Society for Ambulatory Anesthesia Consensus Statement on Perioperative Blood Glucose Management in Diabetic Patients Undergoing Ambulatory Surgery

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Optimal evidence-based perioperative blood glucose control in patients undergoing ambulatory surgical procedures remains controversial. Therefore, the Society for Ambulatory Anesthesia has developed a consensus statement on perioperative glycemic management in patients undergoing ambulatory surgery. A systematic review of the literature was conducted according to the protocol recommended by the Cochrane Collaboration. The consensus panel used the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system for providing suggestions. It was revealed that there is insufficient evidence to provide strong recommendations for the posed clinical questions. In the absence of high-quality evidence, recommendations were based on general principles of blood glucose control in diabetics, drug pharmacology, and data from inpatient surgical population, as well as clinical experience and judgment. In addition, areas of further research were also identified. (Anesth Analg 2010;111:1378–87)

Given the escalation in the prevalence of diabetes mellitus worldwide and a significant increase in surgical procedures performed on an outpatient basis, anesthesiologists will encounter diabetic patients in the ambulatory setting with increasing frequency. Surgical stress response can lead to relative insulin deficiency through increased insulin resistance and reduced insulin secretion, which elevate blood glucose levels.1 Hyperglycemia in the perioperative period can cause dehydration, fluid shifts, electrolyte abnormalities, a predisposition to infection, and impaired wound healing, as well as ketoacidosis and hyperosmolar states.1

In critically ill patients and in patients undergoing major surgical procedures, hyperglycemia may be associated with increased perioperative morbidity and mortality.1 However, several randomized controlled trials (RCTs) evaluating tight perioperative glycemic control (blood glucose levels between 80 and 110 mg/dL) have reported inconsistent results, including some studies reporting harm to the patients.1–3 In addition, tight control demands frequent measurements of glucose levels, which may further increase the complexity of perioperative glucose management. Nevertheless, tight glycemic control during the perioperative period has been recommended by several professional organizations and has been targeted as a national quality improvement initiative by the Centers for Medicare and Medicaid Services.4

Although a recent consensus statement of the American Association of Clinical Endocrinologists (AACE) and the American Diabetes Association (ADA) issued clinical recommendations for the management of hyperglycemia in hospitalized patients, including the critically ill and those undergoing major surgical procedures; perioperative blood glucose control in patients undergoing ambulatory surgical procedures was not addressed.5

On the basis of the demands from members of the Society for Ambulatory Anesthesia (SAMBA), the Task Force on Clinical Practice Guidelines developed a consensus statement on perioperative glycemic management in patients undergoing ambulatory surgery. In approving this document as a consensus statement, a similar process was used as created by the SAMBA Board of Directors for the development of the SAMBA consensus guidelines for the management of postoperative nausea and vomiting.6

METHODS

A systematic review of the literature concerning perioperative blood glucose management in adult patients undergoing ambulatory surgery was conducted according to the protocol recommended by the Cochrane Collaboration.7 We searched the Cochrane Controlled Trials Register, the Cochrane Library (Issue 4, 2009), MEDLINE, and EMBASE from January 1980 to November 2009. A reference librarian familiar with literature search protocol of the Cochrane Collaboration (Marina Englesakis, Toronto, Ontario, Canada) designed and conducted the electronic search strategy.
recommendation was offered when the desirable effects of
sensus panel (Table 1).

were considered to ensure that the recommendations main-
and risks of interventions and clinical practice information
the recommendations.9–11 The strength of recommenda-
Development, and Evaluation (GRADE) system for grading

ther Delphi rounds to achieve final consensus.8 The benefits
individual comments on the evidence and draft recommen-
der Delphi group, using the Delphi method to collate rounds of
operative surgical procedures in which perioperative management
number of and reason for excluded studies in this step was
read the abstract or full text of the papers for inclusion. The
screened by the authors in a stepwise manner to identify
eligible studies. In the first step we screened the titles,
were subsequently excluded for reasons that are given in
trial was 309 studies were considered for inclusion, but 299 studies
after title review, 8179 irrelevant studies were excluded and
We screened 8488 abstracts yielded by our search strategy;
limited to only English language and human trials. The
librarian deleted duplicate records. The search results were
screened by the authors in a stepwise manner to identify the
eigible studies. In the first step we screened the titles, and irrelevant papers were excluded. In the next step, we read the abstract or full text of the papers for inclusion. The
number of and reason for excluded studies in this step was
recorded. We selected all reviews, trials, or RCTs of ambula-
tory surgical procedures in which perioperative management of
adult (age ≥18 years) diabetic patients was studied.

