Perioperative Management of Diabetic Patients

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Diabetes mellitus is the most common metabolic disease. New classifications have recently been proposed by the American Diabetes Association (ADA) and the World Health Organization (WHO).[1] Type 1 (formerly insulin-dependent diabetes mellitus IDDM) is immune-mediated and leads to absolute insulin deficiency. Type 2 diabetes (formerly non-insulin-dependent diabetes mellitus [NIDDM]) is a disease of adult onset and is associated with insulin resistance. Type 3 corresponds to a wide range of specific types of diabetes, including various genetic defects of beta-cell function and insulin action, diseases of exocrine pancreas, endocrinopathies, and drug-induced diabetes. Type 4 is gestational diabetes (Table 1).

Diabetics undergoing surgery have increased mortality, and type 1 diabetics are particularly at risk of postoperative complications.[2] Wound complications are increased in diabetics, and healing is severely impaired when glycemic control is poor.[3] However, with the use of modern management plans, the major outcome measures of surgery are comparable in diabetic and nondiabetic patients.[4] Successful management of surgery in diabetic patients requires simple and safe protocols, which are fully understood by all staff and a close liaison among the surgeons, diabetes care team, and anesthetists.

There is no consensus on the optimal metabolic management of the diabetic patient during surgery. Several surveys have highlighted the inconsistency with which surgical problems are managed in diabetic patients.[5,6] The aim of this article is to provide protocols to achieve sensible and practical glycemic control in diabetic patients undergoing surgery. (Curr Surg 60: 607-611. © 2003 by the Association of Program Directors in Surgery.)

KEY WORDS: diabetes mellitus, perioperative, surgery

TABLE 1. Classification of Diabetes Mellitus

Type 1	Associated with absolute insulin deficiency
	A. Immune-mediated
	B. Idiopathic
Type 2	Adult-onset, Associated with insulin resistance
Type 3	A. Genetic defects of β-cell function
	B. Genetic defects in insulin action
	C. Diseases of exocrine pancreas
	D. Endocrinopathies
	E. Drug-or chemical-induced
	F. Infections
	G. Uncommon forms of immune-mediated diabetes
	H. Other genetic syndromes sometimes associated with diabetes
Type 4	Gestational diabetes mellitus

METABOLIC CONSEQUENCES OF SURGERY AND ANAESTHESIA

Trauma of surgery results in increased secretion of stress hormones, particularly cortisol and catecholamines.[7,8] The magnitude of the counter-regulatory response depends on the severity of surgery and any complications that may develop, such as sepsis. Both cortisol and catecholamines reduce insulin sensitivity. Sympathetic activity is also increased, resulting in reduced insulin secretion. The secretions of glucagon and growth hormone are also increased.[9,10] In a diabetic patient with absolute or relative insulin deficiency, the sequence of these complex hormonal and metabolic changes in response to surgery results in a marked catabolic response. Gluconeogenesis, glycogenolysis, proteolysis, lipolysis, and ketogenesis are all increased, which leads to a state of hyperglycemia and ketosis. This problem is compounded by perioperative starvation.[11]

In contrast to general anesthesia, epidural anesthesia has minimal effect on glucose metabolism.[12] Circulating glucose, noradrenaline, and cortisol concentrations are not raised in patients undergoing epidural anesthesia. Epidural anesthesia blocks catecholamine release, irrespective of the segmental level.[13] Insulin response to a bolus of glucose is also preserved in low spinal anesthesia.[14] Regional anesthesia, however, may carry greater risks in the diabetic patient with autonomic neuropathy and may result in profound hypotension, which can have deleterious consequences in patients with ischemic heart disease or cerebrovascular disease. Epidural abscesses also occur more commonly after spinal and epidural anesthesia. The anesthetic technique chosen should ensure a rapid return to con-

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sciousness to obviate the masking of hyperglycemic or hypoglycemic coma.

The usual intravenous induction agents have negligible effect on the blood glucose concentration although ketamine may cause significant hyperglycemia.[15] Etomidate is an induction agent associated with rapid recovery without hangover effects. It causes less hypotension than other drugs used for induction. Repeated doses of etomidate have a suppressant effect on adrenocortical function, as it blocks steroidogenesis by its action on 11β-hydroxylase and cholesterol cleavage enzymes. It consequently decreases the hyperglycemic response to surgery.[16] Benzodiazepines decrease the secretion of ACTH when used in high doses during surgery.[17] They also reduce sympathetic stimulation but stimulate growth hormone secretion. The overall result is a decrease in the glycemic response to surgery. High-dose opiates block the sympathetic nervous system and hypothalamic-pituitary axis, therefore abolishing the hyperglycemia response to surgery.[18] However, increased glucose plasma concentrations have been observed in patients receiving fentanyl/midazolam anesthesia and are thought to be caused by a decrease in whole-body glucose clearance.

