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Pharmacological Modulation of Glycemic Homeostasis in the Canine Diabetic Patients: Review of Perioperative Management of Insulin-Anesthesia Interaction. Part (1)

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Abstract— Type 2 Diabetes Mellitus (T2DM) is a prevalent chronic metabolic disorder in dogs, characterized by persistent hyperglycemia and insulin resistance. Diabetic dogs undergoing general anesthesia present unique perioperative challenges, as anesthesia itself can exacerbate insulin resistance and glycemic instability, thereby increasing the risk of life-threatening complications. This review summarizes the pathophysiology of diabetes in dogs, current antidiabetic treatment strategies, and the physiological alterations relevant to anesthetic management. Key perioperative considerations include preoperative stabilization of blood glucose, electrolytes, and hydration; appropriate insulin dosing protocols; and vigilant intraoperative monitoring of glycemia, hemodynamics, and electrolyte balance. Specific anesthetic agents and their interactions with glycemic control are discussed, with particular attention to the hyperglycemic effects of alpha-2 agonists and inhalant anesthetics. The review also provides a synthesis of recent epidemiological data on insulin-resistant canine diabetes from 2005 to 2025. Optimal perioperative glycemic control, guided by regular blood glucose monitoring and individualized anesthetic protocols, is essential for reducing morbidity and mortality in diabetic dogs undergoing surgery.

Keywords: Anesthesia; Diabetes type 2; Dogs; Insulin resistance; Perioperative management

INTRODUCTION

Type 2 Diabetes Mellitus (T2DM), also referred to as diabetes mellitus (DM), is a common chronic metabolic disorder in dogs characterized by persistent elevation of blood glucose concentration (hyperglycemia) and insulin resistance. T2DM occurs when blood glucose fails to enter cells due to the inability of insulin to activate its receptor effectively, producing an intracellular signal too weak to facilitate glucose uptake. This results in glucose accumulation in the bloodstream while cells remain energy-depleted. Over the long term, this metabolic disruption leads to tissue damage in the liver and kidneys. Additional complications include cataract formation (due to sorbitol accumulation in the ocular lens, frequently leading to sudden blindness), diabetic ketoacidosis, cardiac arrhythmias, peripheral neuropathy, and recurrent infections, particularly urinary tract infections (UTIs) (1).

Clinically, diabetic dogs commonly present with polydipsia, polyuria, weight loss despite polyphagia, weakness, and bilateral lens opacity. Medical intervention is critical for survival, with the primary goal of maintaining blood glucose within normal physiological limits to minimize chronic complications. Early diagnosis, adherence to veterinary instructions, and dietary management are key determinants of outcome. Diabetic dogs undergoing surgical procedures are at substantially elevated risk during general anesthesia (GA), necessitating a structured perioperative management approach (2).

Anesthesia plays an indispensable role in veterinary medicine, providing reversible loss of consciousness and analgesia to enable safe surgical and diagnostic procedures. Diabetic dogs require special consideration during anesthesia; maintaining optimal glycemic control in the perioperative period is essential to reduce the risk of mortality and postoperative complications. The current review highlights the importance of perioperative glycemic control in diabetic dogs and discusses antidiabetic agents used to achieve optimal glycemic management across the perioperative continuum.

Types of Diabetes

Type 1 Diabetes (T1DM): Insulin-dependent diabetes involving autoimmune destruction of pancreatic β-cells. This is the most common form in dogs and requires insulin replacement therapy.

Type 2 Diabetes (T2DM): Characterized by insufficient insulin secretion and/or altered insulin action. While dogs may develop this form, it often also requires insulin therapy. There is currently no reliable practical test to clearly differentiate T1DM from T2DM in dogs (2). A subset of these cases, particularly those involving hormonal-mediated insulin resistance without primary immune-mediated beta-cell destruction, may also be classified under the broader term "Secondary Diabetes / Hormonal Insulin Resistance" (2).

