Perioperative Management of Surgical Patients with Diabetes Mellitus

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Despite our technical ability to nearly normalize blood glucose concentrations in many patients with in-

sulin-dependent diabetes mellitus (IDDM) or non–insulin-dependent diabetes mellitus (NIDDM), longstanding diabetes leads to a number of complications that require surgical intervention. During the 1960s, it was estimated that diabetic patients had a 50% chance of undergoing surgery at some time during their life.¹ Due to advances in medical and surgical therapies, it is likely that diabetic individuals have an even greater chance of undergoing surgery today. Vitrectomy, cataract extraction, kidney transplantation, penile prosthesis implantation, ulcer debridement, and vascular repairs are commonly performed on diabetic patients. Furthermore, they are subject to the same operations required by nondiabetic patients.

There are several reasons to attempt to stabilize plasma glucose concentrations in the perioperative period. In the case of IDDM, inadequate control of blood glucose levels can lead to ketosis and acidemia, and all patients with glucose intolerance are susceptible to electrolyte abnormalities and volume depletion from osmotic diuresis. There are also data indicating impaired wound strength and wound healing—when plasma glucose levels are greater than 11.1 mm (200 mg/dl). In addition, hyperglycemia interferes with leukocyte chemotaxis, opsonization, and phagocytosis.² Both animal and human studies also suggest that hyperglycemia exacerbates ischemic brain damage.³–⁵ Although one study showed no difference in morbidity (or mortality) in diabetic patients after vascular surgery,⁶ many other studies have reported increased mortality during surgery in patients with diabetes.⁷–⁹ Despite the technical ability to nearly normalize glycemia, prospective data comparing surgical outcomes following improved blood glucose control during the perioperative period are not available.

Adapting a diabetic patient’s therapeutic regimen to accommodate a surgical procedure is a challenging problem. Unfortunately, there is no consensus on the optimal manner in which to manage the metabolic changes that occur during surgery in patients with diabetes.¹⁰–¹³ The objective of this article is to review the various options available to the anesthesiologist caring for a patient with diabetes.
Metabolic Effects of Surgery and Anesthesia

Hormones play a key role in the regulation of metabolic pathways (table 1). A simplified approach is to consider insulin the prime anabolic hormone, and epinephrine, glucagon, cortisol, and growth hormone (GH) as the main catabolic (or counterregulatory) hormones. After a meal, insulin is secreted and promotes glucose uptake and glycogen formation by insulin-sensitive tissues (liver and muscle). Insulin also stabilizes fatty acid transport and triglyceride synthesis in adipose tissue and amino acid transport and protein synthesis in muscle. However, insulin also has significant antineoplastic effects. For example, it inhibits glycogenolysis, gluconeogenesis, and ketogenesis in the liver; inhibits lipolysis in adipose tissue; and inhibits protein catabolism in muscle. In the fasting state, the insulin level decreases and the counterregulatory hormones are secreted at relatively high rates to provide a continuous supply of glucose, fatty acids, and ketone bodies. Insulin deficiency, as in patients with IDDM, leads to a total loss of these anabolic and antineoplastic effects and can eventually lead to diabetic ketoacidosis (DKA).

As indicated in table 1, cortisol and GH have the ability to produce anabolic effects as well as their well-known catabolic actions. For example, GH has anabolic effects directed at protein preservation. Like insulin, cortisol causes glycogen deposition, and cortisol is also anabolic with respect to fat metabolism. Glucagon, in contrast, has no known physiologic effects on protein and lipid anabolism. Besides stimulating glycogenolysis and gluconeogenesis, glucagon stimulates hepatic ketogenesis. Finally, the catecholamines are not catabolic with regard to protein breakdown. For example, an epinephrine infusion will decrease proteolysis and thereby reduce circulating amino acids (except alanine) levels.

Surgery produces a stress response that is a function of the degree of trauma and can be modified by anesthesia. Hyperglycemia intraoperatively or postoperatively is not uncommon in nondiabetic patients. The hormonal etiology of this hyperglycemic state includes (relative) insulin hyposecretion and insulin resistance. The precise cause of the latter phenomenon is unclear, but it is believed to be due largely to elevated counterregulatory hormone levels. Catecholamines increase are common during surgery, although this too is modified depending on the anesthetic regimen. Adrenocorticotrophic hormone (ACTH) and cortisol levels are also elevated to varying degrees during the peroperative period. Similarly, in most studies, GH has been shown to be increased peroperatively. Glucagon levels have been the most variable of the counterregulatory hormones in measurement: decreases, increases, and stable levels have been reported. However, changes in hepatic portal venous glucagon concentrations have not been studied, and glucagon assays can include cross-reacting, biologically inactive species. Thus, one would expect the peroperative hormonal milieu to result in protein and fat breakdown. However, glyceral and free fatty acid (FFA) concentrations are lower in surgical patients than in subjects not undergoing surgery and fasted for a similar period. This relative impairment of lipolysis is most likely due to increased insulin levels, a result of insulin resistance.

These catabolic effects compound the state of absolute insulin deficiency and can potentially lead to metabolic decompensation in the patient with IDDM. Although plasma glucose elevations may be only modest if sufficient insulin and fluids are given and renal function is adequate, clinically important lipolysis can lead to ketosis and acidosis in the peroperative period. It is possible for a patient with IDDM to develop an acidemia with a plasma glucose concentration that is only moderately elevated. Indeed, 17% of all diagnoses of DKA are in patients with plasma glucose concentrations less than 16.7 mM (300 mg/dl), and values less than 5.6 mM (100 mg/dl) have been reported. This phenomenon is called “euglycemic DKA.” Although less marked in the patient with NIDDM, changes in protein and fat metabolism can occur in more severely affected patients as a result of the inability to increase insulin secretion in response to the surgery-in-

### Table 1. Metabolic Effects of Anabolic and Catabolic Hormones

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Anabolic Effects</th>
<th>Catabolic Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Glycogenesis</td>
<td>Lipogenesis</td>
</tr>
<tr>
<td>Insulin</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>Glucagon</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>Cortisol</td>
<td>+/−</td>
<td>+/−</td>
</tr>
<tr>
<td>Growth hormone</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

* Effects increased with nonphysiologic concentrations.
† Effects important in the absence of insulin.
duced hyperglycemia. In both groups of patients, frequent monitoring of plasma glucose and urinary ketones is required to avoid metabolic deterioration.

