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REVIEW ARTICLE

Anesthetic considerations in diabetic patients. Part I: preoperative considerations of patients with diabetes mellitus

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Abstract Diabetes mellitus is an increasingly common disease that affects people of all ages, resulting in significant morbidity and mortality. Diabetic patients require perioperative care more frequently than their nondiabetic counterparts. The major risk factors for diabetics undergoing surgery are the associated end-organ diseases: cardiovascular disease, autonomic neuropathy, joint collagen tissue, and immune deficiency. Physicians need to pay extra attention to preoperative and preprocedure evaluation and treatment of these diseases to ensure optimal perioperative management.

Keywords Diabetes mellitus · Preoperative management · Glycosylated hemoglobin

Introduction

During the past 20–30 years, the prevalence of diabetes mellitus (DM) has rapidly increased throughout the world, the prediction being that it will increase by 200% in the next several decades [1–4]. Inevitably, physicians will be confronted with an increasing population of diabetic patients undergoing anesthesia and surgery who may have serious complications, such as hypertension, ischemic heart disease, nephropathy, and autonomic neuropathy [1, 2]. Compared with the standard population, diabetics have as much as a two- to threefold greater frequency of cardiovascular disorders [4], the mortality rate from which is three times higher than in the standard population. Hospital mortality rates among diabetics are also significantly increased; patients with DM had postoperative strokes more often and spent, on average, more days in hospital [3]. In Part I of this review, we focus on anesthetic considerations in diabetic patients during the preoperative period.

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Prevalence of diabetes mellitus

The drastic increase in the incidence of DM appears to be multifactorial though most heavily impacted by aging of the population and the expanding epidemic of obesity and inactivity. Other factors that impact the development of diabetes appear to be related to chronic inflammatory processes, therapies that result in glucose intolerance, and a genetic tendency to abnormal mitochondrial oxidative phosphorylation [5].

It is widely known that the presence of DM greatly affects perioperative mortality and morbidity. Szabó et al. [6] examined 2,779 consecutive diabetic patients undergoing coronary artery bypass graft (CABG) surgery. They showed that time spent in the intensive care unit and hospital was prolonged and that the need for inotropic agents, hemotransfusions, and dialysis was higher in the diabetic group compared with nondiabetic patients. In addition, renal failure, stroke (4.3 vs. 1.7%), mediastinitis, and wound infections were more frequently encountered in diabetic patients. They also found that although the 30-day mortality rate in diabetic patients was 2.6 versus 1.6% in nondiabetic patients ($p = 0.15$), cumulative 5-year survival in diabetic patients was 84.4 versus 91.3% in nondiabetic patients ($p < 0.001$).

An important concern about diabetic patients is that a significant number with type 2 DM do not know that they are diabetic until the time of surgery. Lauruschkat et al. [7] evaluated the prevalence and risk of undiagnosed DM in 7,310 patients who underwent CABG between 1996 and 2003. Their study is interesting in that it shows that undiagnosed diabetic patients more frequently required resuscitation (nondiabetic 1.7%, known diabetic 1.5%, undiagnosed diabetic 4.2%) and reintubation (nondiabetic 2.1%, known diabetic: 3.5%, undiagnosed diabetic 5.0%), and often required a longer period of ventilation (nondiabetic 5.6%, known diabetic 7.4%, undiagnosed diabetic 10.5%). In addition, perioperative mortality rates were highest in undiagnosed diabetic patients (nondiabetic 0.9%, known diabetic 1.4%, undiagnosed diabetic 2.4%). Hence, in addition to the usual history and physical examination, it is important to evaluate all patients presenting for surgery for the presence of DM and subsequently initiating treatment, such as diet, oral antidiabetic drugs, or insulin.

Diabetes related complications

Since long-standing hyperglycemia in most patients compromises one or more end organs, coexisting pathologies must be identified and carefully managed perioperatively.

