



Top 10 Facts to Know About Inpatient Glycemic Control

William B. Horton, MD,^a Jose S. Subauste, MD^{a,b,c}

^aDepartment of Medicine and ^bDivision of Endocrinology, University of Mississippi Medical Center, Jackson; ^cDepartment of Medicine, G.V. Montgomery VA Medical Center, Jackson, Miss.

ABSTRACT

Uncontrolled hyperglycemia in hospitalized patients with or without a previous diagnosis of diabetes is associated with adverse outcomes and longer lengths of hospital stay. It is estimated that one-third of hospitalized patients will experience significant hyperglycemia, and the cost associated with hospitalization for patients with diabetes accounts for half of all health care expenditures for this disease. Optimizing glycemic control should be a priority for all health care providers in the inpatient setting. Appropriate management strategies should include identification of appropriate glycemic targets, prevention of hypoglycemia, initiation of appropriate basal-plus-bolus insulin regimens, and planning for the transition from inpatient to outpatient therapy before hospital discharge.

© 2016 Elsevier Inc. All rights reserved. • *The American Journal of Medicine* (2016) 129, 139-142

KEYWORDS: Hyperglycemia; Hypoglycemia; Insulin

Uncontrolled hyperglycemia in hospitalized patients with or without a previous diagnosis of diabetes is associated with adverse outcomes and longer lengths of hospital stay.¹ It is estimated that one-third of hospitalized patients will experience significant hyperglycemia,² and the cost associated with hospitalization for patients with diabetes accounts for half of all health care expenditures for this disease.³ Many patients without preexisting diabetes will also experience stress-related hyperglycemia while hospitalized.⁴ Optimizing glycemic control should be a priority for all health care providers in the inpatient setting.

CONSENSUS GUIDELINES EXIST FOR THE MANAGEMENT OF INPATIENT HYPERGLYCEMIA

The American Diabetes Association and the American Association of Clinical Endocrinologists released a consensus statement on inpatient glycemic control in 2009.⁵ These guidelines note that insulin therapy is the preferred method for

achieving inpatient glycemic control. In the intensive care unit, intravenous (IV) infusion is the preferred route of insulin administration. Outside of critical care units, scheduled subcutaneous administration of insulin consisting of basal, nutritional, and supplemental (correction) components is preferred.^{1,5}

GLYCEMIC TARGETS VARY BY PATIENT POPULATION

In critically ill patients on IV insulin therapy, the blood glucose (BG) level should be maintained between 140 and 180 mg/dL. Targets <110 mg/dL are not recommended for this patient population. For noncritically ill patients treated with subcutaneous insulin, premeal glucose targets should generally be <140 mg/dL in conjunction with random glucose targets <180 mg/dL, as long as these targets can be safely achieved. Higher glucose ranges may be acceptable in terminally ill patients or patients with severe comorbidities. Consideration should be given to reassessing the insulin regimen if BG levels are consistently <100 mg/dL, for avoidance of hypoglycemia.⁵

INPATIENT HYPERGLYCEMIA IS BEST MANAGED WITH INSULIN

Typically, oral agents have a limited role in the inpatient setting and should be discontinued during acute illness

Funding: None.

Conflict of Interest: None to disclose.

Authorship: Both authors had access to data and contributed equally to writing the manuscript.

Requests for reprints should be addressed to William B. Horton, MD, University of Mississippi Medical Center, 2500 North State Street, Jackson, MS 39216.

E-mail address: wbhorton@umc.edu

unless it is a very brief hospitalization.^{1,5} Metformin cannot be used when there is any possibility of the need for iodinated contrast studies or renal insufficiency.¹ Sulfonylureas and metaglinides can cause unpredictable hypoglycemia in patients who are not eating consistently.¹ Thiazolidinediones cause fluid retention (especially in combination with insulin) and parenteral glucagon-like peptide-1, and amylin agonists can cause nausea and should be withheld in acutely ill patients.¹ Insulin works reliably and can be quickly titrated based on changes in diet or glucose levels, making it ideal in the inpatient setting. The **Table** and the **Figure** detail the onset and duration of action characteristics by insulin type.

