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Inpatient Glycemic Control: Best Practice Advice From the Clinical Guidelines Committee of the American College of Physicians

Amir Qaseem, MD, PhD, MHA,[1] Roger Chou, MD,[2] Linda L. Humphrey, MD, MPH,[2] and Paul Shekelle, MD, PhD[3] for the Clinical Guidelines Committee of the American College of Physicians

Abstract

Hyperglycemia is associated with poor outcomes in hospitalized medical and surgical patients. Although some early evidence showed benefits of intensive insulin therapy (IIT), recent evidence does not show a consistent benefit and even shows harm associated with the use of IIT. The overuse of some therapeutic interventions and the resulting harms to a patient are an important component of unnecessary health care costs. The goal of this article is to address the management of hyperglycemia and evaluate the benefits and harms associated with the use of IIT to achieve tight glycemic control in hospitalized patients with or without diabetes mellitus. This article is based on the evidence review and the guideline developed by the American College of Physicians on this topic. Best Practice Advice 1: Clinicians should target a blood glucose level of 7.8 to 11.1 mmol/L (140 to 200 mg/dL) if insulin therapy is used in SICU/MICU patients. Best Practice Advice 2: Clinicians should avoid targets less than 7.8 mmol/L (<140mg/dL) because harms are likely to increase with lower blood glucose targets.

Keywords

high-value care, inpatient glycemic control, intensive insulin therapy, blood glucose level

Hyperglycemia is associated with poor outcomes in hospitalized medical and surgical patients.[1-6] Although some early evidence showed benefits of intensive insulin therapy (IIT), recent evidence does not show a consistent benefit and even shows harm associated with the use of IIT.[7-11] In addition, IIT consumes more resources and is a more expensive approach to managing hyperglycemia than standard therapy.[12] Thus, it is important to evaluate the health benefits of IIT in order to justify its harms and costs.[13] The American College of Physicians (ACP) developed this Best Practice Advice paper to discuss evidence on the management of hyperglycemia with the use of IIT in hospitalized patients. The goal of ACP's High-Value Care initiative is to promote the use of diagnostic tests and therapeutic interventions that provide high value while discouraging the use of low-value tests and interventions that are not beneficial or may be harmful. This article is based on the evidence review and ACP guideline on inpatient glycemic control.[14,15] The target audience for this article is all clinicians, and the target patient population is all adults with hyperglycemia in a hospital setting. In this study, *IIT* is defined as the use of intravenous insulin to achieve a targeted blood glucose level with frequent blood glucose testing and adjustment of insulin doses.[14,15] In intensive care unit (ICU) settings, the usual target of IIT is normoglycemia (blood glucose level = 4.4-6.1 mmol/L [80-110 mg/dL]), whereas targets in non-ICU settings have been more variable (ranging from normoglycemia to <11.1 mmol/L [<200 mg/dL]).

Benefits of IIT

The potential benefit of a well-controlled glucose level is a reduction in morbidity and mortality and improved health outcomes in hospitalized patients. However, evidence comparing IIT with normoglycemia or targeted strict blood glucose control in patients with or without diabetes mellitus has not shown decreased mortality

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among patients in the medical intensive care unit (MICU) or surgical intensive care unit (SICU), in patients with myocardial infarction, stroke, or acute brain injury, or in the perioperative setting.[14] Data on the effects of IIT targeted to normoglycemia on reduction in length of ICU stay are mixed. In addition, studies evaluating the incidence of infection with the use of IIT showed that there is some evidence of a marginally significant reduction in the risk of sepsis and a nonsignificant reduction in the incidence of infection.[14]

Harms of IIT

The major harm of IIT is an increased risk of hypoglycemia; all of the studies showed the excess risk, especially in critically ill patients.[16-19] Although the evidence is not clear regarding the consequences of hypoglycemia in hospitalized patients, some studies have shown that increased mortality is associated with IIT and hypoglycemia[20] or extended length of stay among patients experiencing 1 or more episodes of hypoglycemia.[21-24] Additional concerns about the impact of hypoglycemia include an increased risk for dementia,[25] transient ischemia, and catecholamine surges.[26-28] Although the target blood glucose levels in the trials evaluated in the evidence review ranged widely, avoiding targets less than 7.8 mmol/L (<140 mg/dL) should be a priority because harms are likely to increase at lower blood glucose targets.