The recommendations were formulated by the consen-
sus group, using the Delphi method to collate rounds of
individual comments on the evidence and draft recommenda-
tions, followed by roundtable discussions and then fur-
ther Delphi rounds to achieve final consensus.8 The benefits
and risks of interventions and clinical practice information
were considered to ensure that the recommendations main-
tain patient safety and have clinical validity and usefulness.
The categories of evidence were based upon the level of
evidence and agreement among the members of the con-
sensus panel (Table 1).

We used the Grading of Recommendations, Assessment,
Development, and Evaluation (GRADE) system for grading
the recommendations.9–11 The strength of recommenda-
tions was graded either as “strong” or “weak.” A strong
recommendation was offered when the desirable effects of
an intervention clearly outweighed or clearly did not out-
weigh the undesirable effects. A weak recommendation was
offered if the overall effects were less certain, either because of
low-quality evidence or because evidence suggested that
desirable and undesirable effects were closely balanced.

The consensus panel considered the following clinical
questions:

1. What, if any, preoperative information specifically related to glycemic control should be obtained about diabetic patients?
2. How do we manage preoperative oral antidiabetic and noninsulin injectable therapy?
3. How do we manage preoperative insulin therapy?
4. Is there a preoperative blood glucose level above which one should postpone elective surgery?
5. What is the optimal intraoperative period blood glucose level?
6. How do we maintain optimal blood glucose levels?
7. Should an insulin-naïve patient receive insulin to optimize blood glucose levels?
8. What are the other considerations specific to glycemic control in diabetic outpatients?
9. What is the optimal perioperative blood glucose monitoring?
10. How should we identify and manage perioperative hypoglycemia?
11. What are the discharge considerations for diabetic outpatients?
12. What advice should we give to patients for glucose control after discharge home?
13. What are the areas for future research?

RESULTS

The Quality of Reporting of Meta-analysis (QUORUM) guide-
lines were followed for the description of this study (Fig. 1). We
screened 8488 abstracts yielded by our search strategy;
after title review, 8179 irrelevant studies were excluded and
309 studies were considered for inclusion, but 299 studies
were subsequently excluded for reasons that are given in
detail in Figure 1. We eventually included only 1 systematic
review and 9 trials including 5 RCTs.12–21

Overall, studies evaluating perioperative glycemic con-
control in patients undergoing ambulatory surgery are sparse
and of limited quality. Thus, there is insufficient evidence
to provide strong recommendations for the posed ques-
tions regarding perioperative blood glucose management
of diabetics undergoing ambulatory surgery. In the absence
of high-quality evidence, recommendations were based on
general principles of blood glucose control in diabetics,
drug pharmacology, data from inpatient surgical popula-
tion, and review articles,22–32 as well as clinical experience
and judgment.

DISCUSSION

In an ambulatory surgery setting, the primary goals are the
avoidance of hypoglycemia and maintenance of adequate
blood glucose control. This is accomplished with minimal
disruption in the patients’ antidiabetic therapy, frequent
blood glucose monitoring, and prompt resumption of oral
intake after the surgery.

<table>
<thead>
<tr>
<th>Table 1. Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category 1</td>
</tr>
<tr>
<td>High-level evidence (i.e., high-powered randomized clinical trials or meta-analyses), and the panel has reached uniform (near unanimous) consensus.</td>
</tr>
<tr>
<td>Category 2A</td>
</tr>
<tr>
<td>Lower-level evidence (phase II or large cohort studies), but despite the absence of higher-level studies, there is uniform consensus that the recommendation is appropriate. It is assumed that these recommendations may be modified as higher-level evidence becomes available.</td>
</tr>
<tr>
<td>Category 2B</td>
</tr>
<tr>
<td>Lower-level evidence, and there is nonuniform consensus that the recommendation should be made. This suggests to the practitioner that there could be more than one approach to the question in statement.</td>
</tr>
<tr>
<td>Category 3</td>
</tr>
<tr>
<td>A major disagreement among the panel members. The level of evidence is not pertinent in this category, because experts can disagree about the significance of high-level trials. This category directs the practitioners that there is a major interpretation issue in the data and directs them to the manuscript for an explanation of the controversy.</td>
</tr>
</tbody>
</table>
What, if Any, Preoperative Information Specifically Related to Glycemic Control Should Be Obtained About Diabetic Patients?