Stiff-joint syndrome

The syndrome of joint contractions and nonfamilial short stature in patients with juvenile-onset DM was first reported by Rosenbloom and Frias [8]. They reported three adolescent patients with stiffness of the fingers, wrists, ankles, and elbows, with tight skin over the affected joints. One patient had spine involvement as well. In another study by the same group, Grgic et al. [9] found that the syndrome occurred in 65 of 229 adolescents with juvenile-onset DM. Subsequently, in a 1981 study of 309 patients, they found a positive correlation with microvascular disease, the incidence being unrelated to the adequacy of blood glucose control or insulin dose [10]. Twenty-seven of these patients had either cervical spine involvement or obvious hand deformity at rest. This symptom typically begins in the metacarpophalangeal and proximal interphalangeal joints of the fifth finger and spreads medially. Other large joints, including the cervical and thoracolumbar spine, can also be affected. When affecting cervical joints, it can result in limited joint mobility, called stiff-joint syndrome. The mechanism of stiff-joint syndrome in diabetic patients is, however, unknown. One possibility is that the chronic hyperglycemia of diabetes can induce abnormal cross-linkage of collagen by nonenzymatic glycosylation in connective tissues.

Salzarulo and Taylor [11] first reported a case of difficult endotracheal intubation due to diabetic stiff-joint syndrome in 1986 in a 36-year-old man with juvenile-onset DM who could not be intubated due to severe limitation of tilting the head on the atlas. In 1988, Hogan et al. [12] retrospectively examined the incidence of difficult laryngoscopy in 40 diabetic patients undergoing pancreatic transplantation and in 75 diabetic and 112 nondiabetic patients undergoing kidney transplantation. They found that 32% of the 115 diabetic patients had a difficult laryngoscopy compared with 2.7% of 112 nondiabetic patients. In 1995, Beebe et al. [13] reviewed their experience with perioperative management of diabetic pancreatic transplant patients and found that seven (13%) of their 55 patients had this problem. Reissell et al. [14] examined the difficult laryngoscopy conditions in 31% of 62 diabetic patients who underwent renal transplantation or vitrectomy. Warner et al. [15] examined 725 patients who underwent renal or pancreatic transplantations under general anesthesia with endotracheal intubation. Patients with diabetes were found to have a significantly ($p = 0.002$) higher frequency of difficult laryngoscopy [4.8%, 95% confidence interval (CI) 2.3–8.6%] versus patients without diabetes (1.0%, 95% CI 0.3–2.2%). A recent study from Mashour et al. [16] demonstrated that the presence of DM is one predictor of difficult laryngoscopy in the morbidly obese. Their study interestingly noted that diabetic patients with easy laryngoscopy (Cormack–Lehane laryngoscopic view grades 1 and 2) had a mean glycosylated hemoglobin (HbA1c) of $6.2 \pm 1.3\%$, whereas those with difficult laryngoscopy (Cormack–Lehane laryngoscopic view grades 3 and 4) had a mean HbA1c of $8.7 \pm 1.9\%$. Some reports show the efficacy of the palm print as a sensitive predictor of difficult laryngoscopy in diabetic patients [14, 17]. In contrast, Erden et al. [18] reported no relationship between the "prayer sign" (inability to approximate the palmar surfaces of the phalangeal joints despite maximum effort) and difficult laryngoscopy.

Cardiovascular disease

The chronic effects of DM can be divided into microvascular (including diabetic retinopathy and nephropathy), neuropathic (autonomic and peripheral), and macrovascular complications (atherosclerotic disease). Perioperative cardiovascular morbidity and mortality are increased two- to threefold in patients with diabetes [4]. Diabetic patients have an increased risk of various cardiovascular pathologies, including hypertension, coronary artery disease, peripheral arterial disease, systolic and diastolic cardiac dysfunction, and congestive heart failure. Cardiovascular pathology is the cause of death in 80% of diabetic patients. The recent American College of Cardiology/American

Heart Association updated guidelines on perioperative cardiac assessment of patients undergoing noncardiac surgery place diabetics, especially those receiving insulin, at a minimum of intermediate risk [19]. They also state that the vast majority of diabetic patients >65 years of age have significant symptomatic or asymptomatic coronary artery disease, with a greater incidence of silent ischemia. Reduced appreciation for ischemic pain can impair timely recognition of myocardial ischemia or infarction, thereby delaying appropriate therapy. Silent ischemia in diabetic patients may result from either autonomic neuropathy, coronary artery disease itself, or both [20, 21]. In the Framingham study [22], the rates of unrecognized myocardial infarction were 39% in diabetic patients and 22% in nondiabetic patients. In a survey from the National Registry of Myocardial Infarction 2 (NRMI-2), of 434,877 patients presenting with myocardial infarction, 33% did not have chest pain [23]. Thirty-two percent of those presenting without chest pain had diabetes versus 25.4% in the group with chest pain. The mechanisms of painless myocardial ischemia are, however, complex and not fully understood. In the Detection of Ischemia in Asymptomatic Diabetics (DIAD) study in 1,123 patients with type 2 diabetes, cardiac autonomic dysfunction was a strong predictor of ischemia [24]. Thus, patients with autonomic neuropathy warrant more careful attention, and cardiovascular autonomic function testing may be an important component in the risk assessment of diabetic patients with coronary artery disease.

