Original Article

Perioperative Management of Adult Patients with Diabetes Mellitus

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Abstract

Background: Diabetic patients often undergo surgeries due to diabetes complications.
Objective: The critical appraisal of studies regarding the perioperative diabetes management.
Methodology: A database search (Pubmed, Cinahl, Cochrane), with the keywords "diabetes", "surgery", "perioperative management", "operation", "adult surgical patient" and a manual search were conducted. The criteria for the inclusion of articles in the review included studies relating to the glycemic control management for diabetic adults who undergo surgery.
Results: Diabetes' perioperative management is better performed by a multidisciplinary team, in order for the needs of each patient to be covered holistically and individually. There are no evidence-based guidelines for the optimal perioperative management of diabetic patients. Patients who achieve good glycemic control with proper diet and exercise may not need supplemental perioperative care, in addition to monitoring of blood glucose. In type 2 diabetes and good glycemic control by oral antidiabetics, these are usually continued postoperatively with the first meal. The insulinotherapy in type 1 diabetes is not interrupted, but there are variations concerning the optimal doses. Administration of insulin intravenously can be a great way to manage diabetes perioperatively.
Conclusions: There is controversy in the literature regarding the ideal values of blood glucose, the influence of the glycated hemoglobin values on recovery, and the insulin administration regimens. However, there is agreement on issues such as that diabetic patients should be placed first on the operating list, the routine monitoring of blood glucose, the effectiveness of insulin pumps and the resumption of food intake as soon as possible postoperatively.

Key words: diabetes, surgery / surgery, perioperative period, management of diabetes mellitus

Introduction

Diabetic patients often undergo surgeries due to diabetes complications (Plodkowski & Edelman 2001), and present increased morbidity and mortality (Jackson et al 2012). A Blood Glucose (BG) increase by 20mg/dl perioperatively leads to a 30% rise of complications (Alexanian et al 2011).

Common problems perioperatively include the increased catabolism due to stress hormones, the inhibition of insulin secretion (Guyton 1990), the interruption of food intake (McAnulty et al 2000), the reduced level of consciousness (anesthetics' administration, McAnulty et al 2000), and the cardiovascular complications due to e.g. anesthetics (National Formulary 2007).

The acute perioperative complications include dehydration (osmotic diuresis), acidosis (increased lactate and ketones), fatigue, and loss of body weight (lipolysis, protein catabolism) (McAnulty et al 2000). Surgical stress, infections, and decreased insulin secretion modify patients' insulin needs and can lead to ketoacidosis or hyperosmolar hyperglycemic nonketotic coma (French 2000). Hyperglycemia affects leukocyte function, increasing the risk for infections and impaired wound healing (Dagogo-Jack & Alberti 2002), while there is an increased risk of thrombosis, due to the coagulation abnormalities (Rizvi et al 2010, Godoy et al 2012). The long-term complications of diabetes (e.g., angiopathy, neuropathy), are involved in complications postoperatively (McAnulty et al 2000, Plodkowski & Edelman 2001). In patients with autonomic neuropathy, insulin can lower blood pressure in the supine position, leading to hypotension (McAnulty et al 2000). The diabetic gastroparesis can lead to aspiration and pneumonia (Plodkowski & Edelman 2001). Due to the glycosylation of collagen in the cervical vertebrae joints, people with diabetes are likely to exhibit arduous intubation (McAnulty et al 2000). However, complications and mortality of surgical diabetic patients can be prevented with efficient glycemic control perioperatively, i.e., during the preoperative, intraoperative, and postoperative period. The purpose of this review was to critically assess studies regarding the current practices of diabetes management perioperatively.

Methodology

A databases search (Pubmed, Cinahl, Cochrane) was performed in December 2014- January 2015, using the keywords "diabetes", "surgery", "perioperative management", "operation", "adult surgical patient", to identify studies on diabetes management perioperatively. A manual search was conducted also, to identify articles not cited electronically, both in journals and in the retrieved studies' references. The inclusion criteria were the following:

1. Studies published in English,
2. Studies examining practices regarding the glycemic control of adult diabetic patients having surgeries, irrespectively of the type of surgery,
3. Studies more recently published, in order to reflect the contemporary clinical practice, apart from points on which there was no more recently published literature.