With regard to blood glucose management, preoperative evaluation may include the level of glycemic control (as is assessed by blood glucose levels and glycosylated hemoglobin A1c [HbA1c]). The HbA1c reflects the average glycemic levels over the previous 3 to 4 months and therefore is a good indicator of long-term glycemic control. The evaluation should also include the type and dose of antidiabetic therapy (i.e., oral antidiabetics and insulin), the occurrence and frequency of hypoglycemia, the manifestations of hypoglycemia and blood glucose level at which hypoglycemic symptoms occur, and hospital admissions due to glycemic control issues. The ability of the patient to reliably test blood glucose levels as well as to understand and manage diabetes should also be noted, because this would guide perioperative treatment goals.5

How Do We Manage Preoperative Oral Antidiabetic and Noninsulin Injectable Therapy?

Antidiabetics (Table 2) and noninsulin injectables (Table 3) suggest that hypoglycemia rarely occurs with these medications, except occasionally with sulfonylureas, meglitinides, and noninsulin injectables.22,23,32–35 In addition, there is no evidence that metformin is associated with an increased risk of perioperative lactic acidosis (level of evidence [LoE] category 1).36,37 Nevertheless, in patients with renal dysfunction and those who might receive IV contrast, metformin may be discontinued 24 to 48 hours before surgery.

Overall, it may not be necessary to discontinue oral antidiabetics before the day of surgery (LoE category 2A). However, we suggest that oral antidiabetics and noninsulin injectables should not be taken on the day of surgery (LoE category 2A) until normal food intake is resumed.

How Do We Manage Preoperative Insulin Therapy?

There is insufficient evidence regarding preoperative management of insulin. In the absence of evidence, patient instructions regarding preoperative insulin use should be based on safety concerns (i.e., avoidance of hypoglycemia) as well as maintenance of adequate glucose control. Suggestions for perioperative insulin use are based upon principles for insulin administration to maintain blood glucose levels.
glucose control, which mimics physiologic insulin release consisting of both a basal component (targeting fasting or interprandial [between meals] hyperglycemia) and a correction component (targeting postprandial hyperglycemia). Basal glycemic control is usually accomplished by using long- or intermediate-acting insulin or continuous subcutaneous insulin infusion of rapid-acting insulin delivered via an insulin pump. Postprandial glycemic control is usually accomplished by using short-acting or rapid-acting insulin (Table 4). The basal-bolus insulin regimens have been used with increasing frequency in recent years.22–24

Because basal insulin regimens are generally used to maintain blood glucose control between meals, patients should not experience hypoglycemia with these regimens, even if meals are missed (e.g., during preoperative and postoperative fasting). Thus, there should be minimal alterations in the basal insulin doses on the day before surgery unless the patient reports a history of hypoglycemia at night, in the morning, or with missed meals and in patients on diet restriction preoperatively (e.g., bowel preparation). On the other hand, patients using insulin in combination with oral antidiabetics38 or regimens using intermediate-acting insulins with a peak effect (e.g., NPH, Lente, and Protamine lispro) may experience hypoglycemia, if a meal is omitted.25,39

Plans for preoperative insulin management should consider the level of preoperative glycemic control (i.e., fasting blood glucose level and HbA1c); for example, patients with tight glycemic control or those with a wide range of daily blood glucose values and those using complex insulin regimens are more likely to experience hypoglycemia if meals are omitted. Patients’ ability to check blood glucose levels and follow instructions regarding appropriate dose adjustments is critical in avoiding hypoglycemia. In addition, the timing of surgery and the expected time to

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**Table 2. Pharmacology of Oral Antidiabetic Agents**