Another concern is that diabetic cardiomyopathy is a common feature in diabetic patients [25]. Diabetes predisposes to the development of a specific cardiomyopathy that contributes to increasing cardiovascular risk. Diabetic cardiomyopathy progresses from impaired ventricular relaxation to diastolic dysfunction with high left ventricular filling pressures and finally to overt heart failure. As many as 60–75% of asymptomatic, well-controlled patients with type II diabetes demonstrate diastolic dysfunction with increased left ventricular filling pressures [26].

Hypertension develops more commonly in diabetic than in nondiabetic patients and increases in frequency over time and is closely related to the development of progressive nephropathy [27]. Hypertension usually develops within 3 years of the onset of microalbuminuria. The risk of hypertension and renal insufficiency is greatest in African Americans. In type 2 diabetic patients, modest blood pressure control may be more important than chronic glycemic control [27]. In this trial, the UK Prospective Diabetes Study Group reported that blood pressure control using an angiotensin-converting enzyme inhibitor or beta-blocker significantly reduced the risk of death from diabetes-induced macrovascular pathology [28]. Current recommendations are to target a blood pressure of <130/80 mmHg in hypertensive diabetics.

Diabetic autonomic neuropathy

Diabetic autonomic neuropathy is a serious and common complication of diabetes that can affect many organ systems throughout the body, such as the gastrointestinal, genitourinary, and cardiovascular systems. The major clinical manifestations of diabetic autonomic neuropathy include resting tachycardia, exercise intolerance, orthostatic hypotension, constipation, gastroparesis, sudomotor dysfunction, impaired neurovascular function, and hypoglycemic autonomic failure. Determination of the presence of diabetic autonomic neuropathy is based on a battery of autonomic function tests. R–R variation, Valsalva maneuver, and postural blood pressure tests can be useful in determining the presence of cardiovascular autonomic dysfunction. Other tests for autonomic neuropathy are less standardized and less available than commonly used tests of cardiovascular autonomic function. Interpretability of heart rate variability testing requires accurate, precise, and reproducible procedures that use established maneuvers. Detailed practical testing is amply described in other reviews [20, 21].

Gastroparesis

Gastrointestinal symptoms are relatively common in patients with diabetes and often reflect diabetic gastrointestinal autonomic neuropathy [21]. Esophageal dysfunction, the symptoms of which include heartburn and dysphagia for solids, results in part from vagal neuropathy [29]. Via the use of radioisotopic techniques that quantify gastric emptying, it appears that ~50% of patients with long-standing diabetes have delayed gastric emptying (gastroparesis) [30]. Gastric emptying largely depends on vagus nerve function, which can be severely disrupted in patients with DM. Gastroparesis in DM is usually silent, although severe diabetic gastroparesis is one of the most debilitating of all diabetic gastrointestinal complications. The major clinical features of this disorder are early satiety, anorexia, nausea, vomiting, epigastric discomfort, and bloating. Wright et al. [31], using radionuclide techniques, assessed the gastric emptying of fluids and solids in diabetic patients and showed that although the gastric emptying rate of fluids was similar between nondiabetic and diabetic patients, the gastric emptying rate of solids was markedly delayed in diabetic patients compared with that in nondiabetic patients. This study interestingly noted that metoclopramide infusion (10 mg IV bolus) normalized delayed solid emptying rates without affecting fluid emptying rates. Cavallo-Perin et al. [32] demonstrated that the acetaminophen test (rate of acetaminophen absorption after ingestion of 1,500 mg of the drug) is a simple, safe, and noninvasive test for the quantitative assessment of gastric emptying in diabetic patients.

The increased volume of gastric contents associated with diabetic gastroparesis enhances the risk of acid aspiration during the induction of anesthesia. These patients are often asymptomatic, which—together with unpredictable difficulties in tracheal intubation due to the possibility of diabetic stiff-joint syndrome—further increases the risk of aspiration. In contrast to the efficacy of metoclopramide infusion in normalizing delayed solid emptying rates, 10 mg of cisapride 100 min before anesthesia failed to demonstrate any effects on gastric contents and postoperative gastrointestinal motility [33].

