Perioperative Management of Diabetes

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Maintaining glycemic and metabolic control is difficult in diabetic patients who are undergoing surgery. The preoperative evaluation of all patients with diabetes should include careful screening for asymptomatic cardiac or renal disease. Frequent self-monitoring of glucose levels is important in the week before surgery so that insulin regimens can be adjusted as needed. Oral agents and long-acting insulin are usually discontinued before surgery, although the newer long-acting insulin analog glargine may be appropriately administered for basal insulin coverage throughout the surgical period. The usual regimen of sliding scale subcutaneous insulin for perioperative glycemic control may be a less preferable method because it can have unreliable absorption and lead to erratic blood glucose levels. Intravenous insulin infusion offers advantages because of the more predictable absorption rates and ability to rapidly titrate insulin delivery up or down to maintain proper glycemic control. Insulin is typically infused at 1 to 2 U per hour and adjusted according to the results of frequent blood glucose checks. A separate infusion of dextrose prevents hypoglycemia. Potassium is usually added to the dextrose infusion at 10 to 20 mEq per L in patients with normal renal function and normal preoperative serum potassium levels. Frequent monitoring of electrolytes and acid-base status is important during the perioperative period, especially in patients with type 1 diabetes because ketoacidosis can develop at modest levels of hyperglycemia. (Am Fam Physician 2003;67:93-100. Copyright© 2003 American Academy of Family Physicians.)

Diabetic patients who require surgery present special challenges in perioperative management. Special attention must be paid to prevention and treatment of metabolic derangements. Vigilance for the development of acute complications that lead to higher rates of surgical morbidity and mortality is also critical.

Maintaining Glycemic Control

Glycemic control is maintained by a balance between insulin and the counterregulatory hormones glucagon, epinephrine, cortisol, and growth hormone. Insulin stimulates glucose uptake and utilization by muscle and fat tissue. It also suppresses hepatic glucose production from gluconeogenesis and glycogenolysis. Insulin prevents development of ketosis and protein breakdown. During the perioperative period, adequate insulin must be present to prevent metabolic decompensation.

Perioperative Response to Surgery and Anesthesia

Surgery and anesthesia invoke a neuroendocrine stress response with release of counterregulatory hormones,[1] which results in peripheral insulin resistance, increased hepatic glucose production, impaired insulin secretion, and fat and protein breakdown, with potential hyperglycemia and even ketosis in some cases. The degree of this response depends on the complexity of the surgery and any postsurgical complications.

In addition to counter-regulatory hormone excess and relative insulin deficiency, fasting and volume depletion contribute to metabolic decompensation.[2] Diabetic ketoacidosis occurs infrequently in patients with type 2 diabetes, but hyperglycemic hyperosmolar nonketotic states are well described. The latter are characterized by extreme hyperglycemia, hyperosmolarity, volume depletion, and associated changes in mental status resulting from inadequate insulin action, osmotic diuresis, fluid losses from surgery or overuse of diuretics, and volume under-replacement.[3] In patients with type 1 diabetes, diabetic ketoacidosis may develop in the absence of severe hyperglycemia because of inadequate insulin availability during a time of increased demand.

Hyperglycemia inhibits host defenses against infection,[4-6] including many leukocyte functions.[7-10] Hyperglycemia also impairs wound healing because of its detrimental effects on

Hyperglycemia inhibits host defenses against infection and impairs wound healing.

collagen formation and resulting diminished wound tensile strength.[11,12]

Preoperative Evaluation

In elective surgical procedures, potential problems should be identified, corrected, and stabilized before surgery. Preoperative evaluation includes assessment of metabolic control and any diabetes-associated complications, including cardiovascular disease, autonomic neuropathy, and nephropathy, which could affect the surgical outcome.

Asymptomatic cardiac ischemia occurs relatively often in patients with diabetes.[13] The presence of cardiovascular risk factors should prompt a thorough evaluation. At minimum, resting electrocardiography should be performed, but a stress test is often justified if there is suspicion for cardiovascular disease. Cardiac autonomic neuropathy may predispose patients to perioperative hypotension,[14] so the presence of resting tachycardia, orthostatic hypotension, peripheral neuropathy, and loss of normal respiratory heart rate variability should be sought.

