Intraoperative Management of Diabetes in Diabetic Adults

Gülhan Akbaba¹, Yusuf Aydın²

¹Department Endocrinology and Metabolism Diseases, Mugla Sitki Kocman University Faculty of Medicine, Mugla, Turkey.  
²Department of Endocrinology and Metabolism Diseases, Düzce University Faculty of Medicine, Düzce, Turkey.

Abstract

According to TURDEP-II study, the prevalence of diabetes has reached 13.7% in Turkey. Diabetes mellitus is rapidly increasing, and diabetic patients are likely to undergo surgical procedures more frequently than non-diabetic patients. Observational and prospective studies have demonstrated that hyperglycemia correlates with increased morbidity and mortality associated with surgery. Stress hormones such as epinephrine, norepinephrine, cortisol, glucagon, and growth hormone are mostly augmented, and insulin resistance develops during surgery. All diabetic patients undergoing surgery should have comprehensive preoperative evaluation due to the risk of both hypoglycemia and hyperglycemia during surgical procedures. In this article we aimed to review the diabetes treatment protocols for preoperative and postoperative assessment of adult diabetic patients undergoing surgery.

Keywords: Diabetes Mellitus, perioperative management, perioperative insulin.

Introduction

According to TURDEP-II study, the prevalence of diabetes has reached 13.7% in Turkey (1). Diabetes mellitus is rapidly increasing, and diabetic patients are likely to undergo surgical procedures more frequently than non-diabetic patients (2,3). Several studies have shown that hyperglycemia is associated with poor outcomes in critically ill patients admitted to an intensive care unit or those undergoing cardiac surgery (4-6). Observational and prospective studies have demonstrated that hyperglycemia correlates with increased morbidity and mortality (5,7,8), and intense glucose control reduces the risk of multiorgan failure and systemic infections and decreases both short- and long-term mortality (4,5). Surgical procedure itself can make the body susceptible to diabetic coma (diabetic ketoacidosis and hyperosmolar hyperglycemic state) during and after surgery. The patients may experience nausea, vomiting or dehydration after surgery due to a reaction to the anesthesia and other drugs administered, or stress. This may increase osmotic diuresis secondary to sustained hyperglycemia, thereby increasing the risk for ischemic events and acute renal failure (9). All diabetic patients undergoing surgery should have comprehensive preoperative evaluation due to the risk of both hypoglycemia and hyperglycemia during surgical procedures. In our article we aimed to evaluate the diabetes treatment protocols for preoperative and postoperative assessment of adult diabetic patients undergoing surgery.

Metabolic Effect of Surgical Stress

Stress hormones such as epinephrine, norepinephrine, cortisol, glucagon, and growth hormone are mostly augmented, and insulin resistance develops during surgery (10-15). In addition to insulin resistance, surgical stress has a deleterious effect on pancreatic beta-cell function. Insulin secretory responses to glucose become impaired and plasma insulin levels fall during surgery (16-18). One study found that there was a negative correlation between insulin and plasma epinephrine level in the postoperative phase (16). Elevated catecholamine levels during surgery lead to increased gluconeogenesis and glycogenolysis and inhibit glucose utilization by peripheral tissues and insulin secretion. The hyperglycemic effect is further exacerbated by glucagon secretion-enhancing effect of epinephrine and norepinephrine. Also, catecholamines express a catabolic effect which increases lipogenesis and ketogenesis. Epinephrine activates hormone sensitive lipase, thus stimulates lipolysis, releasing free fatty acids into the circulation. Similarly, the increase in glucagon levels, stimulated by increased catecholamines, exerts an anti-insulin effect. Growth hormone and glucocorticoids can enhance the catabolic effects of catecholamines and glucagon (19). Relative insulin deficiency, insulin resistance and catabolic effects of increased stress hormones can cause serious glucose metabolism disorders especially in poorly controlled diabetic patients.
**Table 1.** Non-insulin treatments before and during the operation

<table>
<thead>
<tr>
<th>MEDICATION</th>
<th>The day before the operation</th>
<th>Morning operation</th>
<th>The operation day</th>
<th>Afternoon operation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acarbose</td>
<td>Treatment continued</td>
<td>Morning dose is skipped</td>
<td>Morning dose as usual if the patient eats breakfast</td>
<td></td>
</tr>
<tr>
<td>Glinides</td>
<td>Treatment continued</td>
<td>Morning dose is skipped</td>
<td>Morning dose as usual if the patient eats breakfast</td>
<td></td>
</tr>
<tr>
<td>Metformin (if contrast material is not used in the procedure)</td>
<td>Treatment continued</td>
<td>Continue treatment</td>
<td>Continue treatment</td>
<td></td>
</tr>
<tr>
<td>Sulfonylureas</td>
<td>Treatment continued</td>
<td>Single daily morning dose is skipped</td>
<td>Single daily morning dose is skipped</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>If the pills are taken twice daily, the morning dose is skipped</td>
<td>If the pills are taken twice daily, the morning dose is skipped, and evening dose is given if the patient eats dinner</td>
<td></td>
</tr>
<tr>
<td>Pioglitazone DPP-IV inhibitors</td>
<td>Treatment continued</td>
<td>Continue treatment</td>
<td>Continue treatment</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Treatment continued</td>
<td>The dose is skipped on the day of surgery</td>
<td>The dose is skipped on the day of surgery</td>
<td></td>
</tr>
<tr>
<td>GLP-1 analogues</td>
<td>Treatment continued</td>
<td>The dose is skipped on the day of surgery</td>
<td>The dose is skipped on the day of surgery</td>
<td></td>
</tr>
</tbody>
</table>

**Hemodynamic Imbalance**

Hemodynamic instability that occurs during surgery in diabetic patients requires intravenous fluid resuscitation and vasopressor support (27).