Hypoglycemia unawareness

Preoperative fasting for several hours before anesthesia and surgery, in order to empty gastric contents and protect against gastric aspiration during the induction of anesthesia, is a prerequisite for elective anesthesia and surgery. Although most patients can safely fast for several hours before surgery, it is possible that diabetic autonomic neuropathy in these patients can cause or contribute to hypoglycemia unawareness with several hours of preoperative fasting. Although the relationship between diabetic autonomic neuropathy and hypoglycemia unawareness is complex, it is possible that the presence of autonomic neuropathy attenuates the epinephrine response to hypoglycemia in diabetic individuals [34]. Hence, to avoid hypoglycemia in diabetic patients with autonomic neuropathy, in whom hypoglycemia unawareness can lead to silent hypoglycemia, glucose-containing fluids, such as orange juice, should be at the bedside or in the car for emergency use.

Other concerns related to diabetic neuropathy

About 30 years ago, Page and Watkins [35] reported the unusual pattern of cardiorespiratory arrest in eight patients with diabetic neuropathy in whom the possible mechanism was likely related to impaired respiratory responses to hypoxia and susceptibility to drugs with respiratory depressant effects. Controversial data exists regarding the ventilatory responses to hypoxia and hypercapnia in patients with DM [36–45]. An early study from Soler and Eagleton [41] demonstrated preservation of ventilatory responses to hypoxia in diabetics. Subsequently, Calverley et al. [40] demonstrated preservation of the hypoxic drive to breathing in patients with diabetic autonomic neuropathy. However, many other reports confirmed that the ventilatory response to hypoxia was impaired in diabetic patients compared with that in nondiabetic patients [37, 38, 41, 44, 45]. Conversely, conflicting evidence exists concerning the response of the respiratory center to hypercapnia in diabetics [42–45]: in different populations of diabetics suffering from autonomic neuropathy, the hypercapnic drive to breathing was found to be increased, unchanged, or decreased compared with diabetics without autonomic neuropathy and/or healthy individuals. Among the many reports examining the ventilatory response of diabetic patients to hypercapnia is a study by Tantucci et al. [43] demonstrating that diabetic patients without autonomic neuropathy showed a reduction in the hypercapnic respiratory drive, as was seen in diabetic patients with autonomic neuropathy with parasympathetic nervous system damage. Hence, the authors speculated that the sympathetic nervous system (SNS) might modulate the output of the respiratory centers in response to hypercapnic stimuli. The underlying mechanisms of sleep disturbances and impairment of the respiratory system in diabetic patients are poorly understood [46, 47], and further studies are needed to elucidate them.

Postoperative respiratory arrest is sometimes observed in diabetic patients [48]. Acute, unexpected respiratory problems in the recovery room are more common in men, in those aged >60 years, and in obese or diabetic patients [48]. Physicians should exert extra caution while using sedative or analgesic agents in diabetic patients and should be vigilant for unexpected respiratory depression during the postoperative period because of their impaired respiratory response to hypoxia and hypercapnia.

Diabetic neuropathy also affects the thermoregulatory response to hypothermia during surgery. Kitamura et al. [49] showed that the core temperature of diabetic patients with autonomic dysfunction was lower from 120 min into the surgery (35.1°C) onward compared with nondiabetics and diabetic patients without autonomic dysfunction and that perioperative vasoconstriction, evaluated using the forearm–fingertip skin-surface temperature gradient was delayed in patients with autonomic neuropathy compared with the others. They concluded that diabetic patients with autonomic neuropathy might fail to develop a normal core temperature plateau.