It appears that central neural blockade has only a limited impact on metabolic function. No significant changes have been noted in blood glucose, lactate, alanine, FFA, glycerol, and ketones during epidural anesthesia.\footnote{Available data also suggest that epidural anesthesia has no clinically important effect on plasma cortisol and GH levels.} Plasma epinephrine and norepinephrine concentrations decrease in proportion to the level of sensory analgesia during spinal anesthesia with tetracaine.\footnote{The insulin response to hyperglycemia appears to be inhibited by a high thoracic (T2–T6) blockade, whereas a low blockade (T9–T12) has no effect on insulin secretion. These earlier studies are supported by a more recent report, which showed a marked amelioration of the metabolic and endocrine response to surgery in patients given a splanchnic nerve block.} The insulin response to hyperglycemia appears to be inhibited by a high thoracic (T2–T6) blockade, whereas a low blockade (T9–T12) has no effect on insulin secretion. These earlier studies are supported by a more recent report, which showed a marked amelioration of the metabolic and endocrine response to surgery in patients given a splanchnic nerve block.\footnote{The insulin response to hyperglycemia appears to be inhibited by a high thoracic (T2–T6) blockade, whereas a low blockade (T9–T12) has no effect on insulin secretion. These earlier studies are supported by a more recent report, which showed a marked amelioration of the metabolic and endocrine response to surgery in patients given a splanchnic nerve block.}

**Treatment Goals for the Diabetic Patient during the Perioperative Period**

In order to minimize morbidity in the diabetic patient undergoing elective surgery, the anesthesiologist should mimic normal metabolism as closely as possible by avoiding hypoglycemia, excessive hyperglycemia, lipolysis, ketogenesis, protein catabolism, and electrolyte disturbances. This goal is best achieved by providing adequate insulin to counterbalance the catabolic response described above. Adequate glucose should be provided to meet the increased requirements of the surgical stress in addition to basal caloric requirements. Finally, a regimen that is simple and minimizes the possibilities of error in administration must be devised.

**Insulin-dependent Diabetes Mellitus: Elective Surgery**

**Preoperative Issues**

Although many protocols have been suggested for the perioperative management of patients with IDDM, only a few prospective studies have compared two or more treatment regimens.\footnote{However, there are several preoperative issues that need to be considered before the patient is taken to surgery (table 2).} Since surgery is associated with a variety of potentially deleterious metabolic effects, preoperative evaluation and treatment to correct hyperglycemia and electrolyte abnormalities are imperative. Earlier reviews suggested admitting patients with IDDM 48–72 h before surgery to improve metabolic control and to assess cardiovascular status.\footnote{However, the high costs involved limit this option. Indeed, many diabetic patients now are admitted on the morning of surgery. With the widespread use and accessibility of home blood glucose monitoring, it usually is possible to correct serious hyperglycemia without hospital admission.}

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**Table 2. Preoperative Management for Patients with IDDM Scheduled for Elective Surgery**

| 1. | Frequent home blood glucose monitoring before admission to hospital or ambulatory surgical unit |
| 2. | Preoperatively, assess metabolic, renal and cardiac status (electrolytes, blood glucose and creatinine, urine dipstick for ketones and protein, EKG) |
| 4. | For patients with excessive hyperglycemia (blood glucose concentration >16.6 mmol/L, or electrolyte abnormalities, suggest preadmission to hospital for insulin infusion therapy (glucose-insulin-potassium infusion or variable-rate insulin infusion); arterial blood gases should be measured for these patients |
| 5. | Bedside capillary glucose levels should be measured every one hour after the insulin infusion is started |
| 6. | Sufficient glucose (e.g. 5–10 g/h) and potassium (e.g. 2–4 mEq/h) need to be administered to prevent hypoglycemia and hypokalemia |

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Given the high prevalence of cardiovascular disease in the diabetic population, it is not surprising that one series found the most common cause of perioperative mortality to be coronary artery disease (29%).\footnote{In addition, end-stage renal disease from diabetic nephropathy will develop in about 35% of patients with IDDM. Therefore, preoperative assessment should include basic renal and cardiovascular testing (e.g., urinalysis, electrolyte panel, and ECG). For the former, a serum creatinine test alone is not sufficient since its level usually remains normal until renal disease is advanced.\footnote{Minimum renal function testing therefore should also include urinary dip-stick determination for proteinuria. The existence of proteinuria, even with a normal serum creatinine level, should make the anesthesiologist consider other less harmful agents when potentially nephrotoxic drugs are considered (e.g., aminoglycosides). Finally, a recent report suggests that diabetic patients should also be screened for autonomic neuropathy prior to surgery, since this population is at high risk for developing perioperative hypotension.\footnote{This can be accomplished by measuring variation in RR (interval between QRS complexes on an ECG) during deep breathing, heart rate response to Valsalva's maneuver, and the blood pressure and heart rate response to standing.\footnote{The regimen for achieving optimal preadmission glycemic control is arbitrary. Most patients with IDDM take two injections of intermediate-acting (NPH or Lente) and short-acting (regular) insulin each day. There has been an increase in use of long-acting (Ultralente) insulin over the past few years. The animal preparations of this insulin have a duration of 36 h, and provide "basal" serum insulin levels throughout the day. The human Ultralente preparation has a shorter profile, one that persists}}}}

The regimen for achieving optimal preadmission glycemic control is arbitrary. Most patients with IDDM take two injections of intermediate-acting (NPH or Lente) and short-acting (regular) insulin each day. There has been an increase in use of long-acting (Ultralente) insulin over the past few years. The animal preparations of this insulin have a duration of 36 h, and provide "basal" serum insulin levels throughout the day. The human Ultralente preparation has a shorter profile, one that persists...
for 24 h, with a broad peak lasting 12–16 h. Preoperatively, one may wish to stop the Ultralente insulin 3 days prior to surgery and switch to an intermediate-acting insulin. However, some would consider this inconvenient, and no studies have documented perioperative problems with long-acting insulin preparations.