There are no evidence-based guidelines regarding the optimal perioperative management of patients with diabetes. In this review several management methods are presented, according to what has been published internationally.

Results

General Care Plan

Diabetes' perioperative management is better performed by a multidisciplinary team (endocrinologists, anesthesiologists, surgeons, nurses, etc), in order for the needs of each patient to be covered holistically, from admission to discharge (Girard & Schricker 2011). The purpose of BG management perioperatively is to avoid both hypoglycemia and hyperglycemia (Plodkowski & Edelman 2001, Ablove 2010), as BG fluctuations are as important as maintaining normal BG values (Ferrari 2008).

The admission of patients who will undergo elective surgery is better to occur 1-2 days preoperatively, for the target BG values to be achieved (Draper 2011) and to determine which medications will be discontinued (Plodkowski & Edelman 2001). If BG values range ≤180mg/dl, patients can be scheduled for surgery without further management, but for values ranging between 181-300mg/dl, the possibility for an insulin pump preoperatively can be considered (Alexanian et al 2011).

An individualized plan must be developed for each patient (Girard & Schricker 2011), according to co-morbidity, body weight (University of California 2014), type of diabetes, type of surgery, antidiabetic medications (Loh-Trivedi & Schwer 2013), anesthesia (Dagogo-Jack & Alberti 2002), and BG values (Alexanian et al 2011). Surgeries are categorized into major and minor according to their duration (major operations last >2 hours or require prolonged fasting period postoperatively) (French 2000).

Diabetic patients are better to be first on the operating list, to shorten the preoperative fasting period and to allow food consumption later that day (Draper 2011). The administration of medications for cardiac and/ or respiratory diseases, epilepsy etc, usually continues until the day of surgery, unless there are other reasons for discontinuation (UVHS 2011).

Fasting of patients is common for diabetes mellitus type 1 (DMT1) and 2 (DMT2); if the surgery is scheduled before 12:00, patients usually remain nil by mouth from 24.00 of the previous day (Draper 2011), while if the surgery is scheduled after 12:00, patients can consume oral fluids until 06:00 of the same day (UVHS 2011). In any case, the fasting period for solid foods must have a minimum duration of 6 hours and for clear fluids (no milk, no carbonated drinks) of 2 hours (American Society of Anesthesiologists 2011).

There are differences between the studies regarding the target BG values and the optimal management of diabetes perioperatively (Rogers & Zinner 2009, Wallia et al 2011). A strict glycemic control to maintain low BG values (e.g. 81-108mg/dl) is associated with increased risk of hypoglycemia, while there are no indications that it leads to improved outcomes (Kansagara et al 2011, Schiffner 2014). However, high BG values (>200mg/dl) have negative effects on wound healing (Ablove 2010).

Furthermore, the results are conflicting regarding BG values above which the hyperglycemia has to be treated (e.g., ≥200mg/dl or ≥180mg/dl), and to the values that, when exceeded, require surgery's postponement. However, BG between 150-200mg/dl without blood ketones are expected postoperatively (Shah 1992).

As high levels of glycated hemoglobin (HbA1c) may lead to complications, optimal values must be <6% preoperatively (Vann 2009). However, according to other studies, HbA1c does not play important role (McAnulty et al 2000), but rather that a strict control may result to hypoglycemia (Clement et al 2004). Therefore, the correlation between recovery and optimal HbA1c values needs further investigation.

Preoperatively, BG measurements can take place every 4 hours for insulin dependent patients and every 8 hours for non-dependent patients. In major operations, BG must also be measured every hour intraoperatively. The measurements carried out with an ordinary glucometer are sufficient, unless the BG values are too high or too low, where laboratory analysis is required (Plodkowski & Edelman 2001). Intraoperatively, blood pressure is measured every 5 minutes, to avoid sudden rises, because these can further damage the ocular vessels (French 2000). Regular monitoring of skin color and body temperature contributes to early recognition of hypoglycemia (French 2000).