All volatile anesthetic agents, including halothane, enflurane, and isoflurane, inhibit the insulin response to glucose in a dose dependent manner in vitro.[19] The hyperglycemic response during inhaled anesthesia with isoflurane is a consequence of both impaired glucose clearance and increased glucose production.[20] The clinical significance of these findings is not clear in diabetic patients undergoing surgery.

Most anesthetic agents cause hyperglycemia; the choice of anesthetic agent will be influenced by the severity of systemic diseases, such as coronary artery disease, nephropathy, and hypertension, and the choice of neuromuscular blocking agent will be affected by renal function. Mivacurium and cis-atracurium have more predictable elimination than do rocuronium and vecuronium in the presence of renal dysfunction. Although abnormalities of transmission across the neuromuscular junction can occur in diabetics, the clinical response to neuromuscular blocking agents is normal. The use of suxamethonium in extensive diabetic neuropathy, however, is inadvisable because of excessive potassium release from denervated muscle.[21]

GENERAL PRINCIPLES

Aims of successful perioperative management of diabetes are as follows:

Reducing mortality and morbidity
Avoiding excessive hyperglycemia
Avoiding ketosis
Avoiding hypoglycemia

Glycemic control should be monitored carefully during the period before admission, aiming for HbA1c of less than 7%. For most patients, reasonable metabolic control can be achieved on an outpatient basis. Clinical examination should include cardiovascular examination, measurement of renal function, and examination for autonomic neuropathy. Urinalysis, biochemical profile, and echocardiogram should be obtained. Urine should be dip-sticked for proteinuria, the existence of which should alert the anesthetist of the potentially harmful effects of nephrotoxic drugs. Autonomic neuropathy can lead to perioperative hypotension and intraoperative cardiorespiratory arrest.[22,23] The resulting gastroparesis also carries an increased risk of regurgitation and aspiration on induction of anesthesia. Examination of autonomic nervous system can be accomplished by measuring variation in RR interval during deep breathing, heart rate response to Valsalva's maneuver, and the blood pressure and heart rate response to standing. Examination of the muskuloskeletal system is important as the presence of stiff-joint-syndrome or diabetic cheiroarthropathy may make endotracheal intubation difficult.[24] This is because of the impaired mobility of the neck due to limited extension of the atlanto-axial joint. Fundoscopy may reveal presence of diabetic retinopathy, and if proliferative retinopathy is present, marked increases in arterial pressure may result in vitreous hemorrhage and should be avoided. Standard procedure for most patients undergoing surgery usually is starvation after midnight. However, this may not be appropriate for the diabetic patient because the patient may have undiagnosed gastroparesis that may prolong retention of food in the stomach, thus increasing the danger of aspiration during anesthesia induction. A 12-hour fast is therefore recommended in diabetic patients before surgery. Hartmann's solution should be avoided in diabetic patients, as infused lactate is rapidly converted to glucose with resulting hyperglycemia. Diabetics are particularly prone to cerebrovascular and cardiac disease. Ganglion-blocking agents may block sympathetically mediated hepatic gluconeogenesis with resultant hypoglycemia. The use of beta-blockers is associated with slower recovery from hypoglycemia.

Fasting blood glucose should be measured on the day of operation. A further check should be made preoperatively or every 2 hours if the operation is delayed. If the operation is long, intraoperative measurement and an additional measurement in the recovery room should be made. Thereafter, it should be measured once after 2 hours and then every 4 hours.

SURGERY IN NIDDM PATIENTS NOT TREATED WITH INSULIN

Oral agents are generally administered on the day before surgery and withheld on the day of surgery. Metformin is withheld because of concerns about altered renal function in the acutely ill, and alpha-glucosidase inhibitors are withheld because they are effective only when taken with food. Hyperglycemia is treated with supplemental short-acting insulin, usually administered subcutaneously.

In patients who achieve good control and who are undergoing minor surgery, simple observation is required. However, if the glycemic control is poor ie, a fasting blood glucose of greater than 10 mmol (180 mg/dL), they should be treated with stan-

TABLE 2. Standard GIK

- 500 ml 10% dextrose solution
  + 15 units short-acting insulin
  + 10 mmol KCl
- Infuse over 5 hours (100ml/h)

dard GIK (glucose-insulin-potassium).[25] Another approach is to try a short-/rapid-acting insulin for 24 to 48 hours to asses insulin requirements and to switch to an intermediate-acting insulin a day or two before surgery is planned. On the day of surgery, breakfast is omitted and preoperative insulin is administered. The dose is reduced by two-thirds to one-third of the total daily dose depending on whether the patient takes two or three insulin doses per day and on the likelihood of having lunch.[26]

Non-insulin-dependent diabetes mellitus patients undergoing major surgery are best managed using GIK. Two GIK regimens have been proposed—one based on 10% glucose and one on 5% glucose, both given at 100 mL/hr. The insulin/glucose ratio is 0.32 U/g, although lower ratios have been used[27,28] (Table 2). Oral hypoglycemic drugs should be restarted with first postoperative meal. Other alternatives are intermittent, small intravenous boluses of regular insulin and variable separate infusion of glucose and regular insulin. The superiority of any method remains controversial.[29] In the intermittent bolus technique, 10 units of regular insulin is administered every 2 hours and supplemented by 5 units every 60 minutes for blood glucose levels greater than 11 mmol/L (198 mg/dL).[30] Continuous intravenous insulin infusion rates are 0.5 to 5 units per hour, corresponding with the amount of glucose infused.

