practical diabetology

Management of Diabetes in Patients Undergoing Surgery

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An estimated 25% of patients with diabetes will require surgery, and advances in perioperative care of these patients allow them to safely undergo the most complicated surgical procedures (1–4). Today, more surgery is performed in an outpatient setting than ever before, and for those procedures performed on inpatients, the length of hospital stay is being shortened dramatically.

The successful perioperative management of patients with diabetes mellitus is principally a logistical challenge. Many factors are involved in determining the glycemic response to a surgical procedure. Although some of these indices may be adequately anticipated, others are difficult to predict. Insulin secretory capability, insulin sensitivity, overall metabolism, and nutritional intake may change radically from the preoperative period through the postoperative recuperation and may also differ greatly from one procedure to another. For this reason, health-care providers must be proactive in their management of hyperglycemia in patients with diabetes who are undergoing surgery. Significant hyperglycemia should be prevented because it may cause dehydration and electrolyte abnormalities, impair wound healing, and predispose to infection or diabetic ketoacidosis in patients with Type 1 diabetes mellitus (5, 6).

Preoperative Evaluation and Preparation

For any patient about to undergo a surgical procedure, it is important to evaluate and optimize cardiac, pulmonary, renal and electrolyte, and hematologic status before surgery. Additionally, for the patient with diabetes, the preoperative evaluation should focus on the chronic complications of diabetes (microvascular, macrovascular, and neuropathic), which may further potentiate operative risk (Figure 1).

Because cardiovascular disease in patients with diabetes mellitus is common and frequently underdiagnosed (7, 8), assessment of cardiac risk assumes a high priority in the preoperative evaluation. In persons with diabetes and a history of myocardial infarction or unstable angina, the risk of postoperative cardiac complications may be decreased if coronary angiography is done. If warranted, angioplasty or coronary artery bypass surgery should be performed before other elective surgery (9). Renal disease may complicate this cardiac evaluation in addition to increasing operative risk. Diabetic autonomic neuropathy may further complicate and prolong the postoperative recovery phase and has been associated with nonsurgical excess mortality.

FIGURE 1.

PREOPERATIVE ASSESSMENT OF SURGICAL CANDIDATES WITH DIABETES MELLITUS

- OPERATIVE RISK ASSESSMENT
  - Routine risk factors
    - Cardiac
    - Pulmonary
    - Renal
    - Hematologic
  - Diabetes-related risk factors
    - Macrovascular complications
    - Microvascular complications
    - Neuropathic complications
- DIABETES THERAPEUTIC REGIMEN
  - Verify diagnostic classification of diabetes
  - Pharmacologic regimen
    - Medication type
    - Dosage
    - Timing
  - Meal plan
    - Carbohydrate content
    - Timing of meals
  - Activity level
  - Hypoglycemia
    - Frequency
    - Awareness
    - Severity
- SURGERY
  - Type of surgical procedure
  - Inpatient or outpatient
  - Type of anesthesia
  - Scheduled start time
  - Duration of procedure

Although near-normal glycemic control has been recommended for elective surgical procedures (5), little evidence exists to substantiate the benefits of short-term, preoperative tight metabolic control independent of its effects on the chronic complications of diabetes. Nutritional status (5, 6) and hypertension (7) should be optimized before elective surgery if time permits. These recommendations represent the ideal, and the relative contraindications to the operative procedure must be balanced against the urgency and benefit of the procedure itself.

The attainment of glycemic control is challenged by the numerous variables important to the diabetes regimen and their interplay with the surgical procedure (for example, the variety of diabetes treatment regimens for both Type 1 and Type 2 diabetes and the many different types of surgical procedures, compounded by varying start times, durations, and anesthetic approaches). A detailed history of the patient's diabetes therapy is fundamental to anticipating the changes caused by the surgery. The physician should reconfirm the type of diabetes, because this may ultimately influence future pharmacologic requirements and the risk of metabolic complications, and obtain details about the pharmacologic regimen and the caloric prescription and carbohydrate content of the meal plan. It is important to elicit daily routines such as mealtimes, usual level of activity, and exact timing of medication (e.g., taking care to differentiate a PM insulin dose as either before supper or before bedtime) to understand in what manner routines will be disrupted in the hospital. In addition, the physician should determine what glycemic levels are associated with this regimen, the patient's degree of adherence, and the patient's experience with hypoglycemia (e.g., frequency, degree of hypoglycemia awareness, and history of recent neuroglycopenia).

