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The Importance of Glycemic Control in the Hospital and the Role of the Infusion Nurse

ABSTRACT

Diabetes is reaching epidemic proportions. Patients undergoing surgery, regardless of diabetes history, are at high risk for complications of poor glycemic control, including infection, mortality, and longer lengths of stay. This article provides an overview of the evidence about glycemic control in the hospital, risk factors for hyperglycemia and hypoglycemia, and the role of infusion nurses in improving outcomes for hospitalized patients with diabetes.

Key words: diabetes, glycemic control, hyperglycemia, hypoglycemia, hospital

The Centers for Disease Control and Prevention estimates that 29.1 million people, or 9.3% of the population of the United States, have diabetes.[1] Another 86 million have prediabetes,[1] a precursor to diabetes in which blood glucose values are higher than normal but not yet high enough to diagnose diabetes. People with prediabetes have a greater risk of developing type 2 diabetes. There is also an economic burden of diabetes. A study conducted by the American Diabetes Association (ADA) found that $176 billion are spent on direct medical costs; this is 2.3 times more than the costs for those without diabetes.[2] More than 40% of the costs result from the higher hospital admission rates and longer lengths of stay for those with diabetes.[2] Indirect costs—such as those associated with disability, work loss, and premature death—account for an additional $69 billion.[2] As the population of those with diabetes increases and the economic burden of the disease worsens, health care professionals must understand how to best manage diabetes when patients are acutely or critically ill.

The benefits and risks of achieving glycemic control in hospitalized patients have been studied increasingly during the past 10 to 15 years. The most recent studies challenge the long-standing notion that tight glycemic control is best for hospitalized patients, including those undergoing surgery. These patients have an increased risk of hyperglycemia, which may affect healing, infection risk, length of stay, and other outcomes. The negative impact of hypoglycemia also has gained more attention and has led to a shift toward more moderate glycemic targets. As the complexity of diabetes care intensifies, infusion nurses can play an important role in promoting and providing safe, evidence-based care for patients with diabetes and hyperglycemia.

PATHOPHYSIOLOGY OF HYPERGLYCEMIA

The stress of surgery and illness causes a release of counterregulatory hormones, including catecholamines, cortisol, glucagon, and growth hormone. Surgical tissue trauma induces the same response.[3] This release of hormones triggers a decrease in insulin secretion, increased gluconeogenesis and glycogenolysis, and greater insulin resistance. These factors all contribute to hyperglycemia regardless of whether the patient has a history of diabetes. Proinflammatory cytokines also contribute to hyperglycemia through indirect release of counterregulatory hormones.[4] This leads to capillary basement membrane thickening, oxidative stress, increased C-reactive protein levels, increased platelet adhesion

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TABLE 1

Causes of and Risk Factors for Hyperglycemia and Hypoglycemia

Hyperglycemia	Hypoglycemia
• Physiologic stress of illness/surgery	• Anesthesia and/or analgesia effects causing inability of patient to self-report signs/symptoms of hypoglycemia
• Psychological stress	• Failure to adjust insulin and other antihyperglycemic agents
• Renal dysfunction	• Steroid taper
• Hepatic dysfunction	• Hyperkalemia treatment
• Infection	• Renal dysfunction
• Severity of illness	• Hepatic dysfunction
• Medications (ie, corticosteroids, immunosuppressants, and vasopressors)	• Lack of coordination of glucose monitoring, insulin, and meals
• Inappropriate discontinuation or withholding of antihyperglycemic medications preoperatively or postoperatively	• Sepsis
• Poor transition from IV to SC insulin	• Severity of illness
• Enteral/parenteral nutrition	• Inadequate oral intake
• Lack of coordination of glucose monitoring, insulin, and meals	• Interruptions in meals or enteral/parenteral nutrition
• Fear of hypoglycemia	

Abbreviations: IV, intravenous; SC, subcutaneous.

and coagulation factors, and decreased vasodilation.[5,6] Adverse outcomes also include impaired phagocytosis, decreased neutrophil activity, and altered tissue metabolism. These effects contribute to increased infection risk and impaired wound healing.

CAUSES OF HYPERGLYCEMIA

In addition to physiologic and psychological stress, there are many causes of hyperglycemia in hospitalized patients, including those undergoing surgery (Table 1). Clinical conditions including new or worsening hepatic or renal function, infection, and severity of illness may have a negative impact on glycemic control. Medications such as corticosteroids, immunosuppressants, and vasopressors increase blood glucose levels. Such medications are often necessary treatments for other conditions, but complicate diabetes care. Antihyperglycemic medications may be appropriately discontinued during acute or critical illness, or inappropriately withheld because of concerns about hypoglycemia or lack of knowledge about the necessity of glycemic control. For patients requiring intraveneous (IV) insulin infusions, transitions to subcutaneous insulin may result in rebound hyperglycemia if protocols are not in place or not followed.