Preoperative Management

Patients' evaluation starts with a detailed medical history [dietary habits, body weight, physical activity, medications, medical tests' results, complications (e.g., hypoglycemia), recent infections, ulcers (diabetic foot), risk factors for atherosclerosis, socioeconomic factors that may affect diabetes management (Draper 2011)] and continues with the physical examination [autonomic neuropathy, orthostatic hypotension, paraesthesia], assessment of the cardiovascular, liver, and renal function, eye examination (Loh-Trivedi & Schwer 2013), detection of foot ulcers, and blood tests [complete blood count, serum electrolytes, urea, creatinine etc] (Draper 2011). Severe metabolic and electrolyte imbalances should be corrected preoperatively (Plodkowski & Edelman 2001). Blood pressure values should also be well controlled, with maximum values at 140/90mmHg (Plodkowski & Edelman 2001).

Patients with diabetes are prone to respiratory infections, and therefore, need a chest x-ray preoperatively and respiratory physiotherapy postoperatively (Draper 2011). All preexisting infections should be treated preoperatively, as in people without diabetes (French 2000). Neurological function must be evaluated, in order to recognize nerve damages before anesthesia (Loh-Trivedi & Schwer 2013). Thyroid function must be assessed preoperatively, as patients with diabetes have a higher prevalence of thyroid disorders (Loh-Trivedi & Schwer 2013).

Temperature measurements help to ensure that there is neither hypothermia (hence, no risk for peripheral insulin resistance, hyperglycemia, impaired healing), nor hyperthermia (infection). The placement of an arterial catheter intraoperatively provides a line through which blood samples can be drawn (Loh-Trivedi & Schwer 2013).

There are no contraindications to the administration of anesthetics, while only in vitro it has been shown that halothane, enflurane, and isoflurane may effect on glucose metabolism through their action on the sympathetic nervous system (McAnulty et al 2000), or on insulin secretion (Loh-Trivedi & Schwer 2013). The effects of propofol are not known, but, as diabetic patients have reduced ability to metabolize lipids, the long-term administration of propofol may be associated with complications (McAnulty et al 2000). There is no evidence that regional block anesthesia is more preferable than general anesthesia in regards to complications (McAnulty et al 2000).

The advantages of regional block anesthesia include the reduction of surgical stress response, the rapid detection of hypoglycemia intraoperatively, and the lower rates of nausea. In general anesthesia, the presence of cardiovascular and/or renal disease, the risk of undetected hypoglycemia, and protection of areas bearing prolonged pressure are taken into account (Draper 2011). Patients at high risk for gastroparesis should be administered laxatives and antiemetics prior to anesthesia, to reduce the risk of aspiration (Loh-Trivedi & Schwer 2013). Ringer's lactate should be avoided in diabetes, as lactate is a substrate for gluconeogenesis (Shah 1992, French 2000).

Surgical Diabetic Patients who Regulate BG Through a Healthy Lifestyle

Patients who achieve good glycemic control only with proper diet and exercise may not need supplemental care, apart from regular monitoring (Plodkowski & Edelman 2001, Draper 2011). It is important for BG measurements to take place on the morning of surgery and that monitoring is continued hourly intraoperatively if the procedure lasts over an hour. In the case of a major operation or poor glycemic control (e.g., BG>180mg/dl), glucose and insulin solutions can be administered, as described below. In this case, BG must also be determined hourly intraoperatively (Dagogo-Jack & Alberti 2002). Postoperatively, BG measurements can be performed every 2 hours until food resumption (Ekoé 2011).

Surgical Diabetic Patients who Regulate BG with Oral Antidiabetics

In patients who receive oral antidiabetics and present poor glycemic control, the management is the same as for patients undergoing major surgery (French 2000, see below), or for patients with DMT1 (McAnulty et al 2000), with infusion of glucose and insulin, even when they are undergoing minor surgeries. Patients with DMT2 and adequate glycemic control can continue taking their oral antidiabetics (Shah 1992, McAnulty et al 2000), except the day before surgery and the morning of surgery. Postoperatively, they can resume taking their oral antidiabetics with their first meal (Ekoé 2011).

