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REVIEW ARTICLE

Anesthetic considerations in diabetic patients. Part II: intraoperative and postoperative management of patients with diabetes mellitus

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Abstract Some studies have reported that tight glycemic control in diabetic patients undergoing major surgery improves perioperative morbidity and mortality rates. Recently, however, large randomized studies have shown such control increases the mortality rate, since aggressive glycemic control induces more frequent incidences of hypoglycemia. Diabetic patients have cerebral complications during the perioperative period more often than their nondiabetic counterparts. Further, anesthetic agents have some effects on cerebral circulation and cerebrovascular carbon dioxide reactivity. Hence, anesthesiologists should have adequate knowledge about anesthetic agents that maintain the integrity of the cerebral circulation. Patients with diabetes mellitus (DM) have an increased susceptibility to perioperative infections. Recent work confirmed that a combination of intravenous and subcutaneous insulin as a glucose management strategy had beneficial effects identical with intravenous insulin therapy alone on the reduction of infection rates during the postoperative period.

Keywords Diabetes mellitus · Tight glycemic control · Perioperative management

Introduction

In Part I of the anesthetic considerations in diabetic patients, we discussed the preoperative management of patients with diabetes mellitus (DM). In this review, we primarily discuss perioperative glucose control in diabetic patients during anesthesia and surgery and in the postoperative period. Additionally, it is widely known that diabetic patients often have cerebral complications during the perioperative period. Thourani et al. [1] showed that diabetic patients undergoing coronary artery bypass graft (CABG) surgery had a higher incidence of postoperative death (3.9% vs. 1.6%) and stroke (2.9% vs. 1.4%) ($p \leq 0.05$ in both). We therefore discuss cerebral circulation during the perioperative period in diabetic patients. In addition, it is widely known that patients with DM have an increased susceptibility to perioperative infections, so we also discuss perioperative infections in these patients.

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Intraoperative management of diabetic patients

Hemodynamic instability

There are many reports related to hemodynamic instability during induction and maintenance of anesthesia in diabetic patients [2–7]. Burgos et al. [2] examined the effects of diabetes on hemodynamic instability in patients undergoing elective ophthalmic surgery under general anesthesia. They showed that heart rate and blood pressure declined to a greater degree during anesthesia induction in diabetics compared with controls, and there was less of an increase in these same parameters in diabetic patients following tracheal intubation. In addition, they found that 35% of diabetics required intraoperative vasopressors compared with only 5% of controls. They concluded that diabetics are at risk for cardiovascular lability under general anesthesia. In contrast, Keyl et al. [8] found no relationship between hemodynamic instability during anesthetic induction and abnormal autonomic function tests, although most of the

diabetic patients they studied had impaired autonomic function. However, many other reports [2–7, 9] emphasize the importance of diabetic neuropathy in patients with hemodynamic instability during the perioperative period. Latson et al. [7] speculated several probable mechanisms for this hemodynamic instability. One is that in patients with autonomic neuropathy, homeostatic reflexes are less able to compensate for the effects of anesthetic induction on venous return, vascular tone, and myocardial contractility. Alternatively, patients with autonomic neuropathy may be less able to tolerate further depression of homeostatic reflexes by the administered anesthetics. A third possible mechanism is that preexisting alterations in autonomic neuropathy may influence the indirect effects of anesthetics on vascular and myocardial function.

It is important to prevent hemodynamic instability during surgery in diabetic patients, especially in those prone to develop renal and cardiac complications postoperatively [10]. Thus, anesthesiologists should be aware of the preoperative presence of diabetic neuropathy and be extra cautious about preventing severe hypotension during anesthesia induction and the perioperative period. Treatment of perioperative hemodynamic instability in diabetic patients may require administration of IV fluids and the use of vasopressors. Although there is no clinical evidence regarding the value of intraoperative transesophageal echocardiography (TEE) in guiding this management in such patients, TEE may be clinically helpful in assessing left ventricular filling, preload responsiveness, and overall cardiac performance. Other hemodynamic monitoring techniques, such as pulmonary artery catheter, central venous pressure, or continuous arterial pressure monitoring, may also be clinically helpful in assessing hemodynamics and treating hemodynamic instability.