Earlier admission may be required for an individual patient, especially if he or she is acidic or if there are major electrolyte disturbances. Most patients with poorly controlled diabetes can be “fine-tuned” 12 h prior to elective surgery (table 2). Therefore, preadmission should be considered only for those patients with poorly controlled IDDM.

**INSULIN**

Use of a continuous intravenous (iv) insulin infusion is the most rational way to manage a patient with IDDM before, during, and immediately after major surgery. Numerous factors affect serum insulin concentrations after subcutaneous (sc) injection of insulin. In addition, there are marked intra- and intersubject variations in insulin absorption after sc insulin injection. Although the effects of surgery on sc insulin have not been studied, it seems reasonable to assume that the fluid shifts and hemodynamic changes that occur during and after surgery would alter cutaneous blood flow and result in highly unpredictable differences in serum insulin concentrations.

The safety of an iv insulin infusion has been demonstrated by many authors. Nevertheless, only a few investigators have studied the blood glucose concentration differences after iv compared to sc insulin administration. In one of their earlier reports, Alberti and Thomas showed clear improvements in plasma glucose and ketone body concentrations with a glucose–insulin–potassium (GIK) infusion compared to sc insulin. Pezzarossa et al. later demonstrated that iv insulin administration offered better glycemic control compared to the “standard” sc insulin administration during the intraoperative period, whereas it did not offer any advantages over the sc route during the pre- and postoperative periods. These investigators stated that their infusion of glucose (10 g · h⁻¹), potassium chloride (2 mmol · h⁻¹), and insulin was easily applicable without the aid of a diabetologist.

In another study, Watts et al. showed a wide range of insulin requirements (0.5–5.0 U · h⁻¹) during insulin infusion, based on an algorithm-dependent program in a group of patients with IDDM and NIDDM. Within 8 h, the mean blood glucose level was within the target range of 5.7–10.0 mmol (120–180 mg/dl), and it remained stable for the remainder of the study period (24 h after surgery). However, the standard treatment group who received either sc sliding-scale or fixed-rate iv insulin infusion had a final glucose concentration ranging from 1.7–17.0 mmol (30–306 mg/dl) at 12–24 h after surgery. This demonstrates marked variability in plasma glucose concentrations, ranging from dangerous hypoglycemia to excessive hyperglycemia. In addition, control patients had higher mean plasma glucose concentrations than did patients receiving the algorithm-based infusion (11.6 ± 1.1 mmol vs. 7.6 ± 0.8 mmol [208 ± 20 mg/dl vs. 136 ± 15 mg/dl], P < 0.05). On the other hand, two other studies have reported that the use of a fixed-rate insulin infusion provides glucose control similar to that achieved by sc sliding-scale insulin.

The safest method to administer insulin in the perioperative period is by iv infusion. To do this effectively, the prior insulin regimen may need to be adjusted so that only a small effect remains from previously administered sc insulin. Starting the insulin infusion the evening before surgery will guarantee proper preparation of the patient. The poorly controlled patient (random blood glucose > 16.6 mmol [300 mg/dl]) taking a “split–mixed” regimen of NPH and regular insulin before breakfast and supper should take the normal morning dose the day before surgery. The evening dose should consist only of the regular insulin (the supper NPH insulin should be withheld). The patient who takes NPH and regular insulin before breakfast, regular insulin before supper, and NPH insulin at bedtime, should simply have the bedtime NPH injection withheld. If preadmission is not possible, all insulin should be discontinued. The patient should only return the usual evening insulin dose that evening. The patient who takes NPH and regular insulin before breakfast, regular insulin before supper, and NPH insulin at bedtime, should simply have the bedtime NPH injection withheld. If preadmission is not possible, all insulin should be discontinued. The patient should only return the usual evening insulin dose that evening.

### Table 3. IV Insulin Infusion Algorithm for Use Prior to Elective Surgery

<table>
<thead>
<tr>
<th>Glucose Level (mmol)</th>
<th>Infusion Algorithm</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;4.4</td>
<td>Turn infusion off for 30 min; give 25 ml 50% dextrose; recheck glucose level in 30 min†</td>
</tr>
<tr>
<td>4.5–6.7</td>
<td>Decrease insulin infusion by 0.3 U · h⁻¹</td>
</tr>
<tr>
<td>6.7–10.0</td>
<td>No change in insulin infusion rate</td>
</tr>
<tr>
<td>10.1–13.3</td>
<td>Increase insulin infusion by 0.3 U · h⁻¹</td>
</tr>
<tr>
<td>&gt;13.3</td>
<td>Increase insulin infusion by 0.5 U · h⁻¹</td>
</tr>
</tbody>
</table>

* Modified from reference 58.
† Restart insulin infusion between 0.3 and 0.6 U · h⁻¹ only after blood glucose is greater than 6.7 mmol.
be administered in the usual doses on the day prior to surgery. However, in the well-controlled patient, initiation of an insulin infusion early in the morning will be acceptable. The insulin infusion should be started no later than 7:00 AM, even if the procedure is scheduled for later in the day.

There is no consensus concerning the optimal perioperative insulin regimen for patients receiving Ultralente insulin. Although some would consider stopping the insulin preparation 3 days prior to surgery, others find this scheme too complicated. Furthermore, the shorter duration of action of human Ultralente insulin makes these changes unnecessary. If it is decided to continue administering the animal preparation of Ultralente insulin until surgery, it is appropriate to give the entire sc dose at the usual time on the day of surgery. Withholding or administering half of the usual dose just prior to surgery will have little effect during the operation. Furthermore, insulin levels would be lower on the day after surgery.