Impact of IIT on Costs

Currently, there are no cost-effectiveness studies that have incorporated results from the recent trials to evaluate the impact of IIT in light of the new evidence.

There is some evidence evaluating the impact of IIT on resource utilization, and a multicenter ICU study showed that intensive glucose monitoring and dosing adjustments could cost up to 2 hours of nursing personnel time for a given patient per 24-hour period ($182 488 nurses' salaries and $58 500 for supplies per year).[29]

Current Practice

In the United States, many hospitals and health care systems developed protocols intended to implement IIT routinely in critically ill patients[30,31] based on evidence from one trial that showed mortality benefit.[10] However, there is no evidence supporting that the benefits of IIT outweigh its harms. Even in light of the new evidence, many systems continue to recommend moderate blood glucose control because of the association of high blood glucose with infection, poor wound healing, dehydration, and other complications. Clinicians caring for these patients must keep the harms of hypoglycemia in mind when managing hyperglycemia and should avoid aggressive glucose management.

ACP Best Practice Advice

Best Practice Advice 1: Clinicians should target a blood glucose level of 7.8 to 11.1 mmol/L (140-200 mg/dL) if insulin therapy is used in SICU/MICU patients.

Best Practice Advice 2: Clinicians should avoid targets less than 7.8 mmol/L (<140 mg/dL) because harms are likely to increase with lower blood glucose targets.

Our review of the evidence shows that IIT with a goal of achieving normoglycemia or near-normoglycemia in patients with or without diabetes does not provide any beneficial effects and may lead to harm. The results from various studies indicate that using IIT to achieve strict glucose control compared to standard therapy with less strict control did not reduce mortality or length of hospital stay but did substantially increase the risk for severe hypoglycemia. In addition, aside from the costs associated with the implementation of IIT in a hospital, there are also downstream costs that are incurred with the management of consequent harms. Hence, IIT should not be used to strictly control blood glucose or to normalize blood glucose in SICU and MICU patients with or without diabetes mellitus. However, it is important to keep in mind that poorly controlled hyperglycemia is associated with increased morbidity, mortality, and worsened health outcomes in patients in the ICU. Although the evidence is not sufficient to give a precise range for blood glucose levels, target values of 7.8 to 11.1 mmol/L (140-200 mg/dL) is a reasonable option for patients in the ICU because insulin therapy targeted at blood glucose levels of 7.8 to 11.1 mmol/L (140-200 mg/dL) is associated with similar mortality outcomes as IIT targeted at blood glucose levels of 4.4 to 6.1 mmol/L (80-110 mg/dL) and is associated with a lower risk for hypoglycemia.

Table 1 summarizes ACP's Best Practice Advice for managing inpatient hyperglycemia with evidence-based guidance for providing high-value care that is safe, effective, and cost-conscious.

Members of the Clinical Guidelines Committee

Individuals who served on the Clinical Guidelines Committee from initiation of the project until its approval: Paul Shekelle, MD, PhD, Chair; Roger Chou, MD; Paul Dallas, MD; Thomas D. Denberg, MD, PhD; Nick Fitterman, MD; Mary Ann Forciea, MD; Robert

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Table 1. The American College of Physicians Best Practice Advice: Inpatient Glycemic Control.

The American College of Physicians Best Practice Advice: Inpatient Glycemic Control	
Disease/condition	Inpatient hyperglycemia
Target audience	Internists, family physicians, physicians caring for hospitalized patients, other clinicians
Target patient population	Hospitalized adults with hyperglycemia
Interventions	Intensive insulin therapy (IIT)
Outcomes	Short-term mortality (28-day, hospital, intensive care unit)
Evidence on the use of IIT to treat inpatient hyperglycemia	• There is no difference in mortality for insulin therapy targeted at blood glucose levels of 7.8 to 11.1 mmol/L (140-200 mg/dL) compared to IIT targeted at blood glucose levels of 4.4 to 6.1 mmol/L (80-110 mg/dL). • The use of IIT is associated with an excess risk of hypoglycemia (relative risk = 6.00; confidence interval = 4.06-8.87)
Best practice advice	*Best Practice Advice 1*: Clinicians should target a blood glucose level of 7.8 to 11.1 mmol/L (140-200 mg/dL) if insulin therapy is used in SICU/MICU patients. *Best Practice Advice 2*: Clinicians should avoid targets less than 7.8 mmol/L (<140 mg/dL) because harms are likely to increase with lower blood glucose targets.