Intravenous vasodilators, such as nitroglycerin or a recombinant brain natriuretic peptide, are effective in decreasing ventricular filling pressure, although excessive decreases in preload can compromise cardiac output and may cause hypotension. In some cases, the use of positive inotropic drugs, such as dopamine or dobutamine, may be required. Vasopressor support is needed more often in diabetic patients with autonomic neuropathy than in those without autonomic neuropathy. However, these inotropic drugs may not adequately stabilize hemodynamics.

In clinical practice, for intraoperative management of hemodynamic instability in diabetics, dopamine or dobutamine infusions are started at a continuous rate of 3–5 μg/kg per minute. Higher dosages are sometimes needed in patients with cardiomyopathy or neuropathy. Continuous infusions of nitroglycerin are started at a rate of 0.5–1.0 μg/kg per minute, although a change in infusion dosage is often needed. Bolus infusion of ephedrine, phenylephrine, or atropine sulfate may be used for transient improvement of hemodynamics. However, these drugs may not be efficacious in maintaining systemic hemodynamics, as shown in the report by Tsueda et al. [11], which showed that the atropine-induced heart rate in diabetics was significantly lower than that in nondiabetics (95 ± 14 beats/min vs. 109 ± 12 beats/min, respectively), the heart rate being closely related to preoperative orthostatic diastolic blood pressure changes.

Glucose control

Recent studies suggest that aggressive glucose control would result in improved survival, decreased incidence of ischemic events, and reduced rate of complications [12–15]. Van Den Berghe et al. [12], using intensive insulin therapy, shed new light on the issue of glucose control in critically ill patients. They reported that tight glucose control could be maintained using insulin infusions, even in patients who received early nutritional support via the enteral or parenteral route, and that improved glucose control resulted in fewer complications and better survival rate. Data from this sentinel network was widely disseminated, generated significant commentary, and stimulated achievement of the common goal of euglycemia in most intensive care units (ICUs). Since then, there have been some published reports proving the efficacy of tight glycemic control during the perioperative period in diabetic patients. Lazar et al. [14] examined whether a glucose–insulin–potassium (GIK) infusion in 141 diabetic CABG patients could improve perioperative outcomes and found that GIK patients had lower serum glucose levels (138 ± 4 vs. 260 ± 6 mg/dl; $P < 0.0001$), a lower incidence of atrial fibrillation (16.6% vs. 42%; $P = 0.0017$), and a shorter postoperative length of hospital stay (6.5 ± 0.1 vs. 9.2 ± 0.3 days; $P = 0.003$). GIK patients also showed a survival advantage during the initial 2 years after surgery ($P = 0.04$), with decreased episodes of recurrent ischemia (5% vs. 19%; $P = 0.01$) and fewer recurrent wound infections (1% vs. 10%, $P = 0.03$). Ouattara et al. [13] also demonstrated the efficacy of tight perioperative blood glucose control in improving the outcome of cardiac surgery in diabetic patients. In addition, Doenst et al. [15] reported that a high peak serum glucose level during cardiopulmonary bypass was an independent risk factor for death and morbidity in diabetic and, unexpectedly, nondiabetic patients. These reports highlight the importance of tight glycemic control during the perioperative period in diabetic patients undergoing CABG surgery.

Recently, in contrast, large, prospective, randomized, studies [16–18] addressed the question of whether tight glycemic control during the perioperative period actually improves postoperative outcome. The Efficacy of Volume Substitution and insulin Therapy in Severe Sepsis (VISEP)