The physician responsible for management of the diabetes (if other than the surgeon) should be aware of the details of the surgical procedure, in particular the inpatient or outpatient status of the procedure, the anticipated start time and duration, and the type of anesthesia administered. If the procedure is short and can be performed early in the day, and if the patient can be expected to eat shortly after the surgery, the patient's diabetes regimen can be shifted to a few hours later in the day. The easiest course of management is to perturb the diabetes routine as little as possible.

Glycemic Goals During Surgery

Surgical stress and some general anesthetics are associated with increases in counterregulatory hormones, which will result in an increase in hepatic glucose production and a decrease in peripheral glucose utilization (5, 6). This process will promote hyperglycemia in all patients with diabetes and additionally ketogenesis (and potentially ketoacidosis) in patients with Type 1 diabetes. Patients taking pharmacologic therapy, however, may also be at risk for developing hypoglycemia, especially if they have fasted preoperatively to minimize the risks of emesis and aspiration of gastric con-

tents during induction of anesthesia. To avoid being caught up in this glycemic balancing act, many physicians may unfortunately elect to permit shortterm hyperglycemia. In general, the goal for glucose control during surgery is to maintain the glucose level between 140 and 200 mg/dl to protect against hypoglycemia (5, 6, 10–18). Anticipation of the metabolic effects of surgery on glucose control is difficult and requires bedside glucose monitoring (13–15). Obviously, the more unstable the diabetes, the greater the need for frequent glucose monitoring.

Diabetes Therapy Before and During Surgery

Type 2 diabetes treated with diet alone. For those patients with Type 2 diabetes who are treated with diet alone, a retroactive approach is taken to the management of glucose control. Patients usually fast overnight, and hydration may be maintained with an intravenous solution, possibly containing dextrose. Blood glucose may be measured before and after the operative procedure and intraoperatively if the procedure is long. Hyperglycemia is treated with subcutaneous short-acting insulin (Regular or insulin lispro). In these individuals, the stress of the surgery may lead to decompensation of glycemic control, requiring more prolonged pharmacologic intervention (15). In the case of outpatient surgery, it is prudent to remind these patients before discharge from the ambulatory surgical center of the signs and symptoms of hyperglycemia and of guidelines for contacting their physician.

Type 2 diabetes treated with oral antidiabetes agents. For those patients treated with oral agents, these agents are generally administered on the day before surgery and are withheld on the day of surgery. If patients present with significant hyperglycemia, supplemental insulin should be administered to achieve better glycemic control, and the surgery may be performed if electrolyte levels are acceptable. Further correction of hyperglycemia during the perioperative period in patients previously treated with these agents should be made with insulin. If patients have inadvertently taken their medications on the operative day, more frequent glucose monitoring in addition to continuous intravenous dextrose infusion are appropriate.

Recommendations for specific agents are as follows.