SURGERY IN INSULIN TREATED PATIENTS

Long-acting insulin should be stopped several days before operation and be replaced with intermediate-acting insulin, or with multiple injections of short-acting insulin through the day with an intermediate-acting preparation at night. This regimen can be continued until the morning of operation. Use of short-/rapid-acting insulin by sliding scale as the patient's only insulin is discouraged because of the greater likelihood of fluctuations in blood glucose levels.

Glucose-insulin-potassium should be started on the morning of operation and should be continued until the patient is ready to eat, at which time, subcutaneous insulin can be reinstituted. Subcutaneous insulin should be restarted before first postoperative meal, and GIK should be discontinued 2 to 3 hours later (Table 3).

EMERGENCY SURGERY

Diabetic patients needing urgent surgery need full assessment both clinically and biochemically because any acute illness can cause metabolic decompensation. This should first be corrected if possible. It is also important to note the time of the last injection or dose of sulphonylurea, because their continuing absorption can markedly affect glycemic control during and after surgery. Blood glucose should be monitored frequently.

TABLE 3. Protocol For Managing Diabetic Patients Undergoing Surgery

1- Ensure satisfactory pre-operative control.
2- Operate in morning if possible.
3- Omit breakfast, and insulin or oral hypoglycaemic drugs morning of surgery.
4- NIDM patients not treated with insulin, having minor surgery, need observation only.
5- GIK is used in all other cases.
6- Check blood glucose 2-hourly initially and aim for 6-11 mmol/l
   - if >11mmol/l, change to GIK with 20 units insulin
   - if <6mmol/l, change to GIK with 10 units insulin
7- Continue GIK until patients eat, then revert to oral hypoglycaemic drugs with the first meal in case of NIDDM patients not treated with insulin.
8- Patients on insulin should be continued on GIK for 2-3 hours after the first dose of subcutaneous insulin, which is given before the first meal.

OPEN-HEART SURGERY

Insulin requirements are much more in cardiac surgery with cardiopulmonary bypass than in other operations. The reason for the high insulin requirements of diabetics undergoing cardiopulmonary bypass is multifactorial. These include insulin resistance caused by hypothermia, infusion of dead space of the bypass machine with glucose solution, and the hyperglycemic effects of adrenergic drugs. Therefore, a separate-line system for insulin administration as opposed to GIK infusion is recommended.

CAESAREAN SECTION

Most patients in late pregnancy require relatively higher doses of insulin. Women with diabetes become increasingly insulin resistant during the third trimester of pregnancy. To maintain optimal glycaemic control, it is usually necessary to increase doses of insulin to as much as 100% to 200%. Use of β-adrenergic agonist, ritodrine or dexamethasone, will also increase insulin requirements. Therefore, an infusion containing 20 units soluble insulin in 500 mL 10% dextrose should be commenced. Insulin requirements fall dramatically after delivery of the placenta, and the GIK should be stopped at this time. Glucose-insulin-potassium should be restarted later in the recovery or labor room with a GIK solution containing 10 to 15 units of insulin. When subcutaneous insulin is restarted with the first meal, doses approximating to those used before pregnancy and not those used in the third trimester must be used.

PANCREATIC DIABETES

Patients with this disorder are unique in that they have low glucagon levels that respond abnormally to several physiological stimuli, blunted epinephrine responses to insulin-induced hypoglycemia, and malabsorption.[31,32] The clinical symptoms of diabetes caused by pancreatic disease do not differ from those of other types of diabetes mellitus. The development of ketosis is, however, exceptional.[33] In contrast, insulin-induced hypoglycemia is frequent.[34] Moreover, recovery from hypoglycemia may be impaired, and this may be due to inadequate glucagon response.[35] Patients with pancreatic diabetes have increased levels of circulating gluconeogenic amino acids and decreased insulin requirements. Low daily requirements of insulin and high frequency of severe hypoglycemic events in pancreatic diabetes have been ascribed to the absence of glucagon. A conservative approach with regard to intensive insulin therapy and tight blood glucose control has been suggested.[36] Frequent monitoring of blood glucose levels is of paramount importance.

CONCLUSION

Several regimens have been proposed for the perioperative management of diabetic patients. A simple, easily understandable approach is required for optimal management of these patients. A careful preoperative assessment of the metabolic status and chronic complications of diabetes, use of GIK during and in the immediate postoperative period, and frequent monitoring of the patient's metabolic state can minimize the metabolic derangements associated with surgical stress. This can be safely done on a ward where staff is familiar with glucose monitoring and insulin-giving devices as long as the patient has no diabetes-related complications needing intensive unit care.

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