Patients using continuous sc insulin infusion (CSI) are actually the simplest to prepare since they receive only regular insulin from their pump. These patients need only to take off the pump prior to surgery, and at that time have the insulin infusion initiated. No studies have examined the use of CSI during surgery; however, due to the potential insulin absorption problems discussed above, CSI should be avoided during this period.

There are currently two accepted regimens for initiating iv insulin infusions. The GIK infusion proposed by Alberti et al. has the disadvantage of having a fixed insulin concentration, such that the entire bag must change each time the plasma glucose is outside of targeted values. This problem is resolved with a separate variable-rate insulin infusion as described by Watts et al. (Table 3). The adsorption of insulin to plastic is a theoretical problem and can be avoided by flushing 50 ml of the infusion mixture through the tubing before connecting it to the patient. With both the GIK infusion and the variable-rate infusion, the insulin can be concentrated further if excessive fluid administration is a concern.

It is possible that for some smaller hospitals the variable-rate insulin infusion may be too complex. In this situation, the GIK infusion is perhaps the better alternative. Whichever is used, if it is determined to preclude the poorly controlled patient to initiate an insulin infusion, one can administer the usual dose of regular insulin with supper and begin the infusion between 10:00 and 11:00 PM. Although the insulin dose required for optimal control varies, the usual starting dose for the variable-rate infusion is 1.0 U·h⁻¹. It is reasonable to start thin women, who tend to be more sensitive to insulin, at 0.5 U·h⁻¹. There does not appear to be general agreement regarding the frequency of bedside capillary glucose monitoring; however, a schedule of glucose checks every 1 h for the first 4 h after the insulin infusion is started, and then every 2 h until surgery, is recommended. In the operating room, the blood glucose should be estimated every 1 h.

Other clinically important points are: 1) A blood glucose meter, rather than visually read capillary glucose estimation, should be used for patients receiving an insulin infusion. 2) The nurse or physician using the meter should be properly trained in its use. 3) At least one plasma glucose sample (eg, the fasting blood glucose concentration) should be sent to the laboratory for confirmation of the meter’s accuracy. This check sample should be drawn simultaneously with the capillary meter test.

As a general guideline, patients receiving an insulin infusion require 0.3–0.4 U of insulin per gram glucose per hour (U·g⁻¹·h⁻¹). Higher insulin requirements and thus higher insulin infusion rates are necessary for some patients with liver disease (0.5–0.6 U·g⁻¹·h⁻¹), obesity (0.4–0.6 U·g⁻¹·h⁻¹), or severe infections (0.6–0.8 U·g⁻¹·h⁻¹); for those receiving steroid therapy (0.5–0.8 U·g⁻¹·h⁻¹); and for those undergoing cardiopulmonary bypass (0.8–1.2 U·g⁻¹·h⁻¹). The latter situation may be related to increased insulin resistance during hypothermia. It necessitates even more frequent glucose monitoring (every 15 min) during the hypothermic phase of open heart surgery.

Another controversial issue regarding iv insulin administration concerns the practice of injecting large bolus doses of iv insulin without an insulin drip. Despite the paucity of literature concerning this regimen (only the studies by Wals et al. and Meyers et al. have examined it), this iv bolus insulin administration was found to be the most common practice of intraoperative insulin administration at a large university-affiliated tertiary care medical center. Eighty percent of surgical patients with IDDM who received intraoperative insulin were given their insulin as iv boluses. This practice could be considered both unphysiologic and potentially dangerous. The half-life of iv insulin is 4–5 min and the biologic half-life less than 20 min (except in patients with antibodies to insulin). Depending on initial plasma glucose levels, patients given iv insulin injection may manifest very high (but short-lived) insulin concentrations, which may cause hypoglycemia. Since intraoperative glucose monitoring was performed infrequently (35% of patients had no glucose measurements during the surgery), the actual incidence of hypoglycemia during the intraoperative period may be much higher than that which was actually observed (only 1 of 85 patients had a capillary glucose concentration less than 3.3 mm [60 mg/dl] detected). In addition, the insulin concentrations can be expected to be extremely low in the 60–120-min period prior to the administration of the second bolus of insulin. This “roller coaster” approach to glucose regulation may result in an even greater rate of lipolysis and ketogenesis. Indeed, patients with
electrolytes measured on the day of surgery had a reduced serum bicarbonate (<22 mm), which presumably was due to ketoacidemia resulting from hypoinsulinemia. Finally, a large insulin bolus can cause a significant extracellular-to-intracellular shift of potassium, phosphorus, and magnesium, and may therefore predispose patients to cardiac arrhythmias.

**GLUCOSE**

The average nondiabetic adult needs a minimum of 100–125 g (400–500 calories) of exogenous glucose each day for protein sparing and ketosis prevention. Although this quantity of glucose was considered adequate to produce a 50% decrease in protein catabolism during starvation, a more recent study found that normal subjects receiving 100 g glucose per day had only a 23% decrease in urinary nitrogen compared to control subjects eating a normal diet.

Wolfe and Peters have recently shown that in fasting normal volunteers, glucose infused at the rate of 1 mg · kg⁻¹ · min⁻¹ (4.2 g · h⁻¹ for a 70-kg man) had no effect on the rate of appearance of glycerol (glycerol Ra) or FFA (FFA Ra). However, at 4 mg · kg⁻¹ · min⁻¹ (16.8 g · h⁻¹ for a 70-kg man), both glycerol Ra and FFA Ra were suppressed. This type of kinetic study has not yet been attempted during surgery. The prevention of ketone body and FFA accumulation in all surgical patients is theoretically important since elevated levels of circulating FFA have been shown to increase myocardial oxygen consumption, and in some instances, the risk of arrhythmias and ketoacidosis.

Sufficient glucose to prevent hypoglycemia and to provide the basal energy requirements should be administered during surgery in the insulinopenic patients. Some authors recommend 10 g glucose per hour (2.4 mg · kg⁻¹ · min⁻¹), whereas most infuse 5 g each hour (1.2 mg · kg⁻¹ · min⁻¹). Further studies are needed to determine the optimal dose of glucose to prevent unnecessary fat and protein catabolism during and after surgery.

