Perioperative Management of Oral Antidiabetic Drugs and Non-Insulin Injectables: A Review Article

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ABSTRACT

Perioperative management of diabetes and hyperglycemia is still a challenging dilemma. For complications prevention, maintaining optimal diabetes control for surgical procedures is crucial. The purpose of this review is to evaluate available data regarding perioperative management of oral antidiabetic drugs (OADs) and non-insulin injectables, and to provide recommendation to guide the use of these agents. An in-depth literature review and discussion of the current guidelines. Perioperative management of diabetes and hyperglycemia is a common and yet a challenging clinical scenario. Insulin remains the cornerstone of perioperative hyperglycemia. Professional guidelines are brief and nonspecific regarding perioperative management of diabetes and hyperglycemia, especially OADs and non-insulin injectables. Effective perioperative management requires a comprehensive approach. Preoperative assessment is critical to minimize morbidity and mortality. Most associations recommended stopping the consumption of OADs and non-insulin injectables on the day of surgery, except for dipeptidyl peptidase-4 (DPP-4) inhibitors. DPP-4 inhibitors-based therapies are safe and effective in perioperative hyperglycemia management, either alone or in combination with basal insulin. Current guidelines need to be updated to reflect the new findings concerning the perioperative use of OADs and non-insulin injectables.

Keywords: Diabetes mellitus; Management; Oral antidiabetic; Perioperative; Non-insulin

INTRODUCTION

More than 825 million adult people (aged ≥18 years) worldwide have diabetes in 2022, and among them, 445 million patients (aged ≥30 years) did not receive therapy [1]. During their lifespan, as many as half of diabetics will need to undergo operations [2, 3]. Perioperative hyperglycemia with or without diabetes has been shown to influence clinical outcomes with an increased risk of cardiovascular complications, thromboembolic events, infections, a longer length of hospital stay, and higher hospitalization costs [4-8]. Although older studies have shown mixed results, newer studies have indicated that higher hemoglobin A1c (HbA1c) is associated with worse surgical outcomes as an independent risk factor [9, 10]. A prior study reported that the rate of perioperative mortality for diabetic individuals is as much as 50% more elevated than that for individuals without diabetes [6]. Thus, meticulous preoperative management of patients with diabetes is critical to minimize morbidity and mortality during the operation [11]. Despite these, perioperative management of diabetes and hyperglycemia is still a challenging dilemma. Professional guidelines have been short and nonspecific regarding perioperative management of diabetes and hyperglycemia, especially oral antidiabetic drugs (OADs) and non-insulin injectables [12-15]. Insulin remains the cornerstone of treatment for perioperative hyperglycemia [12]. Overall, the target range for perioperative glycemic control should be 80-180 mg/dL (4.4 – 10.0 mmol/L). Generally, the American Diabetes Association (ADA) recommends withholding metformin or any other glucose lowering agent on the morning of surgery and administering 50% of the NPH insulin dose or 60-80% of the long-acting basal insulin analog or basal pump insulin dose [12]. Recently, many new classes of anti-diabetic agents were introduced. A list of the available OADs and non-insulin injectables is found in Table 1 [16-21]. Diabetologists have proposed revisiting our practice habits regarding inpatient use of OADs and non-insulin injectables [22]. This article reviewed the evidence-based and current guidelines regarding perioperative management of oral antidiabetic drugs and non-insulin injectables, focusing on the newer antidiabetic agents.

Table 1. Classes of oral antidiabetic drugs and non-insulin injectables

Class	Generic name	Brand name
Newer antidiabetic agents:		
SGLT-2 inhibitors	Empagliflozin Dapagliflozin Canagliflozin Ertugliflozin	Jardiance Farxiga Invokana
Incretin-based therapy	Exanatide Liraglutide Lixisenatide Dulaglutide Semaglutide Albiglutide Tirzepatide	Bydureon, Byetta Saxenda, Victoza Adlyxin Trulicity Ozempic, Rybelsus, Mounjaro
DPP-4 inhibitors	Sitagliptin Saxagliptin Linagliptin Alogliptin Vildagliptin	Januvia Onglyza Tradjenta Nesina
Older OAD agents:		
Sulfonylureas	1st Generation: Acetohexamide Chlorpropamide Tolazamide Tolbutamide 2nd Generation: Glipizide Glyburide/ Glibenclamide Glimepiride Gliclazide	 Glipizide XL, Glucotrol Glynase Amaryl

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Biguanide	Metfromin	Fortamet, Glucophage, Glucophage, Glumetza, Riomet
Thiazolidinediones	Pioglitazone Rosiglitazone	Actos Avandia
Meglitinides	Nateglinide Repaglinide	Starlix Prandin
Alpha-glucosidase inhibitors	Acarbose Miglitol Voglibose	Precose Glyset

Dopamine receptor agonists	Bromocriptine
Bile acid sequestrants	Colesevelam
Amylin analog	Pramlintide acetate

SGLT2: sodium-glucose cotransporter, GLP-1: glucagon-like peptide, DPP-4: dipeptidyl peptidase-4.

Preoperative Assessment:

A comprehensive preoperative assessment of diabetes patients is required, particularly for patients at risk of diabetes-related complications [23]. Preoperative evaluations for diabetes patients encompass collecting patient clinical history, focusing on the type of diabetes, risk of diabetes-related complications, drug therapy, current glycemic control, susceptibility to hypoglycemia, and surgery (figure 1) [24-26].

Perioperative Risk of Hypoglycemia:

Hypoglycemia is diagnosed when plasma glucose levels < 3.9 mmol/L and can also suspected according to neuroglycopenic or adrenergic manifestations [27]. In the fasting state, meglitinides and sulfonylureas can result in hypoglycemia because they stimulate insulin release regardless of glucose levels [27, 28]. In the perioperative period, hypoglycemia is linked to diverse negative consequences, such as mortality, morbidity, cardiovascular events, brain damage, and cognitive dysfunctions [29-31]. Accordingly, minimizing and managing perioperative hypoglycemia is crucial. Treatment of hypoglycemia includes oral glucose (if patients can swallow safely) or IV dextrose. Careful monitoring and repeated tests are mandatory after hypoglycemia resolves [27]. Still, in some cases, particularly patients on old sulfonylureas, severe hypoglycemia may persist after treatment. Hence, sulfonylureas must be avoided on the day of surgery, particularly in older patients and patients experiencing renal dysfunction [32]. Enhancing preoperative diabetes management aids in reducing the length of hospitalization and diminishing the incidence of hypoglycemia after surgery [33]. Finally, utilizing a prediction model for perioperative hypoglycemic risk is reported to be valid and reliable, and it may decrease hypoglycemia risk and associated complications [34].