HYPOGLYCEMIA SHOULD BE PREVENTED

Hypoglycemia (both spontaneous and iatrogenic) has been associated with higher risk of complications among hospitalized patients, including longer and more expensive hospital stays and increased mortality rates.⁶⁻⁸ Hospitalized patients who are elderly or severely ill are especially vulnerable to the adverse effects of hypoglycemia.⁶ Hypoglycemia is defined as any BG <70 mg/dL.⁹ For avoidance of hypoglycemia, consideration should be given to reassessing the insulin regimen if BGs <100 mg/dL are consistently noted. Modification of the regimen is necessary when BG values are <70 mg/dL, unless the event is easily explained by other factors such as a missed meal.⁵ It is also important to avoid routine use of correctional insulin doses at bedtime so as to prevent nocturnal hypoglycemia.⁵

Table Duration and Onset of Action Characteristics by Insulin Type

Insulin Type	Onset of Action	Peak of Action	Duration of Action
Mealtime insulins			
Regular	15-60 min	2-4 h	6-8 h
Lispro	10-15 min	1 h	3-4 h
Aspart	10-15 min	1 h	3-4 h
Glulisine	10-15 min	1 h	3-4 h
Basal insulins			
NPH	1-3 h	6-8 h	12-16 h
Glargine	1-3 h	No peak	Up to 24 h
Detemir	1-3 h	No peak	Up to 24 h

NPH = Neutral Protamine Hagedorn.

CLINICAL SIGNIFICANCE

- Uncontrolled hyperglycemia in hospitalized patients with or without a previous diagnosis of diabetes is associated with adverse outcomes and longer lengths of hospital stay.
- Most hyperglycemic inpatients will require basal plus insulin regimens to mimic normal pancreatic physiology. Insulin-naïve patients can safely initiate treatment by calculating total daily dose.
- Sliding scale insulin alone is insufficient treatment for sustained hyperglycemia.

GLYCEMIC MONITORING VARIES BY DIETARY NEEDS

Bedside capillary point-of-care (POC) testing is the preferred method for guiding ongoing glyceemic management.¹⁰ Recommendations include POC testing before meals and at bedtime in patients who are eating usual meals.^{5,10} POC testing should be performed every 4-6 hours in patients who are not allowed anything by mouth or who are receiving continuous enteral or parenteral nutrition.^{5,10} More frequent POC testing, ranging from every 30 minutes to every 2 hours, is required for patients receiving IV insulin infusions.⁵

TREATMENT OF INPATIENT HYPERGLYCEMIA IS COST-EFFECTIVE

In the Portland Diabetic Project, institution of continuous IV insulin therapy to achieve predetermined target BG values in diabetic patients undergoing open-heart surgical procedures reduced the incidence of deep sternal wound infections by 66%, resulting in a total net savings to the hospital of \$4638 per patient.¹¹ In another study, intensive glyceemic control in 1600 patients treated in a medical ICU was associated with a total cost savings of \$1580 per patient.¹² Optimization of inpatient glyceemic management is not only effective in reducing morbidity and mortality, but also is cost-effective.⁵

TRANSITIONING FROM INPATIENT TO OUTPATIENT GLYCEMIC MANAGEMENT IS IMPORTANT

Hospitalization provides a unique opportunity for addressing a patient's education in diabetes management.² Preparation for transition to the outpatient setting is an important goal of inpatient diabetes management and begins with hospital admission.⁵ Successful coordination of this transition requires a team approach that includes physicians, nurses, dietitians, case managers, and social workers.¹³ An outpatient follow-up visit with the primary care provider, endocrinologist, or diabetes educator within 1 month after discharge from the hospital is advised for all patients experiencing hyperglycemia while hospitalized.¹³