Serum creatinine levels should be measured, but they are not a sensitive indicator of early renal dysfunction, which is usually advanced before an elevation in creatinine develops. Kidney function can be estimated by using creatinine clearance formulas but, if a high index of suspicion for renal impairment exists, a measured creatinine level from a 24-hour urine collection is the best gauge of renal function. Diabetic patients with proteinuria or abnormal creatinine clearance have a greater risk of developing acute renal failure.

GLYCEMIC CONTROL

Establishing good glycemic control and correcting any other metabolic abnormalities are usually accomplished on an outpatient basis before surgery because most patients are hospitalized just before surgery.

To stabilize glycemic control in patients taking insulin, frequent glucose monitoring should be performed, with insulin dosages adjusted appropriately. Ideally, patients should monitor blood glucose levels before meals, after meals, and at bedtime. Long-acting insulin (e.g., ultralente, glargine [Lantus]) can be discontinued one to two days before surgery, and glucose levels can be stabilized with a regimen of intermediate insulin (e.g., NPH, lente) mixed with short-acting insulin (e.g., regular, lispro [Humalog] or aspart [Novolog]) twice daily or short-acting insulin before every meal. However, on the day before surgery, long-acting insulin can be continued throughout the day if the patient's control is good, particularly if the patient is using glargine. Since this newer insulin analog maintains a stable level throughout the day, more experience with its use may demonstrate its safety as a basal insulin throughout the perioperative period.

Oral agents are generally discontinued before surgery. Long-acting sulfonylureas (e.g., chlorpropamide [Diabinese]) are stopped 48 to 72 hours before surgery, while short-acting sulfonylureas, other insulin secretagogues, and metformin [Glucophage] can be withheld the night before or the day of surgery. No recommendations exist for discontinuation of thiazolidinediones (e.g. rosiglitazone [Avandia], pioglitazone [Actos]) before surgery; their extremely long duration of action probably indicates no rationale for stopping them at all.

In patients with good metabolic control who are undergoing relatively minor surgery, antihyperglycemic treatment may not be needed on the day of surgery. Otherwise, insulin will generally be used.

EVALUATION FOR EMERGENCY SURGERY

Many patients with diabetes who require emergency surgery will not be in good meta-

bolic control at that time and may even have diabetic ketoacidosis. The first priority is to assess glycemic, acid-base, electrolyte, and fluid status, and correct any derangements before surgery. This step is especially critical if acidosis or potassium abnormalities are present. Surgery should be delayed, if possible, to stabilize metabolic status. *Table 1* presents considerations to bear in mind in preparing patients with diabetes for emergency surgery.

Intraoperative Management

INSULIN

All patients with type 1 diabetes and many with type 2 diabetes require insulin intraoperatively to maintain glycemic control. Patients with type 2 diabetes who are chronically treated with only diet or small doses of oral agents and who are in good control (fasting blood glucose level of less than 140 mg per dL [7.78 mmol per L]) before surgery may not require insulin if the surgery is relatively short. In many situations, including chronic poor control or complicated surgical procedures, patients with type 2 diabetes benefit from insulin treatment to maintain glycemic control.

The best method of providing insulin during surgery is debatable. Few data clearly demonstrate the superiority of one regimen over another. Any regimen should (1) maintain good glycemic control to avoid hyperglycemia and hypoglycemia; (2) prevent other metabolic disturbances; (3) be relatively easy to understand; and (4) be applicable to a variety of situations (operating room, recovery room, and general medical and surgical wards). The key to success of any regimen is careful, frequent monitoring to detect any alterations in metabolic control and correct them before they become severe.