trial from Germany in 2008 [16] reported that there were no significant differences between the intensive and conventional insulin therapy groups in the death rate or mean score for organ failure at 28 days. In addition, they found that the rate of severe hypoglycemia (glucose level ≤40 mg/dl) was higher in the intensive-therapy group than in the conventional-therapy group (17.0% vs. 4.1%, $P < 0.001$, respectively), as was the rate of serious adverse events (10.9% vs. 5.2%, $P = 0.01$, respectively). The Glucontrol study from Europe in 2009 [17] had to be discontinued because the rate of hypoglycemia was higher in the intensive insulin therapy group (8.7%) than in the conventional insulin therapy group (2.7%, $P < 0.0001$). The Normoglycemia in Intensive Care Evaluation-Survival Using Glucose Algorithm Regulation (NICE-SUGAR) trial in 2009 [18] was designed to be a pivotal multicenter, multinational trial involving 42 hospitals in Australia, New Zealand, Canada, and the USA. In this study, of the 6,104 patients who underwent randomization, 3,054 were assigned to the intensive therapy group and 3,050 to the conventional insulin therapy group. The study found that 829 patients (27.5%) in the intensive therapy group and 751 (24.9%) in the conventional insulin therapy group died [odds ratio (OR) for intensive therapy 1.14; 95% confidence interval (CI) 1.02–1.28; $P = 0.02$]. In addition, severe hypoglycemia (blood glucose level ≤40 mg/dl) was reported in 206 patients (6.8%) in the intensive therapy group and 15 (0.5%) in the conventional insulin group ($P < 0.001$). These studies [16–18] indicate that tight glycemic control during the perioperative period may not always be beneficial.

So, why did the NICE-SUGAR trial and other studies show such different outcomes from the results of van den Berghe et al. [12]? Why did intensive insulin therapy in the ICU result in increased mortality? Several possibilities exist. Parenteral nutrition, enteral feeding, or combined feeding was provided to all patients within 24 h of admission to the ICU. Further, experimental data has demonstrated that both insulin and hypoglycemia may induce hypotension resulting from nitric oxide release, leading to reduced sympathetic nervous system (SNS) response to stress. These effects may alter systemic and peripheral hemodynamics in humans. Finally, the incidence of hypoglycemia in the Van Den Berghe report [12] was low, seen in only 5% of the study group and 0.7% of the control group, with no reported neuroglycopenic complications. The authors concluded that well-educated staff using a standard insulin infusion protocol can minimize hypoglycemic events. However, Vriesendorp et al. [19] demonstrated that DM is a predisposing factors for hypoglycemia in the ICU. In addition, Egi et al. [20] recently found a relationship between hypoglycemia and adverse outcomes in diabetic patients in ICUs. It is reasonable to infer that hypoglycemia may be becoming more prevalent as patients are set strict glucose control targets during the perioperative period. Physicians must bear in mind that hypoglycemia remains a major problem in the management of diabetes, particularly in patients treated with insulin.

Many institutes or physicians have published therapeutic regimes for glycemic control [12–18]. Wilson et al. [21] reviewed the performance characteristics of 12 insulin infusion protocols, and found that there was great variability in protocols, the areas of variation including differences in initiation and titration of insulin, use of bolus dosing, calculations used for adjustment of the insulin infusion, and method of insulin protocol adjustments. It is, however, proven that continuous infusion of insulin is superior to intermittent infusion of insulin for tight blood glucose control [22]. The key to managing blood glucose levels perioperatively in diabetic patients is, thus, to set clear goals (target blood glucose levels during the perioperative period) and monitor blood glucose levels frequently enough to adjust therapy to achieve these goals.

It is known that surgery causes a marked, though transient reduction in insulin sensitivity [23, 24], the degree of reduction being related to the magnitude of the surgery. Although the mechanism of this reduction in insulin sensitivity during the perioperative period has not been completely proven, Thorell et al. [25] showed the relationship between postoperative insulin sensitivity and interluekin-6 levels.

Neuromuscular agents

Some researchers demonstrated that recovery from the nondepolarizing neuromuscular agent, vecuronium, is delayed in diabetic patients compared with nondiabetic patients [26–28] because diabetic patients exhibit degeneration, demyelination, or axon loss in the motor nerve ending of the neuromuscular junction and infarction or atrophy in the skeletal muscle. It is known that volatile anesthetics such as sevoflurane or isoflurane enhance the action of neuromuscular relaxants, so that physicians must be aware of delayed recovery from the effects of nondepolarizing neuromuscular-blocking agents under volatile anesthetics in diabetic patients.