Surgical Patients with Diabetes who Regulate their BG with Insulin

The insulin needs of DMT1 patients are constant, even if the patients are not eating (Maynard et al 2008), and cannot be met solely with rapid-acting insulins (Alexanian et al 2011). During hospital treatment an individualized management plan is followed (Plodkowski & Edelman 2001), with basal insulin (e.g., intravenous insulin infusion, intermediate- or long-acting insulin, and rapid acting insulin prior to meals) (ADA 2015). In the case of poor glycemic control, and/ or major surgery (University of California 2014), or if the patient is receiving insulin with a pump, the intravenous administration of insulin preoperatively constitutes safe method (Alexanian et al 2011, see below).

In patients already receiving insulin with a pump, the insulin administration can continue, either at the same rate (University of California 2014) or less (Ablove 2010), e.g. reduced by 20% from midnight before surgery (Alexanian et al 2011). With food resumption postoperatively, the insulin pump rate is adjusted accordingly (UVHS 2011).

In insulin dependent patients, both insulin type and timing of insulin administration must be taken into account, i.e. if a patient receives insulin on the morning and on the evening, the evening dose can be administered as usual, but the dose of intermediate-acting or long-acting insulins must be reduced by 20% on the evening before surgery. On the day of surgery, the morning rapid insulin is omitted and the dose of intermediate-acting or/and long-acting insulin is reduced by 50%, and is only administered in BG ≥120mg/dl. If a patient is taking premixed insulin, the evening dose is reduced by 20% while no insulin is given on the morning (Alexanian et al 2011). Obese patients often present insulin resistance and require higher insulin doses (University of California 2014).

Usually, good glycemic control can be achieved with the administration of short-acting insulins or a combination of short-acting and intermediate-acting insulins twice a day (Draper 2011). Short-acting insulins must be stopped until food resumption postoperatively, both in patients with DMT1 and DMT2 (Alexanian et al 2011, University of California 2014). For patients receiving only intermediate-acting insulins there is a need for adjustment of the insulin doses; the usual dose on the night before surgery can be administered (UVHS 2011) and the morning dose is decreased by 1/3 if the operation is performed early in the morning or by ½ if the operation is performed in the afternoon (UVHS 2011). At the same time, a glucose solution can be allowed to avoid hypoglycemia (University of California 2014). Intermediate-acting insulins are better not to be discontinued, in order to prevent ketoacidosis. The same instructions apply both to DMT1 and DMT2 patients (University of California 2014). Patients who control their BG with a combination of rapid-acting and long-acting insulin can also be given intermediate-acting insulins perioperatively (University of California 2014).

Alternatively, the doses of intermediate-acting insulin can be determined by BG values, e.g. in patients with BG between 70-150mg/dl, a 50% of the usual dose of intermediate-acting insulin can be given, for values between 151-250mg/dl the 67% of the usual dose can be given, and for values between 251-350mg/dl the 75% of the usual dose can be administered (Plodkowski & Edelman 2001).

Patients using only long-acting insulins can receive their usual evening dose (University of California 2014) or they can reduce it the night before surgery by 20% (UVHS 2011), or they can even receive an intermediate-acting insulin for 1-2 days before an elective surgery (McAnulty et al 2000). However, there is controversy regarding the continuation of long-acting insulin in patients with DMT1, because according to some authors the long-acting insulin can be continued perioperatively (University of California 2014) and according to others it must be replaced by a combination of intermediate and short-acting insulins (Plodkowski & Edelman 2001). Similar instructions, with a reduction of the dose of long-acting insulin by ½ or ¾ on the night before surgery, or its discontinuation with simultaneous initiation of intravenous insulin on the day of a major surgery, also apply to DMT2 patients (University of California 2014). Postoperatively, the administration of long-acting insulin can be reinitiated (Alexanian et al 2011).

