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Clinical Practice Guidelines

In-hospital Management of Diabetes

Canadian Diabetes Association Clinical Practice Guidelines Expert Committee

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KEY MESSAGES

- Hyperglycemia is common in hospitalized patients, even in those without a previous history of diabetes, and is associated with increased in-hospital complications, length of hospital stay and mortality.
- Insulin is the most appropriate agent for effectively controlling glycemia in-hospital. A proactive approach to management using scheduled basal, bolus and correction (supplemental) insulin is the preferred method. The use of sliding-scale insulin (SSI), which treats hyperglycemia after it has occurred, should be discouraged.
- For the majority of noncritically ill patients treated with insulin, preprandial blood glucose (BG) targets should be 5.0 to 8.0 mmol/L, in conjunction with random BG values <10.0 mmol/L, as long as these targets can be safely achieved. For critically ill patients, BG levels should be maintained between 8.0 and 10.0 mmol/L.

Introduction

Diabetes increases the risk for disorders that predispose individuals to hospitalization, including cardiovascular disease, nephropathy, infection, cancer and lower-extremity amputations. In-hospital hyperglycemia is common. Umpierrez et al. (1) reviewed the medical records of over 2000 adult patients admitted to a community teaching hospital in the United States (>85% were non-intensive care unit [non-ICU] patients) and found that hyperglycemia was present in 38% of patients. Of these patients, 26% had a known history of diabetes, and 12% had no history of diabetes prior to admission (1). Diabetes has been reported to be the fourth most common comorbid condition listed on all hospital discharges (2).

Acute illness results in a number of physiological changes (e.g. increases in circulating concentrations of stress hormones) or therapeutic choices (e.g. glucocorticoid use) that can exacerbate hyperglycemia. Hyperglycemia, in turn, causes physiological changes that can exacerbate acute illness, such as decreased immune function and increased oxidative stress. This leads to a vicious cycle of worsening illness and poor glucose control (3).

Although a growing body of literature supports the need for targeted glycemic control in the hospital setting, blood glucose (BG) continues to be poorly controlled and is frequently overlooked in general medicine and surgery services. This is largely explained by the fact that the majority of hospitalizations for patients with diabetes are not directly related to the metabolic state, and diabetes management is rarely the primary focus of care. Therefore, glycemic control and other diabetes care issues are often not adequately addressed (4).

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Diagnosis of Diabetes and Hyperglycemia in the Hospital Setting

A history of diabetes should be elicited in all patients admitted to hospital and, if present, should be clearly identified on the medical record. In view of the high prevalence of inpatient hyperglycemia with associated poor outcomes, an admission BG measurement should be considered for all patients even in the absence of a prior diagnosis of diabetes (1). In-hospital hyperglycemia is defined as any glucose value >7.8 mmol/L (5). A glycated hemoglobin (A1C) level should be drawn in all patients with known diabetes or with hyperglycemia if this has not been performed within 2 to 3 months of the admission. For patients with known diabetes, the A1C identifies patients who would benefit from efforts to improve glycemic control. For patients with newly recognized hyperglycemia, an elevated A1C may help differentiate patients with previously undiagnosed diabetes from those with stress-induced hyperglycemia (6).

Glycemic Control in the Noncritically Ill Patient

A number of studies have demonstrated that inpatient hyperglycemia is associated with increased morbidity and mortality in noncritically ill hospitalized patients (1,7–9). However, due to a paucity of randomized controlled trials on the benefits and risks of “loose” vs. “tight” glycemic control in noncritically ill patients, it is difficult to define glycemic targets for this population. Current recommendations are based on clinical experience and judgement. Glycemic targets for hospitalized patients are modestly higher than those routinely advised for outpatients with diabetes given that the hospital setting presents unique challenges for the management of hyperglycemia, such as variations in patient nutritional status and the presence of acute illness. For the majority of noncritically ill patients treated with insulin, preprandial glucose targets should be 5.0 to 8.0 mmol/L, in conjunction with random BG values <10.0 mmol/L, as long as these targets can be safely achieved. Lower targets may be considered in clinically stable patients with a prior history of successful tight glycemic control in the outpatient setting, while higher targets may be acceptable in terminally ill patients or in

those with severe comorbidities. If BG values are ≤3.9 mmol/L, the glucose-lowering therapy should be modified, unless the event is easily explained by other factors (e.g. a missed meal) (5).