For nondiabetic pediatric patients, there continues to be controversy regarding the use of glucose-containing solutions in the perioperative period. One group of investigators found asymptomatic hypoglycemia in some otherwise healthy children presenting for elective outpatient surgery. Unfortunately, when a solution of 5% dextrose with lactated Ringer’s (LR) solution was administered, glucose concentrations increased to 13.6 ± 3.3 mm (mean ± SD) compared to 4.6 ± 0.8 mm in the group not receiving glucose. These authors later reported that this hyperglycemic response could be prevented by giving 2.5% glucose in LR. At the infusion rates used, this provided glucose at a rate of 5.3 ± 1.6 mg · kg⁻¹ · min⁻¹.

Since glucose requirements in healthy children are about 5.0 mg · kg⁻¹ · min⁻¹, these authors recommend a 2.5% dextrose-containing solution for children presenting for outpatient surgery. Nevertheless, another group found no hypoglycemia during the perioperative period in pediatric patients receiving non–glucose-containing solutions, and these investigators concluded that glucose-containing solutions were not necessary in this population.

In diabetic pediatric patients, sufficient glucose must be administered to provide adequate energy requirements as well as to prevent hypoglycemia. Since there are no systematic data on the glucose and insulin requirements of this patient population currently available, it is difficult to make any recommendations regarding these issues. Until these questions are resolved, these patients should receive 5.0 mg · kg⁻¹ · min⁻¹ (300 mg · kg⁻¹ · h⁻¹) of glucose with adequate insulin to achieve the desired blood glucose control.

**POTASSIUM**

Since only 2% of total body potassium is extracellular, a normal serum potassium concentration does not necessarily reflect a normal total body potassium. In addition, there are several metabolic factors that will influence the serum potassium level: 1) changes in insulin concentration, i.e., changes in serum insulin levels, are capable of stimulating potassium uptake by muscle, liver, and adipose tissue; 2) small incremental changes in blood tonicity as seen with dehydration or hyperglycemia can cause a shift of water and potassium from the intracellular to the extracellular space; and 3) changes in acid–base balance, e.g., acidosis, result in hyperkalemia as hydrogen ions are exchanged with intracellular potassium. If a poorly controlled (i.e., volume-depleted, insulinopenic, and acidicemic) diabetic patient is admitted with a normal serum potassium level, the fluid administration and an insulin infusion may result in severe hypokalemia unless supplemental potassium is provided.

In the normokalemic diabetic patient with normal renal function, 20 mEq of potassium chloride should be added to each liter of fluid. However, additional potassium may be required, especially in an insulin-resistant patient who requires large doses of insulin. In a poorly controlled patient, it is reasonable to check the serum potassium level 6–8 h after the insulin infusion is started. All diabetic patients should have their glucose and electrolytes concentrations remeasured while in the recovery room.

**FLUIDS**

If a patient is receiving adequate insulin, glucose, and potassium, any additional fluids given during surgery (e.g., to treat intraoperative blood loss) should be non–glucose-containing. In general, glucose is provided in a solution...
of 5 or 10% dextrose in 0.45% saline. However, if fluids need to be restricted, the glucose can be given as 20 or 50% solutions at lower rates. When these concentrated solutions are used, infusion via a central venous catheter is recommended because of the increased risk of peripheral venous thrombosis with these solutions.

Although the use of LR solution during surgery is common, its use for diabetic patients is controversial. Lactate is a gluconeogenic precursor that is rapidly metabolized, particularly in a starved or catabolic state. Thomas and Alberti showed that patients with NIDDM who were not receiving iv fluids during surgery had a mean plasma glucose increase of 2.2 mM (40 mg/dl), whereas those receiving LR (29–44 mmol) had a mean plasma glucose increase of 7.5 mM (135 mg/dl). Higher insulin doses may be required for diabetic patients receiving LR during the perioperative period. In a more recent study, it was shown that the infusion of lactate at the rate of 25 μmol·kg⁻¹·min⁻¹ over 5 h (approximately 300 mmol) in nondiabetic subjects did not alter plasma glucose production.

In addition, Degoulet and colleagues showed, in a group of nondiabetic patients undergoing infrarenal abdominal aortic surgery, that intraoperative glucose infusion provokes greater blood lactate accumulation than does infusion of LR. However, the group receiving 5% glucose was given a mean of 200 g (50 g·h⁻¹) glucose intraoperatively. This supraphysiologic quantity of glucose may have caused an excessive hyperglycemia and lactate accumulation. In addition, since FFA and β-hydroxybutyrate levels were not measured, lipolysis and ketogenesis may have been increased in the LR group. As noted above, these issues are more than academic, since elevated levels of FFA have been shown to increase myocardial oxygen consumption and the risk for cardiac arrhythmias. Furthermore, elevated ketone levels can further increase the risk of metabolic deterioration in patients with diabetes. Although enough glucose should be provided to prevent these catabolic processes, 50 g·h⁻¹ is excessive. Until further studies are performed, the suggested glucose infusion rate of 5–10 g·h⁻¹ seems reasonable.

GENERAL RECOMMENDATIONS

Most experts on diabetes management agree that operations on diabetic patients should be scheduled early in the day. However, if this is not possible, the use of a variable-rate insulin infusion or GIK infusion minimizes the previous problems of hypoglycemia or excessive hyperglycemia seen with the more traditional insulin regimens. Although there have been many recommendations for the postoperative management of patients with diabetes, no controlled studies have been performed to compare postoperative regimens when the preoperative and intraoperative regimens were similar. There appears to be no advantage in using a sliding-scale sc insulin based on glycosuria. Although this is a simple method for administering insulin to diabetic patients after surgery, traditional sliding-scale regimens are based on retrospective hyperglycemia and thus tend to induce major swings in plasma glucose concentrations. In addition, absorption of sc insulin in the immediate postoperative period is highly variable due to fluid shifts. Thus, the sliding scale itself is based primarily on guess work.