Newer antidiabetic agents:

Sodium-glucose co-transporter 2 inhibitors:

Sodium-glucose co-transporter 2 (SGLT-2) inhibitors work by an insulin-independent mechanism producing modest glycemic control by increasing the renal excretion of glucose. SGLT-2 inhibitors are shown to have tremendous benefits for patients with type 2 diabetes mellitus (T2DM) in the outpatient setting, including improved glycemic control, low risk of hypoglycemia, and cardiorenal protective effects [35-38]. It is important to note that they have been associated with an increased risk of urogenital infections, diabetic ketoacidosis (DKA), and dehydration in numerous clinical trials in the outpatient setting [39-42].

There is limited data about SGLT-2 inhibitor use in the hospital or the perioperative period. A retrospective, multicenter, controlled cohort study showed an increased risk of development of DKA in hospitalized

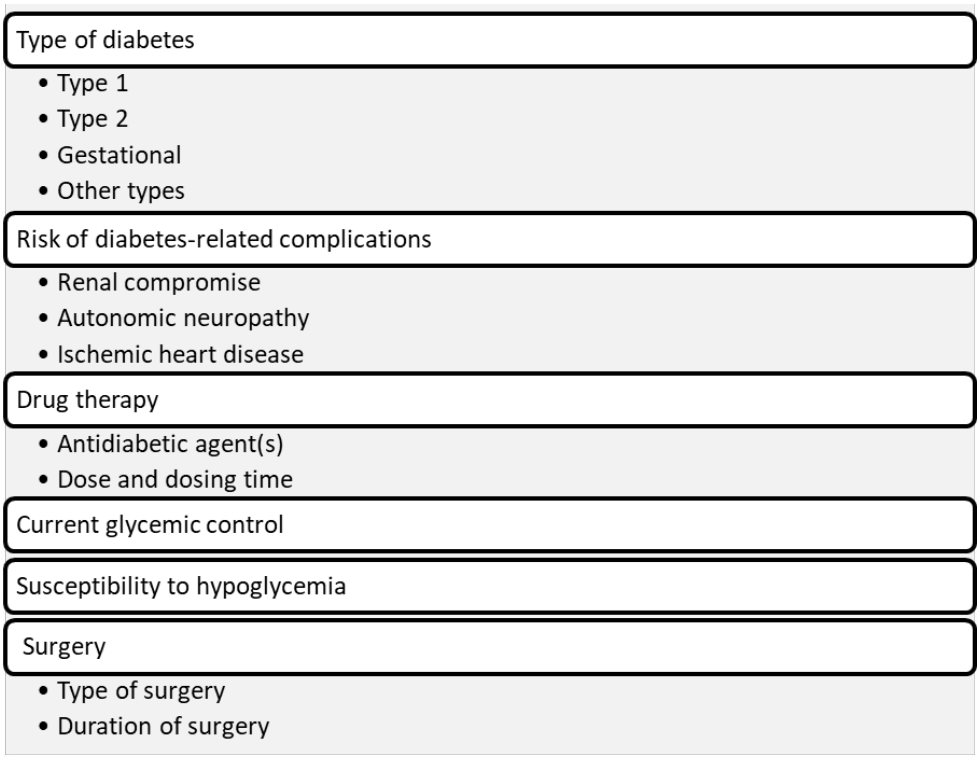

Figure 1. preoperative assessment of diabetes patients

Table 2. Recommended perioperative management for oral antidiabetic drugs and non-insulin injectables

Class	The day before the surgery	Day of surgery	When to restart
Newer antidiabetic agents:			
SGLT-2 inhibitors	According to FDA 2020, ertugliflozin should suspended minimally 4 days before, and empagliflozin, dapagliflozin, and canagliflozin should suspended minimally 3 days before.	Treat hyperglycemia with insulin, monitor acid/base status and intravascular volume, and avoid glucocorticoids.	Resume when the patient is eating and drinking normally.
Incretin-based therapy	Take as usual	Take as usual if there is no concern for gastrointestinal side effects. If needed, add insulin based on glycemic control.	
DPP-4 inhibitors	Take as usual	Take as usual. If needed, add insulin based on glycemic control.	
Older OAD agents:			
Sulfonylureas	Take as usual	Hold and give insulin	When the patient is eating and drinking normally
Biguanide	Take as usual	Hold and give insulin	When the patient is eating and drinking normally, consider checking kidney function when contrast media given, hypotension or any condition that increase risk of kidney dysfunction.
Thiazolidinediones	Take as usual	Hold and give insulin	When the patient is eating and drinking normally and no concern for heart failure
Meglitinides	Take as usual	Hold and give insulin	When the patient is eating and drinking normally
Alpha-glucosidase inhibitors	Take as usual	Hold and give insulin	When the patient is eating and drinking normally if there is no concern for gastrointestinal side effects.

SGLT2: sodium-glucose cotransporter, GLP-1: glucagon-like peptide, DPP-4: dipeptidyl peptidase-4.

SGLT-2 inhibitor users compared to hospitalized SGLT-2 inhibitor nonusers [43]. In a small retrospective study, initiation of SGLT-2 inhibitors for patients admitted with acute heart failure was associated with a lower incidence of acute kidney injury and a decreased number of diuretics used at the time of discharge [44]. SGLT-2 inhibitors should be held on the day of surgery and may be resumed when the patient is eating and drinking normally and there is no concern for dehydration and hypotension. Table 2 lists evidence-based recommendations for oral antidiabetic drugs and non-insulin injectables used for perioperative management [12, 15, 45, 46]. The ADA recommends that SGLT-2 inhibitors should be avoided in the immediate preoperative period in patients who are being held NPO and in those who are severely ill. The ADA recommends against routine inpatient use of SGLT-2 inhibitors [12].

Incretin-based therapies:

GLP-1 receptor agonists:

Glucagon-like peptide-1 (GLP-1) receptor agonists work to improve glycemic control through different mechanisms, which include improving insulin secretion, slowing gastric emptying, and reducing glucagon levels after meals. Randomized controlled trials (RCTs) have shown significant cardiovascular benefits with GLP-1 receptor agonist use [47-49]. Given the low risk of hypoglycemia and cardioprotective benefits associated with this class of medication, the use of GLP-1 receptor agonists preoperatively and, in the hospital, have been studied. In a non-blinded randomized superiority trial with 104 patients, exenatide administered by bolus of 0.05 µg/min then continuous infusion of 0.025 µg/min, reduced the total insulin dose and increased the time to the start of insulin compared to intravenous insulin protocol. However, exenatide was not superior in increasing the percentage of patients who spent more than 50% of the study period within the target blood glucose range of 100-139 mg/dL. There was a small increase in nausea in the exenatide group, but no other statistically significant adverse events or postoperative complications were reported up to 30 days later [50]. A pilot study showed that exenatide alone or in combination with basal insulin is safe and effective for the management of hospitalized general medical and surgical patients with T2DM. There was a small but not statistically significant increase in gastrointestinal adverse events [51]. In an open-labelled multicenter RCT with 150 patients, liraglutide started the night before surgery and given the morning of surgery led to lower plasma glucose levels one hour postoperatively. However, liraglutide increased preoperative nausea compared to patients treated with insulin infusion 30-minutes preoperatively or patients who were given 50% of their long-acting basal insulin. There was no difference in hypoglycemia risk between the three groups [52]. In a blinded placebo-controlled multicenter randomized superiority trial with 278 patients, two preoperative doses of liraglutide given as 0.6 mg subcutaneous injection on the evening before surgery and 1.2 mg subcutaneous injection given after induction of anesthesia, improved perioperative control, while reducing insulin requirements

compared with placebo. Both groups were on a continuous insulin infusion protocol. There was no difference in hypoglycemia, nausea, vomiting, mortality, or postoperative complications [53]. In a randomized controlled pilot study, dulaglutide in combination with basal plus correction insulin therapy was shown to reduce the frequency of hyperglycemia and hypoglycemia compared to basal plus correction insulin therapy. There was no difference in the reported side-effects between the two groups [54].