Glycemic Control in the Critically Ill Patient

Acute hyperglycemia in the intensive care setting is not unusual and results from a number of factors, including stress-induced counterregulatory hormone secretion and the effects of medications administered in the ICU (10). Appropriate glycemic targets for patients with preexisting diabetes who are critically ill (ICU setting) have not been firmly established. Some trials showed that achieving normoglycemia (4.4 to 6.1 mmol/L) in cardiac surgery patients or patients in postoperative surgical ICU settings may reduce mortality (11). However, subsequent trials in mixed populations of critically ill patients did not show a benefit of targeting BG levels of 4.4 to 8.3 mmol/L. A meta-analysis of trials of intensive insulin therapy in the ICU setting suggested some benefit of intensive insulin therapy in surgical patients, but not in medical patients (12). However, this benefit in surgical ICU patients was not demonstrated in the Normoglycemia in Intensive Care Evaluation-Survival Using Glucose Algorithm Regulation (NICE-SUGAR) study, the largest trial to date of intensive glucose control in critically ill patients (13). Furthermore, intensive insulin therapy has been associated with an increased risk of hypoglycemia in the ICU setting (12). Therefore, it is recommended to maintain BG levels between 8.0 and 10.0 mmol/L in critically ill patients; a lower BG target (but not <6.0 mmol/L) may be appropriate in select patients. Insulin infusion protocols with proven efficacy and safety are recommended to minimize the risk of hypoglycemia (5).

Perioperative glycemic control

The management of individuals with diabetes at the time of surgery poses a number of challenges. Acute hyperglycemia is common secondary to the physiological stress associated with surgery. Preexisting diabetes-related complications and comorbidities may also influence clinical outcomes. Acute hyperglycemia has been shown to adversely affect immune function (14) and wound healing (15) in animal models. Observational studies in humans have shown that hyperglycemia increases the risk of postoperative infections (16–18) and renal allograft rejection (19), and is associated with increased resource utilization (20). In patients undergoing coronary artery bypass grafting (CABG), a preexisting diagnosis of diabetes has been identified as a risk factor for postoperative sternal wound infections, delirium, renal dysfunction, respiratory insufficiency and prolonged hospital stays (21–23). Intraoperative hyperglycemia during cardiopulmonary bypass has been associated with increased morbidity and mortality rates in individuals with and without diabetes (24–26).

Minor and moderate surgery

The appropriate perioperative glycemic targets for minor or moderate surgeries are less clear. There are few intervention studies assessing the impact of tight glycemic control on morbidity or mortality in these settings; however, a number of small studies that compared different methods of achieving glycemic control during minor and moderate surgeries did not demonstrate any adverse effects of maintaining perioperative glycemic levels between 5.0 and 11.0 mmol/L (27–29).

Rapid institution of perioperative control should be carefully considered in patients with poorly controlled type 2 diabetes undergoing monocular phacoemulsification cataract surgery with moderate to severe nonproliferative diabetic retinopathy because of the possible increased risk of postoperative progression of retinopathy and maculopathy (30). The outcome of vitrectomy does not appear to be influenced by perioperative control (31).

Given the data supporting tighter perioperative glycemic control during major surgeries and the compelling data showing the adverse effects of hyperglycemia, it is reasonable to target glycemic levels between 5.0 and 10.0 mmol/L for minor and moderate surgeries. However, the benefits of improved perioperative glycemic control must be weighed against the risk of perioperative hypoglycemia. Anesthetic agents and postoperative analgesia may alter the patient's level of consciousness and awareness of hypoglycemia. The risk of hypoglycemia can be reduced by frequent BG monitoring and carefully designed management protocols.

