Glucose Control in Hospitalized Patients

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Evidence indicates that hospitalized patients with hyperglycemia do not benefit from tight blood glucose control. Maintaining a blood glucose level of less than 180 mg per dL (9.99 mmol per L) will minimize symptoms of hyperglycemia and hypoglycemia without adversely affecting patient-oriented health outcomes. In the absence of modifying factors, physicians should continue patients' at-home diabetes mellitus medications and randomly check glucose levels once daily. Sulfonylureas should be withheld to avoid hypoglycemia in patients with limited caloric intake. Patients with cardiovascular conditions may benefit from temporarily stopping treatment with thiazolidinediones to avoid precipitating heart failure. Metformin should be temporarily withheld in patients who have worsening renal function or who will undergo an imaging study that uses contrast. When patients need to be treated with insulin in the short term, using a long-acting basal insulin combined with a short-acting insulin before meals (with the goal of keeping blood glucose less than 180 mg per dL) better approximates normal physiology and uses fewer nursing resources than sliding-scale insulin approaches. Most studies have found that infusion with glucose, insulin, and potassium does not improve mortality in patients with acute myocardial infarction. Patients admitted with acute myocardial infarction should have moderate control of blood glucose using home regimens or basal insulin with correctional doses. (*Am Fam Physician*. 2010;81(9):1121-1124. Copyright © 2010 American Academy of Family Physicians.)

▶ **See related article on page 1130, and editorial on page 1078.**

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Hyperglycemia commonly complicates the treatment of adult patients hospitalized for other reasons. Stress, medications, and changes in diet during hospitalization can elevate or lower blood glucose levels. Physicians often do not know whether high glucose levels are from acute changes or if the levels were present before admission.

Diabetic ketoacidosis or hyperosmolar states caused by critical increases in blood glucose levels have well-established management protocols. This article reviews the rationale and evidence for blood glucose control in hospitalized patients with noncritical hyperglycemia and recommends methods for achieving blood glucose goals.

Effects of Tight Glucose Control in Hospitalized Patients

The concern with hyperglycemia in hospitalized patients is the effect of elevated blood glucose on the immune system and the body's susceptibility to pathogens. Elevated blood glucose levels impair neutrophil adhesion and phagocytosis and may alter the virulence of some pathogens, resulting in increased risk of infection, including sepsis.[1] There is no research assessing the value of tightly controlling blood glucose in hospitalized patients who are not in intensive care units. Hypoglycemic episodes occur in approximately 7.7 percent of patients admitted with diabetes mellitus to a general hospital ward; each episode is associated with an increased risk of inpatient mortality, as well as an increase in the risk of death in the following year.[2]

In severely ill patients, preliminary research points to a benefit of controlling hyperglycemia.[3,4] Studies that evaluated epidemiologic data or that were controlled studies of patients in surgical intensive care or of patients with acute myocardial infarction (MI) found that intensive control aimed at maintaining glucose concentrations between 80 to 110 mg per dL (4.44 to 6.11 mmol per L) decreased mortality, morbidity, and length of hospitalization.[5,6]

However, confirmatory studies have found no benefit and have provided evidence of harm from tight glucose control in critically ill adult patients.[7,8] A meta-analysis of 29 studies that enrolled a total of 8,432 patients found that intensive control decreased the risk of septicemia, but was not associated with a decrease in hospital mortality and was associated with an increased risk of severe hypoglycemia (i.e., blood glucose level less than 40 mg per dL [2.22 mmol per L]).[7] A recent study of more than 6,000 patients

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	*Evidence rating*	*References*	*Comments*
For patients who are in the surgical ICU, insulin drip and tight glucose control decreases the risk of septicemia, but increases hypoglycemic episodes and has no mortality benefit.	A	7	Meta-analysis of RCTs
Intensive blood glucose protocols (goal of 81 to 108 mg per dL [4.50 to 5.99 mmol per L]) for patients in the ICU increase mortality compared with less intensive treatment (i.e., goal of 180 mg per dL [9.99 mmol per L] or less).	B	8	Large RCT that showed increased mortality with strict glucose control, and no difference in length of hospitalization or need for mechanical ventilation or dialysis
In hospitalized patients, home diabetes mellitus treatment regimens should be continued in the absence of specific contraindications.	B	9	—
Metformin (Glucophage) should be discontinued in patients with diabetes who have a serum creatinine level greater than 1.5 mg per dL (132.60 µmol per L) for men, and greater than 1.4 mg per dL (123.76 µmol per L) for women.	C	13, 14	Consensus statement from working group on contrast-induced nephropathy
Sliding-scale insulin regimens have no benefit over continuation of home diabetes treatment regimens.	B	19	Comparative study evaluating the benefit of sliding-scale insulin versus home regimens found no difference in glucose control

ICU = intensive care unit; RCT = randomized controlled trial.