Abbreviations: SICU, surgical intensive care unit; MICU, medical intensive care unit.

H. Hopkins Jr, MD; Linda L. Humphrey, MD, MPH; Tanveer P. Mir, MD; Holger J. Schünemann, MD, PhD; Donna E. Sweet, MD; and David S. Weinberg, MD, MSc.

Authors' Note

The authors of this article are responsible for its contents, including any clinical or treatment recommendations.

Conflicts of Interest

The authors declared no conflicts of interest with respect to the research, authorship, and/or publication of this article. Any financial and nonfinancial conflicts of interest of the group members were declared, discussed, and resolved. A record of conflicts of interest is kept for each Clinical Guidelines Committee meeting and conference call and can be viewed at www.acponline.org/clinical_information/guidelines/guidelines/conflicts_cgc.htm.

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References

1. Bochicchio GV, Salzano L, Joshi M, Bochicchio K, Scalea TM. Admission preoperative glucose is predictive of morbidity and mortality in trauma patients who require immediate operative intervention. *Am Surg*. 2005;71:171-174.
2. Capes SE, Hunt D, Malmberg K, Gerstein HC. Stress hyperglycaemia and increased risk of death after myocardial infarction in patients with and without diabetes: a systematic overview. *Lancet*. 2000;355:773-778.
3. Capes SE, Hunt D, Malmberg K, Pathak P, Gerstein HC. Stress hyperglycemia and prognosis of stroke in nondiabetic and diabetic patients. *Stroke*. 2001;32:2426-2432.
4. Furnary AP, Gao G, Grunkemeier GL, et al. Continuous insulin infusion reduces mortality in patients with diabetes undergoing coronary artery bypass grafting. *J Thorac Cardiovasc Surg*. 2003;125:1007-1021.
5. Pomposelli JJ, Baxter JK 3rd, Babineau TJ, et al. Early postoperative glucose control predicts nosocomial infection rate in diabetic patients. *JPEN J Parenter Enteral Nutr*. 1998;22(2):77-81.
6. Umpierrez G, Isaacs S, Bazargan N, You X, Thaler L, Kitabchi A. Hyperglycemia: an independent marker of in-hospital mortality in patients with undiagnosed diabetes. *J Clin Endocrinol Metab*. 2002;87:978-982.
7. NICE-SUGAR Study Investigators, Finfer S, Chittock DR, Su SY, et al. Intensive versus conventional glucose control in critically ill patients. *N Engl J Med*. 2009;360:1283-1297.
8. Furnary AP, Cheek DB, Holmes SC, Howell WL, Kelly SP. Achieving tight glycemic control in the operating room: lessons learned from 12 years in the trenches of a paradigm