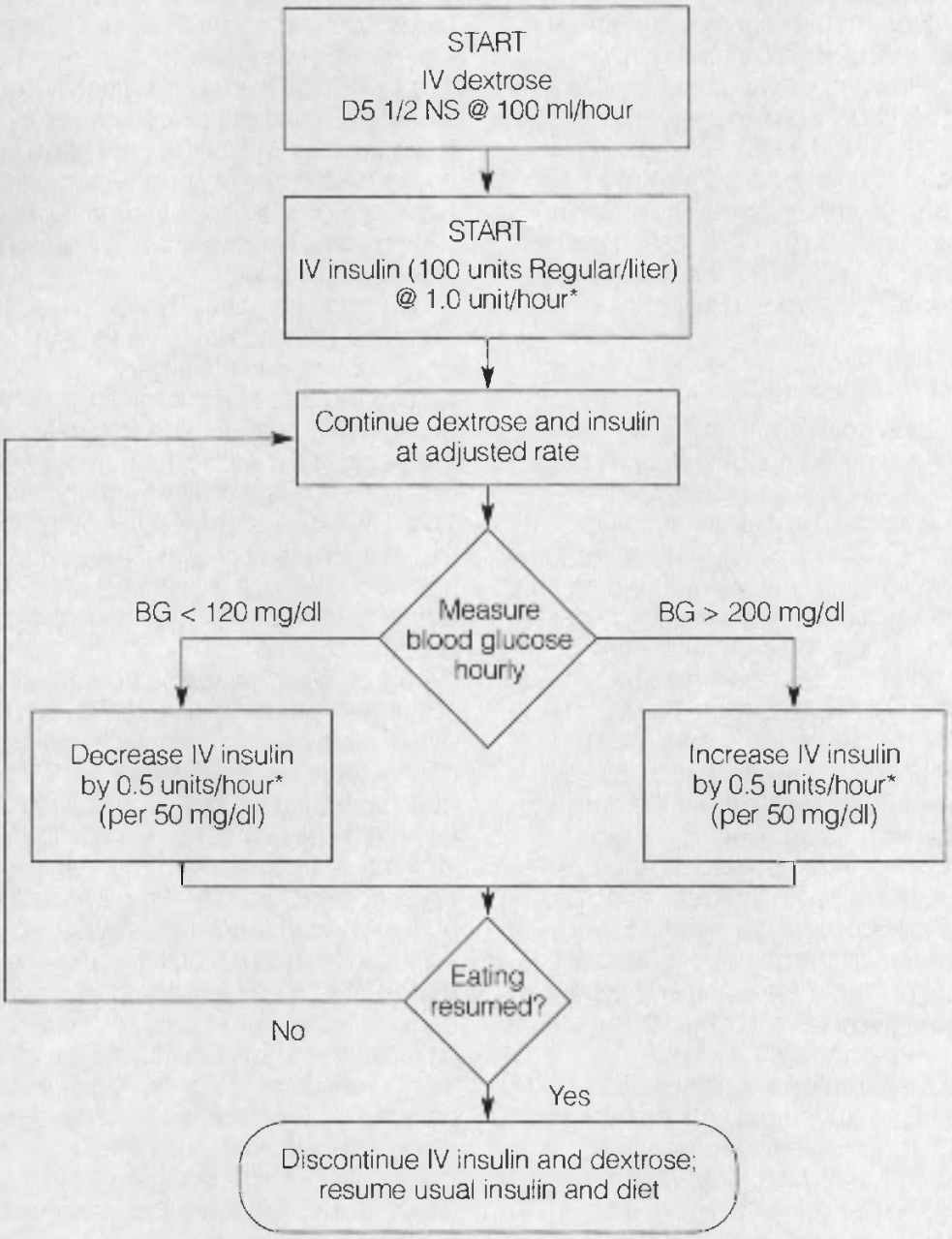
- Alpha-glucosidase inhibitors. These agents (acarbose and miglitol) are not effective in the fasting state. Therefore, there is no utility in administering an alpha-glucosidase inhibitor until the patient resumes eating.
- Biguanides. Metformin should be discontinued on the day of surgery because complications or alterations in renal function arising intraoperatively may increase the risk of lactic acidosis.
- Thiazolidinediones. This drug class (rosiglitazone and pioglitazone) may be discontinued on the day of surgery.
- Sulfonylureas and other insulin secretagogues (e.g., repaglinide and nateglinide). These agents may produce hypoglycemia during fasting associated with the surgery. This risk is dependent on the duration of action of the particular agent, but it can be minimized by glucose monitoring and administration of dextrose-containing intravenous solutions.

Type 1 or Type 2 diabetes treated with insulin. Although in many insulin-treated patients, the disease may be managed with adjustments of their routine insulin regimens (5, 6, 10–18), more control over unforeseen glycemic complications may be achieved with continuous intravenous insulin regimens. Although this approach may initially require more training of nursing staff, continuous intravenous insulin can be used effectively and safely on routine medical or surgical nursing units. Because intravenous insulin has such a short half-life (less than 20 minutes), rapid adjustments can be made in the regimen to compensate for unanticipated excursions of glucose levels. Many diabetes specialists prefer this form of management to the more conventional, reduced-dose subcutaneous insulin regimens.

On the evening before the scheduled surgical procedure, most patients require little alteration of their usual subcutaneous insulin regimen. For individuals taking long-acting insulin (i.e., Ultralente or glargine), a switch to an intermediate-acting insulin a day or two before the planned surgery is appropriate. If this cannot be accomplished, then more intensive glucose monitoring and appropriate adjustment of the dextrose infusion rate should be performed to prevent hypoglycemia and significant hyperglycemia. If patients experience

FIGURE 2.

MANAGEMENT ALGORITHM FOR SEPARATE GLUCOSE AND INSULIN INFUSIONS



NS indicates normal saline; BG indicates blood glucose.