Role of Subcutaneous Insulin

In general, insulin is the preferred treatment for hyperglycemia in hospitalized patients with diabetes (5). Patients with type 1 diabetes must be maintained on insulin therapy at all times to prevent diabetic ketoacidosis (DKA). Scheduled subcutaneous (SC) insulin administration that consists of basal, bolus (prandial) and correction (supplemental) insulin components is the preferred method for achieving and maintaining glucose control in non-critically ill patients with diabetes or stress hyperglycemia who are eating (5). Bolus insulin can be withheld or reduced in patients who are not eating regularly; basal insulin should not be withheld. Stable patients can usually be maintained on their home insulin regimen with adjustments made to accommodate for differences in meals and activity levels, the effects of illness and the effects of other medications. In the hospital setting, rapid-acting insulin analogues are the preferred SC bolus insulins (32). Sliding-scale insulin (SSI) (defined as the administration of a preestablished amount of short-acting insulin in response to hyperglycemia) as the sole regimen for the management of hyperglycemia in the hospital setting is ineffective in the majority of patients and, therefore, is not recommended (5,33–36). Insulin is often required temporarily in-hospital, even in patients with type 2 diabetes not previously treated with insulin. In these insulin-naïve patients, there is evidence demonstrating the superiority of basal-bolus-supplemental insulin regimens over SSI (37,38). These studies have typically started patients on 0.4 to 0.5 units of insulin per kilogram of body weight per day, with 40% to 50% of the total daily dose (TDD) given as basal insulin (detemir, glargine, NPH) and the balance given as bolus (rapid or short-acting) insulin divided equally before each meal (i.e. breakfast, lunch, and dinner); supplemental doses of the bolus insulin are to be provided if BG values are above target. The patient's BG measurements should be reviewed daily and the insulin dose adjusted as required.

Role of Oral Antihyperglycemic Drugs

To date, no large studies have investigated the use of oral antihyperglycemic drugs (OADs) on outcomes in hospitalized patients with diabetes. There are often short- and/or long-term contraindications to the use of OADs in the hospital setting, such as irregular eating, acute or chronic renal failure, and exposure to intravenous (IV) contrast dye (39). Stable patients without these contraindications can often have their home medications continued while in the hospital. However, if contraindications develop or if glycemic control is inadequate, these drugs should be discontinued and the patient should be started on a basal-bolus-supplemental insulin regimen.

Role of Medical Nutrition Therapy

Medical nutrition therapy is an essential component of inpatient glycemic management programs and should include nutritional

assessment and individualized meal planning. A consistent carbohydrate meal planning system may facilitate glycemic control in hospitalized patients and facilitate matching the prandial insulin dose to the amount of carbohydrate consumed (35,40).

Special Clinical Situations

Patients receiving enteral or parenteral feedings

In patients receiving parenteral nutrition (PN), insulin can be administered with the nutrition. An IV infusion of regular insulin is often used initially to estimate the TDD of insulin required. Approximately 80% of the TDD of insulin needed to maintain BG levels within the target range on IV insulin is added to the PN bags as regular insulin. SC correction (supplemental) insulin is often used in addition to the insulin mixed with PN for unusual hyperglycemia. The dose of insulin is adjusted based on BG monitoring results. To prevent ketoacidosis, patients with type 1 diabetes must be given subcutaneous insulin if the total parenteral nutrition (TPN) is interrupted. As an alternative to adding insulin to the PN, a separate IV insulin infusion may be used.

Since nutrition is being provided continuously in patients receiving continuous enteral feeds, the TDD of insulin can be administered as a long-acting, nonpeaking basal insulin alone (once-daily glargine or twice daily detemir). Patients receiving bolus enteral feeds are typically treated like patients who are eating meals. Approximately 50% of the TDD is provided as basal insulin and 50% as bolus insulin, which is administered in divided doses to match feed times (39). Short-acting regular insulin is usually selected over rapid-acting insulin in this group of patients because of the longer duration of action. Supplemental insulin should be administered as needed with the bolus insulin. In the event that tube feeds are interrupted, IV dextrose may be required to prevent hypoglycemia.

Patients receiving corticosteroid therapy

Hyperglycemia is a common complication of corticosteroid therapy, with prevalence between 20% and 50% among patients without a previous history of diabetes (41). Although the optimal management of hyperglycemia in patients receiving high-dose oral corticosteroids has not been clearly defined, glycemic monitoring for at least 48 hours is recommended for patients with or without a history of diabetes (5). For management, insulin is generally preferred, with an emphasis on adjusting bolus insulin doses. Depending on the glucose monitoring results, gradual, persistent insulin adjustments should be made to prevent hyper- and hypoglycemia. During corticosteroid tapers, insulin dosing should be proactively adjusted to prevent hypoglycemia.

