

CLINICAL DECISIONS
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Management of Hyperglycemia in Hospitalized, Non–Critically Ill Adults

This interactive feature addresses the approach to a clinical issue. A case vignette is followed by specific options, neither of which can be considered either correct or incorrect. In short essays, experts in the field then argue for each of the options as assigned. Readers can participate in forming community opinion by choosing one of the options and, if they like, providing their reasons.

CASE VIGNETTE

A Hospitalized Woman with Type 2 Diabetes

Leslie L. Chang, M.D.

A 72-year-old woman with a body-mass index (the weight in kilograms divided by the square of the height in meters) of 35 and a 5-year history of type 2 non–insulin-dependent diabetes mellitus without complications presents to the emergency department with fevers, cough, and decreased oral intake. On arrival, she has a temperature of 38.1°C; her oxygen saturation is 88% while she is breathing ambient air, and she is given supplemental oxygen. Her condition is otherwise hemodynamically stable. Laboratory tests are performed and show a neutrophil-predominant leukocytosis. Blood lactate and liver enzyme levels are within normal limits. A chest radiograph reveals an opacity in the left lower lobe, and intravenous antibiotics are initiated for treatment of community-acquired pneumonia. She is admitted to your general medicine service for further care.

On admission, you confirm her home medications, which include metformin, 500 mg twice a day. Her last glycated hemoglobin measurement in clinic 2 months ago was 7.7%. You re-

view her laboratory results and note a fasting glucose level of 175 mg per deciliter (9.7 mmol per liter) and a creatinine level of 0.9 mg per deciliter (80 μ mol per liter), which was similar to the level 2 months previously. She appears tired but is alert and oriented and is breathing comfortably. You notice that she has finished only about a quarter of the food on her lunch tray.

You must make a decision regarding management of her type 2 diabetes while she is an inpatient. Would you recommend that she continue to receive metformin, as she had been at home, or that the metformin be stopped and insulin therapy initiated?

TREATMENT OPTIONS

Which one of the following approaches would you take for this patient? Base your choice on the published literature, your own experience, published guidelines, and other information sources.

1. Recommend continuing metformin.
2. Recommend stopping metformin and initiating insulin.

To aid in your decision making, each of these approaches is defended in a short essay by an expert in the field. Given your knowledge of the patient and the points made by the experts, which approach would you choose?

OPTION 1

Recommend Continuing Metformin

Guillermo E. Umpierrez, M.D.

Dysglycemia has become so common that metformin and other oral glucose-lowering agents

are used in up to 30% of patients admitted to medical and surgical services of a hospital.¹ Metformin has important glycemic and nonglycemic benefits and does not cause hypoglycemia — factors that have led to its frequent use. When patients with type 2 diabetes and mild-to-moderate hyperglycemia who are receiving metformin

and are in clinically stable condition are admitted to the hospital, routinely stopping metformin is unnecessary and may, in fact, lead to worsened glycemic control and increased use of insulin, both of which may result in adverse patient outcomes.

Several observational studies have shown that the use of oral glucose-lowering medications in hospitalized patients may be associated with outcomes better than those with insulin therapy. A matched cohort study comparing the use of oral hypoglycemic agents (metformin, thiazolidines, or sulfonylureas) with insulin therapy in patients undergoing emergency abdominal surgery showed that patients treated with insulin had worse outcomes, including more postoperative complications, longer hospital stays, and higher 30-day mortality, than those treated with oral agents.² Reitz et al.³ reported that among 10,088 patients with diabetes who underwent a major surgical intervention, preoperative metformin use was associated with lower 30-day and 90-day mortality and fewer hospital readmissions than those in patients who received non-metformin therapy.

The in-hospital use of metformin has not been recommended by clinical guidelines owing to concerns that it poses a risk of lactic acidosis. However, several studies and systematic reviews have shown that metformin-associated lactic acidosis is rare in the absence of advanced kidney failure. A Cochrane review identified no cases of fatal or nonfatal lactic acidosis in 59,321 patient-years of metformin use.⁴ Although the use of iodinated contrast material has been cited as a contraindication to metformin therapy, published evidence indicates that metformin does not put patients with normal kidney function at increased risk for acute kidney injury, increased lactate levels, or lactic acidosis. However, in patients with an estimated glomerular filtration rate of less than 30 ml per minute per 1.73 m² of body-surface area, severe heart failure, liver disease, or shock, the risk of lactic acidosis is higher, and metformin should be discontinued.