Based on the available data, GLP-1 receptor agonists are safe and effective in controlling perioperative hyperglycemia while decreasing the risk of hypoglycemia. Given the gastrointestinal side effects and the risk of slowed gastric motility, caution should be used when considering GLP-1 receptor agonists for patients who have or who are at risk of gastrointestinal issues. The ADA did not provide specific recommendations for the perioperative use of GLP-1 receptor agonists.

Dipeptidyl peptidase 4 (DPP-4) inhibitors:

DPP-4 inhibitors are another class of medication which exert a glycemic effect through the GLP-1 pathway. DPP-4 is an enzyme that deactivates multiple peptides, including GLP-1 and glucose-dependent insulinotropic polypeptide (GIP). By inhibiting GLP-1 deactivation, DPP-4 inhibitors have a modest effect on the GLP-1 level and glycemic control compared to GLP-1 receptor agonists. DDP-4 inhibitors were initially thought to have a neutral effect on cardiovascular risk, but since two studies showed an association between heart failure hospitalization with saxagliptin and alogliptin, the Food and Drug Administration (FDA) added a warning to these two medications, which later have been expanded to include all the DDP-4 inhibitors [55, 56]. The warning is to exercise caution when using this class of medications for patients who are at a high risk of heart failure and to consider discontinuation if heart failure develops [57, 58]. It is important to note that various cardiovascular outcome trials and a recent meta-analysis failed to show a significant increase in heart failure hospitalization with DPP-4 inhibitors [59-63]. Multiple studies have assessed DDP-4 inhibitor use in surgical patients [64-67].

In a pilot RCT, 90 general medicine and surgery patients with T2DM, sitagliptin alone or with basal insulin was as effective as basal plus bolus insulin. The sitagliptin groups required a lower dose of insulin. There was no significant difference in hypoglycemia or other adverse effects [64]. In a non-inferiority RCT with 277 general medicine and surgery patients with mild to moderate hyperglycemia defined as blood glucose (BG) < 200 mg/dL, sitagliptin plus basal insulin was an effective and safe alternative to basal-bolus insulin [65]. In another RTC with 250 patients with T2DM undergoing non-cardiac surgery who presented with mild to moderate hyperglycemia (BG <200 mg/dL), daily linagliptin alone was effective in achieving good glycemic control while resulting in lower hypoglycemia compared to basal-bolus insulin [66]. In a multicenter observational study of patients with T2DM hospitalized in non-cardiac surgery departments with mild to moderate hyperglycemia (BG<240 mg/dL), linagliptin combined with basal insulin was shown to provide similar glycemic control with less hypoglycemia compared to basal-bolus insulin [67]. Based on the available data, DDP-4 inhibitors alone or in combination with basal insulin are a safe and effective way to achieve good glycemic control for surgical patients with mild to moderate hyperglycemia. However, cation should be used with patients who are at high risk for heart failure. The ADA did not provide specific recommendations for the perioperative use of DPP-4 inhibitors.

Older OAD agents:

Sulfonylureas:

Sulfonylureas manifest their glycemic control by increasing insulin secretion due to an increase in the responsiveness of adenosine triphosphate-sensitive potassium channels in the pancreatic beta cells. Sulfonylureas are usually used in combination with other diabetes medications as a second or third add on agent [13] Sulfonylureas continue to be commonly utilized globally [68]. Sulfonylureas are used as a first line agent for the treatment of MODY type 1 and 3. In addition to permanent neonatal diabetes mellitus [69, 70]. Sulfonylureas are inexpensive and effective. In a meta-analysis, sulfonylurea monotherapy lowered HbA1c by 1.51% more than placebo, and sulfonylureas added to oral diabetes treatment lowered HbA1c by 1.62% compared with placebo. In the same meta-analysis, sulfonylurea treatment increased the risk of hypoglycemia [71]. There is a concern about cardiovascular safety with older sulfonylureas, namely tolbutamide [72]. However, newer RCTs with glimepiride demonstrated that sulfonylureas do not increase cardiovascular risk compared to linagliptin, suggesting that sulfonylureas are safe to use [73]. Sulfonylureas are associated with modest weight gain [74]. Inpatient use of sulfonylureas demonstrates an increase in the risk of hypoglycemia when used in older patients and patients with eGFR <30 mL/min/1.73 m^2 [75, 76]. Although sulfonylurea use is discouraged in the inpatient setting due to the risk of hypoglycemia [77], a study estimated that 28% of US patients with diabetes, were administered a sulfonylurea when they required hospitalization from 2010-2012 [78]. Overall, it has been recommended that sulfonylureas be avoided on the day of surgery [14, 24].

Metformin:

Metformin is a biguanide derivative. It is one of the oldest diabetes medications that has been used in Europe since 1957 and in the US since 1995 [79]. Despite being available for this duration, the mechanism of action of metformin is not fully understood. It is suggested that metformin exerts an effect on glycemic control via inhibiting hepatic gluconeogenesis; also, it enhances glucose utilization in the muscle, liver, and other peripheral tissues. Other suggested mechanisms involve the mitochondria and gastrointestinal tract [80]. Metformin is considered the first line medication for blood glucose lowering in most patients with T2DM by the ADA and EASD [13, 81]. Metformin has been shown in multiple trials to either help in achieving modest weight loss or preventing weight gain [82-84]. Metformin is well tolerated, with the most common side effect being gastrointestinal symptoms. Lactic acidosis is a rare but concerning side effect because of the high fatality rate [85, 86]. Metformin was associated with improving cardiovascular outcomes, compared with placebo and sulfonylureas, in multiple studies and by a recent meta-analysis [87-90]. The FDA has lessened the labeling for metformin to be contraindicated in eGFR <30 mL/min/1.73 m^2, while the FDA does not recommend starting metformin if the eGFR is between 30 and 45 mL/min/1.73 m^2[89]. Currently, the ADA recommends holding metformin on the day of surgery [12]. The Society for Ambulatory Anesthesia also concurs with the ADA regarding this subject [24]. However, the Association of Anesthetists of Great Britain and Ireland and Joint British Diabetes Societies, state that it is safe to continue metformin on the day of surgery, if it does not require contrast media and if the patient will be missing only one meal [15]. There is limited data about metformin perioperative use. A recent RCT demonstrated lower perioperative BG levels and no hypoglycemia or other serious adverse events in patients who were continued on metformin or sulfonylurea during surgery [91]. We agree with the ADA

recommendation to hold metformin on the day of surgery. After resuming the diet, metformin maybe restarted if the eGFR >30 mL/min/1.73 m^2. Careful consideration should be given in patients who received contrast media or had hypotension given the higher risk of kidney dysfunction**.**