There are multiple factors related to nutrition that contribute to hyperglycemia for postsurgical patients. Patients may be unable to eat or have significant delays in resuming adequate oral intake. In some cases, hyperglycemia treatment may be withheld because of concerns about hypoglycemia risk while not eating. Some patients may require enteral or parenteral nutrition; these therapies can have a significant impact on glycemic control given the carbohydrate-rich content of the formulations. One prospective, multicenter study showed a higher risk of in-hospital mortality for noncritically ill patients who received total parenteral nutrition and had mean blood glucose levels greater than 180 mg/dL.[7] As surgical patients begin to eat meals, new challenges exist. Patients' intake may be unpredictable and variable, making it difficult to anticipate treatment needs. Nurses and providers may underestimate insulin requirements during this time. It is also a considerable challenge for nursing staff to coordinate glucose monitoring and nutritional insulin administration, especially if on-demand meal delivery programs are in place.

RECOMMENDATIONS FOR OPTIMAL GLYCEMIC CONTROL

Interest in glycemic control in hospital settings began to grow in the late 1990s as researchers investigated the benefits of glycemic control in certain patient populations, such as cardiac surgery patients and patients in intensive care units (ICUs).[8-12] Clinical outcomes evaluated included postoperative infection rates, deep sternal

wound infections, arrhythmias, and mortality. Intensive hyperglycemic management was strongly embraced after the landmark single-center randomized controlled trial (RCT) was published by Van den Berghe and colleagues in 2001.[13] Surgical ICU patients in the treatment group with tight glycemic control (80-110 mg/dL) showed statistically significant reductions in sepsis, renal impairment requiring dialysis, polyneuropathy, blood transfusions, length of stay in the ICU, and in-hospital mortality.[12] Position statements were subsequently issued by national diabetes organizations promoting tight glycemic control.[14,15] In 2006, Van den Berghe and colleagues repeated the study with medical ICU patients, but outcomes were not as favorable. The mortality benefit was achieved only for patients with a length of stay greater than or equal to 5 days.[16] Other researchers also were unable to replicate outcomes of Van den Berghe and colleagues' initial trial.

In 2009, the Normoglycemia in Intensive Care Evaluation and Survival Using Glucose Algorithm Regulation (NICE-SUGAR) study was published.[17] This multicenter, multinational RCT included 6104 patients in medical and surgical ICUs. Intensive glycemic control (80-108 mg/dL) was compared with moderate control (blood glucose < 180 mg/dL) for patients in the conventional group. Study patients who were intensively managed had higher mortality rates at 90 days. They also had a 14-fold increase in overall hypoglycemia rates compared with the conventional group. Severe hypoglycemia (defined as ≤ 40 mg/dL) occurred in 0.5% of patients in the group with moderate control compared with 6.8% in the intensively managed group.[17]

Based on the available evidence, the American Association of Clinical Endocrinologists and the ADA published a consensus statement in 2009[18] and yearly clinical practice guidelines[19] that reflect a shift away from tight glycemic control for most patients. Critically ill patients should maintain blood glucose levels between 140 and 180 mg/dL, with a suggestion that a greater benefit may be seen at the lower end of this range.[18,19] Patients who are not in the ICU should have premeal glucose levels lower than 140 mg/dL and random glucose levels lower than 180 mg/dL[18,19] (Table 2). Given the conflicting data and controversial nature of the evidence, diabetes experts recommend that glucose targets be individualized for specific patient populations as long as hypoglycemia can be avoided.[19,20]

TABLE 2

Glycemic Targets for Hospitalized Patients[18,19]

Noncritically ill patients
• Premeal: generally < 140 mg/dL
• Random glucoses < 180 mg/dL
Critically ill patients
• 140-180 mg/dL (lower targets for some patients, if hypoglycemia can be avoided)
• Less than 110 mg/dL is not recommended

HYPOGLYCEMIA

Evidence from the NICE-SUGAR study[17] and subsequent guidelines[18,19] have led clinicians to focus more closely on avoiding hypoglycemia in hospitalized patients. The ADA defines hypoglycemia as a blood glucose less than 70 mg/dL.[16] Many studies evaluate overall hypoglycemia rates as well as the number of severe hypoglycemic events, often defined as less than 50 mg/dL or less than 40 mg/dL by study investigators. Organizations often select 1 of these thresholds to define the critical value for hypoglycemia. A number of adverse effects have been associated with hypoglycemia, including cognitive impairment, seizures, cardiac arrhythmias, prolonged hospital lengths of stay, and mortality.[21,22] Clinicians also may become fearful of repeated hypoglycemic events, which can lead to ineffective management of hyperglycemia.