Diabetic retinopathy

The retinal and cerebral microvasculatures share many morphological and physiological properties because embryologically, the retina is an extension of the diencephalon, and both organs share a similar pattern of vascularization during development [50]. In addition, there is a close anatomical correlation between both the macrovascular and microvascular blood supply to the brain and the retina, and both vascular networks share similar vascular regulatory processes [50]. Assessment of the cerebral vasculature is important in determining individual risks of cerebrovascular diseases, such as vascular dementia and stroke. Owing to the homology between retinal and

cerebral microvasculatures, changes in retinal vasculature may reflect similar changes in the cerebral vasculature. Using the retinal vasculature as a marker of the state of the cerebral vasculature is advantageous owing to the ease with which the retinal vasculature can be directly visualized. Diabetic retinopathy is one of the microvascular complications of DM, its severity being directly related to the severity and duration of hyperglycemia. The presence of diabetic retinopathy may thus indicate impairment of microvascular circulation in the brain as well. Ono et al. [51] examined the impact of diabetic retinopathy on long-term outcome in diabetic patients undergoing CABG surgery and demonstrated it was a strong independent predictor of overall mortality (relative risk 4.0), possibly due to the fact that diabetics with retinopathy have had a longer-period of poorly controlled diabetes and, therefore, are much more likely to have additional comorbidities, such as progressive cerebral atherosclerosis or impaired cerebral microcirculation. We examined the relationship between diabetic retinopathy and postoperative cognitive dysfunction in patients undergoing CABG surgery [52, 53] and showed that it was a predictor of postoperative cognitive dysfunction because of coexisting impaired cerebral circulation (Table 1).

From the above studies, it appears that retinal circulation may be an alternative, useful predictor of the state of the cerebral circulation. The preoperative presence of diabetic retinopathy is, thus, an important indicator of the risk of postoperative cerebral dysfunction or increased mortality risk and should be assessed in all diabetic patients.

Table 1 Independent predictors of cognitive impairment at 7 days or 6 months after cardiac surgery in diabetic patients

	Odds ratio (95% CI)	*p* value
All cognitive impairment		
HbA1c (%)	2.0 (1.5–3.3)	0.042
Diabetic retinopathy	2.4 (1.4–2.9)	0.01
Insulin therapy	2.1 (1.4–3.5)	0.01
Short-term cognitive impairment		
Age	1.5 (1.3–1.8)	0.03
Ascending aorta atherosclerosis	1.5 (1.1–1.9)	0.01
SjvO2 <50% time	1.5 (1.1–2.6)	0.04
Hypertension	1.8 (1.3–2.0)	0.01
Diabetic retinopathy	2.0 (1.3–3.0)	0.01
Insulin therapy	2.0 (1.3–3.0)	0.049
Long-term cognitive impairment		
HbA1c (%)	1.9 (1.3–3.1)	0.047
Diabetic retinopathy	2.1 (1.2–2.7)	0.01
Insulin therapy	2.0 (1.3–3.8)	0.01

CI confidence interval, *HbA1c* hemoglobin, *SjvO2* jugular venous oxygen saturation, *SjvO2 <50% time* time at which SjvO2 was <50% during cardiopulmonary bypass period

From Kadoi et al. [52]

Anesthetic agents and diabetes mellitus

Anesthetic agents may affect glucose homeostasis perioperatively in diabetic patients either indirectly, by decreasing catabolic hormone secretion, or directly, by altering insulin secretion. The latter mechanism is relevant only in patients with some residual insulin secretion (type 2 diabetes).

Fragen et al. [54] reported that etomidate inhibits adrenal steroid genesis and may induce a decrease in the glycemic response to surgery. In general, gamma-aminobutyric acid (GABA) agonists reduce the secretion of adrenocorticotrophic hormone (ACTH) and consequently cortisol, and stimulate basal secretion of growth hormone (GH). Several studies have investigated modification of hormonal and metabolic response to surgery by benzodiazepines, such as midazolam. In a study by Desborough et al. [55], midazolam was infused at 0.42 mg/kg followed by infusion of 0.125 mg/kg for 1 h. They found that midazolam infusion decreased cortisol and insulin secretion and an increased GH secretion. These effects are believed to be minimal when midazolam is given at the usual sedative dosage but may be relevant if given by continuous infusion to patients in intensive care units.

The alpha 2 agonist, clonidine, reduces sympathetic tone and the release of norepinephrine from nerve terminals. There is controversy regarding the effect of clonidine on the pituitary–adrenocortical system, but decreased release of ACTH and cortisol has been reported with its use [56, 57]. The use of clonidine during surgery has been proposed as a way of improving perioperative hemodynamics while decreasing anesthetic requirements. The effects of clonidine, administered either as premedication or as a coinduction agent, on the glucose response to surgery in nondiabetic patients are inconsistent [56–58]. In contrast, Belhoula et al. [59] reported that premedication of type 2 diabetic patients with clonidine 90 min before surgery improved blood glucose control and decreased insulin requirements during ophthalmic surgery, because clonidine decreased circulating catecholamines despite having no effect on cortisol concentrations and GH secretion. However, Venn et al. [60] reported that dexmedetomidine, a highly selective and potent alpha-2 agonist, decreased insulin secretion after major surgery without exacerbating the glycemic response. This report suggested that impaired insulin secretion was balanced by reduced sympathetic activity. At present, it would be reasonable to accept that alpha-2 agonists, such as clonidine or dexmedetomidine, modify insulin secretion without exacerbating the glycemic response.