Surgical Patients with Diabetes who Undergo Major Surgery

Rapid-acting insulins, which can be administered intravenously (e.g. insulin regular), are preferred, because they require shorter monitoring and because the absorption of subcutaneous insulin can be affected by various factors perioperatively (Loh-Trivedi & Schwer 2013). The doses' titration is performed individually for each patient; for example, cardiac surgery patients who undergo extracorporeal circulation may require more insulin compared to patients who undergo general surgery, due to the induced hypothermia and the use of adrenergic agents (Shah 1992).

The continuous intravenous administration of insulin is preferable to the subcutaneous (e.g., with sliding scales, whose use is now controversial) and the intermittent intravenous, which is difficult to apply (Dagogo-Jack & Alberti 2002). The advantage of continuous intravenous insulin administration is that the risk of hypoglycemia is avoided, as insulin and glucose are usually administered concomitantly (Shah 1992).

Before the administration of the insulin solution, a 50ml flush of the same solution is used to saturate the binding sites of the plastic tube of the infusion set and prevent the further binding of insulin (McAnulty et al 2000). The minimum needs in glucose for an adult are 120g per day (Dagogo-Jack & Alberti 2002), to meet the patient's needs during fasting. Glucose may be administered either as 5% dextrose or as 10% dextrose solution. In the case of 5% dextrose solution, an infusion rate of 100ml/h provides the patient with 5g of glucose per hour. If fluid restrictions are required (e.g. fluid overload, renal failure) a 10% dextrose solution is preferred, due to higher glucose concentration. Usually, 0.3 units of insulin are administered per gram of glucose. These requirements, however, increase in patients with sepsis, obesity, or in unstable condition (Dagogo-Jack & Alberti 2002).

There are two main methods of insulin (and glucose) administration: a) insulin drip (with or without concomitant administration of glucose as a separate solution), or b) insulin in combination with glucose and/ or potassium (Shah 1992, French 2000). For an insulin drip, 25 units of regular insulin can be added in 250ml of Normal Saline- N/S 0.9%, resulting in 0.1 insulin units per 1ml of solution. The initial infusion rate can be at 5ml/h (i.e. 0.5 insulin units per hour) in thin women and at 10ml/h (i.e. 1 insulin unit per hour) in other patients (Dagogo-Jack & Alberti 2002) (Table 1).

Another way of insulin administration is for 100 units of regular insulin to be added in 100ml N/S 0.9% (1 insulin unit/ 1ml of solution) (French 2000, Loh-Trivedi & Schwer 2013); the infusion rate can be determined either by the formula:

Table 1. Insulin drip (25 units of regular insulin in 250ml N/S 0.9%, **Source:** Dagogo-Jack & Alberti 2002).

Blood Glucose (mg/dl)	**Infusion rate**
<80	BG measurement after 15 minutes
80-140	Reduction by 0.4 units (4ml/h)
141-180	No change needed
181-220	Increase by 0.4 units (4ml/h)
221-250	Increase by 0.6 units (6ml/h)
251-300	Increase by 0.8 units (8ml/h)
>300	Increase by 1 units (10ml/h)

Table 2. Insulin drip (100 units of regular insulin in 100ml N/S 0.9%, **Source:** French 2000).

Blood Glucose (mg/dl)	**Insulin (units/ h)**
< 90	0
90 - 180	1
180 - 270	2
270 - 360	3
> 360	6 (monitoring, test urine for ketones)

Table 3. Infusion rate of Glucose-Insulin-Potassium solution (**Source:** Dagogo-Jack & Alberti 2002).

Blood Glucose (mg/dl)	**Infusion rate**	
	5% Dextrose	**10% Dextrose**
<80	↓5 units	↓10 units
<120	↓3 units	↓5 units
120-180	No change needed	No change needed
181-270	↑3 units	↑5 units
>270	↑5 units	↑10 units

Table 4. Units of insulin that need to be added in Glucose-Insulin-Potassium solutions in patients undergoing major surgeries (**Source:** French 2000).