With a variable-rate iv insulin infusion or GIK infusion, postoperative management is simple and flexible. The capillary glucose should be monitored at the bedside every 1–2 h while insulin is being infused. The variable-rate insulin infusion should be changed as suggested previously to achieve a target goal of 6.7–10.0 mM (120–180 mg/dl). Serum potassium concentrations should be also be monitored daily until the insulin infusion is discontinued. It is recommended that the insulin infusion be continued through the first light meal and discontinued immediately before the subsequent meal. This can be easily accomplished with the midday meal, since NPH or Ultralente insulin is not usually given at this time. Thus, the usual mealtime dose of regular insulin can be given before the midday meal. If the patient does not tolerate the food, the insulin infusion can be restarted later in the day without the potential problem of hypoglycemia resulting from the longer-acting insulin. If the meal is well tolerated, the usual supper and bedtime insulin doses can be given.

AMBULATORY (OUTPATIENT) SURGERY

The types of operations that are performed on an outpatient basis are changing. Although the procedures might be considered minor, general anesthesia is still required in a majority of the cases. Not only is the definition of "minor surgery" changing; it also varies from surgeon to surgeon. Due to the known hyperglycemic effects of surgical stimulation, variation in sc insulin absorption can occur even during seemingly "minor" procedures.

Despite the increasing emphasis on ambulatory surgery, there are few studies examining the metabolic effects after common outpatient operations in patients with IDDM. Two studies have shown that plasma glucose concentrations can be well controlled during "minor" surgery with insulin-glucose infusions. However, as with "major" surgery, large prospective outcome studies in patients with IDDM undergoing minor procedures need to examine important issues such as infections, wound healing, volume depletion (due to hyperglycemia), and the incidence of DKA.

Christiansen et al. recently compared two groups of "insulin-dependent" diabetic patients undergoing minor
surgery under general anesthesia. One group received a GIK infusion, and the other conventional sc insulin therapy. The former group had significantly better perioperative blood glucose control (from the day of surgery until the second postoperative day), although there were no differences between the two groups in lactate, β-hydroxybutyrate, and glycerol levels (FFA were not measured). Unfortunately, C-peptide measurements (to measure endogenous insulin secretion) were not reported. Since the mean age of both groups of patients was 52 yr (and both groups included patients greater than 70 yr old), it is likely that some of these subjects actually were patients with NIDDM. Thus, residual endogenous insulin secretion, at least in part, may explain why there were no differences in the measured metabolites.

For brief outpatient surgical procedures, it is often advisable to deviate from the iv insulin infusion regimen suggested above. The option not to begin an insulin infusion will depend on: 1) the outpatient’s current metabolic status (e.g., the individual with marked hyperglycemia and/or acidemia should be placed on an insulin infusion); 2) preoperative insulin regimen (e.g., it would be easier to continue with sc insulin for those patients receiving animal-species Ultralente insulin); 3) the diet (or lack of) that the outpatient will be allowed to eat after the surgery; and 4) the physician’s ability to handle a metabolic crisis related to prolonged postoperative nausea and vomiting, a common complication after outpatient anesthesia. Indeed, it was recently reported that 18% of unanticipated hospital admissions after ambulatory surgery for a general patient population were due to intractable vomiting.

Gastroparesis occurs in 20–30% of all diabetic patients. Although often asymptomatic, gastroparesis presents clinically as nausea, postprandial fullness, early satiety, epigastric pain, and sometimes protracted vomiting. Although there are no data indicating that patients with diabetes have an increased risk of perioperative vomiting, this complication can lead to regurgitation and aspiration. In the patient with IDDM receiving sc insulin, the inability to eat after surgery might complicate the medical management. Glucose infusions can be titrated for a targeted glucose level; however, if the serum insulin levels are declining while the glucose infusion is increasing, the patient is at risk for hyperglycemia and ketosis. The alternate approach—a variable-rate iv insulin infusion or GIK infusion—diminishes the metabolic risks during the postoperative period.

The treatment of postoperative nausea and vomiting in this population deserves further study. Metoclopramide, a gastriokinetic agent that increases gastric motility, can be an effective antiemetic in patients with gastroparesis. Thus, until further studies are completed, this agent appears to be the drug of choice for initial therapy of postoperative nausea and vomiting in patients with diabetes. Other useful drugs include the butyrophenones (e.g., droperidol) and antihistamines (e.g., hydroxyzine).

All sc insulin regimens must achieve adequate plasma insulin concentrations to prevent excessive gluconeogenesis, glycogenolysis, lipolysis, and ketogenesis. There are several strategies that can be used for this purpose. If the patient normally takes NPH and regular insulin before breakfast and supper, one half to two thirds the usual dose of each type of insulin can be given in the morning unless there is evidence of fasting hypoglycemia. In the latter case, the regular insulin dose can be withheld until the capillary glucose concentration rises. The lower dose of NPH insulin will reduce the risk of afternoon hypoglycemia if surgery is delayed or postoperative vomiting develops. Since supplemental regular insulin can be given later in the day, the full dose of NPH is not necessary. The patient also will require a glucose infusion (5 g·h⁻¹), and capillary glucose levels should be checked hourly. If oral intake is allowed immediately after the procedure, the remainder of the morning regular insulin should be given 20–30 min before eating. However, additional sc regular insulin should be given if the capillary glucose level is greater than 11.1 mM (200 mg/dl). The NPH insulin given in the morning will have its onset of action approximately 2 h after injection, and its peak effect at approximately 8–12 h; therefore, one should not be overly aggressive with supplemental regular insulin if the patient is capable of eating at between 2:00 and 4:00 PM. This regimen depends on a degree of guess work and may be vulnerable to misjudgment.

