Inpatient Diabetes Management

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Editor's note: *This article is the 11th in a 12-part series reviewing the fundamentals of diabetes care for physicians in training. Previous articles in the series can be viewed at the* Clinical Diabetes *website (http://clinical.diabetesjournals.org).*

The epidemic of diabetes continues to flourish in the United States and throughout the world. Nowhere is the diabetes epidemic as apparent as in the inpatient hospital setting. Diabetes mellitus increases the risk of disorders such as coronary artery disease, cerebrovascular occlusion, peripheral artery disease, renal insufficiency, peripheral neuropathy, lower-extremity infection, ulceration, and amputation, and other disorders. Such complications frequently require admission into the hospital for evaluation and treatment.

It is not surprising, therefore, that patients with diabetes compose a disproportionately high number of hospital inpatients. Approximately 12–25% of hospitalized patients have diabetes, and the diagnosis of diabetes at hospital admission has increased 2.3-fold to 5.1 million from 1980 to 2003. An increasing number of studies have associated hyperglycemia with adverse outcomes during hospitalization, but outcomes of interventional studies that attempt to decrease such complications by aggressively treating hyperglycemia are mixed.[1,2]

Observational Studies

It has long been observed that patients with diabetes or who develop hyperglycemia in response to the stress of illness may have poor hospital outcomes and higher rates of complications when hospitalized. This trend has shown itself in patients with mild degrees of illness and small surgical procedures, as well as critically ill patients and those undergoing major surgery. Recently, several studies have attempted to quantify the increased risk of patients with diabetes in the hospital setting and determine whether aggressive intervention improves such risks.

One of the first studies that attempted to actually quantify the extent of increased risk to noncritically ill patients was conducted by Umpierrez et al.[3] They analyzed the hospital records of more than 2,000 patients who were admitted in general hospital wards in a community hospital. The study included both medical and surgical patients. Of the patients studied, 26% had known diabetes, and 12% were newly diagnosed as hyperglycemic based on a fasting glucose level ≥ 126 mg/dl or random glucose measurements ≥ 200 mg/dl on two occasions. Impressively, 38% of all patients admitted into general hospital wards in this study were diabetic or hyperglycemic, illustrating how important inpatient glucose management has become.

In this study, patients with a preexisting diagnosis of diabetes experienced a 2.7-fold increase in risk of in-hospital mortality compared to patients with normoglycemia. Perhaps even more strikingly, patients with newly diagnosed hyperglycemia had an 18-fold increase in risk of mortality. Patients with newly diagnosed hyperglycemia were also found to have a longer length of hospital stay and a higher risk of admission into the intensive care unit (ICU) and were less likely to be discharged to home, often requiring nursing or rehabilitation facility placement.[2,3]

The relationship between high glucose levels and poor outcomes is also true for patients with more severe illnesses such as ischemic injuries. Patients experiencing myocardial infarction (MI) with hyperglycemia have higher risk of death than patients without hyperglycemia. Furthermore, such patients with hyperglycemia also experience higher likelihood of congestive heart failure or cardiogenic shock compared to patients who are normoglycemic.[4] Stroke patients who are hyperglycemic also experience a higher risk of death or poor functional recovery compared to patients who do not experience hyperglycemia. One possible explanation is that hyperglycemia may increase the oxygen demands of ischemic tissue in both circumstances, thus exacerbating injury.[4,5] This information is especially salient because patients with diabetes have higher rates of stroke and MI.

In patients with diabetes who are hospitalized, there appears to be increased risk associated with higher glucose levels. Patients undergoing surgery who experience hyperglycemia with glucose > 220 mg/dl exhibit an infection rate 2.7 times higher than patients with diabetes who do not experience glucose > 220 mg/dl. Furthermore, when minor urinary tract infections are excluded, the relative risk of infection is increased to 5.7 if glucose exceeds 220 mg/dl on the first postoperative day.[6]

Trauma patients experience similar risks associated with stress hyperglycemia after hospitalization. A recent study identified a higher risk of infection and mortality rates in trauma patients who experience glucose levels > 200 mg/dl in the first 2 days after hospitalization. This association remained significant independent of injury characteristics but not for lesser degrees of hyperglycemia.[7]

Surgical patients with high glucose levels, therefore, are at elevated risk for adverse outcomes even if their glucose level is elevated in the absence of history of known diabetes. This information helps to identify patients who are at elevated risk to develop complications while hospitalized, but perhaps a more important question may be whether normalizing glucose levels reduces such risk.