<table>
<thead>
<tr>
<th>Drug class: generic (trade name)</th>
<th>Mechanism of action</th>
<th>Half-life (hours)</th>
<th>Adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biguanides</td>
<td>Decrease hepatic gluconeogenesis, increase insulin sensitivity.</td>
<td>6–18 24</td>
<td>Diarrhea, nausea, vomiting, lactic acidosis (avoid in renal &amp; liver disease, congestive heart failure).</td>
</tr>
<tr>
<td>Metformin (Glucophage)</td>
<td>Stimulate insulin secretion, decrease insulin resistance.</td>
<td>2–10</td>
<td>Hypoglycemia (caution in elderly &amp; renal disease). Gastrointestinal disturbance.</td>
</tr>
<tr>
<td>Metformin extended release</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sulphonylureas</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chlorpropamide (Diabenese)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tolbutamide (Orinase)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glimepiride (Amaryl)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glyburide (DiaBeta, Micronase)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meglitinides</td>
<td>Stimulate pancreatic insulin secretion.</td>
<td>1</td>
<td>Hypoglycemia, but less common in comparison with sulfonylureas.</td>
</tr>
<tr>
<td>Repaglinide (Prandin)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nateglinide (Starlix)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thiazolidinediones</td>
<td>Regulate carbohydrate and lipid metabolism, reduce insulin resistance and hepatic glucose production.</td>
<td>3–8</td>
<td>Fluid retention, increased cardiac risk including congestive heart failure. Hepatotoxicity.</td>
</tr>
<tr>
<td>Rosiglitazone (Avandia)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pioglitazone (Actos)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alpha-glucosidase inhibitors</td>
<td>Reduce the intestinal absorption of ingested glucose.</td>
<td>2–4</td>
<td>Gastrointestinal irritation, flatus.</td>
</tr>
<tr>
<td>Acarbose (Precose)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Miglitol (Glyset)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dipeptidyl peptidase-4 (DPP-4)</td>
<td>Reduces breakdown of gastrointestinal hormone-incretins (glucagon-like peptide type-1, enhance insulin secretion, decrease glucagon.</td>
<td>8–14</td>
<td>Infection.</td>
</tr>
<tr>
<td>inhibitors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sitagliptin (Januvia)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saxagliptin (Onglyza)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table 3. Noninsulin Injectables**

<table>
<thead>
<tr>
<th>Drug class: generic (trade name)</th>
<th>Mechanism of action</th>
<th>Half-life (hours)</th>
<th>Adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exenatide (Byetta)</td>
<td>Synthetic form of exendin 4, which has actions similar to glucagon-like peptide type-1 (GLP-1). Suppresses glucagon secretion and hepatic glucose production. Suppresses appetite. Delays gastric emptying.</td>
<td>6–10</td>
<td>Nausea, vomiting, weight loss, hypoglycemia when combined with sulfonylureas.</td>
</tr>
<tr>
<td>Pramlintide (Symlin)</td>
<td>Synthetic form of amylin, a naturally occurring peptide that is cosecreted with insulin by beta cells. Suppresses postprandial glucagon secretion and hepatic glucose production. Enhances the effects of insulin. Suppresses appetite. Delays gastric emptying.</td>
<td>2–4</td>
<td>Nausea, vomiting, weight loss, hypoglycemia with insulin.</td>
</tr>
</tbody>
</table>

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resumption of regular diet after surgery should also be considered. The suggestions for preoperative insulin administration are included in Table 5 (LoE category 2A).

Is There a Preoperative Blood Glucose Level Above Which One Should Postpone Elective Surgery?

There are insufficient data to specifically recommend the level of preoperative fasting blood glucose or HbA1c levels above which elective ambulatory surgery should be postponed. In addition to inadequate long-term glycemic control, preoperative hyperglycemia is commonly due to inappropriate discontinuation of preoperative antidiabetic therapy and preoperative stress response. Surgery should be postponed in patients with significant complications of hyperglycemia such as severe dehydration, ketoacidosis, and hyperosmolar nonketotic states (LoE category 2A).¹

It may be acceptable to proceed with surgery in patients with preoperative hyperglycemia but with adequate long-term glycemic control (LoE category 2A). The ADA recommends that outpatient management of diabetes should ideally include a combination of a target HbA1c <7% (normal 4%–7%), a preprandial blood glucose level of 90 to 130 mg/dL and a peak postprandial blood glucose level of <180 mg/dL,²² although this has not been verified in the ambulatory surgical population.

In chronically poorly controlled diabetic patients, the decision to proceed with ambulatory surgery should be made in conjunction with the surgeon while taking into consideration the presence of other comorbidities and the potential risks of surgical complications (e.g., delayed wound healing and wound infection). There are no RCTs evaluating the effects of preoperative glycemic control on postoperative infection in ambulatory surgical procedures.⁴⁰ However, a review of outcomes after noncardiac surgery found that HbA1c <7% was associated with a significantly lower incidence of postoperative infections.⁴¹

What Is the Optimal Intraoperative Blood Glucose Level?