A second option for outpatients who take their insulin before breakfast and supper is to give the NPH insulin (from the second injection) at bedtime, on the night before surgery. If he or she usually takes NPH insulin at bedtime, no change needs to be made. On the morning of the procedure, one half to two thirds the usual dose of NPH insulin can be administered and little or no regular insulin given, since plasma insulin levels should be sufficient from the NPH insulin administered the night before. As suggested previously, a glucose infusion is started and capillary glucose levels checked hourly. Blood glucose concentrations above 11.1 mM (200 mg/dl) require treatment with supplemental regular insulin. However, the “peaking” NPH insulin given the night before needs to be considered, since serum insulin levels will be highest between 6:00 and 9:00 AM. If the patient is capable of eating immediately after the surgery, one half to two thirds the usual sc dose of regular insulin can be given immediately before the meal.

Patients taking Ultralente insulin should be given the usual dose of insulin. Regular insulin is necessary only for capillary glucose concentrations greater than 11.1 mM.
(200 mg/dl). Because of the long duration of action of Ultralente insulin (56 h for the animal preparations and 24 h for the human preparation), the patient should have adequate insulin levels from the insulin given the previous day. Decreasing the Ultralente dose on the morning of surgery will have little, if any, effect on plasma glucose concentrations during the procedure. Changing to a different type of insulin preparation before the procedure is unnecessarily complicated for patients undergoing brief ambulatory surgical procedures.

All of these sc insulin regimens should be considered only as guidelines. Individual situations may warrant different action. One group has argued that all patients with IDDM should be placed on a GIK infusion regardless of the severity of surgery. Although one study does support the use of the GIK infusion during minor surgery for patients with IDDM, retrospective reports have shown that in the United States, sc insulin administration is the most common for both minor and major surgery. In addition, a recent British study reported that the majority of anesthesiologists opt not to use a GIK infusion during minor surgery. Therefore, until further studies document advantages for the iv insulin infusion during minor surgery, it is prudent to follow these general guidelines for sc insulin administration.

Non-Insulin-dependent Diabetes Mellitus: Elective Surgery

GENERAL PRINCIPLES

The majority of diabetic patients undergoing surgery have NIDDM as opposed to IDDM. Whereas microvascular complications predominate in patients with IDDM, those with NIDDM have a much higher prevalence of macrovascular disease. Many of these NIDDM patients are taking insulin although they are not "insulin-dependent" in the true sense. Some of these patients, especially if not obese, behave metabolically like the classic IDDM patient and therefore should be treated in a likewise manner during surgery. Indeed, it is not uncommon for IDDM to present in adulthood, since the age of onset has been shown to be bimodal. Finally, IDDM can present in patients with NIDDM who have "pancreatic exhaustion" and "conversion" to IDDM.

AMBULATORY (OUTPATIENT) SURGERY

Most authors agree that well-controlled, diet-treated patients with NIDDM do not require any special treatment before and during surgery. Indeed, one study showed that 93% of patients with NIDDM can be managed without insulin. If the fasting plasma glucose is lower than 7.8 mM (140 mg/dl), these patients can be treated initially with close observation. Glucose concentrations should be measured hourly. Patients with this degree of glycemic control treated with an oral hypoglycemic agent (OHA) can be given their medication and started on a glucose infusion at the usual time (approximately 7:00 AM). Some suggest stopping the OHA the evening before surgery (or discontinuing the longer-acting chlorpropamide 48–72 h preoperatively). Treatment decisions for patients with higher glucose concentrations are more controversial. Perioperative insulin therapy should be considered when blood glucose concentrations (fasting or random) exceed 11.1 mM (200 mg/dl) and definitely should be initiated when they are in excess of 13.9 mM (250 mg/dl). These values are chosen for the following reasons. First, fasting plasma glucose concentrations exceeding 11.1 mM tend to manifest absolute deficiency with respect to insulin secretion. Second, the renal threshold for glucose is approximately 10.0–11.1 mM in patients with normal renal function. Osmotic diuresis with resulting water and electrolyte losses occur when this glucose level is exceeded. Finally, the literature suggests that impaired wound healing and strength occurs when plasma glucose levels exceed 11.1 mM.

The decision to begin a variable-rate insulin infusion or GIK infusion should be individualized according to the patient and type of operative procedure. If an infusion is not started, sc regular insulin should be given. It is difficult to give a precise recommendation for the amount of insulin that should be administered to maintain euglycemia during and after the procedure. Regular insulin, 4–6 U sc, is a reasonable initial dose for a surgical patient not previously treated with insulin. More significant hyperglycemia (≥19.4 mM) should be treated with an iv insulin infusion.

Malling and colleagues recently studied two groups of well-controlled patients with NIDDM prior to minor surgery (e.g., vitrectomy, hand surgery, and digital amputations). The patients were treated with either a GIK infusion or sc insulin followed by an infusion of glucose. Mean fasting glucose levels were less than 8 mM (144 mg/dl), and all subjects were taking an OHA at home. There was no difference between the two groups in blood glucose levels and metabolic (β-hydroxybutyrate, lactate, glycerol, and alanine) or hormonal (insulin, glucagon, and GH) parameters. Therefore, both of these treatment options are reasonable for this patient population.

In caring for patients with NIDDM taking insulin at home, the anesthesiologist has the option of administering an iv insulin infusion or sc insulin. The same principles of insulin administration discussed for patients with IDDM apply to this population. Some of these patients are actually insulinopenic and thus behave metabolically like those with IDDM. Finally, for any patient who requires insulin, there is less guess work with an insulin infusion compared with sc insulin, particularly for patients at risk for developing postoperative nausea and vomiting.
NEUROLOGICAL, MAJOR INTRACAVITARY AND OPEN HEART SURGERY

The metabolic responses to major surgery have been discussed previously. Patients with NIDDM are insulin-resistant. Surgical stress potentiates this insulin resistance and larger doses of insulin are required to prevent hyperglycemia. Patients treated with diet alone who have fasting plasma glucose concentrations <7.9 mM (140 mg/dl) can be treated initially with close observation, but insulin therapy most likely will be required during the operation. An insulin infusion should be initiated if the capillary glucose rises above 11.1 mM (200 mg/dl) during the operation. Besides the reasons listed previously for beginning an insulin infusion at this blood glucose concentration, hyperglycemia has been shown to worsen neurologic outcome for patients after ischemic stroke. Although there are several possible mechanisms by which hyperglycemia may exacerbate cerebral ischemia, the reason for this relationship is unknown. Nevertheless, until further data become available, the prudent course of action is to minimize hyperglycemia in patients undergoing neurosurgical procedures.