**Glucose Control**

Perioperative insulin resistance makes glucose control difficult. Intraoperative management of diabetes varies according to the type of diabetes, operation time, pregnancy status and preoperative glucose control status. An upper limit of HbA1c<8.5% is acceptable prior to elective surgery (28). All type 1 diabetic patients undergoing major or minor surgery and type 2 diabetics undergoing major surgery should receive intensive perioperative insulin and dextrose infusion (9).

There are contradictory publications about the optimal blood glucose target in hospitalized patients and in those scheduled for surgery. Some recent studies have shown that the cases with well controlled blood glucose showed higher survival rate and a lower complication and ischemic event rates (5,29,30). The research by Van den Berghe et al. suggested that controlling hyperglycemia by insulin infusion in critically ill patients improved survival and reduced complications (5). The beneficial effects of perioperative tight blood glucose control have been proven by several studies. Tight control of blood glucose can greatly improve clinical outcomes of patients undergoing cardiac surgery (29,30). On the
contrary, a series of large studies were designed to establish whether perioperative tight blood glucose control could substantially improve postoperative outcomes (31-33). The authors sought to assess the efficacy of intensive insulin therapy compared with conventional insulin therapy in patients with severe sepsis, and at 28 days, there was no significant difference between the two groups in the rate of death or the mean score for organ failure. However, the rate of severe hypoglycemia (glucose level ≤ 40 mg/dl) was higher in the intensive therapy group than in the conventional therapy group (17% vs. 4.1%, respectively, p<0.001) (31). Similarly, it has been shown that tight blood glucose control did not decrease morbidity or mortality in patients hospitalized in a mixed medical/surgical ICU, instead, the intervention was associated with a five-fold increased risk of hypoglycemia (33). Moreover, in “Normoglycemia in Intensive Care Evaluation - Survival Using Glucose Algorithm Regulation” (NICE-SUGAR) study, a multicentre trial involving 6104 patients, the mortality rate in the intensive treatment group was 27.5% versus 24.9% in the conventional group [odds ratio (OR) for intensive treatment group 1.14; 95% confidence interval (CI) 1.02–1.28; P = 0.02]. The blood glucose level was maintained between 80-110 mg/dl in the intensive treatment group and 140-180 mg/dl in the conventional group. In addition, 6.8% of patients in the intensive treatment group vs. 0.5% of patients in the conventional group had severe hypoglycemia (blood glucose level ≤ 40 mg/dl) (p<0.001) (32). These studies show that tight perioperative glucose control is not always associated with good results (31,32). American Association of Clinical Endocrinologists (AACE) and American Diabetes Association (ADA) issued a guideline in 2009 for the desired blood glucose goal range in hospitalized patients. This guideline recommends a target blood glucose level of 140-180 mg/dl in patients hospitalized in intensive care unit, < 140 mg/dl in patients admitted to a medical-surgical intensive care unit, and random blood glucose level of < 180 mg/dl (34).

**Patients with controlled blood glucose levels through diet and exercise**

Any special treatment is not recommended for the patients with well controlled blood glucose level through diet and exercise who undergo to a minor surgery. Blood glucose levels must be monitored hourly throughout the morning of the surgery, and during surgery if the operation lasts more than one hour. Insulin and dextrose infusion should be initiated in patients who do not meet target blood glucose levels or undergo major surgery (9).

**Patients using oral antidiabetic drugs**

Long-acting sulfonylureas should be withheld one day before surgical procedures, short-acting oral hypoglycemic drugs should be given to patients undergoing minor surgery, and the patients undergoing major surgery should be hospitalized in order to initiate the insulin treatment. Other oral medications can be continued until the day of surgery. However, metformin should be withdrawn 48-72 hours prior to surgery, and it can only be restarted if serum creatinine level remains normal for 48-72 hours. Patients, in need of minor operations and are expected to miss one meal, are being monitored hourly for blood glucose, and are advised to take prescribed oral dose with their next meal (Table-1) (28). For a blood sugar reading of > 200 mg/dl during minor operation, 4-10 units of short-acting insulin are given subcutaneously. If the patient is undergoing major surgery and if more than one meal is to be missed, intravenous insulin and dextrose infusion should be started (see below) (9).

**Patients using insulin**

The management of patients, treated with insulin and not expected to miss more than one meal, is summarized in Table 2 (28). Type 2 diabetic patients on insulin therapy are hospitalized 2 to 3 days before the major surgery. When blood glucose levels meet the surgical criteria, cardiovascular status, serum electrolyte concentrations and renal function must be monitored, and electrolyte abnormalities, if found, should be corrected before surgery (9).