Thiazolidinediones:

These agents have not been widely used given the increased risk of heart failure. Rosiglitazone and pioglitazone are the only thiazolidinediones approved by the FDA [92]. The FDA restricted prescribing rosiglitazone due to the increased risk of cardiovascular deaths and acute myocardial infarction. However, in 2013 these restrictions were removed based on the result of Rosiglitazone Evaluated for Cardiac Outcomes and Regulation of Glycaemia in Diabetes (RECORD) study. This study showed inconclusive results about the effect of rosiglitazone on myocardial infarction (MI) but did not show an increased risk of overall cardiovascular morbidity or mortality in the rosiglitazone group compared to the control group including metformin and sulfonylurea. The same study confirmed the increased risk for heart failure and fractures due to rosiglitazone [93, 94]. Pioglitazone shares the same risk in regards to heart failure, but does not seem to increase MI risk and, may even decrease the risk of MI [95-98]. Pioglitazone may have a resurgence in its use, given the increased interest in using the drug as treatment for nonalcoholic steatohepatitis, and newer studies which demonstrate a decrease in the risk of recurrent stroke [99, 100]. Given the concerns of heart failure and fluid retention, thiazolidinediones are generally avoided in the hospital setting. The ADA has not provided a specific recommendation for perioperative use, but the Association of Anesthetists of Great Britain and Ireland and Joint British Diabetes Societies list that thiazolidinediones are safe when taken on the morning of surgery, if no more than one missed meal occurs on that day [15]. Giving the lack of robust data, thiazolidinedione should be held on the day of surgery. They may be resumed when the patient is eating if there is no concern about volume status.

Non-sulfonylurea secretagogues/ meglitinides (repaglinide, nateglinide):

Meglitinides have a similar efficacy on glycemic control compared to sulfonylureas by increasing insulin secretion, but meglitinides work on a different receptor and are more expensive. Since they carry the risk of hypoglycemia, the same rules for sulfonylureas generally apply to meglitinides and recommend avoiding its perioperative use [12].

Alpha-glucosidase inhibitors (acarbose, miglitol):

Alpha-glucosidase inhibitors work by delaying the absorption of carbohydrates from the intestine. Acarbose, voglibose, and miglitol are the three alpha-glucosidase inhibitors available [101, 102]. They have a modest effect on glycemic control and may be used as monotherapy or as an addition to the other diabetes agents. However, compliance is limited due to the high rate of gastrointestinal side effects, especially flatulence, and only 16-20 % of new acarbose users were still taking it after one year of initiation [103, 104]. The gastrointestinal side effects limit the inpatient use. This class of medication should be held on the day of surgery and may be resumed once the patient is tolerating a diet.

Special Considerations:

Managing diabetes in perioperative settings is complex; it necessitates attention to multiple factors that impact surgical outcomes, such as glycemic control, duration and type of surgery, medication interaction, general health, and comorbidities [105]. In order the following points provide key considerations in the perioperative management of patients with diabetes:

Considerations related to glycemic control, type of surgery, general health, and comorbidities:

Patients' age [106] and health state [28] must be considered, as they influence the glycemic target; for example, in stable patients, the glycemic target is <7.8 mmol/L, while in critical patients, it is <10 mmol/L [28]. Moreover, nonemergency surgeries should be evaluated to cancel if a patient has a glucose reading above 22.2–27.8 mmol/L or metabolic abnormalities [28].

Considerations related to medications:

Preoperative management of diabetes medications is significant [32]. Most associations recommend stopping OADs and non-insulin injectables on the morning of surgery [14, 107]. The use of these medications must consider associated complications/benefits in Table 3 [27, 108, 109]. However, surgery may proceed under meticulous monitoring of glucose levels if the patient takes sulfonylurea on the day of surgery by mistake [108, 110].

Table 3. Considerations (complications/benefits) of OADs and non-insulin injectables

Antidiabetic agents	Considerations (complications/benefits)
SGLT-2 inhibitors	Increase DKA and volume depletion risk.
GLP-1 agonists	Result in GI side effects and delayed gastric emptying.
DPP-4 inhibitors	Reduce hypoglycemia risk. Good tolerability.
Sulfonylureas	In the fasting state can result in hypoglycemia.
Metformin	In the fasting state can result in hypoglycemia. Increase lactic acidosis risk. Renal function complications (such as decreased renal perfusion)
Thiazolidinediones	Risk of congestive heart failure, peripheral edema, and fluid retention.

OADs: oral antidiabetic drugs, SGLT2: sodium-glucose cotransporter, DKA: diabetic ketoacidosis. GLP-1: glucagon-like peptide, GI: gastrointestinal, DPP-4: dipeptidyl peptidase-4.

Major vs. Minor Surgery:

Major surgery for patients on OADs is like that for minor surgery. Firstly, the preoperative assessment must be performed, considering the hypoglycemic risk and special considerations [111]. Regarding perioperative management recommendations for OADs and non-insulin injectables, see Table 3.

Emergency Surgeries:

Numerous diabetes patients who require emergency surgery are metabolically unstable and may have DKA. Firstly, it is essential to preoperatively evaluate and correct fluid status, electrolyte, acid-base, and glycemic [112]. Besides, it should be:

Stop OADs and non-insulin injectable medications immediately [26].

Recurring monitoring of blood glucose [28].

Determine the last dose of sulfonylureas; it may influence glycemic control [113, 114].

Postpone the surgery, if feasible, to stabilize metabolic status [112].

Future research examining the optimum perioperative management of diabetes practices is warranted. This include identifying high risk population.

CONCLUSION

Perioperative management of diabetes and hyperglycemia is a challenging dilemma. Insulin is used as the primary antidiabetic agent to control perioperative hyperglycemia [12]. Oral antidiabetic drugs (OADs) and non-insulin injectables are reviewed for possible perioperative use.