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shift in anesthetic care. *Semin Thorac Cardiovasc Surg*. 2006;18:339-345.
9. Malmberg K, Rydén L, Efendic S, et al. Randomized trial of insulin-glucose infusion followed by subcutaneous insulin treatment in diabetic patients with acute myocardial infarction (DIGAMI study): effects on mortality at 1 year. *J Am Coll Cardiol*. 1995;26:57-65.
10. Van den Berghe G, Wouters P, Weekers F, et al. Intensive insulin therapy in critically ill patients. *N Engl J Med*. 2001;345:1359-1367.
11. Zerr KJ, Furnary AP, Grunkemeier GL, Bookin S, Kanhere V, Starr A. Glucose control lowers the risk of wound infection in diabetics after open heart operations. *Ann Thorac Surg*. 1997;63:356-361.
12. Lifetime benefits and costs of intensive therapy as practiced in the diabetes control and complications trial. The Diabetes Control and Complications Trial Research Group. *JAMA*. 1996;276:1409-1415.
13. Owens D, Qaseem A, Chou R, Shekelle P. High-value, cost conscious care: concepts for clinicians to evaluate benefits, harms, and costs of medical interventions. *Ann Intern Med*. 2011;154:174-180.
14. Kansagara D, Fu R, Freeman M, Wolf F, Helfand M. Intensive insulin therapy in hospitalized patients: a systematic review. *Ann Intern Med*. 2011;154:268-282.
15. Qaseem A, Humphrey LL, Chou R, Snow V, Shekelle P. Use of intensive insulin therapy for the management of glycemic control in hospitalized patients: a clinical practice guideline from the American College of Physicians. *Ann Intern Med*. 2011;154:260-267.
16. Fischer KF, Lees JA, Newman JH. Hypoglycemia in hospitalized patients. *N Engl J Med*. 1986;315:1245-1250.
17. Krinsley J. Glycemic control in critically ill patients. *Chest*. 2007;132:1-2.
18. Shilo S, Berezovsky S, Friedlander Y, Sonnenblick M. Hypoglycemia in hospitalized nondiabetic older patients. *J Am Geriatr Soc*. 1998;46:978-982.
19. Vriesendorp TM, van Santen S, DeVries JH, et al. Predisposing factors for hypoglycemia in the intensive care unit. *Crit Care Med*. 2006;34:96-101.
20. Svensson AM, McGuire DK, Abrahamsson P, Dellborg M. Association between hyper- and hypoglycaemia and 2 year all-cause mortality risk in diabetic patients with acute coronary events. *Eur Heart J*. 2005;26:1255-1261.
21. Arabi YM, Dabbagh OC, Tamim HM, et al. Intensive versus conventional insulin therapy: a randomized controlled trial in medical and surgical critically ill patients. *Crit Care Med*. 2008;36:3190-3197.
22. Brunkhorst FM, Engel C, Bloos F, et al. Intensive insulin therapy and pentastarch resuscitation in severe sepsis. *N Engl J Med*. 2008;358:125-139.
23. Devos P, Preiser J, Melot C. Impact of tight glucose control by intensive insulin therapy on ICU mortality and the rate of hypoglycaemia: final results of the GLUCONTROL study. *Intensive Care Med*. 2007;33 (suppl 2):S189.
24. Krinsley JS. Association between hyperglycemia and increased hospital mortality in a heterogeneous population of critically ill patients. *Mayo Clin Proc*. 2003;78: 1471-1478.
25. Whitmer RA, Karter AJ, Yaffe K, Quesenberry CP, Selby JV. Hypoglycemic episodes and risk of dementia in older patients with type 2 diabetes mellitus. *JAMA*. 2009;301:1565-1572.
26. Desouza C, Salazar H, Cheong B, Murgo J, Fonseca V. Association of hypoglycemia and cardiac ischemia. *Diabetes Care*. 2003;26:1485-1489.
27. Lindström T, Jorfeldt L, Tegler L, Arnqvist HJ. Hypoglycaemia and cardiac arrhythmias in patients with type 2 diabetes mellitus. *Diabet Med*. 1992;9:536-541.
28. Spyer G, Hattersley AT, MacDonald IA, Amiel S, MacLeod KM. Hypoglycaemic counter-regulation at normal blood glucose concentrations in patients with well controlled type-2 diabetes. *Lancet*. 2000;356:1970-1974.
29. Aragon D. Evaluation of nursing work effort and perceptions about blood glucose testing in tight glycemic control. *Am J Crit Care*. 2006;15:370-377.
30. Institute for Health Care Improvement. Establish a glycemic control policy in your ICU. http://www.ihi.org/knowledge/Pages/Changes/EstablishaGlycemicControlPolicyinYourICU.aspx. Accessed May 2012.
31. Clement S, Braithwaite S, Magee M*, et al*. Management of diabetes and hyperglycemia in hospitals. *Diabetes Care*. 2004;27:553-591.

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