There is no evidence in the literature that any particular blood glucose level is either beneficial or harmful for patients undergoing ambulatory surgical procedures. Therefore, the optimal blood glucose level for ambulatory surgical patients remains unknown. In the absence of direct

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### Table 4. Pharmacology of Insulin

<table>
<thead>
<tr>
<th>Drug class: generic (trade name)</th>
<th>Onset</th>
<th>Peak effect</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Short acting and rapid acting</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regular (Novolin R, Humulin R)</td>
<td>30–60 minutes</td>
<td>2–4 hours</td>
<td>6–8 hours</td>
</tr>
<tr>
<td>Lispro (Humalog)</td>
<td>5–15 minutes</td>
<td>30–90 minutes</td>
<td>4–6 hours</td>
</tr>
<tr>
<td>Aspart (Novolog)</td>
<td>5–15 minutes</td>
<td>30–90 minutes</td>
<td>4–6 hours</td>
</tr>
<tr>
<td>Glulisine (Apidra)</td>
<td>5–15 minutes</td>
<td>30–90 minutes</td>
<td>4–6 hours</td>
</tr>
<tr>
<td><strong>Intermediate acting</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NPH (Novolin N, Humulin N-NF)</td>
<td>2–4 hours</td>
<td>4–10 hours</td>
<td>10–16 hours</td>
</tr>
<tr>
<td>Zinc insulin (Lente)</td>
<td>2–4 hours</td>
<td>4–10 hours</td>
<td>12–20 hours</td>
</tr>
<tr>
<td>Extended zinc insulin (Ultralente)</td>
<td>6–10 hours</td>
<td>10–16 hours</td>
<td>18–24 hours</td>
</tr>
<tr>
<td><strong>Long acting (peakless)</strong></td>
<td>2–4 hours</td>
<td>None</td>
<td>20–24 hours</td>
</tr>
<tr>
<td>Glargine (Lantus)</td>
<td>2–4 hours</td>
<td>None</td>
<td>20–24 hours</td>
</tr>
<tr>
<td>Detemir (Levemir)</td>
<td>2–4 hours</td>
<td>None</td>
<td>20–24 hours</td>
</tr>
<tr>
<td><strong>Mixed insulins (NPH + regular)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>70% NPH/30% regular (Novolin 70/30, Humulin 70/30)</td>
<td>30–90 minutes</td>
<td>Dual</td>
<td>10–16 hours</td>
</tr>
<tr>
<td>50% NPH/50% regular (Humulin 50/50)</td>
<td>30–90 minutes</td>
<td>Dual</td>
<td>10–16 hours</td>
</tr>
<tr>
<td><strong>Mixed insulins (intermediate-acting + rapid-acting analogs)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>70% Lispro Protamine suspension/30% Aspart (Novolog mix 70/30)</td>
<td>5–15 minutes</td>
<td>Dual</td>
<td>10–16 hours</td>
</tr>
<tr>
<td>75% Lispro Protamine suspension/25% Lispro (Humalog mix 75/25)</td>
<td>5–15 minutes</td>
<td>Dual</td>
<td>10–16 hours</td>
</tr>
<tr>
<td>50% Lispro Protamine suspension/50% Lispro (Humalog mix 50/50)</td>
<td>5–15 minutes</td>
<td>Dual</td>
<td>10–12 hours</td>
</tr>
</tbody>
</table>

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### Table 5. Instructions to Patient Regarding Preoperative Insulin and Noninsulin Injectable Administration

<table>
<thead>
<tr>
<th>Insulin regimen</th>
<th>Day before surgery</th>
<th>Day of surgery</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin pump</td>
<td>No change</td>
<td>No change</td>
<td>Use “sick day” or “sleep” basal rates. Reduce nighttime dose if history of nocturnal or morning hypoglycemia. On the day of surgery, the morning dose of basal insulin may be administered on arrival to the ambulatory surgery facility. See the comments for long-acting insulins.</td>
</tr>
<tr>
<td>Long-acting, peakless insulins</td>
<td>No change</td>
<td>No change</td>
<td>75%–100% of morning dose</td>
</tr>
<tr>
<td>Intermediate-acting insulins</td>
<td>No change in the daytime dose. 75% of dose if taken in the evening</td>
<td>50%–75% of morning dose</td>
<td></td>
</tr>
<tr>
<td>Fixed combination insulins</td>
<td>No change</td>
<td>50%–75% of morning dose of intermediate-acting component</td>
<td>Lispro-protamine only available in combination; therefore use NPH instead, on day of surgery. See the comments for long-acting insulins.</td>
</tr>
<tr>
<td>Short- and rapid-acting insulin</td>
<td>No change</td>
<td>Hold the dose</td>
<td></td>
</tr>
<tr>
<td>Noninsulin injectables</td>
<td>No change</td>
<td>Hold the dose</td>
<td></td>
</tr>
</tbody>
</table>
evidence, suggestions are based on data from hospitalized surgical patients and a consensus statement of the AACE/ADD.5 We suggest that in patients with well-controlled diabetes, intraoperative blood glucose levels be maintained <180 mg/dL (10.0 mmol/L) (LoE category 2A).