Incretin-based therapies show promise in perioperative hyperglycemia management, with multiple randomized controlled trials demonstrating safety and efficacy of DDP-4 inhibitors alone or in combination with basal insulin for patients with mild to moderate hyperglycemia [64-67]. Additionally, in randomized controlled trials, GLP-1 receptor agonists are shown to provide effective and safe blood glucose control alone or in combination with basal insulin [52-56]. On day of surgery SGLT-2 inhibitor use should be avoided given the risk of DKA and the limited data involving inpatient and perioperative use [12, 43]. The oldest antidiabetic agents, metformin and sulfonylureas, should be held on the day of surgery and then they may be carefully reinitiated after the surgery. There should be further review of the guidelines regarding inpatient use of oral antidiabetic drugs (OADs) and non-insulin injectables [22], and that more studies are needed to explore these agents use in controlling perioperative hyperglycemia.

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REFERENCES

1. Zhou B, Rayner AW, Gregg EW, et al. Worldwide Trends in Diabetes Prevalence and Treatment from 1990 to 2022: A Pooled Analysis of 1108 Population-Representative Studies with 141 Million Participants. Lancet 2024; 404(10467): 2077-93.
2. Dhatariya K, Dhesi J, Selwyn D, et al. Guideline for Perioperative Care for People with Diabetes Mellitus Undergoing Elective and Emergency Surgery [Internet]. 2021 [accessed December 12, 2024]. Available from: https://cpoc.org.uk/sites/cpoc/files/documents/2021-05/CPOC-Diabetes-Guideline2021.pdf.
3. Rotruck LS, Suszan LL, Vigersky R, et al. Should Continuous Subcutaneous Insulin Infusion (Csii) Pumps Be Used during the Perioperative Period? Development of a Clinical Decision Algorithm. AANA J 2018; 86(3): 194-200.
4. Mraovic B, Hipszer BR, Epstein RH, et al. Preadmission Hyperglycemia Is an Independent Risk Factor for in-Hospital Symptomatic Pulmonary Embolism after Major Orthopedic Surgery. J Arthroplasty 2010; 25(1): 64-70.
5. King JT Jr, Goulet JL, Perkal MF, et al. Glycemic Control and Infections in Patients with Diabetes Undergoing Noncardiac Surgery. Ann Surg 2011; 253(1): 158-65.
6. Frisch A, Chandra P, Smiley D, et al. Prevalence and Clinical Outcome of Hyperglycemia in the Perioperative Period in Noncardiac Surgery. Diabetes Care 2010; 33(8): 1783-8.
7. Buehler L, Fayfman M, Alexopoulos AS, et al. The Impact of Hyperglycemia and Obesity on Hospitalization Costs and Clinical Outcome in General Surgery Patients. J Diabetes Comp 2015; 29(8): 1177-82.
8. Long CA, Fang ZB, Hu FY, et al. Poor Glycemic Control Is a Strong Predictor of Postoperative Morbidity and Mortality in Patients Undergoing Vascular Surgery. J Vasc Surg 2019; 69(4): 1219-26.
9. Underwood P, Askari R, Hurwitz S, et al. Preoperative A1c and Clinical Outcomes in Patients with Diabetes Undergoing Major Noncardiac Surgical Procedures. Diabetes Care 2014; 37(3): 611-6.
10. Yong PH, Weinberg L, Torkamani N, et al. The Presence of Diabetes and Higher Hba(1c) Are Independently Associated with Adverse Outcomes after Surgery. Diabetes Care 2018; 41(6): 1172-9.
11. Galway U, Chahar P, Schmidt MT, et al. Perioperative Challenges in Management of Diabetic Patients Undergoing Non-Cardiac Surgery. World J Diabetes 2021; 12(8): 1255-66.
12. American Diabetes Association. Diabetes Care in the Hospital: Standards of Medical Care in Diabetes. Diabetes Care 2020; 43(1): 193-202.
13. Davies MJ, D'Alessio DA, Fradkin J, et al. Management of Hyperglycemia in Type 2 Diabetes, 2018. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (Easd). Diabetes Care 2018; 41(12): 2669-701.
14. Umpierrez GE, Hellman R, Korytkowski MT, et al. Management of Hyperglycemia in Hospitalized Patients in Non-Critical Care Setting: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab 2012; 97(1): 16-38.
15. Barker P, Creasey PE, Dhatariya K, et al. Peri-Operative Management of the Surgical Patient with Diabetes 2015: Association of Anaesthetists of Great Britain and Ireland. Anaesthesia 2015; 70(12): 1427-40.
16. Cornelius BW. Patients with Type 2 Diabetes: Anesthetic Management in the Ambulatory Setting: Part 2: Pharmacology and Guidelines for Perioperative Management. Anesth Prog 2017; 64(1): 39-44.
17. Feingold KR. Oral and Injectable (Non-Insulin) Pharmacological Agents for the Treatment of Type 2 Diabetes. In: Feingold KR, Anawalt B, Blackman MR, et al. Endo 2000; 1(1):1-17.
18. Lorenzati B, Zucco C, Miglietta S, et al. Oral Hypoglycemic Drugs: Pathophysiological Basis of Their Mechanism of Actionoral Hypoglycemic Drugs: Pathophysiological Basis of Their Mechanism of Action. Pharmaceuticals 2010; 3(9): 3005-20.
19. Dahlén AD, Dashi G, Maslov I, et al. Trends in Antidiabetic Drug Discovery: Fda Approved Drugs, New Drugs in Clinical Trials and Global Sales. Front Pharmacol 2021; 12(1): 1-18.
20. Food and Drug Administration. Women and Diabetes - Diabetes Medicines [Internet]. 2019 [accessed December 12, 2024]. Available from: https://www.fda.gov/consumers/womens-health-topics/women-and-diabetes-diabetes-medicines.
21. World Health Organization. Model List of Essential Medicines [Internet]. 2023 [accessed December 12, 2024]. Available from: https://list.essentialmeds.org/?section=423&showRemoved=1.
22. Pasquel FJ, Fayfman M , Umpierrez GE. Debate on Insulin Vs Non-Insulin Use in the Hospital Setting-Is It Time to Revise the Guidelines for the Management of Inpatient Diabetes? Curr Diab Rep 2019; 19(9): 65-9.