Blood Glucose (mg/dl)	**Regular insulin added in the solution (units)**
< 75	No insulin
75 - 110	5
110 - 180	10
180 - 360	15
> 360	20

Insulin units per hour = blood glucose concentration (mg/dl)/ 150 (Loh-Trivedi & Schwer 2013), or according to Table 2 (French 2000). The administration of glucose (e.g. at a rate of 5-10g/h) can take place simultaneously, with hourly BG monitoring. Bolus infusion of glucose (in hypoglycemia) or regular insulin administration (in hyperglycemia) may also occur (Shah 1992).

For a glucose, insulin, and potassium solution (GIK solution), 15 units of regular insulin are added in 1000ml 5% dextrose solution with 20mEq of potassium, or 30 units of regular insulin are added in 1000ml 10% dextrose solution with 20mEq of potassium; the initial infusion rate is 100ml/h (Draper 2011, Ekoé 2011). This combination is effective, safe and adequate for many patients, but the change in the infusion rate in one of its components cannot be made without changing the other (Dagogo-Jack & Alberti 2002). The infusion rates are based in BG values and they are described in Tables 3 and 4.

Insulin increases the permeability of cells to potassium, therefore, plasma potassium concentrations decrease (McAnulty et al 2000). In potassium concentrations ≤3mEq/l, 20mEq KCl can be added into the solution, whereas if potassium concentrations are between 3-5mEq/l, 10mEq KCl can be added (French 2000), provided renal function is normal. The monitoring for BG and potassium one hour preoperatively, 2 hours after the infusion has begun, at least once intraoperatively, and every 1-2 hours postoperatively is very important (Draper 2011, Loh-Trivedi & Schwer 2013). Renal failure, high potassium concentrations repeatedly, and/or electrocardiogram abnormalities, are contraindications for potassium administration (Dagogo-Jack & Alberti 2002). In the case that glucose, insulin, and potassium are administered in separate solutions, the intravenous lines have to be checked, to ensure infusion of all solutions (French 2000).

The infusion of GIK solutions usually begins preoperatively and continues according to the patient's needs (Dagogo-Jack & Alberti 2002); however, with the first postoperative meal its administration can be disrupted and the patient can resume to the preoperative treatment (French 2000). Postoperatively, food resumption must be achieved as soon as possible. If the patient can not receive any food by mouth, the intravenous infusion of 5% or 10% dextrose solutions is continued, accompanied by insulin administration (Shah 1992). An overlap of at least one hour must intercede between the discontinuation of the intravenous insulin and the transition to subcutaneous insulin (French 2000, Dagogo-Jack & Alberti 2002), to prevent hyperglycemia. All our findings are summarized in Figure 1.

Discussion

The perioperative management of diabetes depends on many factors, so it constitutes a complex process; therefore, it is preferable to be performed by a multidisciplinary team. Avoiding fluctuations in BG levels perioperatively is as important as keeping low BG levels, regarding the impact on morbidity and mortality. According to the American Diabetes Association (2015), BG levels in hospitalized patients must remain lower than 180mg/dl at all times. Many treatment practices are currently based on each hospital's protocol, e.g., in patients who receive subcutaneous insulin, their schema is more or less continued during their hospital stay. However, there is agreement on issues such as placement of diabetic patients first on the operating list, BG monitoring perioperatively, the effectiveness of intravenous insulin and/or glucose solutions, and the resumption of food intake postoperatively as soon as possible.

The practices described in the present review are not detailed and extensive; e.g., we have not referred to the general principles of perioperative care, or specifically to patients who are administered corticosteroids, receive parenteral nutrition, suffer from renal impairment etc. Due to the fact that in most of the studies perioperative diabetes management has been investigated in patients undergoing cardiac surgery and in critically ill patients, more research is needed in order to define which interventions are more suitable for patients with diabetes who undergo other operations, e.g. general surgery. In any case, each treatment program has to be designed for the individual needs of each patient, regarding both surgery and diabetes.