Of note, the selection of peroperative blood glucose level should depend upon the duration of surgery, invasiveness of surgical procedure, type of anesthetic technique, and expected time to resume oral intake and routine antidiabetic therapy. For example, higher blood glucose levels may be acceptable in patients undergoing short surgical procedures after which patients are promptly expected to resume oral intake and antidiabetic therapy.

However, in patients with poorly controlled diabetes, if the decision to proceed with the surgery is made, the blood glucose levels should be maintained around their preoperative baseline values rather than temporarily (i.e., peroperatively) normalizing them (LoE category 2A). Chronically elevated blood glucose levels should not be decreased acutely in the perioperative period because the threshold at which a patient experiences symptoms or organ impairment due to hypoglycemia is dynamic and varies with their long-term glycemic control.22–23 Patients with poorly controlled type 2 diabetes have an altered counterregulatory response (i.e., release of epinephrine, norepinephrine, growth hormone, cortisol, and pancreatic polypeptide), resulting in hypoglycemic symptoms at normal blood glucose levels.42–44 Also, significant fluctuations in blood glucose levels caused by acute reduction in chronically elevated blood glucose levels can lead to detrimental biochemical effects including increased oxidative stress response45 and may increase perioperative morbidity and mortality.1,46

How Do We Maintain Optimal Blood Glucose Level?

There are insufficient data regarding the best strategy or regimen to attain target blood glucose levels in ambulatory surgical patients with diabetes mellitus. The type, dose, and route of administration of insulin used to maintain an optimal blood glucose level are discussed below.

Type of insulin (regular insulin vs. rapid-acting insulin).

There is not enough evidence at this time to recommend the use of one type of insulin in preference of another, because there are no studies comparing regular insulin with rapid-acting insulins in ambulatory surgical patients. However, for subcutaneous dosing, rapid-acting insulins have superior pharmacokinetics in comparison with regular insulin (Table 4). Studies in patients with diabetic ketoacidosis demonstrated that subcutaneous doses of rapid-acting insulin administered every 1 to 2 hours closely matched IV infusion of regular insulin with respect to efficacy and safety.47,48 In addition, the use of a subcutaneous rapid-acting insulin approach was less labor-intensive and thus more cost effective. Another benefit of using rapid-acting insulin is that it may reduce the duration of observation required in the postoperative period because the peak blood levels are achieved earlier than with regular insulin (see the Discharge section). Therefore, in an ambulatory setting, subcutaneous rapid-acting insulin analogs may be preferred over regular insulin (LoE category 2A).

Route of insulin administration (IV vs. subcutaneous).

Because IV bolus doses of insulin have a very short duration of action (30 to 40 minutes), which can cause significant fluctuations in blood glucose levels that could be detrimental to the patients,31 it is not recommended (LoE category 2A).

Although IV infusion of regular insulin has been used to maintain optimal blood glucose levels in patients undergoing major surgical procedures and in critically ill patients, the AACE/ADA consensus statement recommends the subcutaneous route for noncritical patients.5 IV insulin infusion requires more frequent monitoring because there are concerns of hypoglycemia. Overall, insulin infusion may not be necessary or practical in the outpatient surgical setting. Furthermore, as is mentioned above, subcutaneous administration of rapid-acting insulin has been shown to provide similar control as IV infusion of regular insulin.47,48 Therefore, subcutaneous administration is the preferred method for achieving and maintaining target glucose levels (LoE category 2A).

Of note, one of the concerns with subcutaneous administration is the possibility of “stacking” of repeated doses, which may result in hypoglycemia. Thus, additional subcutaneous doses of insulin should not be administered until the time to peak effect has passed or blood glucose is being closely monitored.