23. ElSayed NA, Aleppo G, Aroda VR, et al. Diabetes Care in the Hospital: Standards of Care in Diabetes-2023. Diabetes Care 2023; 46(1): 267-78.
24. Joshi GP, Chung F, Vann MA, et al. Society for Ambulatory Anesthesia Consensus Statement on Perioperative Blood Glucose Management in Diabetic Patients Undergoing Ambulatory Surgery. Anesth Analg 2010; 111(6): 1378-87.
25. Grant B , Chowdhury TA. New Guidance on the Perioperative Management of Diabetes. Clin Med 2022; 22(1): 41-4.
26. Dogra P, Anastasopoulou C , Jialal I. Diabetic Perioperative Management. Statpear 2024; 1(1): 1-11.
27. Leung V , Ragbir-Toolsie K. Perioperative Management of Patients with Diabetes. Health Serv Insights 2017; 10(1): 1-17.
28. Sudhakaran S, Surani SR. Guidelines for Perioperative Management of the Diabetic Patient. Surg Res Pract 2015; 2015(1): 1-28.
29. Cruz P. Inpatient Hypoglycemia: The Challenge Remains. J Diabetes Sci Technol 2020; 14(3): 560-6.
30. Brutsaert E, Carey M , Zonszein J. The Clinical Impact of Inpatient Hypoglycemia. J Diabetes Comp 2014; 28(4): 565-72.
31. Xu Y, Wang L, He J, et al. Prevalence and Control of Diabetes in Chinese Adults. JAMA 2013; 310(9): 948-59.
32. Kirk JK , Gonzales CF. Preoperative Considerations for Patients with Diabetes. Expert Rev Endocrinol Metab 2023; 18(6): 503-12.
33. Garg R, Schuman B, Bader A, et al. Effect of Preoperative Diabetes Management on Glycemic Control and Clinical Outcomes after Elective Surgery. Ann Surg 2018; 267(5): 858-62.
34. Han H, Lai J, Yan C, et al. Development and Validation of a Prediction Model of Perioperative Hypoglycemia Risk in Patients with Type 2 Diabetes Undergoing Elective Surgery. BMC Surg 2022; 22(1): 167-70.
35. Neal B, Perkovic V, Mahaffey KW, et al. Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes. N Engl J Med 2017; 377(7): 644-57.
36. Perkovic V, Jardine MJ, Neal B, et al. Canagliflozin and Renal Outcomes in Type 2 Diabetes and Nephropathy. N Engl J Med 2019; 380(24): 2295-306.
37. Wiviott SD, Raz I, Bonaca MP, et al. Dapagliflozin and Cardiovascular Outcomes in Type 2 Diabetes. N Engl J Med 2019; 380(4): 347-57.
38. Zelniker TA, Wiviott SD, Raz I, et al. Sglt2 Inhibitors for Primary and Secondary Prevention of Cardiovascular and Renal Outcomes in Type 2 Diabetes: A Systematic Review and Meta-Analysis of Cardiovascular Outcome Trials. Lancet 2019; 393(10166): 31-9.
39. Zaccardi F, Webb DR, Htike ZZ, et al. Efficacy and Safety of Sodium-Glucose Co-Transporter-2 Inhibitors in Type 2 Diabetes Mellitus: Systematic Review and Network Meta-Analysis. Diabetes Obes Metab 2016; 18(8): 783-94.
40. Peters AL, Buschur EO, Buse JB, et al. Euglycemic Diabetic Ketoacidosis: A Potential Complication of Treatment with Sodium-Glucose Cotransporter 2 Inhibition. Diabetes Care 2015; 38(9): 1687-93.
41. Ueda P, Svanström H, Melbye M, et al. Sodium Glucose Cotransporter 2 Inhibitors and Risk of Serious Adverse Events: Nationwide Register Based Cohort Study. BMJ 2018; 363(1): 1-13.
42. Clar C, Gill JA, Court R, et al. Systematic Review of Sglt2 Receptor Inhibitors in Dual or Triple Therapy in Type 2 Diabetes. BMJ Open 2012; 2(5): 1-14.
43. Hamblin PS, Wong R, Ekinci EI, et al. Sglt2 Inhibitors Increase the Risk of Diabetic Ketoacidosis Developing in the Community and during Hospital Admission. J Clin Endocrinol Metab 2019; 104(8): 3077-87.
44. Kambara T, Shibata R, Osanai H, et al. Importance of Sodium-Glucose Cotransporter 2 Inhibitor Use in Diabetic Patients with Acute Heart Failure. Ther Adv Cardiovasc Dis 2019; 13(1):1- 17.
45. Madhok J , Vanneman MW. Sglt-2 Inhibitors: Proliferating Indications and Perioperative Pitfalls. J Cardiothorac Vasc Anesth 2022; 36(7): 1815-9.
46. Food and Drug Administration. Fda Revises Labels of Sglt2 Inhibitors for Diabetes to Include Warnings About Too Much Acid in the Blood and Serious Urinary Tract Infections [Internet]. 2022 [accessed December 12, 2024]. Available from: https://www.fda.gov/drugs/drug-safety-and-availability/fda-revises-labels-sglt2-inhibitors-diabetes-include-warnings-about-too-much-acid-blood-and-serious.
47. Marso SP, Daniels GH, Brown-Frandsen K, et al. Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes. N Engl J Med 2016; 375(4): 311-22.
48. Marso SP, Bain SC, Consoli A, et al. Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes. N Engl J Med 2016; 375(19): 1834-44.
49. Gerstein HC, Colhoun HM, Dagenais GR, et al. Dulaglutide and Cardiovascular Outcomes in Type 2 Diabetes (Rewind): A Double-Blind, Randomised Placebo-Controlled Trial. Lancet 2019; 394(10193): 121-130.
50. Besch G, Perrotti A, Mauny F, et al. Clinical Effectiveness of Intravenous Exenatide Infusion in Perioperative Glycemic Control after Coronary Artery Bypass Graft Surgery: A Phase Ii/Iii Randomized Trial. Anesthesiology 2017; 127(5): 775-87.
51. Fayfman M, Galindo RJ, Rubin DJ, et al. A Randomized Controlled Trial on the Safety and Efficacy of Exenatide Therapy for the Inpatient Management of General Medicine and Surgery Patients with Type 2 Diabetes. Diabetes Care 2019; 42(3): 450-6.
52. Polderman JAW, van Steen SCJ, Thiel B, et al. Peri-Operative Management of Patients with Type-2 Diabetes Mellitus Undergoing Non-Cardiac Surgery Using Liraglutide, Glucose-Insulin-Potassium Infusion or Intravenous Insulin Bolus Regimens: A Randomised Controlled Trial. Anaesthesia 2018; 73(3): 332-9.
53. Hulst AH, Visscher MJ, Godfried MB, et al. Liraglutide for Perioperative Management of Hyperglycaemia in Cardiac Surgery Patients: A Multicentre Randomized Superiority Trial. Diabetes Obes Metab 2020; 22(4): 557-65.
54. Fushimi N, Shibuya T, Yoshida Y, et al. Dulaglutide-Combined Basal Plus Correction Insulin Therapy Contributes to Ideal Glycemic Control in Non-Critical Hospitalized Patients. J Diabetes Investig 2020; 11(1): 125-31.
55. White WB, Cannon CP, Heller SR, et al. Alogliptin after Acute Coronary Syndrome in Patients with Type 2 Diabetes. N Engl J Med 2013; 369(14): 1327-35.
56. Scirica BM, Bhatt DL, Braunwald E, et al. Saxagliptin and Cardiovascular Outcomes in Patients with Type 2 Diabetes Mellitus. N Engl J Med 2013; 369(14): 1317-26.
57. Food and Drug Administation. FDA Drug Safety Communication: FDA Adds Warnings About Heart Failure Risk to Labels of Type 2 Diabetes Medicines Containing Saxagliptin and Alogliptin [Internet]. 2023 [accessed December 12, 2024]. Available from: https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-adds-warnings-about-heart-failure-risk-labels-type-2-diabetes.
58. Food and Drug Administration. Drug safety [Internet]. 2017 [accessed December 12, 2024]. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/201280s016lbl.pdf.