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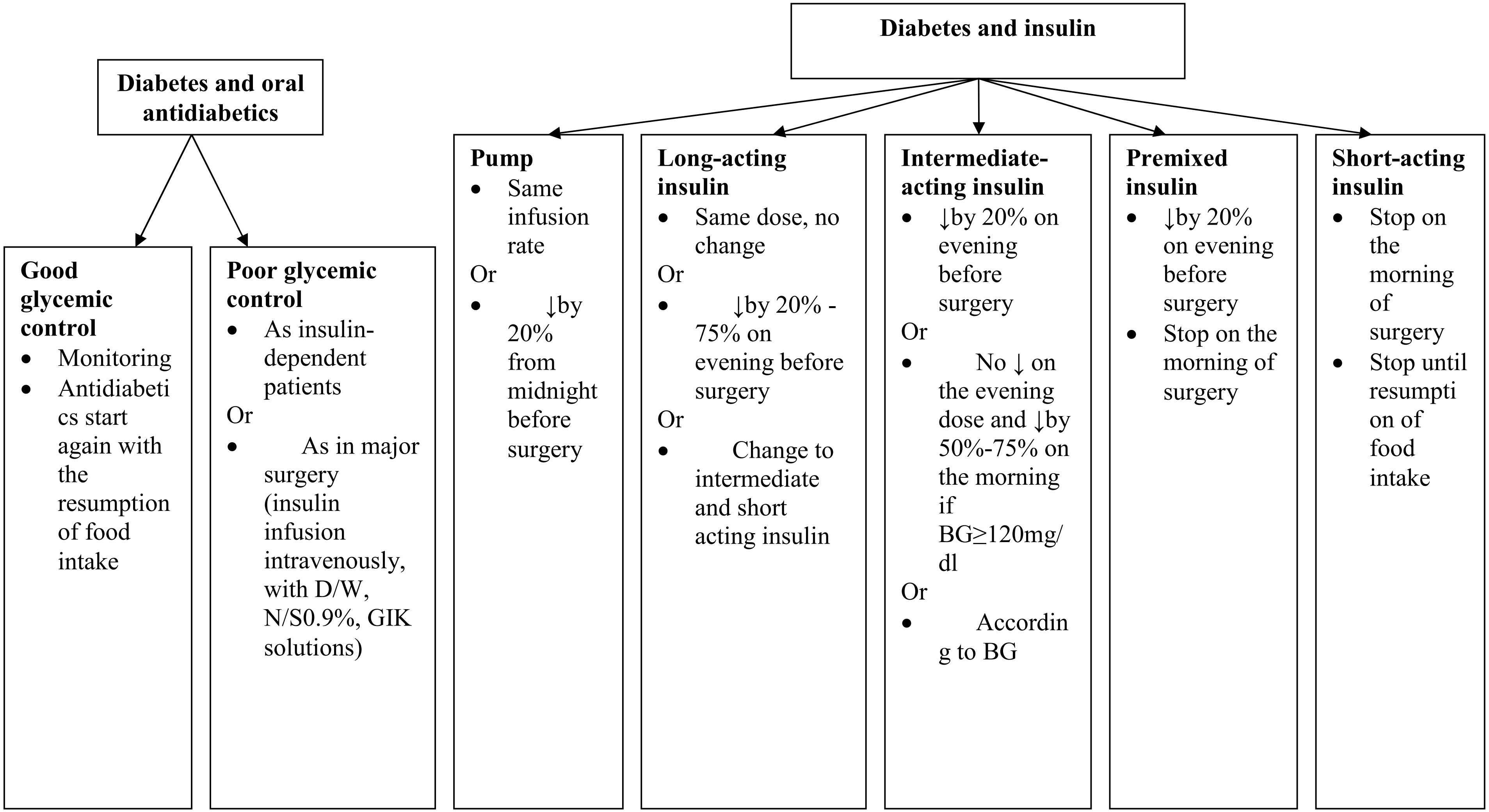

Figure 1. Summarization of review findings.