



Perioperative Management of Diabetes Mellitus: Novel Approaches

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Abstract

Purpose of Review Several studies have demonstrated the benefits of glycemic control in the perioperative period and there is ongoing interest in development of systematic approaches to achieving glycemic control. This review discusses currently available data and proposes a new approach to the management of hyperglycemia in the perioperative period.

Recent Findings In a recent study, we demonstrated that early preoperative identification of patients with poorly controlled diabetes and proactive treatment through various phases of surgery improves glycemic control, lowers the risk of surgical complications, and decreases the length of hospital stay.

Summary Implementation of a perioperative diabetes program that systematically identifies and treats patients with poor glycemic control early in the preoperative period is feasible and improves clinical care of patients undergoing elective surgery.

Keywords Diabetes mellitus · Hyperglycemia · Surgery outcomes · Perioperative treatment · Stress hyperglycemia

Introduction

Several studies have shown that patients with diabetes mellitus have an increased risk of surgical complications. This may be due to severity of the primary condition that led to surgery or hyperglycemia itself may play a role in increasing the risk of post-surgical complications. The stress of surgery also raises blood glucose levels and makes the association between hyperglycemia and surgical complications more complex. Many patients, even those without diabetes, become hyperglycemic during the perioperative period [1]. Observational studies show that perioperative hyperglycemia, with or without established diabetes, predicts clinical outcomes like postoperative infections, thrombo-embolic events,

cardiovascular complications, renal insufficiency, and length of hospital stay [2–5]. However, very few interventional studies have been conducted to investigate the effectiveness of perioperative glycemic control in reducing the risk of surgical complications. This review discusses currently available data and describes a novel approach to the management of hyperglycemia in the perioperative period that improves clinical outcomes.

Basic and Translational Research Suggesting the Importance of Perioperative Glycemic Control

Increased risk of infections and poor wound healing in patients with diabetes is a well-known phenomenon [6]. Multiple pathophysiological changes are present in patients with diabetes that may contribute to this increased risk. Body's defense mechanisms are likely to be activated in the perioperative period to repair the primary condition as well as the tissue damage caused by surgery. In contrast, hyperglycemia is a state of chronic inflammation and endothelial dysfunction with underlying vascular damage [7]. An exaggerated inflammatory response after surgery in patients with diabetes may contribute to poor wound healing. Moreover, neutrophil phagocytic activity is impaired in the presence of hyperglycemia increasing the chances of infection and poor

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wound healing [8]. Improved glycemic control with insulin infusion improves neutrophil phagocytic activity [9, 10]. Additionally, any infection is likely to produce a more severe inflammatory response in the presence of hyperglycemia [11] and normalization of blood glucose levels with insulin infusion can prevent the endotoxin induced hyper-inflammatory response [12, 13]. Hyperglycemia also induces endothelial dysfunction that affects microvascular function critical for wound healing after surgery. Endothelial dysfunction in patients with diabetes along with compromised microvascular function may lead to relative tissue ischemia [14]. Moreover, many patients with diabetes have underlying macrovascular and microvascular disease that may compromise blood supply to the healing tissues. Therefore, maintaining good glycemic control in the perioperative period may improve vascular function and help in healing of the damaged tissues.

Clinical Evidence Supporting Perioperative Glycemic Control

Many observational studies have demonstrated a link between diabetes and poor clinical outcomes after surgery [4, 15–18]. The higher the perioperative blood glucose levels, the higher the risk of complications [17, 19]. It is well known that diabetes mellitus increases short-term mortality and morbidity in patients undergoing coronary artery bypass graft surgery [15]. However, it is difficult to isolate the acute effect of hyperglycemia from the chronic effect that leads to more severe coronary artery disease in patients with diabetes. Some of the early studies in this area, conducted by Furnary and colleagues, showed increased incidence of sternal wound infections in patients with diabetes, with evidence of an effect of acute hyperglycemia in the postoperative period [20]. After implementing a program that included insulin infusion to normalize blood glucose levels for 72 h after cardiac surgery, the incidence of sternal wound infections in patients with diabetes decreased to levels similar to those in patients without diabetes [20]. The use of insulin infusion after cardiac surgery also decreased mortality and several morbidity parameters [21]. Another study showed that tight perioperative glycemic control in patients with diabetes undergoing coronary artery bypass graft surgery improves perioperative outcomes and decreases recurrent ischemic events [22]. Insulin infusion to maintain a tight glycemic control in a surgical intensive care unit that included a large proportion of cardiac surgery patients showed a remarkable reduction in mortality and morbidity [23]. Even more convincing are the data for other types of surgery, for example, vascular surgery, orthopedic surgery, plastic surgery, and colorectal surgery [4, 18, 24].