High doses of opiates induce not only hemodynamic but hormonal and metabolic stability [61]. These anesthetic agents effectively inhibit the entire SNS and the hypothalamic–pituitary axis. Inhibition of the catabolic hormone response to surgery may be beneficial in diabetic patients.

In vitro, volatile anesthetics, such as halothane, enflurane, and isoflurane, inhibit insulin response to glucose in a reversible and dose-dependent manner [62–64]. The clinical study from Diltoer and Camu [64] showed that glucose tolerance was impaired by isoflurane. In an experimental study [65], halogenated anesthetic agents, such as halothane or sevoflurane, produced greater negative inotropic effects in myocardium of diabetic compared with nondiabetic patients, possibly because diabetes exacerbates anesthetic-induced alterations in troponin–tropomyosin complex activity.

The effect of propofol on insulin secretion is not known. It is well known that diabetic patients have a reduced ability to clear lipids from the circulation [66]. However, propofol used only as an induction agent is thought to have no adverse effect in diabetic patients. Alterations in the pharmacokinetics or pharmacodynamics of propofol in rats with DM were reported in an experimental study [67]. There is no data showing whether propofol use can alter lipid clearance from the circulation. An experimental study showed that propofol impairs diastolic left ventricular filling in experimental models and produces negative lusitropic effects in diabetic cardiomyocytes [68]. Thiopental seems to induce greater negative inotropic effects than does pentobarbital in myocardium of diabetics [69]. Keyl et al. [70] showed that induction or maintenance of anesthesia with a combination of etomidate and opioids may reduce hemodynamic instability in diabetic patients with coexisting cardiovascular autonomic neuropathy.

At present, it is uncertain as to which anesthetic agents facilitate adequate glucose control and hemodynamic stability during the perioperative period.

Regional anesthesia

Regional anesthesia, including spinal, epidural, and other regional blocks, may modulate catabolic hormone and insulin secretion. Activation of the SNS and the hypothalamic–pituitary axis, induced by surgical stress under general anesthesia, provokes increases in circulating glucose, epinephrine, and cortisol concentrations, and these increases were prevented by epidural anesthesia [71]. It is interesting to note that Donatelli et al. [72], in a study on epidural anesthesia and analgesia compared with general anesthesia followed by patient-controlled analgesia, demonstrated a decrease in the incidence of insulin resistance soon after and 48 h after surgery only in patients who were insulin resistant before surgery.

Halter and Pflug [73] examined the effects of sympathetic blockade by spinal anesthesia on pancreatic islet function in humans. They showed that high spinal anesthesia (dermatome level T2–T6) induced a reduction in the acute insulin response to glucose, whereas low spinal anesthesia (dermatome level T9–T12) induced no such reduction. Nakao and Miyata [74] found that suppression of insulin secretion by surgical stress was inhibited by the alpha-blocking agent phentolamine. These reports indicate that beta-adrenergic input modulates insulin secretion in the basal state, suggesting that extensive thoracic sympathetic blockade induced by spinal anesthesia may result in reduced insulin secretion. However, it remains unknown whether extensive spinal anesthesia is detrimental in type 2 diabetic patients.

Regional anesthesia for ophthalmic surgery results in more rapid recovery with earlier mobilization, better pain relief, and less nausea and vomiting and earlier oral intake than does general anesthesia. Barker et al. [75] compared the effect of local and general anesthesia on metabolic control in noninsulin-dependent diabetic patients undergoing cataract surgery and showed that marked cortisol and glucose responses to surgery were observed under general anesthesia, these responses being prevented by performing the surgery under local anesthesia. There are, however, some risks associated with ophthalmic surgery under regional anesthesia. In a series of 12,000 cataract extractions under local anesthesia, eight patients showed evidence of brain-stem anesthesia resulting from local anesthesia, and one developed cerebral spread of the local anesthetic solution [76]. As yet, there is no evidence that regional anesthesia is superior to general anesthesia in terms of mortality and major complications in diabetic surgical patients.