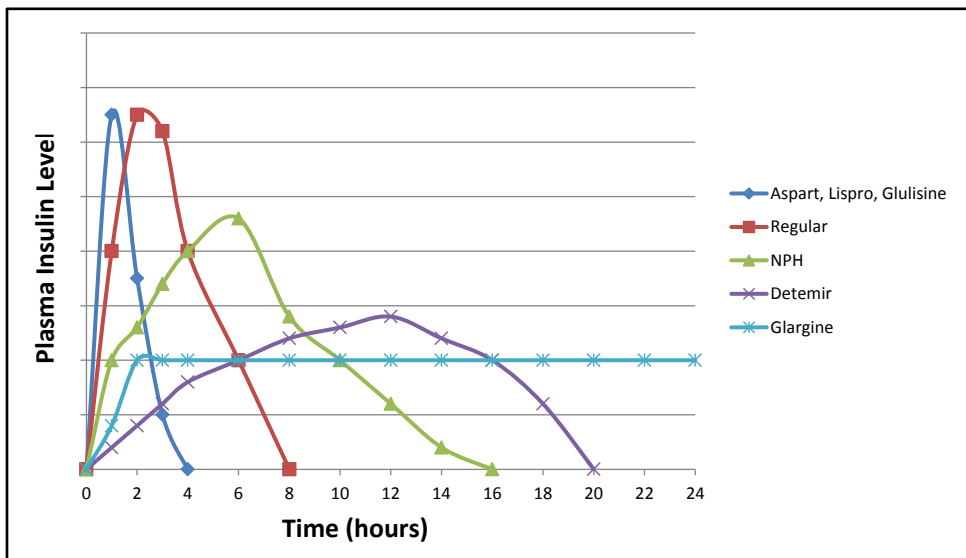


Figure Insulin characteristics by duration and onset of action.

CLINICIANS SHOULD BE AWARE OF MANAGEMENT FOR SPECIAL CLINICAL SITUATIONS

Patients who utilize continuous insulin infusion (pump) therapy in the outpatient setting can be considered for diabetes self-management while hospitalized, provided they have the mental and physical capacity to do so.^{5,13-15} It should be noted that nursing personnel must document basal rates and bolus doses (at least daily) if this occurs.⁵ Persistent hyperglycemia in patients receiving enteral nutrition should be treated with scheduled insulin doses.¹ Once-daily glargine insulin, premixed human 70/30 insulin given every 8 hours, or a combination of Neutral Protamine Hagedorn insulin given every 12 hours and regular insulin given every 6 hours have all been recommended.^{1,13,16,17} Patients receiving glucocorticoids should be treated with scheduled basal/bolus regimens and will likely require an increase in bolus doses while on glucocorticoid therapy.¹ During glucocorticoid tapers, insulin dosing should be proactively adjusted to avoid hypoglycemia.⁵

SLIDING-SCALE INSULIN ALONE IS INSUFFICIENT TREATMENT FOR SUSTAINED HYPERGLYCEMIA

Scheduled basal/bolus insulin regimens mimic normal pancreas hormonal physiology and are designed to prevent hyperglycemia, whereas sliding scale insulin (SSI) alone attempts to lower hyperglycemia only after it has occurred.¹ A study comparing scheduled basal/bolus insulin to SSI alone showed a significantly higher percentage of patients achieving goal glucose levels in the basal/bolus group than in the SSI group (66% vs 38%) without an increase in hypoglycemia.¹⁸

INSULIN-NAÏVE PATIENTS CAN SAFELY INITIATE TREATMENT BY CALCULATING TOTAL DAILY DOSE

For patients who are insulin naïve, insulin therapy can safely be initiated at a total daily dose of 0.3-0.6 units/kg body weight.^{19,20} The lower starting dose is recommended for leaner patients and those with renal insufficiency, while the higher starting dose is recommended for obese patients and those on glucocorticoids.¹ Fifty percent of the calculated total daily dose should be given as a basal component, and the remaining 50% should be split into thirds and given preprandially as the bolus component.^{19,20}

