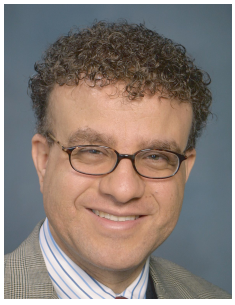
Glycemic control for hospitalized patients with diabetes: strategies for effective management



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'With the rising epidemic of diabetes, accounting for 35–40% of hospitalizations, effective strategies to implement the current evidence are desperately needed.'

Accumulating evidence indicates that tight glycemic control for hospitalized patients improves outcomes, particularly in the post myocardial infarction (MI) and surgical intensive-care unit (ICU) population. With the rising epidemic of diabetes, accounting for 35–40% of hospitalizations, effective strategies to implement the current evidence are desperately needed. Here, we present the status of diabetes care in hospitalized patients, the underlying causes of the largely suboptimal glycemic control, together with proposed therapeutic strategies available to date.

Diabetic patients & increased hospitalization rate

Diabetes mellitus (DM) has become a global epidemic with the number of people with DM estimated to rise from 171 million in the year 2000 to 366 million people in 2030 [1]. Furthermore, there is a six-times higher risk of hospitalization in diabetic compared with non-diabetic patients [2]. With the rising number of patients diagnosed with DM, it is expected that we will see a significant rise in hospitalization attributable to the disease. Therefore, it is imperative that we develop effective strategies for in-patient management.

Hospital outcomes in patients with a primary or secondary DM diagnosis

There are several studies that demonstrated benefits of tight glycemic control in hospitalized patients with either a primary or secondary diagnosis of DM. One of the most significant intervention trials in support of this is the Diabetes mellitus Insulin Glucose infusion in Acute Myocardial Infarction (DIGAMI) study, in which 620 patients were randomized, of whom 306 received intensive insulin treatment and 314 served as controls. The intensive management consisted of insulin–glucose infusion for at least 24 h, followed by multidose insulin treatment. After a mean follow-up period of 3.4 years, there were 102 (33%) deaths in the treatment group compared with 138 (44%) in the control group. The effect was most pronounced in a predefined subgroup that included 272 patients without previous insulin treatment and at a low cardiovascular risk, where there was a significant reduction in mortality during the hospital phase (12 vs 5%; relative risk reduction of 58%; $p < 0.05$) [3,4]. In this study, intensive glycemic control was associated with an absolute reduction in mortality of 11%, meaning that one life was saved for nine treated patients [3].

In addition to improved outcomes, tight glycemic control has also been shown to be associated with a decrease in the length of hospital stay in patients with DM. In a study by our group, involving 212 patients with heart failure, of which 119 were also diagnosed with DM, heart failure patients with DM had a significantly longer hospital stay than those without DM. After adjusting for age, sex, weight and presence of hypertension, hospital stay significantly correlated with the average in-hospital blood glucose ($r = 0.34$, $p = 0.001$) [5].

Tight glucose control has also been shown to decrease the rate of infection and aid in wound healing. Possible factors that may lead to increase risk of infection and poor wound healing in the diabetic patient include altered cellular and humoral immune-defense mechanisms, which may be improved with better glycemic control [6].

Control of hyperglycemia is especially important in the perioperative patient. Golden and colleagues studied 411 adults with DM who underwent coronary artery bypass surgery from 1990 to 1995 in the cardiac surgery service of an urban university hospital. Perioperative glycemic control was characterized by the mean of six capillary glucose measurements taken during the 36-h interval following surgery. The major outcomes studied were infections of leg and chest wounds, development of pneumonia and urinary

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tract infections. Patients with mean glucose concentrations greater than 200 mg/dl within 36 h following surgery were more likely to develop infectious complications than their counterparts who had better glycemic control. These data suggest that postoperative hyperglycemia is an independent predictor of short-term infectious complications [7].

Insights into reasons for poor glycemic control

Glycemic control in hospitalized patients is largely suboptimal and failure of glycemic control is multifactorial, including the comorbid illness that takes priority over glycemic control and also leads to increased stress, which in turn leads to further hyperglycemia. Perhaps one of the frequently cited culprits is the use of sliding-scale insulin. Using insulin sliding scales as the main source of DM treatment without proper control of baseline blood sugars is a significant source of higher in-hospital blood sugars and does not decrease the length of hospital stay compared with standard-dose antihyperglycemic therapy [8,9].

Deleterious effects of acute hyperglycemia

Deleterious effects of hyperglycemia have been studied extensively. Acute hyperglycemia has been shown to lead to increased plasma catecholamines, systolic and diastolic blood pressure and heart rate. It is also associated with decreased blood flow to the leg, suggesting vasoconstriction [10].

Furthermore, hyperglycemia impairs ischemic preconditioning and increases infarct size. It may also activate the coagulation cascade by inducing thrombin activation [10,11].