59. Rosenstock J, Perkovic V, Johansen OE, et al. Effect of Linagliptin Vs Placebo on Major Cardiovascular Events in Adults with Type 2 Diabetes and High Cardiovascular and Renal Risk: The Carmelina Randomized Clinical Trial. JAMA 2019; 321(1): 69-79.
60. Green JB, Bethel MA, Armstrong PW, et al. Effect of Sitagliptin on Cardiovascular Outcomes in Type 2 Diabetes. N Engl J Med 2015; 373(3): 232-42.
61. McMurray JJV, Ponikowski P, Bolli GB, et al. Effects of Vildagliptin on Ventricular Function in Patients with Type 2 Diabetes mellitus and Heart Failure: A Randomized Placebo-Controlled Trial. JACC Heart Fail 2018; 6(1): 8-17.
62. Singh AK , Singh R. Heart Failure Hospitalization with Dpp-4 Inhibitors: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Indian J Endocrinol Metab 2019; 23(1): 128-33.
63. Gantz I, Chen M, Suryawanshi S, et al. A Randomized, Placebo-Controlled Study of the Cardiovascular Safety of the Once-Weekly Dpp-4 Inhibitor Omarigliptin in Patients with Type 2 Diabetes Mellitus. Cardiovasc Diabetol 2017; 16(1): 1-12.
64. Umpierrez GE, Gianchandani R, Smiley D, et al. Safety and Efficacy of Sitagliptin Therapy for the Inpatient Management of General Medicine and Surgery Patients with Type 2 Diabetes: A Pilot, Randomized, Controlled Study. Diabetes Care 2013; 36(11): 3430-5.
65. Pasquel FJ, Gianchandani R, Rubin DJ, et al. Efficacy of Sitagliptin for the Hospital Management of General Medicine and Surgery Patients with Type 2 Diabetes (Sita-Hospital): A Multicentre, Prospective, Open-Label, Non-Inferiority Randomised Trial. Lancet Diabetes Endocrinol 2017; 5(2): 125-33.
66. Vellanki P, Rasouli N, Baldwin D, et al. Glycaemic Efficacy and Safety of Linagliptin Compared to a Basal-Bolus Insulin Regimen in Patients with Type 2 Diabetes Undergoing Non-Cardiac Surgery: A Multicentre Randomized Clinical Trial. Diabetes Obes Metab 2019; 21(4): 837-43.
67. Pérez-Belmonte LM, Osuna-Sánchez J, Millán-Gómez M, et al. Glycaemic Efficacy and Safety of Linagliptin for the Management of Non-Cardiac Surgery Patients with Type 2 Diabetes in a Real-World Setting: Lina-Surg Study. Ann Med 2019; 51(3): 252-61.
68. Tomlinson B, Patil NG, Fok M, et al. The Role of Sulfonylureas in the Treatment of Type 2 Diabetes. Expert Opin Pharmacother 2022; 23(3): 387-403.
69. Pearson ER, Flechtner I, Njølstad PR, et al. Switching from Insulin to Oral Sulfonylureas in Patients with Diabetes Due to Kir6.2 Mutations. N Engl J Med 2006; 355(5): 467-77.
70. Aguilar-Bryan L, Nichols CG, Wechsler SW, et al. Cloning of the Beta Cell High-Affinity Sulfonylurea Receptor: A Regulator of Insulin Secretion. Science 1995; 268(5209): 423-6.
71. Hirst JA, Farmer AJ, Dyar A, et al. Estimating the Effect of Sulfonylurea on Hba1c in Diabetes: A Systematic Review and Meta-Analysis. Diabetologia 2013; 56(5): 973-84.
72. Meinert CL, Knatterud GL, Prout TE, et al. A Study of the Effects of Hypoglycemic Agents on Vascular Complications in Patients with Adult-Onset Diabetes. Mortality Results. Diabetes 1970; 19(1):789-830.
73. Rosenstock J, Kahn SE, Johansen OE, et al. Effect of Linagliptin Vs Glimepiride on Major Adverse Cardiovascular Outcomes in Patients with Type 2 Diabetes: The Carolina Randomized Clinical Trial. JAMA 2019; 322(12): 1155-66.
74. Palmer SC, Mavridis D, Nicolucci A, et al. Comparison of Clinical Outcomes and Adverse Events Associated with Glucose-Lowering Drugs in Patients with Type 2 Diabetes: A Meta-Analysis. JAMA 2016; 316(3): 313-24.
75. Deusenberry CM, Coley KC, Korytkowski MT, et al. Hypoglycemia in Hospitalized Patients Treated with Sulfonylureas. Pharmacotherapy 2012; 32(7): 613-7.
76. Rajendran R, Kerry C , Rayman G. Temporal Patterns of Hypoglycaemia and Burden of Sulfonylurea-Related Hypoglycaemia in Uk Hospitals: A Retrospective Multicentre Audit of Hospitalised Patients with Diabetes. BMJ Open 2014; 4(7): 1-15.
77. Lansang MC , Umpierrez GE. Inpatient Hyperglycemia Management: A Practical Review for Primary Medical and Surgical Teams. Cleve Clin J Med 2016; 83(5): 34-43.
78. Montejano L, Vo L , McMorrow D. Transitions of Care for People with Type 2 Diabetes: Utilization of Antihyperglycemic Agents Pre- and Post-Hospitalization. Diabetes Ther 2016; 7(1): 91-103.
79. Salvatore T, Pafundi PC, Morgillo F, et al. Metformin: An Old Drug against Old Age and Associated Morbidities. Diabetes Res Clin Pract 2020; 160(1): 1-10.
80. Foretz M, Guigas B , Viollet B. Understanding the Glucoregulatory Mechanisms of Metformin in Type 2 Diabetes Mellitus. Nat Rev Endocrinol 2019; 15(10): 569-89.
81. American Diabetes Association. Addendum. Pharmacologic Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes-2020. Diabetes Care 2020;43(1):98-110.
82. United Kingdom Prospective Diabetes Study. Relative Efficacy of Randomly Allocated Diet, Sulphonylurea, Insulin, or Metformin in Patients with Newly Diagnosed Non-Insulin Dependent Diabetes Followed for Three Years. BMJ 1995; 310(6972): 83-8.
83. Hemmingsen B, Schroll JB, Wetterslev J, et al. Sulfonylurea Versus Metformin Monotherapy in Patients with Type 2 Diabetes: A Cochrane Systematic Review and Meta-Analysis of Randomized Clinical Trials and Trial Sequential Analysis. CMAJ Open 2014; 2(3): 162-75.
84. Umpierrez G, Tofé Povedano S, Pérez Manghi F, et al. Efficacy and Safety of Dulaglutide Monotherapy Versus Metformin in Type 2 Diabetes in a Randomized Controlled Trial (Award-3). Diabetes Care 2014; 37(8): 2168-76.
85. Lazarus B, Wu A, Shin JI, et al. Association of Metformin Use with Risk of Lactic Acidosis across the Range of Kidney Function: A Community-Based Cohort Study. JAMA Intern Med 2018; 178(7): 903-10.
86. Salpeter SR, Greyber E, Pasternak GA, et al. Risk of Fatal and Nonfatal Lactic Acidosis with Metformin Use in Type 2 Diabetes Mellitus. Cochrane Database Syst Rev 2010; 1(1): 1-20.
87. Hong J, Zhang Y, Lai S, et al. Effects of Metformin Versus Glipizide on Cardiovascular Outcomes in Patients with Type 2 Diabetes and Coronary Artery Disease. Diabetes Care 2013; 36(5): 1304-11.
88. Kooy A, de Jager J, Lehert P, et al. Long-Term Effects of Metformin on Metabolism and Microvascular and Macrovascular Disease in Patients with Type 2 Diabetes Mellitus. Arch Intern Med 2009; 169(6): 616-25.
89. Maruthur NM, Tseng E, Hutfless S, et al. Diabetes Medications as Monotherapy or Metformin-Based Combination Therapy for Type 2 Diabetes: A Systematic Review and Meta-Analysis. Ann Intern Med 2016; 164(11): 740-51.
90. Roumie CL, Chipman J, Min JY, et al. Association of Treatment with Metformin Vs Sulfonylurea with Major Adverse Cardiovascular Events among Patients with Diabetes and Reduced Kidney Function. JAMA 2019; 322(12): 1167-77.
91. Gasanova I, Meng J, Minhajuddin A, et al. Preoperative Continuation Versus Interruption of Oral Hypoglycemics in Type 2 Diabetic Patients Undergoing Ambulatory Surgery: A Randomized Controlled Trial. Anesth Analg 2018; 127(4): 54-6.