Dosing schedule. There is not enough evidence to recommend a dosing schedule to optimize the blood glucose levels. There are no validated insulin administration protocols that have been shown to be safe and effective in ambulatory surgical patients. Dosing of insulin may depend on the patient’s insulin sensitivity, which is reflected by the patient’s total (basal and prandial) daily dose of insulin. Sliding-scale insulin regimens are commonly used30–32; however, they have been questioned in recent years.5 Another approach to calculating the initial insulin dose is based on the “rule of 1800” (for rapid-acting insulin) or the “rule of 1500” (for regular insulin), which provides the expected decrease in blood glucose with each unit of insulin. The “rule of 1800” is more conservative than the 1500 rule. However, some authors have recommended the use of the “rule of 1500” for all surgical patients.47 Thus, 1800 or 1500 is divided by total daily insulin dose to determine the expected decrease in blood glucose level with 1 unit of insulin. For example, if the patient’s daily insulin requirement is 60 U, each unit of insulin would reduce the blood glucose level by 25 to 30 mg/dL (i.e., 1500/60 or 1800/60).

Should an Insulin-Naive Patient Receive Insulin to Optimize Blood Glucose Levels?

There is insufficient evidence in the literature to guide insulin use in an insulin-naive patient. There has been reluctance on the part of physicians to use insulin in patients with type 2 diabetes who take only oral antidiabetic medications because of concerns of hypoglycemia.49 However, such reluctance may be misplaced because many of these patients eventually require insulin therapy in addition to an oral hypoglycemic drug as part of the natural progression of their disease. In fact, only a relatively low incidence of hypoglycemia has been reported in
used either alone or in combination with other antiemetics. Methasone is a well-established antiemetic and is routinely administered as a single bolus of 20 to 40 mL/kg before surgery (i.e., consumption of water until 2 hours before surgery) and adequate intraoperative crystalloid administration (20 to 40 mL/kg bolus, assuming there are no contraindications such as history of congestive heart failure that might occur in transit. Glucose tablets or gels are usually particulate in nature and therefore should be brought all their insulins with them to the facility and to travel with a suitable treatment such as clear juices for hypoglycemia that might occur in transit. Glucose tablets or gels are usually particulate in nature and therefore should be avoided in the preoperative period. Adequate preoperative hydration (i.e., consumption of water until 2 hours before surgery) and adequate intraoperative crystalloid administration (20 to 40 mL/kg bolus, assuming there are no contraindications such as history of congestive heart failure) should prevent postoperative dehydration.

Aggressive nausea and vomiting prophylaxis and avoidance of factors that might increase postoperative nausea and vomiting (PONV) such as postoperative opioids should allow early resumption of oral intake. Dexamethasone is a well-established antiemetic and is routinely used either alone or in combination with other antiemetics for the prevention of PONV. The use of dexamethasone, even after a relatively modest single dose, has been demonstrated to transiently increase perioperative blood glucose levels.

Dexamethasone in a dose of 10 mg IV has been reported to increase blood glucose concentrations in diabetic and nondiabetic patients. Hans et al. prospectively investigated the change in perioperative blood glucose after dexamethasone 10 mg IV in type 2 diabetic patients who were treated exclusively with oral hypoglycemics and in nondiabetic patients. They found that blood glucose concentrations increased significantly over time (4 hours) and peaked at 2 hours in both groups. The magnitude of increase was around 20% from baseline and was comparable between the 2 groups. Maximum concentrations were higher in the diabetic group (8.97 ± 1.51 mmol/L) than in the nondiabetic group (7.86 ± 1.00 mmol/L). Of interest, 50% of the subjects underwent bariatric surgery, and the authors found that the body mass index and preoperative glycemic control, and those with a history of frequent hypoglycemia. Notably, geriatric patients experience fewer hypoglycemic symptoms. Use of peakless basal insulin analogs (instead of insulins with peak) and rapid-acting prandial insulin analogs (instead of regular insulin)
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and use of continuous subcutaneous insulin infusion result in fewer incidences of hypoglycemia.27,28,29

Patients with long-standing type 2 diabetes are at a risk of developing hypoglycemia-associated autonomic failure because defective glucose counterregulation leads to impairment or even loss of the warning symptoms of hypoglycemia, also termed hypoglycemia unawareness.25,60 Similarly, patients with poorly controlled type 2 diabetes may experience hypoglycemic symptoms at blood glucose levels that are usually considered normal.25 Importantly, adequate perioperative monitoring of blood glucose levels as prescribed above should allow prevention and early diagnosis of hypoglycemia.