While sliding-scale use of subcutaneous insulin has long been a standard method of glucose control in hospitalized patients, many diabetes authorities have recently promoted the use of a variable-rate intravenous (IV) insulin infusion as a more effective approach to perioperative diabetic management.[2,6,15-17] The success of IV insulin infusion lies in its simplicity and the more predictable absorption compared with that of subcutaneous injections. IV insulin infusion uses a simple algorithm to maintain glycemic control over a wide range of insulin requirements.

Most oral diabetes medications are stopped the night before or the morning of surgery, and short-acting insulin is used during the perioperative period.

The goal is to maintain blood glucose levels within a target range (e.g., 120 to 180 mg per dL [6.67 to 10 mmol per L]) during the perioperative period. In a patient with type 1 diabetes, the insulin infusion is started at a rate of 0.5 to 1 U per hour. In a patient with poor control or in one with type 2 diabetes,

TABLE 1
Minimizing the Risks of Emergency Surgery in Patients with Diabetes

Preoperative assessment
Metabolic status: immediate measurement of plasma glucose, pH, creatinine, BUN, electrolytes
Volume status: check for orthostasis, elevated BUN and/or creatinine, urine output
Cardiac status: ECG
Preoperative treatment
Delay surgery if possible until metabolic control and volume status are stabilized.
Maximize glucose, electrolyte, and acid-base status.
Insulin and glucose infusions
Saline infusion if volume is depleted, depending on renal function and cardiac status
Potassium infusion if renal function is normal and serum potassium is normal or low
Bicarbonate infusion only in patients with severe acidosis

BUN = blood urea nitrogen; ECG = electrocardiograph.

Intravenous infusions of insulin provide more predictable absorption than subcutaneous injections.

the starting dose is usually higher, about 2 to 3 U per hour or more. The rate of infusion is adjusted according to a glucose feedback algorithm based on hourly glucose readings. An example of variable rate IV insulin infusion is shown in *Table 2*.

Some protocols also include an algorithm for glucose infusion adjustment.[15] The glycemic target range can be adjusted in particular situations, if needed. In general, however, blood glucose levels above 200 mg per dL (11.1 mmol per L) or below 100 mg per dL (5.56 mmol per L) should be avoided to minimize risks associated with hyperglycemia and hypoglycemia.

Another approach utilizes a single, continuous glucose-insulin-potassium (GIK) infusion.[18] A problem with this method is the inability to independently adjust the insulin and glucose delivery rates as may be required. A new concentration of solution must be prepared if the ratio of insulin to glucose has to be changed. Once the blood glucose level is stabilized, however, the GIK infusion and glycemic control can be simply maintained with this technique.

Subcutaneous insulin injection is frequently used for perioperative management in patients with diabetes. One half the usual dose of long- or intermediate-acting insulin is injected the morning of surgery. This approach can be fraught with problems, how-

TABLE 2
Variable Rate Intravenous Insulin Infusion

Mix 100 U short-acting insulin in 100 mL normal saline (1 U = 1 mL)
Start insulin infusion at 0.5 to 1 U per hour (0.5 to 1 mL per hour)*
Start a separate infusion of 5 percent dextrose in water at 100 to 125 mL per hour
Monitor blood glucose hourly (every two hours when stable) and adjust insulin infusion rate according to the following algorithm:

Blood glucose level, mg per dL (mmol per L)†	*Action*
Below 70 (3.89)	Turn off insulin infusion for 30 minutes, recheck blood glucose level. If blood glucose level is still below 70, give 10 g glucose and recheck blood glucose level every 30 minutes until the level is above 100 (5.56), then restart infusion and decrease rate by 1 U per hour.
71 to120 (3.94 to 6.67)	Decrease insulin infusion rate by 1 U per hour
121 to 180 (6.72 to 10.0)	Continue insulin infusion as is
181 to 250 (10.1 to 13.89)	Increase insulin infusion rate by 2 U per hour
251 to 300 (13.94 to 16.67)	Increase insulin infusion rate by 3 U per hour
301 to 350 (16.72 to 19.4)	Increase insulin infusion rate by 4 U per hour
351 to 400 (19.5 to 22.2)	Increase insulin infusion rate by 5 U per hour
Above 400 (22.2)	Increase insulin infusion rate by 6 U per hour