Practical protocol of perioperative glucose control

Perioperative reduction in insulin sensitivity may result in insulin resistance and difficulty in controlling glucose levels. Managing intraoperative glucose may be dependent on the type of diabetes, type of operation, pregnancy, physician bias, and preoperative glucose control. All type 1

diabetics require insulin to avoid ketogenesis, whereas a significant number of type 2 diabetics require insulin to avoid significant hyperglycemia. However, data indicate that type 2 diabetic patients do not benefit from tight perioperative blood glucose control unless they need intensive care [29].

In all diabetic patients, frequent blood glucose estimations (at a minimum of 2-h intervals) and adequate glucose management (maintaining blood glucose levels <200 mg/dl) during the perioperative period are essential. In addition, plasma potassium should be measured at least every 4 h, and more frequently in case of high insulin requirements. Plasma potassium levels should be maintained in the 4.0–4.5 mEq/L range to decrease the incidence of cardiac arrhythmias due to hypokalemia.

There is much debate regarding the optimal amount of intravenous fluid for diabetic patients [30–32]. Thomas and Alberti [31] showed that 1 L of Hartmann's solution postoperatively was associated with a 7.5-mmol/L (about 136 mg/dl) increase in plasma glucose concentrations compared with an increase of 2.1 mmol/L (38 mg/dl) in diabetic patients who received no IV fluids. In nondiabetic patients who received Hartmann's solution, the increase was 2.5 mmol/L (about 45 mg/dl). They concluded that Hartmann's solution may be metabolically disadvantageous in diabetic patients. However, a recent review [32] suggests that the maximum increase in glucose concentration with 1 L of Hartmann's solution would be about 1 mmol/L (about 18 mg/dl), whereas in clinical practice, the effect on blood glucose will be much less. Currently, it is accepted that Hartmann's solution is unlikely to adversely affect glycemic control [32]. Another concern with regard to IV fluid therapy in diabetic patients is hyponatremia, and postoperative hyponatremia is commonly observed when only glucose-containing solutions are administered. Finally, since glucose and lactate are present in concentrations of red blood cells, their metabolites may influence glycemic control when diabetic patients require blood transfusion.

In 1979, Alberti and Thomas [31] described a simple and safe method of achieving glycemic control whereby GIK were infused at a fixed rate (the GIK system, or Alberti regimen). This regimen rapidly became established practice at a time when infusion pumps were unreliable. The standard IV fluid in the Alberti regimen (500 ml of 10% glucose + 10 U of insulin + 1 g KCL) was infused at a rate of 100–125 ml/h. However, since the risk of hyponatremia from prolonged infusion of glucose solutions is well recognized [31], 0.9% sodium chloride solution is also an acceptable fluid for IV use in diabetic patients. With the Alberti regimen, however, neither glucose nor insulin infusion rates can be independently varied. If blood glucose levels are not adequately controlled, the bag of IV fluid has to be discarded and a new bag of glucose, with the appropriate amount of insulin and potassium, has to be started. Variable rates of insulin regimens became feasible as a result of reliable infusion pumps and the widespread availability of rapid, accurate monitoring of blood glucose concentrations. Recently, many regimens of insulin infusion have been described from different institutes. The most popular and accepted method is summarized in Table 1.

Table 1 Variable rate of intravenous insulin by pump infusion

Place 50 U of regular insulin in 50 ml of 10% dextrose in 0.45% sodium chloride plus potassium in an infusion pump (1 U insulin/ml). Before attaching it to the infusion pump, flush the line with 3 ml of the infusion mixture and discard the flushing solution. This approach saturates insulin-binding sites on the tubing.	
The objective is to maintain blood glucose levels between 100 and 200 mg/dl	
For glucose levels <200 mg/dl and >100 mg/dl, start the infusion at 1 or 2 U/h	
For glucose levels >200 mg/dl, give boluses of 2–4 U and start the infusion at 1 or 2 U/h	
Measure glucose levels every 1 h. Pay close attention to potassium and sodium levels	
Titrate insulin infusion	
Blood glucose mg/dl	Action protocol
<50	Stop infusion for at least 30 min and administer bolus of 50 ml (25 g) of 50% glucose, recheck in 15 min. Redose with glucose as needed. If glucose >70, restart insulin at half the previous rate
50–70	Turn off infusion for 30 min but continue 5–10% glucose infusion, then measure glucose concentration
70–120	Decrease insulin infusion rate by 1 U/h
121–180	Continue insulin infusion at the same rate (0.3 U/g glucose)
181–250	Increase insulin infusion rate by 2 U/h
>250	Bolus of 2–4 U of insulin and increase insulin infusion rate by 3 U/h