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to http://www.aafp.org/afpsort.xml.

also demonstrated that tight glucose control (81 to 108 mg per dL [4.50 to 5.99 mmol per L] in the treatment group versus 180 mg per dL [9.99 mmol per L] or less in control group) increased mortality (odds ratio = 1.14; 95% confidence interval, 1.02 to 1.28; $P = .02$; number needed to harm = 39), with 7 percent of patients experiencing severe hypoglycemia.[8] In this study, there were no differences in median number of days in intensive care or the hospital, or need for mechanical ventilation or dialysis.[8]

Approach to Hospitalized Patients with Hyperglycemia

A reasonable goal for most patients is to maintain a random blood glucose level of less than 180 mg per dL, but only for patients in whom it is safe to do so.[8-10] Instead of frequent blood glucose measurements throughout the day and night, which is bothersome to patients and results in many telephone calls from nursing staff reporting measurements outside of the normal range, a single, random daily determination is often all that is necessary. This level of control is thought to minimize the risk of hypoglycemia, the likelihood of symptoms in patients, and the adverse effect on immune function. Specific patient factors may require more frequent monitoring, such as poor outpatient control of blood glucose, changes in diet, and reactions to stress or medications.

When possible, the patient's previous medications should be continued while in the hospital, except when the patient's situation requires other approaches to treatment.[9] Patients who have no oral intake of medications will need to be treated with subcutaneous or intravenous insulin. Patients with limited caloric intake are at risk of hypoglycemia if they are taking sulfonylureas, and these medications should be withheld until the patient is eating again. Thiazolidinediones should be avoided in patients with new or worsening cardiovascular conditions, given these agents' potential to precipitate or worsen heart failure.[11]

Metformin (Glucophage) does not cause hypoglycemia and may be continued in many hospitalized patients. It has a theoretical risk of inducing lactic acidosis, although the actual risk of this often fatal adverse effect is probably small, considering that a Cochrane review found no cases of fatal or nonfatal lactic acidosis in 59,321 patient-years of metformin use.[12] Because the risk of lactic acidosis increases with declining renal function, product labeling recommends discontinuation of metformin in men with creatinine

levels greater than 1.5 mg per dL (132.60 µmol per L) and in women with levels greater than 1.4 mg per dL (123.76 µmol per L).[13]

Contrast-induced nephropathy can decrease renal function and, theoretically, cause lactic acidosis if a patient is receiving metformin. Current guidelines recommend stopping metformin use before imaging procedures that use contrast, and restarting use 48 hours after the procedure if renal function is unchanged.[13,14] Although the necessity of this prohibition has been questioned,[15] most radiologists will require withholding metformin in all patients for two days before they will perform the imaging study.

Using Insulin in Hospitalized Patients

If it is not possible to continue oral hypoglycemic therapy, insulin may be needed temporarily to maintain blood glucose levels less than 180 mg per dL. Common approaches to insulin dosing in the hospital are the sliding-scale insulin approach and the use of basal insulin dosing with prandial and correctional doses.

SLIDING-SCALE INSULIN

Protocols for reacting to fluctuations in blood glucose have been used for years, and these sliding-scale insulin regimens require measuring blood glucose levels several times per day and administering enough insulin to cover above-normal values. However, the sliding-scale approach makes no physiologic sense and has been compared with giving sliding-scale antibiotics to treat fever.[16] Reacting to high glucose levels has the potential to lower glucose levels too much, creating a physiologic response that sends the glucose level higher than before, leading to higher doses of insulin that only magnify the fluctuations. Reports found that increased length of hospitalization was associated with the use of sliding-scale insulin protocols, prompting concern that it was harmful rather than helpful.[17,18]

One randomized trial evaluated the relative benefit of a sliding-scale approach compared with using patients' prehospitalization dose.[19] Sliding-scale insulin did not produce any greater degree of control than the home dose, with about one third of patients remaining hyperglycemic during their hospitalization, regardless of the method of blood glucose control.[19] The duration of hospitalization was not different with sliding-scale insulin.

BASAL INSULIN WITH PRANDIAL AND CORRECTIONAL DOSES

A more physiologic approach to addressing inpatient hyperglycemia is a weight-based dosing (0.4 to 0.5 units per kg per day) of long-acting basal insulin (glargine [Lantus] or isophane insulin [NPH]), combined with short-acting insulin before meals. Used in insulin-naive patients, this approach will provide lower blood glucose levels than sliding-scale insulin (an average difference of 27 mg per dL [1.50 mmol per L] lower with no increase in hypoglycemic episodes), although it has not been demonstrated to decrease length of stay or affect any patient-oriented outcomes.[20] In addition to making more physiologic sense than a sliding-scale protocol, a basal-insulin–based protocol decreases work for nursing and physician staff, and it decreases the number of finger sticks requested of patients.

A basal-insulin–based protocol for patients in intensive care decreases work for hospital staff.

Insulin to Treat Patients with Acute MI

A combination infusion of glucose, insulin, and potassium (the GIK regimen) was initially used in the 1960s in an attempt to decrease morbidity and mortality in patients with acute MI. The rationale behind the combination was that exogenous insulin would limit myocardial uptake of toxic free fatty acids; glucose would provide energy for the heart; and potassium would replete the losses that occur with ischemia and reduce the likelihood of arrhythmias.

Nine studies have assessed the benefit of the GIK regimen, but only one of these studies demonstrated a decrease in mortality.[21] The other studies, many of them much larger, found no difference in short- or long-term mortality with treatment.[22] Although hyperglycemia is associated with a worse prognosis in patients with acute MI,[23] hypoglycemia

during hospitalization is also associated with increased mortality in patients who have diabetes with non-ST-elevation MI.[24] Therefore, patients admitted with acute MI should have moderate control of blood glucose using home regimens or basal insulin with correctional doses.[9]

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