Type 3 Diabetes (Secondary Diabetes): Occurs secondary to underlying conditions, hormonal changes, or medications that reduce insulin secretion or impair endogenous insulin action. Examples include pancreatic neoplasia, pancreatitis, growth hormone excess, and hypercortisolism (1). In these hormonal forms of secondary diabetes, the underlying endocrine pathophysiology is distinct: cortisol exacerbates hyperglycemia primarily through stimulation of hepatic gluconeogenesis and peripheral insulin antagonism, while growth hormone (GH) induces profound insulin resistance by inhibiting peripheral glucose uptake and promoting lipolysis. Persistent hormonal excess from these conditions leads to transient or permanent secondary diabetes, which is reversible upon resolution of the primary hormonal disorder—distinguishing it from idiopathic T2DM, which is persistent and requires ongoing medical management (3, 4)

Factors implicated in T2DM

Causative factors implicated in T2DM include pathological changes in the exocrine pancreas, progesterone-controlled growth hormone overproduction, and hypercortisolism (2). Glucotoxicity is a well-documented phenomenon in T2DM that further impairs glycemic regulation (3). Environmental factors such as obesity, physical inactivity, and overfeeding are recognized risk factors (4). Common clinical signs include unusual thirst, frequent urination, weight loss despite preserved appetite, weakness or lethargy, and bilateral lens opacity. Diagnosis is based on persistent hyperglycemia and glucosuria, confirmed with the clinical presentation and, in some cases, elevated serum fructosamine concentrations (4).

A chronological synthesis of recent epidemiological data, disease prevalence, and key pharmacological insights regarding insulin-resistant canine diabetes from 2005 to 2025 is systematically summarized in Table (1).

Type 2 DM Treatment

The management of T2DM in dogs includes three principal therapeutic strategies: (1) Insulin Replacement Therapy, (2) Oral Antidiabetic Agents, and (3) Dietary Management.

The major groups of oral hypoglycemic agents used in veterinary practice worldwide are sulfonylureas, biguanides, and thiazolidinediones (5). However, it should be noted that oral hypoglycemic agents are rarely effective or routinely indicated in dogs, as most diabetic dogs lack sufficient functional pancreatic beta-cell mass to respond to these agents. Their use is largely limited to specific experimental or rare clinical scenarios, and insulin therapy remains the cornerstone of canine diabetic management. Critically, any oral antidiabetic agents must be discontinued prior to general anesthesia and replaced with injectable insulin to minimize the risk of unpredictable hypoglycemia during the perioperative period (2).

For insulin therapy, lente or neutral protamine Hagedorn (NPH) insulin are the initial insulin of choice in dogs, with a starting dosage of 0.25–0.5 U/kg subcutaneously every 12 hours. Most dogs require twice-daily insulin injections, and two meals of equal caloric content are provided daily, with one meal served immediately before each insulin administration. For dogs with poorly controlled glycemia on lente or NPH insulin, basal insulin (detemir) at 0.1 U/kg SC every 12 hours should be considered, with glycemic reassessment one week after initiation due to detemir's considerable potency. The detailed pharmacological profiles, onset, peak, and duration of action of these commonly utilized canine insulin formulations are summarized **in Table 2, Part A**. Dietary management should emphasize complex carbohydrates and high-fiber content; high simple-sugar diets should be avoided (4).

Physiological Changes in Diabetic Dogs Relevant to Anesthesia

Anesthesia induces insulin resistance, which may contribute to elevated blood glucose concentrations and adverse postoperative outcomes in critically ill patients, while further impairing glycemic control in diabetic surgical patients (6). Recognition of the effects of hyperglycemia on acid-base status, hydration, and immunity is fundamental to the safe anesthetic management of diabetic dogs. Preoperative stabilization of blood glucose levels, hydration, and electrolyte disturbances are essential for reducing perioperative morbidity and mortality. Perioperative blood glucose monitoring serves as a guide for the administration of dextrose and supplemental insulin (7).

In canine inhalation-based anesthesia, volatile agents—notably isoflurane and sevoflurane—have been shown to cause severe hepatic insulin resistance. Therapeutic strategies targeting the maintenance of hepatic insulin sensitivity may improve surgical outcomes in both healthy and diabetic patients (6). Based on published veterinary studies, the most common anesthesia-related signs in diabetic dogs undergoing phacoemulsification include bradycardia and hypotension (8).