**—Glucose infusion rate can also be increased if tendency toward hypoglycemia persists.*
†—Target blood glucose range is 120 to 180 mg per dL (6.67 to 10.0 mmol per L).

ever. Unpredictable absorption, a difficulty under normal circumstances,[19] may be worse because of changes in tissue perfusion that occur in the perioperative period and may be of particular concern in obese patients.[20] A delay in or prolongation of surgery can result in deterioration of control if the insulin reserve is exhausted before the procedure is performed. However, if hourly glucose monitoring cannot be guaranteed perioperatively, this approach will be relatively safe if the procedure is short.

Glucose should be checked as often as is feasible (e.g., every two hours), and a slow glucose infusion (i.e., 100 to 125 mL per hour in 5 percent dextrose) should be maintained to prevent hypoglycemia. Hyperglycemia can be treated with small periodic doses of a short-acting insulin or analog: regular insulin every four to six hours or lispro every two hours in doses of 0.05 to 0.1 U per kg.

Future experience with glargine will establish whether this long-acting insulin analog, with effects that last for up to 24 hours, will be a useful basal insulin for perioperative glucose management.[21] Use of continuous glucose monitoring systems, as they become more widely available, will make the difficulties of performing frequent glucose measurements obsolete.

Patients on continuous subcutaneous insulin infusion pumps receive only short-acting (regular or lispro) insulin and are easily converted to an IV insulin infusion during surgery. For very short procedures or those using local anesthesia, it may be feasible to continue using the patient's insulin pump but, as described above, problems with subcutaneous insulin infusion can arise.

In patients with type 2 diabetes in good control who will not be given insulin during a surgical procedure, glucose levels should be measured approximately every two hours, and insulin therapy should be initiated if the glucose level approaches 180 to 200 mg per dL. Glycemic control can easily deteriorate in the otherwise well-controlled patient undergoing surgery because of metabolic stress responses. Obesity, sepsis, steroid administration, poor preoperative metabolic control, and recent ketoacidosis also increase perioperative insulin requirements.[22]

Patients with diabetes should receive approximately 5 g of glucose per hour (i.e., 5 percent dextrose solution in water infused at 100 mL per hour) during surgery to prevent the development of hypoglycemia, ketosis, or protein breakdown.

GLUCOSE, FLUID, AND ELECTROLYTE MANAGEMENT

Most authorities recommend that patients with diabetes be given about 5 g of glucose per hour for basal energy requirements and to prevent hypoglycemia, ketosis, and protein breakdown during surgery. More glucose may be needed if conditions are very stressful.[2,23] The choice of dextrose concentration in the IV fluid is based on the anticipated duration of administration and patient restrictions. For example, 5 percent dextrose (contains 50 g glucose per L) in water or 0.45 percent saline at 100 mL per hour is appropriate for relatively short or minor procedures. For longer procedures, using 10 percent dextrose (contains 100 g glucose per L) at 50 mL per hour will avoid excessive fluid administration. A 20 or 50 percent dextrose solution can be given through a central line if fluid restriction is critical. If additional fluids are needed (e.g., to replace blood loss and maintain hemodynamic stability), they should be non–dextrose-containing solutions.

Potassium levels should be monitored at least before and after surgery, remembering that a normal serum potassium level does not necessarily reflect a normal total body potassium concentration. A number of factors can influence serum potassium levels during surgery. Insulin and epinephrine stimulate potassium uptake into cells while hyperosmolarity causes translocation of potassium

out of cells and into the extracellular space. Acidosis can result in hyperkalemia related to the exchange of intracellular potassium for extracellular hydrogen ions. In patients with diabetes with normal renal function and normal serum potassium levels, 10 to 20 mEq per L (10 to 20 mmol per L) of potassium should be added per liter of dextrose-containing fluid. More potassium is given if hypokalemia is present. In patients with hyperkalemia, potassium is not given unless the level falls into the normal range.