Diagnosis of hypoglycemia is based upon symptoms, blood glucose levels, or both. In an awake patient, hypoglycemia may cause sweating, palpitations, weakness, fatigue, confusion, and behavioral changes followed by seizure, loss of consciousness, brain damage, or death. Although there is some disagreement, a blood glucose level of <70 mg/dL is generally considered an alert value for hypoglycemia.25 Use of this value as a trigger for therapy allows time for prevention of symptomatic hypoglycemia, which usually occurs at blood glucose levels of 45 to 55 mg/dL.25

In the symptomatic patient, the preferred method for treatment of hypoglycemia is consumption of 10 to 25 g of glucose, which is repeated until blood glucose increases and symptoms resolve. Clear liquids suitable for treating hypoglycemia include sugary drinks, sodas, electrolyte solutions, and fruit juices (e.g., 4 oz. apple juice). In patients with symptomatic hypoglycemia who are unable to ingest glucose and do not have IV access, subcutaneous glucagon 1 mg may be administered while attempts are made to obtain IV access. If IV access is established, an initial glucose dose of 20 to 50 mL (10 to 25 gm) dextrose 50% may be given.61 Hyperglycemia after glucose administration can have significant detrimental effects, particularly in the presence of significant brain ischemia, and it should be avoided. Of note, the increase in blood glucose levels after oral or IV glucose administration is transient, and patients may require further, sustained glucose therapy after initial improvement in symptoms or blood glucose levels.

What Are the Discharge Considerations for Diabetic Outpatients?
In addition to achieving discharge criteria,62 patients should be observed in an ambulatory facility until the possibility of hypoglycemia from perioperatively administered insulin is excluded. Many ambulatory patients are able to consume adequate oral intake to counteract potential hypoglycemia, but if not, they should be observed for an appropriate period of time after the last dose of insulin. The risk of hypoglycemia with subcutaneous rapid-acting insulin subsides within 1.5 hours, whereas that for subcutaneous regular insulin subsides in about 3 to 4 hours after the last dose is administered.24,25

What Advice Should We Give to Patients for Glucose Control After Discharge Home?
Patients need to receive clear and consistent instructions regarding plans for return to preoperative antidiabetic therapy and management of potential hypoglycemia. They should be instructed to check blood glucose levels frequently while fasting. Patients should carry hypoglycemia treatments while traveling to and from the surgical facility. While patients can resume the preoperative antidiabetic therapy once they are eating, they must be cautious with overlapping times of medication administration due to delayed dosing of morning medications. Resumption of antidiabetic therapy should be based on perioperative course and any treatments received. Because most oral hypoglycemics act on ingested food, these should be restarted once food intake is resumed. Patients should be advised that transition to daily preoperative antidiabetic regimens should be delayed if normal caloric intake is delayed.

What Are the Areas for Future Research?
This review has identified several areas for future research for which current data are insufficient or conflicting. There is a need for further large, adequately powered, well-designed randomized trials to assess all the clinical questions included in this review. In addition, there is a need to evaluate the impact of the recommendations provided in this consensus statement (e.g., preoperative continuation or discontinuation of oral hypoglycemics, risks and benefits of using rapid acting insulin to optimize perioperative blood glucose levels, and need for delaying discharge home after insulin administration).

Other questions that need to be addressed are as follows:

- Does scheduled time of the surgery (i.e., early vs. late) have any significant influence on outcomes, and if so, is there a patient subpopulation for which it does particularly?
- What is the impact of use of various preoperative regimens on short-term (e.g., morbidities and duration of recovery room, hospital stay and quality of recovery) and long-term (e.g., unplanned hospital admission, 30-day unexpected hospitalization, morbidity, and mortality) outcome in the ambulatory setting?
- What is the effect of preoperative insulin therapy on outcome after ambulatory surgery? Is there any benefit to aggressive preoperative glycemic control?
- Are there differences in optimal target blood glucose levels for high-risk outpatients versus low-risk outpatients?
- Are there differences in optimal blood glucose management in type 1 versus type 2 diabetes in the ambulatory setting?
- Are there differences in patient outcome between the various routes of administration of insulin?
- What is the optimal prophylactic antiemetic therapy in diabetic outpatients?
- Are there any predictors (e.g., blood glucose levels, HbA1c levels, and other comorbidities) that suggest avoidance of ambulatory surgery or need for overnight hospital admission?
- What is the impact of anesthetic technique (local/regional anesthesia, sedation/analgesia technique, general anesthesia) on blood glucose control?
REFERENCES