A clinical study by Pacheco et al. (2018) demonstrated that anesthetic complications occur at a high rate in diabetic dogs undergoing ophthalmic surgery. Hypotension was the only complication occurring after anesthetic induction, affecting approximately 80% of diabetic dogs studied (9). Additionally, hyperkalemia has been documented as a serious anesthetic and intraoperative complication in diabetic dogs undergoing solid tumor resection. Routine potassium concentration monitoring and ECG surveillance are recommended during such procedures (10).

Perioperative Management of Antidiabetic Agents

For diabetic patients, it is preferable to schedule procedures early in the day to facilitate a rapid return to normal feeding patterns, timely resumption of the insulin regimen, and close postoperative monitoring. The following perioperative management principles are important:

1. Prior to anesthesia, diabetic patients must be evaluated for stability of hydration, acid-base status, electrolyte balance, and blood glucose levels.

2. There is no universally accepted preoperative insulin protocol; however, administering one-quarter to one-half of the patient's usual insulin dose has demonstrated superiority over complete insulin withdrawal or full dose administration. Blood glucose should be monitored every 30–60 minutes to guide supplemental insulin and dextrose therapy.

3. Anesthetic, analgesic, and sedative agents are not absolutely contraindicated in diabetic dogs; however, caution is warranted with alpha-2 agonists, as they may transiently increase blood glucose concentrations. Protocol selection should be tailored to the patient's overall health status, anticipated degree of pain, and expected procedure duration (2). To ensure patient safety, a structured, step-by-step perioperative glycemic monitoring protocol and corresponding action plans across different surgical phases are provided in **Table 2, Part B**.

Table 1. Incidence and treatment of insulin-resistant canine diabetes (2005–2025) (11-18)

Reference	Year	Study Type / Region	Incidence / Prevalence	Predominant Insulin Therapy	Key Pharmacological Insight
Abhijith *et al*. (11)	2025	Review / Pathogenesis Framework	N/A (Focus on Mechanism)	Insulin Replacement (Primary)	Distinguishes between autoimmune β-cell destruction and secondary resistance (hormonal/pancreatitis) to target therapy.
Brito-Casillas *et al*.(12)	2021	Cohort (Spain)	0.37% (Incidence)	Porcine Lente	Transition from insulin resistance to beta-cell exhaustion is faster in sedentary dogs.
Denyer *et al*. (13)	2025	Registry (UK)	0.26%–0.34%	Caninsulin (Lente)	High prevalence in specific breeds (e.g., Samoyeds) suggests genetic insulin receptor sensitivity.
O'Neill *et al*. (14)	2016	Primary Care (UK)	0.33%	Porcine Lente	Neutering status and age significantly increase the hazard ratio for developing DM.
Mataragka (15)	2025	Mini-review / Global (Multi-taxa)	1.6% (Feline Diabetes)	N/A (Review focus)	Diabetes prevalence rose from 0.4% to 1.6% (2005-2020), driven by the 50-60% obesity rate in pets.
Catchpole *et al*. (16)	2008	Genetic Association Study (UK)	N/A (Genetic focus)	Exogenous Insulin	Identified DLA-DQA1*001 as a common susceptibility allele for canine DM and immune-mediated endocrinopathies.
O'Kell *et al*. (17)	2017	Comparative Pathogenesis Review	Increasing Prevalence (General)	Lifelong Exogenous Insulin	Canine islet architecture and MHC gene associations parallel human T1D, highlighting immune-mediated β-cell loss.
Catchpole *et al*. (18)	2005	Landmark Review	0.32%	NPH / Lente	Established the autoimmune vs. secondary resistance framework for canine diabetes.