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Elevated blood sugars have been shown to cause vascular endothelial cell dysfunction by multiple mechanisms, including increased oxidative stress and impaired nitric oxide function [10,11]. In stroke patients, acute hyperglycemia increases lactate production in the brain and facilitates conversion of hypoperfused at-risk tissue into infarction, which may adversely affect stroke outcomes [12]. Hyperglycemia has also been shown to influence immune function by causing phagocyte dysfunction. This may be an important factor affecting post-surgical infections in diabetic patients [13].

Clement and colleagues proposed a model linking hyperglycemia and poor hospital outcomes. They proposed that metabolic stress leads to hyperglycemia and relative insulin deficiency, which subsequently leads to immune dysfunction, release of fuel substrates and other mediators. Tissue and organ injury occur through the combination of direct fuel-mediated injury, infection and oxidative stress [11].

Therapeutic options for in-patient DM management

In-hospital management of hyperglycemia in patients admitted with DM as either a primary or secondary diagnosis is a significant factor in determining the length of hospital stay and morbidity. We will now discuss treatment approaches that may be helpful in treating these patients.

Use of sliding-scale insulin

As previously mentioned, the use of sliding-scale insulin has been shown to increase the risk of hyperglycemia without any favorable effects on the length of hospital stay [8]. Sliding scales certainly should not be used as the only source of glycemic control and should not be confused with an adjusted premeal supplemental insulin regimen that can be used as an addition to a well-thought-out medication regimen involving oral agents and/or long- or intermediate-acting insulin.

Control of baseline blood sugars with oral agents

Baseline blood sugars should be controlled either with oral agents or long-acting insulin. If a known diabetic was well controlled as an out-patient on a particular oral agent or insulin, it is best to use that same medicine for control as an in-patient with some adjustment in dose as needed. These patients may need a dosage reduction of 25–50% due to better in-hospital dietary compliance [4]. However, if there is a contraindication to the use of a previous medication, such as the new development of congestive heart failure or liver failure in a previously healthy patient who was on a thiazolidinedione, then that medication should be stopped. Additionally, metformin should be discontinued in all patients who may have imaging studies involving the use of contrast dye, patients undergoing surgery, those with poor renal or hepatic function or in whom hydration status may be compromised.

Insulin in the patient who is not eating

Patients with Type 1 DM who are not eating should remain on insulin at two-thirds of their standard dose. Type 2 diabetic patients who are not eating should receive a half of their usual long- or intermediate-acting insulin dose. Insulin-treated Type 1 or Type 2 diabetic patients who are eating in the hospital should receive doses similar to their out-patient requirements with only minor reductions as needed for possible better dietary compliance.

Perioperative management of DM

For perioperative management of DM, Metchick and colleagues describe a well-accepted model for treatment of patients on insulin drips [4]. Type 1 diabetic patients should be placed on an insulin drip at 1–2 U/h with a 5% dextrose solution at 75–125 cc/h. Type 2 diabetic patients should receive a half of their long- or intermediate-acting insulin dose. Blood sugars should be checked hourly for the first 4 h, then every 2 h. The infusion rate can be increased by 50–100% if blood glucose levels are increasing after 2 h. The rate should be decreased by 25–50% if the blood glucose level decreases by more than 100 mg/dl. Infusion rates should be increased by 0.5–2 U/h if the blood glucose level is greater than 200 mg/dl. The drip should be held for 1 h if the blood glucose level is less than 100 mg/dl, then decreased by 0.5–2 U/h. Regular insulin should be given 20–60 min before terminating the infusion.

For Type 2 diabetic patients on oral agents, medication should be held on the day of the procedure and resumed when the patient starts eating [4]. Metformin should be stopped perioperatively due to possible compromise of renal function and hydration with increased risk of lactic acidosis.

Diet

Dietary management is an integral component of any DM treatment plan. All patients who are eating should be placed on standard diabetic diets adjusted for their height and weight. The help of a dietician should be elicited as needed.

Blood glucose monitoring/goals

Blood glucose levels should be monitored at least three times a day, including a 2-h postprandial blood glucose measurement. When blood sugars have been consistently stable for several days, patients may be switched to a twice-a-day monitoring schedule.

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For most patients, the fasting blood glucose goals should be 80–110 mg/dl. If there is any difficulty in achieving these goals, endocrinology consult should be sought as early as possible. Targets may be adjusted for elderly, malnourished, or cognitively impaired patients, as well as patients with liver and renal failure due to the increased risk of hypoglycemia in these patient populations [8–14].

Patient education

The level of DM education and self-management skills should be assessed in all diabetic in-patients. A DM educator should be involved in training the patient and/or family members in any areas where they are deficient

Conclusion

As the epidemic of DM continues, the number of in-patients with the disease will also rise, leading to increased hospitalizations with associated increase in morbidity and mortality. It is therefore imperative that we develop strategies to effectively manage diabetic patients in the hospital. We have presented treatment strategies that can be used in treating such patients. However, further studies are needed in this field to determine the optimal approaches and help develop standardized and evidence-based treatment protocols for both hyperglycemia and hypoglycemia in hospitalized diabetic patients.

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