Since regional anesthesia, such as epidural or spinal anesthesia, can block sympathetic activation and the catabolic hormonal response induced by surgical stress, there may be several risks linked to its use in diabetic patients with autonomic neuropathy. Deleterious hypotension can occur, this hemodynamic instability being of greater significance in diabetic patients with coronary artery or cerebrovascular diseases. In addition, DM is a risk factor for development of epidural abscesses following epidural anesthesia [77, 78]. Eastwood [79] reported a case of anterior spinal artery syndrome arising as a complication of epidural anesthesia in a patient with diabetic scleredema.

High doses of local anesthetics have been reported to induce nerve injury and to reduce nerve blood flow. This indicates that the nerve injury resulting from high doses of local anesthetics is probably ischemic in origin. Fibers in diabetic nerves may, therefore, be more susceptible to

anesthetic toxicity both because they are exposed to a higher local concentration of anesthetics due to impaired blood flow and because they are already stressed by chronic ischemic hypoxia. Kalichman and Calcutt [80] examined the effects of local anesthetics on nerve conduction and nerve-fiber injury in streptozotocin-induced diabetic rats. They showed that nerve-fiber injury, based on light microscopic scoring of axonal degeneration and demyelination, was evident in all lidocaine groups and was significantly greater for nerves of lidocaine-treated diabetic rats compared with lidocaine-treated controls. This data suggests that the risk of local anesthetic-induced nerve injury during regional anesthesia may be greater in diabetic patients. Caution must therefore be exerted in diabetic patients as to the total dosage of local anesthetics used in order to avoid peripheral nerve injury.

Preoperative management of diabetes

In addition to serum glucose levels, the glycosylated HbA1c test is useful in evaluating the efficacy of therapeutic control of the diabetic state. HbA1c is not affected by short-term changes in blood glucose levels but, instead, reflects long-term changes in blood glucose levels. Thus, HbA1c is not useful to monitor acute changes in blood glucose in the perioperative period. However, elevated HbA1c is predictive of the presence of microvascular and macrovascular complications associated with DM. Normally, an HbA1c of 6% indicates that the blood glucose is <120 mg/dl. HbA1c increases to 8% when the blood glucose is 180 mg/dl, to 10% when blood glucose is 240 mg/dl, and to 13% at a blood glucose level of 330 mg/dl.

Diabetic patients present a challenge to physicians, and hence, preoperative evaluation should focus on the type of diabetic disease (type 1 or type 2), method of home monitoring, and usual metabolic control. Knowledge about patients' antidiabetic therapy, such as diet, antihyperglycemic agents, or insulin therapy, is important information for physicians to maintain adequate glucose levels during the perioperative period. Oral hypoglycemic drugs are withheld on the day of surgery for drugs with a short half-life and up to 48 h preoperatively for long-acting drugs such as chlorpropamide. This is done to avoid reactive hypoglycemia, particularly with sulfonylurea compounds, and associated drug-induced toxicities and interactions.

Type 2 diabetic patients with marked hyperglycemia under oral treatment should be switched to insulin preoperatively. The insulin requirements in diabetic patients during surgery vary from 0.25 to 0.40 U/g glucose in normal-weight patients; to 0.4–0.8 U/g glucose in case of obesity, liver disease, steroid therapy, or sepsis; to 0.8–1.2 U/g glucose in patients undergoing cardiopulmonary bypass surgery. Therefore, the appropriate insulin dose has to be determined separately for each individual. The regimen preferred by most authors is based on a variable rate of insulin. Insulin secretion, depending on the extent of hypoinsulinemia, lipolysis, and ketogenesis, is enhanced, which may result in metabolic acidosis with subsequent electrolyte disturbances. Protein catabolism is increased in diabetics because of increased protein breakdown and decreased synthesis. Insulin administration reverses or overcomes most of these disturbances.

Conclusion

Diabetic patients require perioperative care more frequently than their nondiabetic counterparts. The major risk factors for diabetics undergoing surgery are the end-organ diseases associated with diabetes: cardiovascular disease, autonomic neuropathy, joint collagen tissue disorders, and immune deficiency. Hence, physicians should be vigilant about treating these coexisting conditions to ensure optimal perioperative management of diabetic patients.

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