Perioperative hyperglycemia, specifically during the first 24 h after surgery, was associated with high rates of surgical site infections in patients undergoing microvascular head and neck reconstruction surgery in a recent study [25]. In another study conducted using National Surgical Quality Improvement Program database, stress hyperglycemic defined as postoperative blood glucose > 140 mg/dL was found in 46% patients and was associated with increased incidence of surgical site infections [26].

While above data suggest that acute hyperglycemia during the perioperative period is associated with poor surgical outcomes, the effect of chronic hyperglycemia on surgical outcomes is less clear. Some studies have shown an association between HbA1c and surgical outcomes [27, 28, 29, 30]. However, high HbA1c may just be an indicator of poor glycemic control that continues into the perioperative period [31]. For example, in patients undergoing an emergency general surgery, a higher HbA1c was a predictor of higher postoperative blood glucose levels [32]. However, a higher HbA1c and a higher postoperative blood glucose were both independently associated with postoperative complications and the presence of two together was associated with fourfold greater risk of complications suggesting an independent effect of chronic hyperglycemia on surgical outcomes [32]. A recent meta-analysis showed that high HbA1c and high perioperative blood glucose levels are independently associated with increased risk of periprosthetic infections following total joint arthroplasty [33]. The authors of this meta-analysis suggested screening for HbA1c before surgery in addition to achieving a good perioperative glycemic control as a strategy to prevent deep wound infections [33].

Glycemic Goals in the Perioperative Period

Insulin infusion to maintain blood glucose levels in 80–150 mg/dL range in patients with or without diabetes undergoing vascular surgery showed a significant reduction in length of hospital stay and in hospitalization costs [34]. In patients undergoing renal transplantation, optimal inpatient blood glucose levels were suggested to be in 140–180 mg/dL range in one recent study [35]. Most other data also show an increase in infection rates after a glucose threshold of 180 mg/dL. Based on this evidence and in the absence of well-conducted randomized controlled trials, most experts agree on moderate glycemic goals in the perioperative period. French [36] and British [37] societies as well as the American Diabetes Association [38] have made recommendations for perioperative glycemic control and they all agree with a target blood glucose level of < 180 mg/dL. HbA1c can be used as a predictor of postoperative glycemia [31, 32]. Some studies, especially those involving elective procedures like joint arthroplasty, suggest using HbA1c < 8% as a cutoff

for predicting clinical outcomes [31]. In an observational study, we found increased length of hospital stay in patients who underwent non-cardiac surgery with an HbA1c > 8% [39••]. Because high HbA1c is associated with high perioperative blood glucose levels, increased testing and close attention to blood glucose levels after surgery is indicated in patients with high HbA1c [40].