Cerebral circulation in diabetic patients

Many studies show that diabetic patients experience a higher incidence of cerebral complications during the perioperative period compared with patients without diabetes. Arrowsmith et al. [33] reported that diabetes is a key variable predicting major perioperative neurological events. Tao et al. [34] showed that diabetes was an independent predictor of perioperative stroke. One possible cause of postoperative neurological dysfunction in diabetic patients is impaired cerebrovascular circulatory and vasodilatory reserves. Hence, we must have adequate knowledge of the cerebral circulation in diabetic patients undergoing anesthesia. Before discussing the cerebral circulation during anesthesia, it is important to understand cerebral circulation in the awake condition. Controversial data exist regarding whether cerebral autoregulation is intact or not in diabetic patients in the awake state and under anesthesia. It is believed that cerebral blood flow (CBF) is constant between systolic blood pressures of 50 and 150 mmHg under normal conditions. In diabetics, however, compared with normal individuals, the cerebral pressure flow autoregulation curve is shifted toward the right (Fig. 1).

Awake state

In 1975, Bentsen and Larsen [35] examined cerebral pressure flow autoregulation in diabetic patients and found that CBF changed in parallel with blood pressure (Fig. 1). They assumed that cerebral autoregulation was impaired in diabetic patients. Griffith et al. [36] reported that of 22 diabetic patients, 14 responded normally and eight failed to show a significant increase in CBF in response to hypercapnia when the ^{133}Xe-clearance method of analysis was used. Dandona et al. [37] reported that there was a significant variation in CBF after administration of 5% carbon dioxide (CO_2) in insulin-dependent diabetics compared with normal individuals, using the ^{133}Xe-inhalation method, concluding that diabetics had diminished cerebrovascular reserve and were unable to compensate with an increased CBF when necessary. Rodriguez et al. [38] reported that compared with controls, the percentage of global CBF increment measured by the ^{133}Xe-inhalation method after acetazolamide administration was significantly impaired in four insulin-dependent diabetic patients, with two showing a borderline response. These reports [35–37] showed that cerebrovascular CO_2 reactivity and CBF changes were impaired in diabetic patients. In an animal study, Pelligrino and Albrecht [39] demonstrated that cerebral vasodilatory response to hypercapnia is intact during normoglycemia but impaired during hypoglycemia in diabetic rats.

Anesthetic state

Controversial data exists regarding cerebral circulation in diabetic patients during anesthesia [40–45]. Croughwell et al. [40] examined cerebral metabolic autoregulation during the cardiopulmonary bypass period using the ^{133}Xe-clearance method and reported that the CBF of their diabetic group remained constant despite an increase in temperature from 27°C to 37°C, in contrast to an 83% increase in CBF in the control group. They concluded that diabetic patients lose cerebral autoregulation during cardiopulmonary bypass and compensate for an inadequate oxygen delivery by increasing oxygen extraction. In a previous study [41], we found a significant difference in the mean slopes of jugular venous oxygen saturation versus cerebral perfusion pressure (CPP) for increasing CPP, between insulin-dependent diabetic patients and diabetic patients on diet and glibenclamide therapy. In contrast, Kawata et al. [42] examined the effects of DM on CO_2 reactivity using transcranial Doppler (TCD) and found that the relative values of CO_2 reactivity in diabetic patients were equivalent to those of controls during isoflurane

