver disease, pancreatitis, chronic obstructive airway disease (COAD), obesity, and coronary artery disease.
- Enquire about medication history causing hyperglycemia—corticosteroids, octreotide, β-blockers, thiazide diuretics, niacin, protease inhibitors, and antipsychotic agents.

Step 3: Decide on Frequency of Blood Glucose Measurement

- All hemodynamically unstable patients, especially those on intravenous insulin infusion, should have blood glucose checked every hour or even more frequently.
- As the condition stabilizes or in less sick patients, this interval may be prolonged.
- With any change in patients' condition or nutrition delivery regimen, initiate more frequent glucose monitoring.

Step 4: Decide on the Target Blood Glucose Level

- The present recommendation in general medical/surgical ICU patients is to keep blood glucose between 140 and 180 mg/dL.
- Patients with expected length of stay for more than 3 days in ICU will benefit from this control.
- For patients with shorter stay may have a more liberal target sugar control.
- A more liberal blood sugar control is also advised in patients who are diabetic,

Step 5: Decide on Insulin Delivery Route

- All oral hypoglycemic agents and long-acting insulin should be discontinued during initial days of instability.
- Intravenous infusion of short acting regular insulin is the treatment of choice in critically ill patients.
- The following groups of patients may be candidates for periodic subcutaneous insulin:
  - Step-down therapy from intravenous insulin
  - Less sick patients on oral diet

Step 6: Decide on Insulin Delivery Protocol (Tables 6.1 and 6.2)

- Insulin protocol should be institution specific and nurse driven.
- All efforts should be made to educate nurses and residents and ensure compliance by periodic audits.
- Dynamic insulin protocols, ideally computerized, which can monitor trend of rise or fall of blood glucose and adjust insulin doses, tend to keep blood glucose at a more desirable range.
- Use insulin delivery protocol as per Table 6.1 e.g. A diabetic patient with admission blood sugar of 250 mg/dL should get 5 U regular insulin bolus followed by 3 U/h of insulin infusion. Next blood sugar after 1 h is 270 mg/dL, another bolus of 5 U regular insulin and increase insulin infusion to 4 U/h.
- Another insulin delivery protocol which can be used is described in Table 6.2 e.g. A diabetic patient with admission blood sugar of 250 mg/dL and normal renal function may be started on scale 2 at 4 U/h. Patient with impaired renal function could be started on scale 1 and non diabetic patient on scale 3 or 4. Next blood sugar check after 1 h is 270 mg/dL, the scale should shift vertically down (range 251–300) and infusion increased to 6 U/h. Next blood sugar is 264 (target 140–180 mg/dL) the scale should shift horizontally to the right to infusion rate of 9 U/h.

Table 6.1 An example of algorithm of IV insulin therapy in a critically ill patient

	Initiation		Maintenance	
Random blood sugar (RBS) (mg/dL)	Bolus (U)	Infusion (U/h)	At 1–5 U/h	At >5 U/h
151–199	0	2	Increase 1 U/h	Incr 2 U/h
200–249	3	2	Bolus 3 U + incr 1 U/h	Bolus 3 U + incr 2 U/h
250–299	5	3	Bolus 5 U + incr 1 U/h	Bolus 5 U + incr 2 U/h
300–349	8	3	Bolus 8 U + incr 1 U/h	Bolus 8 U + incr 2 U/h
350–399	10	4	Bolus 10 U + incr 2 U/h	Bolus 10 U + incr 3 U/h
400–449	10	5	Bolus 10 U + incr 3 U/h	Bolus 10 U + incr 4 U/h
>450	10	6	Bolus 10 U + incr 4 U/h	Bolus10 U + incr 4 U/h

Target RBS: 140–180 mg/dL

Table 6.2 Another example of algorithm of IV insulin therapy in a critically ill patient

RBS (mg/dL)	Scale 1 (IV—U/h)	Scale 2 (IV—U/h)	Scale 3 (IV—U/h)	Scale 4 (IV—U/h)
<64	Treat as hypoglycemia	Do	Do	Do
64–140	Nil	Nil	Nil	Nil
141–200	1	2	3	4
201–250	2	4	6	8
251–300	3	6	9	12
301–350	4	8	12	16
351–400	5	10	15	20
>400	10	15	20	25

The patient should be started on a particular scale depending on initial sugar and clinical scenario. In this scale, in order to arrive at a target glucose level of 140–180 mg/dL, insulin infusion rate should be shifted horizontally to the next or previous scale in the same row if sugar remains within the range for that row. If sugar increases or decreases to the other range, the infusion rate should be shifted vertically for that range in the same scale
Target RBS: 140–180 mg/dL

Step 7: Avoid Hypoglycemia (Blood Glucose <70 mg/dL)

- Rigorous blood glucose control (80–110 mg/dL) leads to hypoglycemic episodes in a mixed medical/surgical ICU, which may be detrimental to their outcome.
- The following groups of patients are more prone to hypoglycemia:
  - Renal failure
  - Dialysis
  - Liver failure
  - Malnourished
  - Adrenal insufficiency
  - Intolerance to enteral feed
- Stop insulin infusion immediately and give 50 mL of 25% dextrose intravenously and repeat this till blood glucose is more than 90 mg/dL and the patient is asymptomatic.
- Check blood glucose every 15 min and then decrease frequency depending on clinical response.
- Ensure adequacy of carbohydrate calorie intake either enterally or parenterally and avoid abrupt discontinuation.