Alberti and Thomas studied a group of patients with NIDDM who had a mean preoperative plasma glucose level of 8.9 mM (160 mg/dl). When these patients received no insulin (or OHA) therapy for their hyperglycemia, their mean plasma glucose concentration 4 h postoperatively was 14.2 mM (256 mg/dl). These investigators concluded that all patients having major surgery who are taking an OHA should be given an insulin–glucose infusion, since mean plasma glucose concentrations remained the same in the insulin-treated group (10.3–10.1 mM [185–182 mg/dl]) 4 h after surgery compared to the increase from 8.9 to 14.2 mM (160 to 256 mg/dl) in the untreated group. In addition, concentrations of β-hydroxybutyrate and FFA were lower in the insulin-treated group. Optimal management of these patients involves use of a GIK infusion, starting with an insulin dose of 1.0 U·h⁻¹, although much higher insulin doses are likely to be required. Patients with NIDDM who are insulin requiring should be treated as patients with IDDM during major surgery.

Cardiopulmonary bypass surgery deserves special attention since it is associated with potentially greater metabolic derangements. Plasma glucose concentrations can increase to even higher values during this procedure because of the large amounts of glucose that frequently are infused (“cardioplegic solution”), because of insulin resistance during hypothermia, and because of the hyperglycemic effects of the commonly used adrenergic agents. In nondiabetic patients, plasma glucose concentrations as high as 31.8 ± 4.8 mM (572 ± 86 mg/dl) have been reported, and similar values have been found in the diabetic population.

Studies using the artificial endocrine pancreas have shown a progressive increase in insulin requirements during open heart surgery. Preoperative infusion rates of 1.6 U/h had to be progressively increased to 12.3 U/h to maintain euglycemia. Thus, the therapeutic strategies for these procedures include measuring blood glucose concentrations every 15–30 min, limiting the quantity of glucose infused, and increasing the insulin infusion rate as required to prevent excessive hyperglycemia.

Hyperosmolar hyperglycemic nonketotic coma (HHNC) has been reported as a postoperative complication in patients with NIDDM. This syndrome is characterized by marked hyperglycemia, plasma hyperosmolality, profound dehydration, absence of ketoadidas, and variable mental status changes. Due to the increased plasma glucose concentrations and insulin resistance present during coronary artery bypass operations in patients with NIDDM, HHNC is much more likely to occur in this patient population. Seki reported that the high mortality (42%) in patients with HHNC undergoing cardiac operations was related in part to the duration of time between the onset of polyuria and the diagnosis (7.5 ± 0.8 days in the nonsurvivors vs. 4.5 ± 0.8 days in the survivors). Mortality was found to be higher also in those patients without a known diagnosis of diabetes. In an earlier series, 67% of the patients had no history of diabetes. Dehydration in this group of patients is further exacerbated by the postoperative use of loop diuretics. Other factors precipitating HHNC include hyperalimentation and dextrose infusions (without supplemental insulin administration) and certain surgical procedures (e.g., pancreatectomy). This patient population represents a special therapeutic challenge to the anesthesiologist, and frequent intraoperative blood glucose measurements are critical to avoid metabolic decompensation.

Emergency Surgery

In the early series of Galloway and Shuman, 5% of all diabetic patients required emergency surgery. Of the operations performed, appendectomy was the most common major procedure (33% of all major procedures); lower extremity incision and drainage and lower extremity amputation for infection were the most common “minor operations” (89% of all minor procedures). Although data on the number of patients meeting the criteria for DKA were not provided, 31% of all patients were admitted with plasma glucose levels greater than 11.1 mM (200 mg/dl).

A priority for diabetic patients scheduled for emergency surgery is a complete evaluation of the patient’s metabolic status. Plasma glucose, electrolytes, and pH should be measured and urine ketones estimated. A saline infusion should be started, and if clinically indicated, a central venous catheter should be inserted. If DKA is confirmed, surgery should be delayed while standard
treatment for this metabolic emergency is instituted with iv fluids, insulin, and potassium. 126-129 Campbell and associates 126 found that 63% of diabetic patients presenting with DKA and severe abdominal pain and tenderness had disappearance of these signs and symptoms after the DKA was adequately treated. Episodes of unexplained abdominal pain were reported in patients with IDDM who were less than 40 yr old and who were markedly acidemic (serum bicarbonate <10 mEq/l). In addition, Wheelock et al. 126 pointed out that an acute surgical abdomen can initially appear benign in the diabetic patient. The mechanism of this phenomenon is not known, although it probably is due to diabetic neuropathy.

**Conclusion**

Although excessive hyperglycemia, lipolysis, ketogenesis, and proteolysis may adversely affect surgical outcome in patients with diabetes, the evidence to support this view is only indirect. A large, prospective study addressing this issue needs to be performed. By understanding basic physiologic and endocrinologic principles, however, the anesthesiologist can make rational decisions regarding the metabolic care of diabetic patients. In addition to an assessment of the metabolic status of the patient, preoperative evaluation should include assessment of chronic complications of diabetes. Intraoperatively, the use of a carefully titrated variable-rate insulin infusion or a GIK infusion can minimize the metabolic derangements associated with surgical stress. Frequent intraoperative measurement of blood glucose is essential for any regimen to be effective and can be accomplished easily by the use of a capillary glucose device. Finally, the metabolic effects of other factors, such as drugs, obesity, infection, and hypothermia need to be considered.

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**References**


PERIOPERATIVE MANAGEMENT OF DIABETES MELLITUS


