Diabetes Mellitus and Hyperglycemia Management in the Hospitalized Patient

Patricia A. Mackey, FNP-BC, BC-ADM, and Michael D. Whitaker, MD, FRCPC

ABSTRACT

Diabetes mellitus and hyperglycemia are common in hospitalized patients. Uncontrolled hyperglycemia during hospitalization is associated with poor outcomes. A glucose goal of 140-180 mg/dL is recommended. Scheduled subcutaneous insulin with basal, prandial, and correction components is preferred for treating diabetes in non–critically ill patients. The pharmacodynamics of insulins differ, and the type of insulin used should match daily glucose excursions. Varying hospital settings may warrant using a particular insulin type to achieve optimal glucose control. Herein we describe approaches to address hyperglycemia in the hospitalized patient on the basis of insulin pharmacodynamic profiles.

Keywords: basal-bolus insulin, correction insulin, diabetes mellitus, hospitalized patient, hyperglycemia

Optimal glucose control is a challenge for hospitalized patients. Proper treatment of hyperglycemia while avoiding hypoglycemia should be the goal of multidisciplinary teams (endocrinologists, hospitalists, nurses, surgeons, advanced-level practitioners, pharmacists, and intensivists) working together to provide care for the patient with diabetes mellitus or hyperglycemia in the hospital setting. Hyperglycemia in hospitalized patients can represent previously known diabetes, undiagnosed diabetes, or illness-related hyperglycemia. Hemoglobin A_{1c} values $\geq$ 6.5% suggest that diabetes preceded the hospitalization.[1] Numerous studies have indicated that targeted glucose control in the hospital has been shown to improve clinical outcomes; the association between hyperglycemia in hospitalized patients (with or without diabetes) and the increased risk for morbidity and mortality have been well established.[2]

Challenges encountered in the hospital setting can make controlling glucose difficult. These challenges include a new diagnosis of diabetes; infection; a more rigid diet; inactivity; decreased appetite; variable renal and hepatic status; an unpredictable schedule of testing, procedures, and surgical interventions; the use of hyperglycemic-provoking agents (glucocorticoids, octreotide, catecholamines, and calcineurin inhibitors); the administration of contrast agents with certain tests; enteral and total parenteral nutrition (TPN); and the stress induced by the hospitalization itself.

GLYCEMIC GOALS

Although several organizations have issued guidelines for outpatient glucose management, no guidelines or protocols have been formulated for inpatient management. Maintaining glucose levels between 140 and 180 mg/dL is recommended for the majority of hospitalized patients.[1] Individualized goals for younger patients without comorbidities (with previous stable glucose control before admission), or for the elderly, terminally ill, or those with extensive comorbidities (eg, congestive heart failure, cirrhosis, and renal failure), have been established for use in the outpatient setting, but no recommendations exist for inpatient glycemic goals for these different groups.

Standardized glycemic goals for certain populations of hospitalized patients have suggested that targets < 110 mg/dL are not recommended and may lead to poor outcomes, especially in critically ill patients.[1] Recent studies failed to show a significant

improvement in mortality with intensive glycemic control.[3,4]

Hyperglycemia in the hospital (blood glucose > 140 mg/dL) can increase the risk of infections, delay wound healing, and possibly prolong the length of hospital stay. Hyperglycemia has been associated with endothelial dysfunction, oxidative stress, acidosis, caloric and protein losses, electrolyte imbalances, impairment of neutrophil function, and potential exacerbation of myocardial and cerebral ischemia.[2]

Conversely, hypoglycemia (blood glucose < 70 mg/dL), if brief and mild, may not have long-term sequelae, but severe hypoglycemia (blood glucose < 40 mg/dL) could provoke neurologic effects or seizures, or could trigger arrhythmias or other cardiac events.[5] Possible causes of hypoglycemia in the hospital include variability in insulin sensitivity related to the underlying illness, changes in counterregulatory hormonal responses to procedures or illnesses, prolonged nothing-by-mouth (NPO) status, variable doses of dextrose fluids or glucocorticoid therapy, unexpected decreases in food intake or emesis, interruption of enteral or parenteral nutrition, sepsis, concurrent malignancy, use of quinolone antibiotics, or worsening of hepatic or renal function. Providers should be proactive in reducing insulin doses in such settings.

MANAGEMENT OF HYPERGLYCEMIA

Oral Agents

Oral antidiabetic agents used in the hospital are difficult to titrate, have not been studied for safety and efficacy in hospitalized patients, and may predispose patients to hypoglycemia. Also, the use of non-insulin injectable medications, such as the glucagon-like peptide 1 analogs, may be contraindicated in many inpatient settings. Sulfonylureas act by increasing insulin release from islet cells in the pancreas, which can lead to severe, prolonged hypoglycemia, particularly in elderly patients and patients with poor appetite or impaired renal function.[6] Metformin, which suppresses glucose production by the liver, should not be used in patients who have decompensated heart failure, renal insufficiency, or chronic pulmonary disease.[1] Diagnostic tests, such as computed tomography scans, that involve IV contrast dye, can put the patient taking metformin at risk of renal failure or lactic acidosis. Despite being discontinued during the hospital stay, oral agents and non-insulin injectable medications may be resumed at discharge in patients with a history of good glycemic control before hospitalization, who are stable, and have no contraindications.

Insulin

For optimal glucose control, scheduled subcutaneous insulin with basal, prandial, and correction components is the preferred treatment method for the non–critically ill patient in the hospital.[1] There is a paucity of accepted insulin algorithms to facilitate inpatient glucose management. Prudent treatment of hyperglycemia while avoiding hypoglycemia is the primary goal.

With normal endogenous insulin secretion, the body's insulin production increases after each meal with consumption of carbohydrates, and then normalizes between meals, bringing serum glucose levels back to within a normal range (Figure, part A). Even with prolonged fasting, blood glucose rarely falls below 50-60 mg/dL, due to hepatic glycogenolysis and subsequent gluconeogenesis. Moreover, endogenous insulin secretion is present to metabolize hepatic glucose production. Understanding this relationship and trying to mimic a natural, physiologic response requires an understanding of insulin pharmacodynamics. Using rapid-acting insulin at mealtimes and a long-acting basal insulin (programs with multiple daily injections) best mimics the natural physiologic responses of the body (Figure, part B). The pharmacodynamics of types of insulin have differences (Table). In the hospital setting, with many extraneous variables, the appropriate types and timing of insulin doses are paramount, as is consideration of the circumstances and the current clinical condition of the patient.

Basal-Bolus Insulin Therapy

Basal insulin therapy. Long-acting basal insulins, such as glargine, detemir, or intermediate-acting neutral protamine Hagedorn insulin (NPH), are usually given once or twice daily. Basal insulin prevents ketosis in insulinopenic patients (patients with type 1 diabetes mellitus or post-pancreatectomy diabetes) and, if used properly, will manage fasting