Patients using insulin pump therapy

Patients on insulin pump therapy do not necessarily need to discontinue this form of therapy while hospitalized. However, to promote a collaborative relationship between the hospital staff and the patient, and to ensure patient safety, hospitals must have clear policies and procedures in place to guide the continued use of insulin pump therapy in the inpatient setting (42). All patients admitted to hospital using insulin pumps must be assessed for their physical and mental competency to use their respective device. Patients should be asked to demonstrate or describe how to adjust their basal rate, administer a bolus dose, insert an infusion set, fill a reservoir, suspend their pump and correct a capillary BG result outside their target range. The patient should also have adequate insulin pump supplies. If the patient cannot competently demonstrate and/or describe the above-mentioned actions, insulin pump therapy should be discontinued and the patient placed on a SC insulin regimen or an IV insulin infusion.

Role of IV Insulin

Most patients with type 1 or type 2 diabetes admitted to general medical wards can be treated with SC insulin. IV insulin may be appropriate for patients who are critically ill, patients who are not eating or those who require prompt improvement in their glycemic control. Staff education is a critical component of the implementation of an IV insulin infusion protocol. IV insulin protocols should take into account the patient's current and previous BG levels (and, therefore, the rate of change in BG), and the patient's usual insulin dose. Several published insulin infusion protocols appear to be both safe and effective, with low rates of hypoglycemia; however, most of these protocols have only been validated in the ICU setting, where the nurse-to-patient ratio is higher than on general medical and surgical wards (3,43). BG determinations should be performed every 1 to 2 hours until BG stability has been demonstrated. With the exception of the treatment of hyperglycemic emergencies (e.g. DKA, hyperosmolar hyperglycemic state (HHS)), patients receiving IV insulin should receive some form of glucose (e.g. IV glucose or through TPN or enteral feeding).

Transition from IV insulin to SC insulin therapy

All patients with type 1 and type 2 diabetes should be transitioned to scheduled SC insulin therapy from IV insulin. Short- or rapid-acting insulin should be administered 1 to 2 hours before discontinuation of the IV insulin to maintain effective blood levels of insulin. If intermediate- or long-acting insulin is used, it should be given 2 to 3 hours prior to IV insulin discontinuation. Patients without a history of diabetes, who have hyperglycemia requiring more than 2 units of IV insulin per hour, should be transitioned to scheduled SC insulin therapy.

The initial dose and distribution of SC insulin at the time of transition can be determined by extrapolating the IV insulin requirement over the preceding 6- to 8-hour period to a 24-hour period. Administering 60% to 80% of the total daily calculated dose as basal insulin has been demonstrated to be safe and efficacious in surgical patients (44). Dividing the total daily dose as a combination of basal and bolus insulin has been demonstrated to be safe and efficacious in medically ill patients (44,45).

Organization of Care

Healthcare institutions should implement a program to improve glycemic control in the inpatient setting. This should include the formation of a multidisciplinary steering committee to provide educational programs, implement policies to assess and monitor the quality of glycemic management, and produce standardized order sets, protocols and algorithms for diabetes care within the institution. Order sets for basal-bolus-supplemental insulin regimens, insulin management algorithms (46,47), computerized order entry systems (48,49) and specialized nurses reviewing insulin orders (50) all have been shown to improve glycemic control and/or reduce adverse outcomes in hospitalized patients. The timely consultation of glycemic management teams has also been found to improve the quality of care provided, reduce the length of hospital stays and lower costs (51,52).

Patient self-management in the hospital setting may be appropriate for competent, adult patients who successfully self-manage their diabetes at home, have a stable level of consciousness and have the physical skills needed to self-administer insulin and perform self-monitoring of blood glucose (SMBG). For such individuals, a physician order for self-management should be written

with respect to selection of food, SMBG, self-determination and administration of insulin dose and type.

Transition from hospital to home

Patients and their family or caregivers should receive written and oral instructions regarding their diabetes management at the time of hospital discharge. The instructions should include recommendations for timing and frequency of home glucose monitoring; identification and management of hypoglycemia; a reconciled medication list, including insulin and other glucose-lowering medication; and identification and contact information for healthcare providers responsible for ongoing diabetes care and adjustment of glucose-lowering medication. Patients and their primary care providers should be aware of the need for potential adjustments in insulin therapy that may accompany adjustments of other medications prescribed at the time of discharge, such as corticosteroids or octreotide.