*To adjust the insulin infusion rate for insulin resistance, multiply the insulin rate by the total daily insulin dose divided by 30 (TDI/30). To adjust the insulin infusion rate for the operative procedure, multiply the insulin rate by 2 (for renal transplantation) or 3 to 5 (for coronary artery bypass grafting).

well-controlled glycemia or AM hypoglycemia, the PM dose of intermediate-acting insulin may be decreased slightly to produce glycemic levels commensurate with the above stated intraoperative goals.

■ Intravenous insulin regimens. Intravenous Regular human insulin is definitely indicated during the perioperative period for previously insulin-treated patients undergoing long, complex operative procedures; for patients who require emergency surgery while in ketoacidosis; and for those patients with unstable Type 1 diabetes (5, 6, 10–18). In states of peripheral vasoconstriction when the subcutaneous compartment is suboptimally perfused, intravenous insulin administration

TABLE 1.

MANAGEMENT ALGORITHM FOR
SUBCUTANEOUS INSULIN FOR SHORT OPERATIVE PROCEDURES

OUTPATIENT REGIMEN	EARLY-MORNING PROCEDURE	LATE-MORNING PROCEDURE	AFTERNOON PROCEDURE
Oral agents	Delay regimen	Hold oral agents	Hold oral agents
Single-dose insulin	Delay regimen	⅔ total daily dose	½ total daily dose
2- or 3-dose insulin	Delay regimen	½ total AM dose	⅓ total AM dose
Multidose insulin	Delay regimen	⅓ AM dose	⅓ AM and lunch doses
Insulin pump	Basal rate only and delay regimen	Basal rate only	Basal rate only

ensures more controlled and effective delivery to the tissues than subcutaneous administration. Intravenous insulin may be the preferred method for insulin-treated patients because of its powerful flexibility, allowing rapid titration.

Many intravenous insulin protocols have been described and compared (12, 15, 19–27). Intravenous insulin may be administered as variable separate infusions of glucose and Regular human insulin; as variable "single solution" glucose–potassium–insulin infusions; or, least preferably, as intermittent, small intravenous boluses of Regular human insulin (every 2 hours). The superiority of any method remains controversial (25–28) because comparative evaluations have been complicated by inclusion of patients with both Type 1 and Type 2 diabetes, a wide variety of surgical procedures, and lack of randomization.

Continuous intravenous, insulin infusion rates are generally 0.5 to 5.0 units/hour, commensurate with the amount of glucose infused (6, 12, 15). This rate generally translates into infusion of 0.3 units of insulin per gram of glucose, with upward adjustments made for increasing insulin resistance.

The glucose–potassium–insulin infusion is widely used in Europe but not commonly in the United States. It may offer an advantage in its simplicity and single-solution technique (15, 19, 21, 22), but it has less flexibility in the titration of dextrose and insulin because the ratios are fixed in the single solution.

Separate continuous glucose and insulin infusions (6, 12, 27) (Figure 2) may be adjusted quickly and offer greater flexibility in responding to changes in blood glucose and ketosis. Infusion rates of insulin are adjusted to accommodate the following: alterations in blood glucose; insulin sensitivity, as reflected by the patient's preoperative total daily insulin dose; and surgical stress, as indicated by the type of operative procedure. Dextrose 5% is administered at 100 ml/hour and insulin is initiated at 1.0 unit/hour. This initial rate is modulated for the type of procedure (2- to 5-fold increase) and by an "insulin sensitivity" factor (the preoperative total daily insulin dose divided by 30) (12, 29). The insulin infusion rate may be adjusted downward to compensate for hypoglycemia or upward to counteract hyperglycemia. This incremental rate of 0.5 units/hour is also adjusted according to the patient's total daily insulin dose and the operative procedure. For a blood glucose level greater than 200 mg/dl, the increment is increased again at 50-mg/dl levels (e.g., for a blood glucose level of 325 mg/dl, the insulin infusion is increased by 1.5 units/hour to 2.5 units/hour from a starting rate of 1.0 unit/hour). Blood glucose is measured hourly, and potassium is administered as needed.

Cardiopulmonary bypass surgery presents significant challenges to diabetes management because of the stress of the procedure and because dextrose solutions are used to prime the perfusion pump. Organ transplantation is similarly challenging because of the use of immunosuppressive agents and glucocorticosteroids. Such procedures, as well as prolonged neurosurgical procedures, are probably best managed with separate glucose and insulin infusions (15).