There are many contributing factors or causes of iatrogenic hypoglycemia including medication-related factors, comorbid conditions, and nutrition-related factors (Table 1). Most concerning for surgical patients and perioperative clinicians is the risk of hypoglycemia during and immediately after surgery when anesthesia and/or analgesia effects render the patient unable to report signs and symptoms of hypoglycemia. Clinicians must rely on glucose monitoring, which may be challenging to do during the surgical case. Clinicians also must be concerned about insulin or other antihyperglycemic agents taken by patients preoperatively; in some cases, medications are taken inappropriately rather than adjusted or stopped before surgery. Patients who taper off steroids are also at risk for hypoglycemia. As previously mentioned, these medications can cause hyperglycemia. If hyperglycemia treatment is not tapered as the steroid dose is being tapered, then hypoglycemia is predictable. Hyperkalemia treatment, which often involves insulin administration to shift potassium back to the intracellular space, can also increase the risk of hypoglycemia if not balanced with sufficient dextrose and adequate blood glucose monitoring. Examples of comorbid conditions contributing to hypoglycemia risk include those with renal and/or hepatic disease. These conditions interfere with the metabolism of diabetes medications, which can potentiate their effects.[21] In addition, patients who are septic or severely ill are also at high risk. It is sometimes unclear whether hypoglycemia is a marker of critical illness or a contributing factor to poor outcomes.[23]

Postsurgical patients also have a number of nutrition-related factors that contribute to increased hypoglycemia

risk. Their oral intake is restricted before and after surgery in most cases. As restrictions are lifted, intake can often be unpredictable or inadequate because of nausea, vomiting, lack of appetite, interruptions during meals, and various other reasons. One study reported that 44% to 59% of hospitalized patients ate 50% or less of any meal offered, and 18% to 34% of patients ate no food.[24] Unfortunately, insulin doses often are given before the meal, before it is known what the patient will consume. For patients who require enteral or parenteral nutrition and receive insulin to manage the carbohydrate load of the formula, hypoglycemia risk escalates if the feeding is interrupted.

INSULIN SAFETY

Insulin is considered the most appropriate treatment choice for hyperglycemia in hospital settings. It can be given subcutaneously or intraveneously and is often a safer option than the oral antihyperglycemic agents that patients may take at home. Insulin can be titrated to meet the changing clinical needs of the patient, has few side effects (with the exception of hypoglycemia), and is available in rapid-, short-, intermediate-, and long-acting formulations. Human regular insulin is the insulin type used for IV infusions. There is no pharmacologic benefit of using the newer rapid-acting analogues for IV infusions, and doing so would add significant cost to an organization. Regular insulin is stable at room temperature for 24 to 48 hours, depending on the manufacturer's specifications. Insulin has few incompatibilities; it is typically infused with normal saline or dextrose-containing maintenance fluids as drivers.

The Institute for Safe Medication Practices supports a variety of error-reduction strategies.[25] For example, IV insulin should be prepared and dispensed by the pharmacy and prepared with a 1 unit/1 mL concentration. Also, because insulin is considered a high-alert medication, an independent double-check before administration may catch errors before reaching the patient. When new infusions are prepared, tubing must be properly primed by wasting an additional 20 mL to saturate the binding sites of the tubing to prevent delayed hypoglycemia.[26] In addition, high-alert medications should not be infused as a secondary infusion but, rather, as a primary infusion.[27] Last, tubing should be labeled clearly at a point most proximal to the patient and on the channel of the device,[27] and infusion limits should be set to avoid inadvertent overdoses.[25]

ROLE OF INFUSION NURSES

With an estimated 30% to 50% of adult patients having diabetes and/or hyperglycemia during hospitalization,[28] all staff must become more knowledgeable about diabetes care practices that can have a positive impact on clinical outcomes. Infusion nurses can play an important role in the care of these patients. Most important, infusion nurses must be aware of the latest recommendations about glycemic targets. They should proactively advocate for hyperglycemia treatment regardless of a patient's diabetes history. Such efforts have the potential to have an impact on perioperative glycemic control, postoperative healing, and postoperative infection rates. Infusion nurses who are aware of the latest evidence about the negative impact of hypoglycemia can intervene when risk factors are identified or hypoglycemia occurs. Additionally, infusion nurses have the opportunity to share their expertise about infusion therapy with colleagues who may be confused about preparing IV insulin infusions, either through direct consultation or by creating accessible, concise practice reminders. Key points include how to prime tubing, use of maintenance fluids as a continuous primary infusion, and use of appropriate tubing connections when other IV medications are infusing simultaneously. Finally, infusion nurses should partner with teams who are working to help ensure safe use of insulin in the hospital. Dosing limits should be set for IV insulin infusions to prevent inadvertent overdoses. These limits should be most restrictive in pediatric and general care settings; adult intensive care settings and perioperative areas may need higher infusion rate limits.

CONCLUSIONS

Glycemic control in hospitalized patients has an impact on clinical outcomes such as infection rates, length of stay, and mortality. Recommendations about the most beneficial glycemic targets have shifted from the long-standing support of tight glycemic control to a more moderate approach. Infusion nurse specialists must stay abreast of the latest evidence to advocate for patients and support quality improvement work related to reducing infection risk and minimizing the consequences of hypoglycemia and hyperglycemia.

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