An Approach to Improve Perioperative Glycemic Control

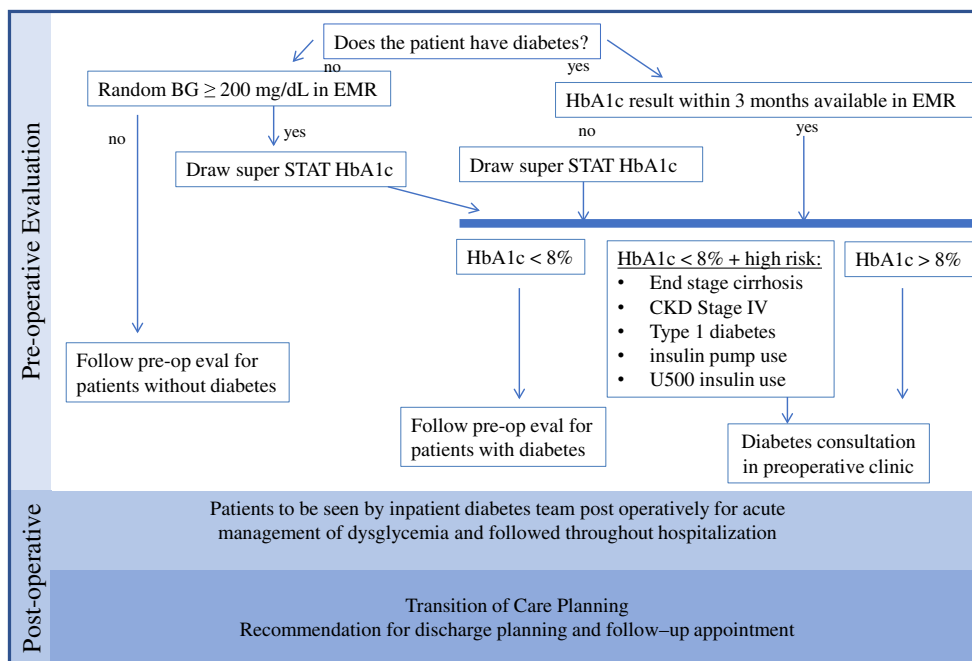
We have developed and successfully implemented a program to identify and treat high-risk patients undergoing an elective surgery (Fig. 1). In this program, diabetes management begins at the time of preoperative evaluation visit and continues through various stages of the surgical course. The program also includes post-discharge management and transition of care planning. High-risk patients are identified during preoperative visit and aggressive treatment of diabetes is started same day. In our program, specialty care is delivered by the inpatient diabetes service even though the patient has still not been admitted to the hospital. Patients are seen in the outpatient setting following the preoperative visit and as a continuity of care, the same diabetes team manages their diabetes during hospitalization.

For the purpose of program implementation, we suggest dividing the perioperative period into preoperative, intraoperative, and postoperative periods even though this is in fact a continuum.

Preoperative Period

Limited data show the importance of preoperative diabetes control to avoid postoperative complications. Based on these data and our own experience, we suggest that if the opportunity exists to improve glycemic control before surgery, it is worth trying to achieve an HbA1c level < 8%. If it is not possible to achieve an HbA1c ≤ 8% before surgery, all attempts should be made to achieve all blood glucose levels < 200 mg/dL preoperatively [19•]. If time permits, referral of patients with poorly controlled diabetes to a diabetes care team before surgery is helpful because aggressive treatment with very close follow-up is often required [41•]. We found that systematic approach of identification and referral of patients with poorly controlled diabetes leads to improved glycemic control at all stages of surgery and decreases the length of hospital stay [42••]. We implemented a program to identify high-risk patients (HbA1c ≥ 8%) at the time of preoperative visit and manage them proactively through the various stages of surgery starting at the preoperative visit. This approach increased the percentage of patients with HbA1c measured in the preoperative period from 31 to 69% pre- and post-implementation respectively. Patients participating in this program were more likely to have glucose levels < 200 mg/dL (86% vs. 71%). It also more than doubled the number of patients who received a diabetes consult during their hospital stay and this may partly be responsible for a significantly lower mean postoperative glucose level (146.4 ± 51.9 mg/dL before the program and 139.9 ± 45.6 mg/dL after the program; P = 0.0028) despite a reduction in the incidence of

Fig. 1 Perioperative collaborative care model



hypoglycemia (patients with any blood glucose < 50 mg/dL 4.93% before the program and 2.48% after the program). [42••]

Preoperative Period in Patients on Enhanced Recovery After Surgery Protocol

Enhanced recovery after surgery (ERAS) pathways are being used more often in the perioperative care of patients. Along with other steps, this pathway includes carbohydrate loading using simple sugars a few hours before surgery. While some investigators have suggested a carbohydrate load (as compared to the traditional overnight fast) may improve insulin resistance, many patients also receive 4–8 mg dexamethasone intravenously to reduce nausea and vomiting which may negate the benefit of this carbohydrate loading and instead cause hyperglycemia. Moreover, ERAS program was not designed for patients with impaired glucose tolerance. The benefits of ERAS protocol on clinical outcomes in patients with diabetes have not been demonstrated at this time. On the other hand, the risk of severe hyperglycemia in patients with diabetes is a certainty. Using complex carbohydrates instead of simple carbohydrates was shown to reduce the incidence of hyperglycemia and was associated with less postoperative complications, and shorter length of hospital stay in patients without diabetes [43]. However, little data exists in patients with diabetes and there is ongoing interest in identifying the best method to modulate hyperglycemia observed following the use of carbohydrate-rich solutions in these patients. Most experts agree that given the lack of data demonstrating benefit in this patient population, it may be best to avoid carbohydrate loading and dexamethasone in patients with known diabetes or newly detected hyperglycemia in the preoperative period [44]. Therefore, we do not recommend use of this part of the ERAS protocol in our perioperative diabetes management program.