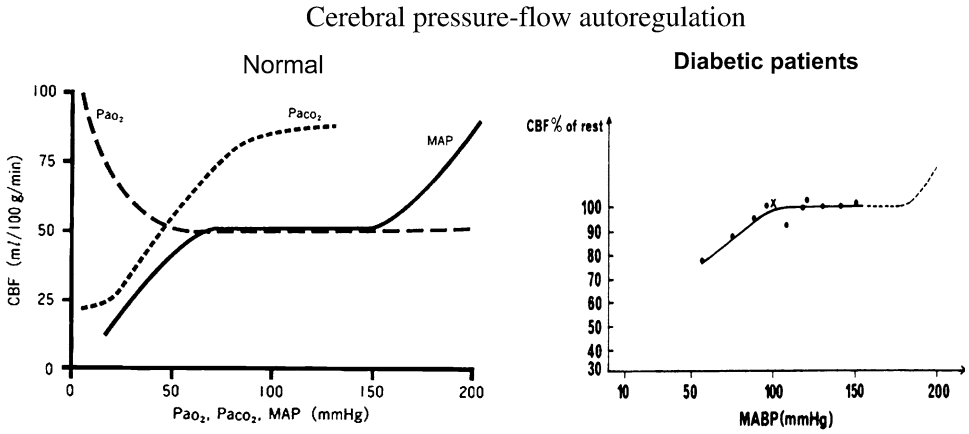

Fig. 1 Cerebral pressure flow autoregulation curve in normal and diabetic patients. Cerebral blood flow is constant between 50 and 150 mmHg in nondiabetic patients. Compared with normal individuals, the cerebral pressure flow autoregulation curve is shifted toward the *right* in diabetic patients

anesthesia. Sieber et al. [43] reported that 4 months of hyperglycemia in an animal model increased both CBF and the cerebral metabolic rate for oxygen. They speculated that the effects of DM on the cerebral vasculature were complicated by a host of factors, including diabetic microangiopathy, atherosclerosis, hypertension, renal disease, and chronic hyperglycemia, and concluded that it was likely that many reported abnormalities in CBF physiology were the result of diabetic vascular disease rather than hyperglycemia. Our previous study [44] showed that diabetic patients with retinopathy had abnormal cerebrovascular CO_2 reactivity compared with diabetic patients without retinopathy and with control groups. In addition, we demonstrated the relationship between glycosylated hemoglobin (HbA1c) and impaired cerebrovascular CO_2 reactivity in diabetic patients (Fig. 2). As mentioned earlier, retinal circulation might reportedly represent the cerebrovascular circulation because the retina develops from the forebrain. Abnormal cerebral microangiopathy in diabetic patients would thus be represented by diabetic retinopathy. In addition, Stratton et al. [45] reported that in patients with type 2 diabetes, the risk of diabetic complications such as macrovascular and microvascular disease was strongly associated with previous hyperglycemia. This implies that the primary cause of microvascular disease is chronic hyperglycemia itself. Klein et al. [46] reported that glycosylated HbA1c predicted the incidence and progression of diabetic retinopathy. In addition, Pallas and Larson [47] noted that hyperglycemia leads to impaired vascular function through endothelial cell function. The pathway that appears most affected by the diabetic state is that of nitric oxide. Loss of this pathway is accompanied by loss of response to partial pressure of carbon dioxide in arterial blood ($PaCO_2$) and lack of autoregulation related to flow-pressure relationships.

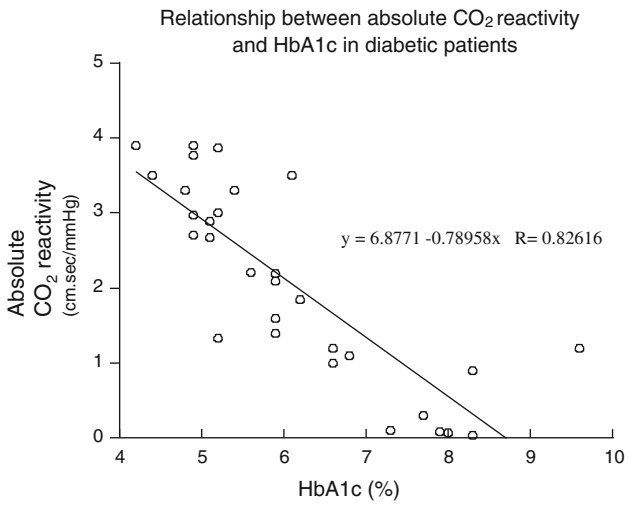

Fig. 2 Relationship between absolute carbon dioxide (CO_2) reactivity and glycosylated hemoglobin (HbA1c) in diabetic patients. Absolute CO_2 reactivity is inversely related to HbA1c

Another consideration is that anesthetic agents may modulate cerebrovascular CO_2 reactivity in diabetic patients. We previously examined the effect of sevoflurane, isoflurane, and propofol on cerebrovascular CO_2 reactivity in diabetic patients [48, 49] and found that different anesthetic agents can differentially modulate their cerebrovascular CO_2 reactivity.