Interventional Studies

Several studies have attempted to reduce the morbidity and mortality of hyperglycemia through improved glucose control. The Diabetes and Insulin Glucose Infusion in Acute Myocardial Infarction study investigated whether intensive insulin therapy for patients with acute MI and high glucose levels would benefit from insulin and dextrose infusion acutely followed by intensive subcutaneous insulin therapy for the 3 months after infarction. Mean blood glucose in the "conventional" group was 210.6 mg/dl and in the treatment arm was 172.8 mg/dl. The study showed that with an average of 3.5 years of follow-up, there was an absolute reduction in mortality of 11%, likely representing one life saved per nine patients treated.[8]

Not all studies, however, have come to the same conclusion. A similar study, the Hyperglycemia: Intensive Insulin Infusion in Infarction Study (HI-5), demonstrated lower incidence of cardiac failure and reinfarction within 3 months with tight glycemic control, but no overall change in mortality was noted.[1,9] Additionally, patients undergoing cardiac surgery who attain good glucose control may have reduced mortality and a lower risk of deep sternal wound infections.[1] These studies suggest that improved glucose control improves risk of morbidity, but mortality benefit may be arguable.

Similar studies have been conducted in surgical intensive care settings. van den Berghe et al.[10] randomized patients with hyperglycemia (with or without previous diagnsosis of diabetes) to receive either intensive insulin therapy intravenously with a target glucose of 80–110 mg/dl or conventional therapy with a target glucose of 180–200 mg/dl. Intensive insulin therapy was associated with a significant reduction in mortality, especially in patients with multiple organ failure with a septic focus. There was reduction in overall in-hospital mortality of 34%, with lower incidence of bloodstream infection, acute renal failure requiring dialysis, and number of red blood cell transfusions.

Another study in the medical intensive care setting did not show difference in mortality but did significantly decrease morbidity by decreasing the risk of newly acquired kidney injury, accelerating weaning from mechanical ventilators, and achieving faster ICU and hospital discharge.[10] It should be noted, however, that other studies have also failed to show survival benefit and have shown higher risk of severe hypoglycemia with intensive insulin therapy. Furthermore, a recent meta-analysis concluded there was no benefit in mortality from intensive glucose control.[1]

Controlling Hyperglycemia

There are many treatment options to control glucose levels in the outpatient setting. Unfortunately, few of these medications translate well into inpatient or acute illness therapy. Some agents are ineffective in acute illness, require long periods of time to be practical in the hospital environment, or may even be detrimental when patients are seriously ill.

Sulfonylureas are very commonly used as an outpatient therapy for type 2 diabetes, typically as a first- or second-line oral agent. In the inpatient setting, they pose significant risk of hypoglycemia because they usually stimulate insulin release from pancreatic β-cells. Patients using these agents may develop hypoglycemia in the fasting state, which is common in the hospital setting because of illness or diagnostic testing. The long half-life of these agents causes them to be relatively nonamenable to acute titration, initiation of therapy, or stopping therapy while patients are hospitalized. Additionally, there is lack of adequate study of such medications showing efficacy in the hospital setting. Metaglinide medications such as nateglinide or repaglinide, although possessing a shorter half-life, could also predispose to hypoglycemia and also lack safety and efficacy data. When initiated, they may also induce nausea. These insulin secretagogues, therefore, do not lend themselves well to hospital use.[1,11]

Exenatide and sitagliptin both act through increasing the effects of glucagon-like peptide 1. They possess a lower risk of causing hypoglycemia than sulfonylureas, but they have a very delayed onset and are not particularly potent agents. Their major action is to control postprandial glucose levels, and therefore they are not attractive agents for the inpatient setting, where many patients are fasting or eating unreliably. They also lack clinical trial data in the inpatient setting.

Thiazolidinediones do not act acutely and in fact may require several months to exert full effect. Additionally, they increase intravascular volume, which may exacerbate congestive heart failure or other conditions of hemodynamic instability. These agents do not appear useful in the inpatient setting.[1,11]

Metformin, although typically a first-line agent in the treatment of type 2 diabetes, has several drawbacks in the inpatient setting. It possesses a very slow onset of action, although the risk of hypoglycemia is relatively low. The major risk regarding metformin is that of lactic acidosis, a rare but potentially fatal complication of metformin therapy. Risk factors for developing lactic acidosis include using metformin in the setting of congestive heart failure, hypoxic states, renal insufficiency, and other causes of hypoperfusion. Because most hospitalized patients are at significant risk to develop such conditions, it is advisable to avoid metformin use in inpatients.