Intraoperative Period

Studies on intraoperative tight glycemic control have often failed to show a significant impact on clinical outcomes [45]. However, a reasonable glycemic control during surgery is desirable. An insulin infusion is the safest and most effective means to achieve glycemic control and is considered if blood glucose is higher than 200 mg/dL.

Postoperative Period

Postoperative treatment of hyperglycemia follows the guidelines established for treatment of hyperglycemia in hospitalized patients. Thus, glycemic goals for patients in the ICU are

140–180 mg/dL and on the general floors 100–180 mg/dL [46]. Patients are preferably treated with insulin infusion if admitted to the intensive care unit and with basal bolus insulin therapy if admitted to the general floors. Patients receiving steroids or agents for hemodynamic support are also candidates for insulin infusion. However, we have shown that stress hyperglycemia after cardiac surgery can be successfully treated with basal insulin alone without the need of insulin infusion [47]. A randomized controlled trial comparing basal bolus insulin versus sliding scale insulin in patients on the general floors after surgery showed improved glycemic control and a reduction in surgical complications with basal bolus insulin [48]. The use of oral agents in milder cases of diabetes in the hospital setting is an interesting idea being explored by multiple groups [49–51]. In recent years, we have found favorable results with the use of DPP4 inhibitors in stable patients on the general floors [49].

Avoiding Hypoglycemia

While treatment of hyperglycemia is important, it is equally important to avoid hypoglycemia. Several factors increase the risk of hypoglycemia after surgery. These factors include older age, impaired renal function, changes in nutritional intake, and interruption in glucose monitoring/failure to adjust therapy [52]. Any hypoglycemia after surgery is associated with increased mortality and morbidity [53]. Therefore, all patients with diabetes should be monitored closely and whenever insulin is ordered, a hypoglycemia protocol should also be ordered. A recent study demonstrated a significantly lower risk of hypoglycemia if the patient is cared by an endocrinology team at all stages of surgery [42••]. Implementation of our program led to a significant reduction in rates of hypoglycemia in the postoperative period [42••].

Insulin Pump

Patients who are proficient with the use of insulin pump and willing to take its responsibility can continue using insulin pump through all stages of surgery. However, some centers limit the use of insulin pumps to surgeries of less than 2-h duration [54]. The basal rate should be lowered to 80% during the intraoperative and postoperative period. Blood glucose should be monitored every hour while the patient is under anesthesia. In case of pump failure, an insulin drip should be promptly started. If the patient or staff is not comfortable with continuing insulin pump during surgery, it is best to switch to insulin infusion during surgery and basal bolus insulin after surgery as appropriate. Pump may be restarted at any stage after the surgery, mostly when the patient is able to manage his/her own pump.

Transition to Outpatient Care

Discharge planning is an important part of the postoperative diabetes management. Patients continue to recover from surgery for a few weeks to months after discharge and during this period, poor glycemic control may complicate their recovery process. Diabetes treatment may need adjustments depending on the type of surgical procedure, postoperative complications, need for rehabilitation, etc. Therefore, the diabetes team should be involved in discharge planning and discharge instructions should be individualized according to patient needs. We recognize this may be challenging for institutions that do not have access to an inpatient diabetes team or rapid evaluation with an endocrinologist. Future work is needed to develop and implement key highlights of this program to assist inpatient providers in optimizing care of postoperative patients with dysglycemia.

Conclusion

While most experts agree there is evidence to support glycemic control in the perioperative period, operationalizing this treatment can be challenging. We have demonstrated implementation of a perioperative program that identifies high-risk patients at the time of preoperative visit and manages them proactively through the various stages of surgery. The program has been associated with improvement in perioperative glycemic control and reduction in length of hospital stay.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest. Many studies performed by the authors are cited in the text.

Human and Animal Right and Informed Consent This is a review article and it did not involve conducting studies with humans or animals.

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- Of importance
- Of major importance

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