The case presented in the vignette involves a 72-year-old woman with diabetes that is well controlled with metformin monotherapy who presents with community-acquired pneumonia and mild hyperglycemia. The patient's condition is clinically stable, and she has normal kidney function without evidence of microvascular or

macrovascular complications of diabetes. In this patient, stopping metformin and starting insulin therapy may be overtreatment and may increase the risk of iatrogenic hypoglycemia.⁵

An individualized approach that is based on diabetes treatment before admission and on the severity of hyperglycemia is the best way to achieve glycemic control while avoiding the risk of iatrogenic hypoglycemia.^{1,5} In the absence of contraindications, continuing metformin therapy with correction doses of rapid-acting insulin before meals is likely to control glucose levels in most patients with mild-to-moderate hyperglycemia.⁵ The practice of stopping oral agents and starting treatment with sliding-scale insulin is not indicated, since that regimen is associated with an increased risk of hyperglycemia and with increased length of stay in the hospital.

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OPTION 2

Recommend Stopping Metformin and Initiating Insulin

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Guidelines from multiple professional organizations have consistently advised that outpatient non-insulin antihyperglycemic medications be discontinued when patients with type 2 diabetes are hospitalized. Instead, guidelines advise using insulin for blood-glucose control.⁶⁻⁸ Such recommendations stem from the lack of efficacy and safety data in the inpatient setting for the use of non-insulin therapies, since studies of these agents have been performed primarily in the outpatient arena. When they are at home, patients consume their usual home diets, whereas in hospital settings, nutritional intake is commonly impaired, which confers a predisposition to hypoglycemia. Although this concern is most relevant for older generations of oral agents such as sulfonylureas, most other agents will also require some consideration about continuation when a patient has an acute illness requiring hospitalization. For example, even the two newest drug categories, the glucagon-like peptide 1 (GLP-1) receptor agonists and the sodium-glucose

cotransporter 2 (SGLT2) inhibitors, which have notable long-term benefits for cardiorenal outcomes, present potential problems. GLP-1 receptor agonists decrease appetite, which may not be desirable during recovery from illness. SGLT2 inhibitors induce a catabolic state, which could confer a predisposition to euglycemic diabetic ketoacidosis, and also may theoretically increase the risk of urinary tract infection, particularly under conditions of bladder catheterization. Thus, insulin still remains the “go to” tool for glycemic control in the inpatient setting.

The question here is whether this specific patient’s metformin regimen, which had been maintaining reasonable glycemic control before admission, should be continued during her hospitalization. In general, if nutritional intake is normal, the hemodynamic condition is stable, kidney function is adequate, there is no acidosis, and there is a low likelihood that any imaging with radiographic contrast material will be performed, metformin could be continued. However, an initially stable condition can easily, quickly, and unpredictably become unstable, and progressive hypoxia, sepsis with acidosis, and impaired renal function can develop. Furthermore, these issues may necessitate imaging studies that involve the use of contrast material. In each of these circumstances, metformin therapy is contraindicated or suboptimal, since the drug may accumulate — thereby increasing the risk of lactic acidosis — when the glomerular filtration rate is reduced below 30 ml per minute per 1.73 m².⁹ In addition, many patients with type 2 diabetes often have improved glycemic control once they are hospitalized, owing to decreased oral intake, and thereby require little to no therapy, whereas others may have clinically significant hyperglycemia from stress and require more aggressive treatment efforts.

Accordingly, it is advisable to stop metformin and use insulin instead to manage hyperglycemia for inpatients. Insulin remains the most flexible form of glucose-lowering therapy; it can be used in both basal and prandial components and can be adjusted frequently to meet the patient’s metabolic needs. Initially, correction insulin (i.e., insulin administered on a sliding scale) can be given before meals in the form of a variable dose of a rapid-acting insulin analogue with the goal of transitioning to a basal–bolus regimen

(i.e., basal insulin once daily or once nightly plus prandial [or nutritional] insulin three times daily before meals) after 24 to 48 hours. Doses would then be adjusted to maintain blood-glucose goals of 100 to 180 mg per deciliter (5.6 to 10.0 mmol per liter), with preprandial levels ideally less than 140 mg per deciliter (7.8 mmol per liter).

It is important to note that on discharge, unless this patient has become unusually and persistently hyperglycemic in the hospital, the metformin should be resumed. Further adjustments of her metformin dose and addition of other agents for blood-glucose control can be made in the outpatient setting.¹⁰

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