Because the half-life of intravenous insulin is so short, continuous intravenous infusions may be preferred over intermittent intravenous bolus therapy for patients with Type 1 dia-

TABLE 2.

ALGORITHM FOR CALCULATING THE COMPENSATORY DOSE OF SUBCUTANEOUS SHORT-ACTING INSULIN

BLOOD GLUCOSE (mg/dl)	INCREMENT FORMULA	CALCULATION	SHORT-ACTING INSULIN (UNITS)
0–200	0	0	0
201–250	1 X (TDI/30)	1 X (120/30)	4
251–300	2 X (TDI/30)	2 X (120/30)	8
301–350	3 X (TDI/30)	3 X (120/30)	12
351–400	4 X (TDI/30)	4 X (120/30)	16
401–500	5 X (TDI/30)	5 X (120/30)	20
>500	Call physician	Call physician	Call physician

Calculations are based on a preoperative total daily insulin dose (TDI) of 120 units.

betes, although this strategy remains controversial when evaluated in insulin-treated patients with Type 2 diabetes (26). In the intermittent bolus technique, 10 units of Regular human insulin is administered every 2 hours and supplemented by 5 units every 60 minutes for blood glucose levels greater than 200 mg/dl (19, 25).

■ Subcutaneous insulin regimens. For early-morning procedures of short duration, after which the patient may be expected to eat according to his or her usual meal plan, it is easiest to give the morning insulin and food after the procedure. Shortening the intervals between later meals may compensate for this delay and gradually realign the patient's mealtimes back to their usual schedule. This operative schedule is the easiest for patients and physicians because it is the least disruptive to the diabetes regimen. Both the patient and physician responsible for managing the diabetes should advocate this type of operative schedule. However, all too frequently these requests cannot be fulfilled.

If surgery cannot be performed without omitting meal(s) and there is reluctance to use a continuous insulin infusion, then preoperative subcutaneous insulin should be administered (5, 6, 10–18). Using this type of regimen requires substantial logistical planning, and recommendations differ depending on the insulin regimen, the meals missed, and the timing of the surgical procedure in relation to the patient's usual insulin schedule (Table 1). Patients treated with continuous insulin infusion therapy (insulin pumps) may be managed with their usual basal infusion rate.

Diabetes Therapy After Surgery

Patients undergoing outpatient surgery may reinstitute their preoperative diabetes therapy when they resume eating. An exception to this approach exists when the procedure is performed in conjunction with iodinated radiocontrast dye in patients treated with metformin. Metformin should not be resumed for 72 hours postoperatively, at which point serum creatinine should be measured to document the absence of dye-induced renal toxicity and normal renal function.

During the postoperative period, diabetes control may be significantly unstable. Operative procedures may necessitate that patients abstain from oral intake for prolonged periods. Many patients are anorectic or may have nausea and vomiting as a result of anesthesia side effects, or they may experience postoperative complications such as ileus. During these intervals of uncertain alimentation, patients may require continued infusion of dextrose or parenteral nutrition for more prolonged periods. Dextrose infusion rates should be sufficient to prevent hypoglycemia and ketosis, at 5–10 g glucose per hour (6). Total daily insulin requirements under these circumstances depend on the rate of administration of dextrose solution and the patient's level of metabolic stress.

If subcutaneous insulin is preferred in this setting, divided doses of intermediate-acting insulin (twice daily) or short-acting insulin (four to six times per day) can be supplemented by subcutaneous insulin doses calculated by an algorithm to compensate for hyperglycemia.

The increment for the insulin algorithm is determined empirically from the patient's total daily dose of insulin, as described previously. The increment to compensate for hyperglycemia above the target glucose level is calculated as the total daily dose divided by 30 for every 50 mg/dl above the goal (Table 2). For those patients treated intraoperatively with intravenous insulin infusions, it is easiest to continue the intravenous insulin along with the dextrose infusion until these patients resume eating (Figure 1). When eating is reliably resumed, the infusions may be discontinued and the usual diabetes regimen (oral agents or insulin) may be reinstated.

Conclusions

The glycemic response in the perioperative period is highly variable and often a challenge to anticipate. There are many different approaches to managing perioperative diabetes, and none demonstrate any clear superiority. Technologically sophisticated methods, such as intravenous insulin infusions with frequent blood glucose monitoring, may be expensive and labor-intensive and often may not be necessary. Although various strategies have been reviewed, managing patients with diabetes who are undergoing surgery remains more art than science, and good clinical judgment is the key to success.

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