Table 2. Comparative Profiles of Canine Insulins and Step-by-Step Perioperative Glycemic Monitoring Protocol Part A: Pharmacological Profiles of Commonly Used Insulins in Dogs

Insulin Type	Formulation Category	Onset of Action	Peak Effect	Duration of Action	Clinical Application & Perioperative Consideration
Porcine Lente *(e.g., Caninsulin / Vetsulin)*	Intermediate-acting (Amorphous & Crystalline zinc suspension)	1 – 2 hours	4 – 8 hours	8 – 14 hours	First-line choice in canine diabetes. Matches well with twice-daily feeding regimes.
NPH *(Neutral Protamine Hagedorn)*	Intermediate-acting (Isophane insulin suspension)	1 – 3 hours	4 – 10 hours	8 – 14 hours	Commonly used alternative. Highly predictable but may have a slightly shorter duration in some individual dogs.
Detemir *(Levemir)*	Long-acting (Basal analogue, acylated insulin)	1 – 2 hours	6 – 12 hours	16 – 24 hours	Highly potent in dogs (requires lower doses, e.g., 0.1 U/kg). Reserved for cases with poor glycemic control on Lente/NPH.
Regular Insulin *(Crystalline)*	Short-acting (Soluble insulin)	10 – 30 mins	1 – 4 hours	3 – 7 hours	Strictly perioperative/emergency use (IV or IM) to correct acute intraoperative hyperglycemia or diabetic ketoacidosis (DKA).

Part B: Step-by-Step Perioperative Glycemic Monitoring Protocol

Perioperative Phase	Monitoring Frequency	Blood Glucose (BG) Target Range	Pharmacological Interventions & Action Plan
1. Pre-induction *(Morning of Surgery)*	Baseline measurement (immediately before any intervention)	150 – 250 mg/dL (8.3 – 13.8 mmol/L)	• **Withhold food.** Administer **1/4 to 1/2** of the normal morning insulin dose. • If BG < 150 mg/dL, start a 5% Dextrose constant rate infusion (CRI).

2. Induction & Maintenance *(Intraoperative Phase)*	**Every 30 – 60 minutes** throughout general anesthesia	150 – 250 mg/dL (8.3 – 13.8 mmol/L)	• **If Hypoglycemia (< 100 mg/dL):** Administer a bolus of 0.5 g/kg of 20%–50% Dextrose IV slowly, then maintain on 5% Dextrose CRI. • **If Hyperglycemia (> 300 mg/dL):** Consider careful administration of Regular Insulin (0.05–0.1 U/kg IM or IV). • *Note:* Anticipate transient spikes if Alpha-2 agonists or volatile anesthetics (Isoflurane) are used.
3. Early Recovery *(Immediate Post-extubation)*	**Every 1 – 2 hours** until the dog is sternal and fully conscious	150 – 250 mg/dL (8.3 – 13.8 mmol/L)	• Continue BG monitoring to guard against delayed anesthetic-induced insulin resistance shifts. • Monitor electrolytes (especially **Potassium**, due to risk of intraoperative hyperkalemia) and hydration status.
4. Late Recovery *(Postoperative to Discharge)*	**Every 4 hours** until the patient resumes normal voluntary feeding	100 – 250 mg/dL (5.5 – 13.8 mmol/L)	• Offer **1/2 of the normal daily food meal** as soon as the dog can safely swallow. • Give the remaining portion of the morning insulin dose based on food intake. • Return to the routine home insulin/feeding schedule the following day.

CONCLUSION

Anesthesia in diabetic dogs presents significant perioperative risks, with several potentially life-threatening pathophysiological alterations requiring active management. Optimal glycemic control must be achieved and maintained before, during, and after surgery, including throughout the induction phase. Appropriate insulin dosing, accurate monitoring of vital signs, and maintenance of electrolyte balance are critical components of the perioperative protocol for diabetic dogs undergoing surgical procedures. Standardized protocols, tailored to the individual patient's metabolic status and comorbidities, remain the cornerstone of safe anesthetic management in this high-risk population.

Conflict of Interest

The authors declare no conflict of interest.

Ethics

This is a review article and did not involve direct animal experimentation. All referenced animal studies were conducted in accordance with applicable ethical guidelines.

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