Step 8: Avoid Large Variations in Glucose Concentrations in ICUs

- Glycemic variability is expressed as the standard deviation of each patient's blood glucose levels.
- Glycemic variability is an independent predictor of mortality in a heterogeneous population of ICU patients.

- The efficacy of continuous or near-continuous glucose monitoring and/or new algorithms targeted more specifically to reduce glycemic variability as well as mean blood glucose requires further clinical studies in ICU patients before the final recommendation is made.

Step 9: Avoid Under or Overtreatment and Safety Issues

- Overtreatment and undertreatment of hyperglycemia represent major safety concerns.
- Education of ICU staff is essential in engaging the support of those involved in the care of inpatients with hyperglycemia.
- Regular audit and process measures should be undertaken to assess compliance with insulin regimens and attainment of target glucose range, avoidance of hypoglycemia and minimising glycemic variability.

Step 10: Change to Intermittent Treatment Once Stable

- Switch over to subcutaneous insulin.
- Long-acting insulin should overlap discontinuation of insulin infusion to prevent hyperglycemia.
- Intermittent short acting insulin (either a fixed dose or based on sliding scale) pre meals or six hourly should be instituted
- Calculate the dosage taking into account the history of diabetes, type of diabetes, previous insulin dose, stress level, steroid use, risk of hypoglycemia, and general clinical status.

Suggested Reading

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Arnold P, Paxton RA. The effect of a hypoglycemia treatment protocol on glycemic variability in critically ill patients. J Intensive Care Med. 2015;30(3):156–64. *Treatment of hypoglycemia with dextrose 50% can overcorrect blood glucose levels and increase glucose variability. This study evaluated the effect of a hypoglycemia treatment protocol focused on minimizing glucose variability in critically ill patients. Implementation of a hypoglycemia treatment protocol led to a reduction in glucose variability, while still providing a safe and effective way to manage hypoglycemia in critically ill patients*

Kalfon P, Giraudeau B, Ichai C. Tight computerized versus conventional glucose control in the ICU: a randomized controlled trial. Intensive Care Med. 2014;40(2):171–81. *A multi-center randomized trial in 34 French ICU. Adult patients expected to require treatment in the ICU for at least 3 days were randomly assigned without blinding to undergo tight computerized glucose control with the or conventional glucose control with blood glucose targets of 4.4-6.1 and <10.0 mmol/L, respectively. The primary outcome was all-cause death within 90 days after ICU admission. Primary outcome was available for 1,335 and 1,311 patients, respectively.*

The conclusion was that tight computerized glucose control with the computerised algorithm did not significantly change 90-day mortality and was associated with more frequent severe hypoglycemia episodes in comparison with conventional glucose control

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Marik PE, Preiser JC. Toward understanding tight glycemic control in the ICU: a systematic review and metaanalysis. Chest. 2010;137:544–51. *The goal of this systematic review was to determine the benefits and risks of tight glycemic control in ICU patients and to explain the differences in outcomes in reported trials. There is no evidence to support the use of intensive insulin therapy in general medical/surgical ICU patients who are fed according to current guidelines. Tight glycemic control is associated with a high incidence of hypoglycemia and an increased risk of death in patients not receiving parenteral nutrition*

NICE-SUGAR Study Investigators for the Australian and New Zealand Intensive Care Society Clinical Trials Group and the Canadian Critical Care Trials Group, Finfer S, Chittock D, Li Y, Foster D, Dhingra V, Bellomo R, Cook D, Dodek P, Hebert P, Henderson W, Heyland D, Higgins A, McArthur C, Mitchell I, Myburgh J, Robinson B, Ronco J. Intensive versus conventional glucose control in critically ill patients with traumatic brain injury: long-term follow-up of a subgroup of patients from the NICE-SUGAR study. Intensive Care Med. 2015;41(6):1037–47. *Randomized trial of target blood glucose (BG) range of either 4.5-6.0 mmol/L (intensive control) or <10 mmol/L (conventional control). Subgroup analysis of traumatic brain injury (TBI) and extended Glasgow outcome score (includes mortality) at 24 months. Patients with traumatic brain injury randomly assigned to intensive compared to conventional glucose control experienced moderate and severe hypoglycemia more frequently, no significant difference in other clinically important outcomes was noticed*

Rhodes A, Evans LE, Alhazzani W, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. Intensive Care Med. 2017;43(3):304–77. *Guidelines on glycemic control in sepsis patients*

Van den Berghe G, Wilmer A, Hermans G, et al. Intensive insulin therapy in the medical ICU. N Engl J Med. 2006;354:449–61. *Intensive insulin therapy significantly reduced morbidity but not mortality in all patients in the medical ICU. Although the risk of subsequent death and disease was reduced in patients treated for three or more days, and these patients could not be identified before therapy*

Van den Berghe G, Wouters P, Weekers F, et al. Intensive insulin therapy in critically ill patients. N Engl J Med. 2001;345:1359–67. *Intensive insulin therapy to maintain blood glucose at or below 110 mg/dL reduces morbidity and mortality in critically ill patients in the surgical intensive care unit*