Insulin, therefore, is the treatment of choice for most hospitalized patients with diabetes.[1,11] Insulin should be used to control glucose level in most hospitalized patients who are not critically ill. Ideally, subcutaneously administered insulin should be given in scheduled doses, with a correction dose algorithm that allows for and quantifies increases in insulin doses. Patients should receive both scheduled intermediate- or long-acting insulin to cover basal requirements and short- or rapid-acting insulin to cover carbohydrate consumption and other sources of carbohydrate, such as intravenous dextrose, dextrose derived from dialysate, and tube enteral feeding. This may be accomplished through the use of various insulin preparations, but it is important to note that several intermediate-acting insulin preparations, such as NPH or premixed insulin containing NPH, may exceed basal insulin requirements for several hours and therefore cause hypoglycemia in patients who are not eating.

Correction insulin should not be administered in isolation to control glucose levels. Use of correction insulin alone in essence waits for patients to become hyperglycemic before they are treated. It also may predispose them to hypoglycemia.[1,11,12]

In acute illnesses, including diabetic ketoacidosis (DKA) and hyperglycemic hyperosmolar states, intravenous regular insulin is frequently used to control hyperglycemia. It offers the advantage of very rapid effect and rapid dissipation of effect if stopped. Many hospital settings now have algorithms to allow nursing staff to adjust insulin infusion rates, although no particular infusion protocol has been proven superior to others. Intravenous insulin may also be used as a way to identify insulin requirements in patients with either type 1 or type 2 diabetes.[1]

As in the treatment of DKA, patients receiving intravenous insulin infusion should resume rapid-acting insulin at meals and intermediate- or long-acting insulin when they are recovering and are able to eat substantial carbohydrate. It is important to continue intravenous insulin several hours after resumption of subcutaneous insulin to avoid recurrent hyperglycemia and possible ketoacidosis, especially in patients with type 1 diabetes.

Controlling Hypoglycemia

Physicians should also be cautious regarding the potential for patients to develop hypoglycemia in the inpatient setting. As described in a previous installment of this series,[13] hypoglycemia is the limiting factor in controlling hyperglycemia. Hypoglycemia may occur with virtually any form of diabetes pharmacotherapy, so clinicians should be aware of its potential and how to treat it appropriately in both outpatient and inpatient settings.

It is important to remember that patients who develop renal, adrenal, hepatic, or cardiac dysfunction and those with limited nutritional intake, sepsis, or malignancies are at particularly increased risk for hypoglycemia. They sometimes exhibit considerable insulin sensitivity and therefore require smaller insulin doses compared to their outpatient regimen or to other patients with diabetes. Additionally, they may also have declining insulin requirements and therefore need frequent insulin adjustments to avoid hypoglycemia.

There should also be a treatment plan for hypoglycemia present in patients' orders.[1] Treatment may take the form or oral carbohydrate, intravenously administered 50% glucose solution, or glucagon.

General Recommendations

Based on the information discussed above and other studies and on clinical experience, the American Diabetes Association offers several guidelines regarding the management of diabetes and hyperglycemia during patients' hospitalization.

Patients admitted into the hospital with diabetes should have

diabetes clearly labeled in their medical record. Glucose monitoring should be ordered for all patients with diabetes, typically before meals and at bedtime in patients who are eating and every 4–6 hours in patients who are not eating. All patients receiving therapy for diabetes should have a plan for treatment of hypoglycemia. Critically ill surgical patients with diabetes should have their glucose level kept as close to 110 mg/dl as possible, and intravenous insulin by established safe protocol is generally the best method for achieving this goal.

As described previously, the evidence suggesting similar goals in critically ill medical patients is less clear. Because some studies have shown benefit in aggressive glucose control, intravenous insulin to maintain glucose levels at < 140 mg/dl is recommended.[1]

Because the above studies show an association of better outcomes in hospitalized patients with fasting glucose levels < 126 mg/dl and random glucose levels < 180–200 mg/dl, these goals are reasonable. Because of the risks of hypoglycemia, there may be situations in which insulin treatment may need to be less aggressive, especially during initial treatment. Scheduled prandial insulin doses should be administered at the appropriate times in relation to meals to avoid glucose fluctuations. Patients should also receive correction insulin doses when needed, but should not be placed on a correction insulin algorithm alone. Patients with hyperglycemia in the hospital who do not have a previous diagnosis of diabetes should have follow-up testing performed after discharge.[1]

Because diabetes is becoming increasingly common in the United States and throughout the world, more and more patients are placed at risk of developing acute and severe illnesses such as MI, congestive heart failure, stroke, and other diseases. These acute illnesses frequently require acute hospitalization, both during their initial onset and also as a result of exacerbations or their sequelae. It is very important, therefore, for physicians working in the world of inpatient medicine to be very adept at treating diabetes. Familiarity with such treatment will likely help improve patient outcomes and minimize complications such as hypoglycemia.

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