References

1. Magaji V, Johnston JM. Inpatient management of hyperglycemia and diabetes. *Clin Diabetes*. 2011;29(1):3-9.
2. Levetan CS, Passaro M, Jablonski K, Kass M, Ratner RE. Unrecognized diabetes among hospitalized patients. *Diabetes Care*. 1998;21(2):246-249.
3. American Diabetes Association. Economic costs of diabetes in the US in 2007. *Diabetes Care*. 2008;31(3):596-615.
4. Centers for Disease Control and Prevention. Crude and age-adjusted percentage of civilian, noninstitutionalized population with diagnosed diabetes, United States, 1980-2011. Available at: <http://www.cdc.gov/diabetes/statistics/us/index.htm>. Accessed August 17, 2014.
5. Moghissi ES, Korytkowski MT, Dinardo M, et al. American Association of Clinical Endocrinologists and American Diabetes Association consensus statement on inpatient glycemic control. *Endocr Pract*. 2009;15(4):353-369.
6. Boucai L, Southern WN, Zonszein J. Hypoglycemia-associated mortality is not drug-associated but linked to comorbidities. *Am J Med*. 2011;124(11):1028-1035.
7. Garg R, Hurwitz S, Turchin A, Trivedi A. Hypoglycemia, with or without insulin therapy, is associated with increased mortality among hospitalized patients. *Diabetes Care*. 2013;36(5):1107-1110.
8. Turchin A, Matheny ME, Shubina M, et al. Hypoglycemia and clinical outcomes in patients with diabetes hospitalized in the general ward. *Diabetes Care*. 2009;32(7):1153-1157.
9. Cryer PE, Davis SN, Shamoon H. Hypoglycemia in diabetes. *Diabetes Care*. 2003;26(6):1902-1912.

10. Umpierrez GE, Hellman R, Korytkowski MT, et al. Management of hyperglycemia in hospitalized patients in non-critical care setting: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab.* 2012;97(1):16-38.
11. Furnary AP, Wu Y, Bookin SO. Effect of hyperglycemia and continuous intravenous insulin infusions on outcomes of cardiac surgical procedures: the Portland Diabetic Project. *Endocr Pract.* 2004;10(Suppl 2):21-33.
12. Krinsley JS, Jones RL. Cost analysis of intensive glycemic control in critically ill adult patients. *Chest.* 2006;129(3):644-650.
13. Clement S, Braithwaite SS, Magee MF, et al. Management of diabetes and hyperglycemia in hospitals. *Diabetes Care.* 2004;27(2):553-591.
14. Cook CB, Boyle ME, Cisar NS, et al. Use of continuous subcutaneous insulin infusion (insulin pump) therapy in the hospital setting: proposed guidelines and outcome measures. *Diabetes Educ.* 2005;31(6):849-857.
15. Bailon RM, Partlow BJ, Miller-Cage V, et al. Continuous subcutaneous insulin infusion (insulin pump) therapy can be safely used in the hospital in select patients. *Endocr Pract.* 2009;15(1):24-29.
16. Korytkowski MT, Salata RJ, Koebel GL, et al. Insulin therapy and glycemic control in hospitalized patients with diabetes during enteral nutrition therapy: a randomized controlled clinical trial. *Diabetes Care.* 2009;32(4):594-596.
17. Leahy JL. Insulin management of diabetic patients on general medical and surgical floors. *Endocr Pract.* 2006;12(Suppl 3):86-90.
18. Umpierrez GE, Smiley D, Zisman A, et al. Randomized study of basal-bolus insulin therapy in the inpatient management of patients with type 2 diabetes (RABBIT 2 trial). *Diabetes Care.* 2007;30(9):2181-2186.
19. Schnipper JL, Ndumele CD, Liang CL, Pendergrass ML. Effects of a subcutaneous insulin protocol, clinical education, and computerized order set on the quality of inpatient management of hyperglycemia: results of a clinical trial. *J Hosp Med.* 2009;4(1):16-27.
20. Maynard G, Lee J, Phillips G, et al. Improved inpatient use of basal insulin, reduced hypoglycemia, and improved glycemic control: effect of structured subcutaneous insulin orders and an insulin management algorithm. *J Hosp Med.* 2009;4(1):3-15.