Postoperative Management

Postoperatively, "sliding scale" subcutaneous insulin schemes are frequently used with short-acting insulin given to correct elevations in measured glucose above a certain level. This approach presents several problems. First, such schemes delay providing insulin until hyperglycemia is present and tend to promote swings in glucose control—high and low.[24] Sliding scale schemes should never be the sole insulin administration regimen in patients with type 1 diabetes because the development of diabetic ketoacidosis is possible before significant hyperglycemia is present. It is important to remember that patients with type 1 diabetes have basal insulin requirements that must be met, even during fasting, to maintain metabolic control.

Use of variable rate insulin infusion in the postoperative period affords the same advantages as noted previously during the intraoperative period. Glucose is measured every one to two hours, and the infusion is adjusted according to the algorithm. Serum electrolytes should be measured postoperatively and daily for as long as the insulin infusion continues, which should be until the patient is ready to resume solid-food intake. When food is given for breakfast or lunch, the patient's usual dose of morning subcutaneous insulin can be given before the meal, and the infusion can be discontinued two hours later. If supper will be the first solid meal, the evening dose of insulin is given in a similar fashion.

In patients who were not previously treated with insulin but who demonstrate a need for insulin during this period, a subcutaneous regimen totaling 0.5 to 0.7 U per kg of body weight is used. This total dose is divided into short-acting insulin before each meal or a combination of intermediate insulin twice daily and short-acting insulin before each meal. Glargine may be a useful basal insulin during this period.

Continuing the insulin infusion while patients are on a liquid diet is preferable. First, caloric intake is likely to be low, and hypoglycemia will be a risk if subcutaneous insulin is being absorbed in the presence of limited amounts of food. Second, liquid diets often have high carbohydrate contents and are consumed in a "grazing" manner throughout the day rather than in meal patterns. This can predispose patients to hyperglycemia and hypoglycemia if the subcutaneous insulin absorption does not match the timing of food absorption. Note that the insulin infusion is discontinued one to two hours after the first subcutaneous dose to prevent a gap in insulin coverage that could lead to loss of metabolic control.

Outpatient Surgery

Currently, many surgical procedures are performed on an outpatient basis. Anesthesia, pain, and anxiety can still invoke minor stress

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reactions and metabolic decompensation. But, by definition, the procedures are minor, and local anesthesia is generally used. Acceptable management of patients with type 1 and type 2 diabetes can be variable-rate IV insulin infusions or subcutaneous insulin strategies. In patients with type 2 diabetes who are taking oral agents, the same management guidelines should be followed as described for elective surgical procedures.

Patients should be given guidelines for postoperative self-monitoring of blood glucose levels that are appropriate to their type of diabetes. In patients taking insulin, glucose monitoring should take place approximately every two hours for several hours, with algorithms for supplemental insulin administration. In patients with type 2 diabetes, monitoring every four hours is usually sufficient, with instructions to call a physician if glucose levels persistently exceed 250 mg per dL (13.9 mmol per L). When a normal or near-normal dietary regimen is resumed, most patients can also resume their preoperative diabetic management regimen.

Final Comment

Although opinions differ, and little data are available to allow specifying optimal treatment goals or the best approach to perioperative management of diabetes, it is clear that surgical outcomes are improved in patients with diabetes who are maintained in good metabolic control. Physicians must be cognizant of patients' preoperative control, their relative need for insulin, and any factors that may be likely to increase insulin requirements.

When insulin requirements are in doubt, it is better to err on the side of providing rather than withholding insulin. The administration of adequate glucose in conjunction with the judicious use of insulin will prevent hypoglycemia. Diabetic ketoacidosis or hyperosmolar states, which may result from inadequate dosing of insulin, are not so easily managed. The key to success of any perioperative management plan is frequent monitoring of glucose, electrolyte, and fluid levels, and acid-base status. Prevention of surgical complications as a result of hyperglycemia is possible with meticulous perioperative glucose management.

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