So far, we have discussed cerebrovascular CO_2 reactivity impairment in diabetic patients under anesthesia. However, is there any clinical implication of this impairment? Gur et al. [50] demonstrated that impaired cerebrovascular CO_2 reactivity could have a prognostic value in predicting cerebral ischemic events. Kessler et al. [51] showed that reduced cerebrovascular CO_2 reactivity is an indicator of postoperative confusion. These two reports show the importance of preoperative examination of cerebrovascular circulation or CO_2 reactivity in diabetic patients.

Perioperative infections

Patients with DM have an increased susceptibility to perioperative infections [52]. Several factors may contribute to the increased complication rate in diabetics, including poor preoperative nutritional status, concurrent obesity, and preexisting immune deficiencies [52]. Hyperglycemia plays an important role in altering leukocyte function, including that of polymorphonuclear neutrophils (PMNs). In 1971, Mowat and Baum [53] demonstrated that PMNs from diabetic patients showed decreased chemotaxis compared with PMNs from nondiabetics. Furthermore, the observed defect in chemotaxis could be corrected by incubating the PMNs with insulin. Bagdade et al. [54] showed that the rate of phagocytosis and bacterial killing by PMNs from patients with poorly controlled diabetes was decreased compared with PMNs from nondiabetics. Rassias et al. [55] examined the effects of an insulin infusion on perioperative neutrophil function in diabetic patients undergoing CABG surgery. They showed that aggressive insulin therapy had a more beneficial effect on neutrophil phagocytic activity compared with standard insulin therapy. Furnary et al. [56] demonstrated that better glycemic control with insulin infusions would reduce the incidence of deep sternal wound infections in diabetic patients undergoing cardiac surgery. Recent work confirmed that a combination of IV and SC insulin as a glucose management strategy had identical beneficial effects as IV insulin therapy alone on reduced infection rates during the postoperative period [57].

Other considerations

There are some concerns about the measurement methods of plasma blood glucose levels. In many institutes, samples for laboratory serum or plasma glucose determination are obtained from either venous or arterial sites. Variability is introduced into the reporting of glucose values because of patient variables and differences between assay methods. Patient variables may include physiology and interfering substances [58] (Table 2). In addition, while analyzing blood glucose results, physicians should bear in mind the differences between assay characteristics, performance of commercial products, sample source, and specimen matrix (plasma vs whole blood).

Conclusion

Diabetic patients require perioperative care more frequently than their nondiabetic counterparts. The major risk factors for diabetics undergoing surgery are associated end-organ diseases: cardiovascular disease, autonomic neuropathy, joint collagen tissue disorders, and immune deficiency. Physicians should be vigilant about treating coexisting conditions to ensure optimal perioperative management. Tight glycemic control in diabetic patients undergoing major surgery has been shown to improve perioperative morbidity and mortality rates. However, this aggressive strategy requires frequent monitoring of blood glucose concentrations to avoid hypoglycemia.

Table 2 Confounding variables in glucose measurement

Variables	Methodology affected	
	Glucose oxidase	Glucose-1-dehydrogenase
Whole blood	↓	↓
Arterial	↑	↑
Capillary	↑	↑
Postprandial state	↑	↑
Hematocrit		
Anemia	↑	↑
Polycythemia	↓	↓
Oxygen concentration		
Hypoxia	↑	–
Oxygen therapy	↓	–
pH (6.8–7.55)	–	–
Low pH	–/↓	–
High pH	–/↑	–
Hypothermia	↑	↓/↑
Hypotension	↑	↑/↓
Drugs		
Ascorbic acid	↓	↑/–
Acetaminophen	↓	↑
Dopamine	–	↓
Icodextrin	–	↑
Mannitol	↑	–

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