92. Eggleton JS , Jialal I. Thiazolidinediones. Statpear 2024; 1(1): 1-16.
93. Home PD, Pocock SJ, Beck-Nielsen H, et al. Rosiglitazone Evaluated for Cardiovascular Outcomes in Oral Agent Combination Therapy for Type 2 Diabetes (Record): A Multicentre, Randomised, Open-Label Trial. Lancet 2009; 373(9681): 2125-35.
94. Food and Drug Administration. FDA Drug Safety Communication: FDA Requires Removal of Some Prescribing and Dispensing Restrictions for Rosiglitazone-Containing Diabetes Medicines [Internet]. 2013 [accessed December 12, 2024]. Available from: https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-requires-removal-some-prescribing-and-dispensing-restrictions.
95. Lincoff AM, Wolski K, Nicholls SJ, et al. Pioglitazone and Risk of Cardiovascular Events in Patients with Type 2 Diabetes Mellitus: A Meta-Analysis of Randomized Trials. JAMA 2007; 298(10): 1180-8.
96. Liao HW, Saver JL, Wu YL, et al. Pioglitazone and Cardiovascular Outcomes in Patients with Insulin Resistance, Pre-Diabetes and Type 2 Diabetes: A Systematic Review and Meta-Analysis. BMJ Open 2017; 7(1): 1-13.
97. Lago RM, Singh PP , Nesto RW. Congestive Heart Failure and Cardiovascular Death in Patients with Prediabetes and Type 2 Diabetes Given Thiazolidinediones: A Meta-Analysis of Randomised Clinical Trials. Lancet 2007; 370(9593): 1129-36.
98. Singh S, Loke YK , Furberg CD. Thiazolidinediones and Heart Failure: A Teleo-Analysis. Diabetes Care 2007; 30(8): 2148-53.
99. Boettcher E, Csako G, Pucino F, et al. Meta-Analysis: Pioglitazone Improves Liver Histology and Fibrosis in Patients with Non-Alcoholic Steatohepatitis. Aliment Pharmacol Ther 2012; 35(1): 66-75.
100. Lee M, Saver JL, Liao HW, et al. Pioglitazone for Secondary Stroke Prevention: A Systematic Review and Meta-Analysis. Stroke 2017; 48(2): 388-93.
101. Sadikot S, Jothydev K, Zargar AH, et al. Clinical Practice Points for Diabetes Management during Ramadan Fast. Diabetes Metab Syndr 2017; 11(2): 811-9.
102. Samson SL, Garber AJ. Prevention of Type 2 Diabetes Mellitus: Potential of Pharmacological Agents. Best Pract Res Clin Endocrinol Metab 2016; 30(3): 357-71.
103. Catalan VS, Couture JA , LeLorier J. Predictors of Persistence of Use of the Novel Antidiabetic Agent Acarbose. Arch Intern Med 2001; 161(8): 1106-12.
104. Chiasson JL, Josse RG, Hunt JA, et al. The Efficacy of Acarbose in the Treatment of Patients with Non-Insulin-Dependent Diabetes Mellitus. A Multicenter Controlled Clinical Trial. Ann Intern Med 1994; 121(12): 928-35.
105. Zaidi SO, Khan Y, Razak BS, et al. Insight into the Perioperative Management of Type 2 Diabetes. Cureus 2020; 12(2): 1-16.
106. ElSayed NA, Aleppo G, Aroda VR, et al. 13. Older Adults: Standards of Care in Diabetes-2023. Diabetes Care 2023; 46(1): 216-29.
107. American Diabetes Association. Diabetes Care in the Hospital. Diabetes Care 2016; 39 (1): 99-104.
108. Williams G. Management of Non-Insulin-Dependent Diabetes Mellitus. Lancet 1994; 343(8889): 95-100.
109. Bailey CJ , Turner RC. Metformin. N Engl J Med 1996; 334(9): 574-9.
110. Groop LC. Sulfonylureas in Niddm. Diabetes Care 1992; 15(6): 737-54.
111. Society AD. Peri-Operative Diabetes Management Guidelines. Aust Diabetes Soc 2012; 30(1): 1-15.
112. Marks JB. Perioperative Management of Diabetes. Am Fam Physician 2003; 67(1): 93-100.
113. Kalimo H , Olsson Y. Effects of Severe Hypoglycemia on the Human Brain. Neuropathological Case Reports. Acta Neurol Scand 1980; 62(6): 345-56.
114. Rehman HU , Mohammed K. Perioperative Management of Diabetic Patients. Curr Surg 2003; 60(6): 607-11.