In 1979, Alberti and Thomas described a simple and safe approach for blood glucose control during surgery with the administration of infusion solution combining glucose, insulin, and potassium (known as GIK regimen or Alberti regimen) (35). Glucose and insulin is supplied in the same route in this widely used method. 10 IU short-acting insulin and 10 mmol KCl (1 ampoule of 7.5% KCl) are added to 500 mL 5% dextrose. Insulin infusion rate is determined by blood glucose levels according to the following protocol (Table 3). NaCl 0.9% can be administered as IV infusion, and if the infusion is continued for longer than 24 hours sodium and potassium must be controlled. The GIK regimen is simple, safe, and effective in many patients, and has also an advantage that does not need infusion pump. But the infusion rates of neither glucose nor insulin can be adjusted separately. The infusion should be discontinued if target level of blood glucose is not achieved, and then reconstituted with appropriate amount of insulin and glucose (27).
Table 2. Insulin treatment before and during the operation

<table>
<thead>
<tr>
<th>MEDICATION</th>
<th>The day before the operation</th>
<th>The operation day</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Single dose insulin at night (detemir, glargine, NPH)</td>
<td>Dose is not changed.*</td>
<td>Blood glucose is measured on hospital admission.</td>
<td></td>
</tr>
<tr>
<td>Single dose insulin at night (detemir, glargine, NPH)</td>
<td>Dose is not changed.</td>
<td>Blood glucose is measured on hospital admission.</td>
<td></td>
</tr>
<tr>
<td>Twice daily ready-mixed or basal insulin</td>
<td>Dose is not changed.</td>
<td>Half of the morning dose is administered. Blood glucose is measured on hospital admission.</td>
<td></td>
</tr>
<tr>
<td>3–4 or 5 times/day injection regimen</td>
<td>Dose is not changed.</td>
<td>Basal-bolus: morning and noon doses of short acting insulin are skipped, but basal dose is not changed.*</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ready-mixed insulin: half of the morning dose is administered, noon dose is skipped. Blood glucose is measured on admission to hospital.</td>
<td></td>
</tr>
</tbody>
</table>

* Some authors suggest a 1/3 reduction of long-acting analogue insulin dose.

There are some intravenous infusion regimens with insulin and glucose being infused separately. Variable rate intravenous insulin infusion (VR III) regimen requires reliable infusion pumps, and a team experienced in the regimen. VR III provides a tighter glucose control, and patients who undergo surgeries, associated with increased insulin requirement, such as cardiac surgery, who develop sepsis, and who take medications, associated with increased insulin requirement, such as corticosteroids may use variable rate intravenous insulin infusion, which is more flexible. 20 mmol KCl is added to 500 mL 5% dextrose and the solution is administered at a rate of 100 mL/hour for glucose administration, and insulin is infused at a rate of 2-4 IU/hour to maintain blood glucose levels within the range of 100 to 125 mg/dl (120-180 mg/dl in patients at high risk of hypoglycemia). An insulin solution is prepared by adding 50 IU short acting insulin to 49.5 mL 0.9% NaCl. Insulin should not be administered intravenously, but should be administered in conjunction with 5% dextrose. Blood glucose should be measured intravenously (Table 4). In patients at risk of fluid overload 5% dextrose solution may be converted to 10% dextrose solution. Mixture of 0.45% saline and 5% dextrose can be recommended as intravenous fluid for patients requiring variable rate intravenous insulin infusion (28).

Table 3. GIK regimen

<table>
<thead>
<tr>
<th>Blood glucose (mg/dl)</th>
<th>Infusion rate (ml/hour)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥280</td>
<td>140</td>
</tr>
<tr>
<td>279-220</td>
<td>120</td>
</tr>
<tr>
<td>219-180</td>
<td>100</td>
</tr>
<tr>
<td>179-120</td>
<td>80</td>
</tr>
<tr>
<td>119-80</td>
<td>60</td>
</tr>
<tr>
<td>&lt;80</td>
<td>The infusion is discontinued for 2 hours.</td>
</tr>
</tbody>
</table>

GIK: glucose-insulin-potassium solution
Emergency Surgery

Unfortunately, poor glycemic control is common amongst patients undergoing emergency surgery. An intravenous route is established immediately; laboratory tests are performed to assess acid-base and electrolyte balance, and blood glucose level. Severe fluid deficits and electrolyte disturbances must be corrected before surgery. If the patient is in diabetic ketoacidosis, the surgery should be delayed long enough to stabilize or partly correct the acid-base imbalance. Patients with non-ketotic hyperosmolar coma suffer from severe dehydration. In these patients, fluid replacement should start as rapidly as possible and metabolic status should be corrected before the surgery. Variable rate intravenous insulin infusion is considered with hourly monitoring for a target blood glucose range of 120 to 180 mg/dl. Serum potassium is monitored every 2 to 4 hours, and replacement is initiated until potassium level comes into the normal range (9, 27).

References