RECOMMENDATIONS

1. Provided that their medical conditions, dietary intake and glycemic control are acceptable, people with diabetes should be maintained on their prehospitalization oral antihyperglycemic agents or insulin regimens [Grade D, Consensus].

2. For hospitalized patients with diabetes treated with insulin, a proactive approach that includes basal, bolus and correction (supplemental) insulin, along with pattern management, should be used to reduce adverse events and improve glycemic control, instead of the reactive sliding-scale insulin approach that uses only short- or rapid-acting insulin [Grade B, Level 2 (37,38)].

3. For the majority of noncritically ill patients treated with insulin, preprandial BG targets should be 5.0 to 8.0 mmol/L in conjunction with random BG values <10.0 mmol/L, as long as these targets can be safely achieved [Grade D, Consensus].

4. For most medical/surgical critically ill patients with hyperglycemia, a continuous IV insulin infusion should be used to maintain glucose levels between 8 and 10 mmol/L [Grade D, Consensus].

5. To maintain intraoperative glycemic levels between 5.5 and 10.0 mmol/L for patients with diabetes undergoing CABG, a continuous IV insulin infusion protocol administered by trained staff [Grade C, Level 3 (60–62)] should be used.

6. Perioperative glycemic levels should be maintained between 5.0 and 10.0 mmol/L for most other surgical situations, with an appropriate protocol and trained staff to ensure the safe and effective implementation of therapy and to minimize the likelihood of hypoglycemia [Grade D, Consensus].

7. In hospitalized patients, hypoglycemia should be avoided.
   - Protocols for hypoglycemia avoidance, recognition and management should be implemented with nurse-initiated treatment, including glucagon for severe hypoglycemia when IV access is not readily available [Grade D, Consensus].
   - Patients at risk of hypoglycemia should have ready access to an appropriate source of glucose (oral or IV) at all times, particularly when NPO or during diagnostic procedures [Grade D, Consensus].

8. Healthcare professional education, insulin protocols and order sets may be used to improve adherence to optimal insulin use and glycemic control [Grade C, Level 3 (46)].

9. Measures to assess, monitor and improve glycemic control within the inpatient setting should be implemented, as well as diabetes-specific discharge planning [Grade D, Consensus].

Abbreviations:
BG, blood glucose; *CABG*, coronary artery bypass grafting; *IV*, intravenous; *NPO*, nothing by mouth.

Bedside BG monitoring

Currently, there are no studies that have examined the effect of the frequency of bedside BG testing on the incidence of hyper- or hypoglycemia in the hospital setting. The frequency and timing of bedside BG monitoring should be individualized; however, monitoring is typically performed before meals and at bedtime in patients who are eating, every 4 to 6 hours in patients who are NPO (nothing by mouth) or receiving continuous enteral feeding, and every 1 to 2 hours for patients on continuous IV insulin. Some bedside BG testing is indicated in individuals without known diabetes but receiving treatments known to be associated with hyperglycemia (glucocorticoids, octreotide, PN, enteral nutrition) (53). Healthcare institutions must implement and maintain a quality control program to ensure the accuracy of bedside BG testing (54,55). The use of meters with bar coding capability has been shown to reduce data entry errors in medical records (56). Data management programs that transfer bedside BG monitoring results into electronic records allow evaluation of hospital-wide glycemic control (57).

Safety

Hypoglycemia

Hypoglycemia remains a major barrier to achieving optimal glycemic control in hospitalized patients. Healthcare institutions should have standardized treatment protocols that address mild, moderate and severe hypoglycemia. Healthcare workers should be educated about factors that increase the risk of hypoglycemia, such as sudden reduction in oral intake, discontinuation of PN or enteral nutrition, unexpected transfer from the nursing unit after rapid-acting insulin administration or a reduction in corticosteroid dose (35).

Insulin administration errors

Insulin causes the most harm and severe adverse events of the high alert medications (58). A systems approach that includes preprinted, approved, unambiguous standard orders for insulin administration and/or a computerized order entry system may help reduce errors (59).

Other Relevant Guidelines

Pharmacotherapy in Type 1 Diabetes, p. S56
Pharmacologic Management of Type 2 Diabetes, p. S61
Hyperglycemic Emergencies in Adults, p. S72
Management of Acute Coronary Syndromes, p. S119
Treatment of Diabetes in Patients with Heart Failure, p. S126

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