Seizure-like reactions induced by propofol in dogs: Prevalence and clinical insight
Reações semelhantes a convulsões induzidas por propofol em cães: Prevalência e visão clínica

ABSTRACT

This study investigated seizure-like reactions induced by propofol in dogs at the Veterinary Hospital of UNIUBE, highlighting their rare occurrence and limited documentation in veterinary literature. Over three years, only one case was reported among dogs receiving propofol for sedation or anesthesia, with a prevalence of 0.02%. A single case was discussed: a three-year-old female dog experienced the reaction during anesthetic induction for elective ovariohysterectomy. The dog was successfully treated with ketamine, allowing the surgery to proceed without complications. Despite their rarity, seizure-like reactions can occur in healthy, young dogs, and ketamine proved effective in halting the crisis in this case.

Keywords: Anesthesia; Anesthetic complication; Epileptic seizure; Ketamine; Small animals
RESUMO
Este estudo investigou reações semelhantes a convulsões induzidas por propofol em cães no Hospital Veterinário da UNIUBE, destacando sua rara ocorrência e a escassa documentação na literatura veterinária. Ao longo de três anos, apenas um caso foi relatado entre os cães que receberam propofol para sedação ou anestesia, com uma prevalência de 0,02%. Um único caso foi discutido: uma cadela de três anos apresentou a reação durante a indução anestésica para ovariohisterectomia eletiva. O animal foi tratado com sucesso com cetamina, permitindo que a cirurgia fosse realizada sem complicações. Apesar de sua raridade, reações semelhantes a convulsões podem ocorrer em cães saudáveis e jovens, e a cetamina mostrou-se eficaz em interromper a crise neste caso.

Palavras-chave: Anestesia; Complicação anestésica; Crise epilética; Cetamina; Pequenos animais.

INTRODUCTION

Propofol is a general anesthetic from the non-barbiturate class (Kay & Rolly, 1977). Currently, it is used in veterinary medicine due to its rapid onset of action, as its metabolism occurs not only in the liver but also in the plasma, kidneys, lungs, and intestines, besides having rapid clearance (Cassidy & Houston, 1984; Cattai et al., 2015). The most commonly observed side effects are apnea and reduced cardiac output (Voss et al., 2015). Central nervous system excitation is rarely seen and is observed as spasms, myoclonus, or seizure-like changes (Seizure-Like) (Ilsander & Vinge, 2000). The Seizure-Like phenomenon is widely reported in human medicine (Meyer et al., 2006; Garg & Dehran, 2009; Cokay-Abut et al., 2018), but still poorly discussed and reported in veterinary literature. Since the 1980s, there have been reports of seizure-like reactions with the use of propofol, with descriptions that the isolated use of this drug resulted in involuntary movements, opisthotonus, hyperextension of limbs, muscle tremors, and mandibular movements in 8% of anesthetized animals (López et al., 1994). The occurrence of Seizure-Like during anesthesia maintenance is uncommon and generally occurs when there are changes in the level of consciousness or variations in propofol plasma concentration, with most reactions observed during induction and recovery from anesthesia (Walder et al., 2002). In this study, we aimed to evaluate the incidence of propofol-induced seizure-like reactions in canine patients seen at the Veterinary Hospital of UNIUBE over the past three years, as well as to study case details. This topic stands out for its low incidence and for being poorly understood and rarely observed in veterinary practice.
MATERIALS AND METHODS

Data were collected from the integrated management system of the Veterinary Hospital of UNIUBE, known as VMS - Veterinary Management System®. Patient records were selected for dogs that received propofol for sedation or anesthesia between January 2021 and February 2024. The frequency of propofol-induced seizure-like reactions was calculated relative to the total number of cases in which propofol was used as a sedation or general anesthesia agent, either as a single agent or in combination with other drugs as part of a multimodal anesthetic protocol.

Comprehensive data were collected, including information on the animal's breed, age, body mass, medical history, clinical and laboratory tests performed, treatments administered, and outcomes obtained in the affected patient. These data were used to better understand the clinical picture and guide treatment.

RESULTS

During the study period, a total of 5,838 dogs received propofol as a sedation or anesthesia agent. The prevalence of propofol-induced seizure-like reactions was 0.02% (1/5,838).

The patient who presented propofol-induced seizure-like reactions was a three-year-old, mixed-breed female dog, weighing 11 kg. She was anesthetized for an elective ovariohysterectomy. According to the owner, the dog did not have access to the street, was fed with commercial food, and was up to date on vaccinations. Additionally, the dog was normodipsic, normouric, normorexic, and had normal feces.

On general physical examination, the dog was agitated. According to Rigueira et al. (2023), her body condition score was 3, with easily palpable ribs and evident abdominal tuck. Her mucous membranes were moist and pink, capillary refill time was two seconds, respiratory rate was 29 breaths per minute, heart rate was 134 beats per minute, and rectal temperature was 38.6°C. Lymph nodes and behavioral and mental status were normal. Preoperative laboratory tests, including hemogram (Red blood cells - 6.01mm3, Hemoglobin - 12%, Hematocrit - 39%, Platelets - 350,000mm3, Total Leukocytes - 8,000mm3) and biochemical (ALT - 80U/L, Creatinine - 0.67mg/dL), were all within normal limits for the species.
According to the American Society of Anesthesiology (ASA), the anesthetic risk was classified as ASA I (healthy patient). In the preoperative period, vital parameters were measured and recorded (Graph 1). As pre-anesthetic medication, ketamine 2 mg/kg (Ketamin®, Syntec, Santana de Parnaíba, SP, Brazil), midazolam 0.15 mg/kg (Dormonid®, Hipolabor, Sabará, MG, Brazil), morphine 0.3 mg/kg (Dimorf®, Cristália, Itapira, SP, Brazil), and dexmedetomidine 1 µg/kg (Dexdomitor®, Zoetis, Campinas, SP, Brazil) were administered intramuscularly (IM). After 20 minutes, the dog was calmer and in lateral recumbency. Before induction, fluid therapy with Ringer's lactate at 2.5mL/kg/h (Eurofarma, Itapevi, SP, Brazil) was initiated, and vital parameters were reassessed and recorded.

For anesthetic induction, fentanyl 5 µg/kg (Fentanest®, Cristália, Itapira, SP, Brazil), diluted in water for injection, was administered intravenously (IV), with half the dose contained in the syringe. During the injection of propofol (Propovan®, Cristália, Itapira, SP, Brazil) at 1.5 mL (15 mg), the dog exhibited a seizure-like reaction, characterized by episodes of myoclonus, rigid extension of the thoracic limbs with paddling, opisthotonus, dystonia, and mandibular movements. The duration of the seizure-like phenomenon was 5 minutes, and it was interrupted with the administration of ketamine 2 mg/kg/IV (Ketamin®, Syntec, Santana de Parnaíba, SP, Brazil). Subsequently, a patent airway was confirmed. For anesthesia maintenance, isoflurane (Isoforine®, Cristália, Itapira, SP, Brazil) at a minimum alveolar concentration of 0.5% was used, along with 100% oxygen, in a valvular circle system.

The surgery was performed conventionally, using the three-clamp technique, as employed by Quadros et al. (2023). Before clamping the ovarian pedicles, lidocaine (Xylestesin® 2%, Cristália, Itapira, SP, Brazil) was instilled at a dose of 2 mg/kg into the pedicles. Vital parameters were monitored during the preoperative, intraoperative, and postoperative periods using a multiparameter monitor SDA12B (SDAMED, Paulínia, SP, Brazil), which includes pulse oximetry (SpO2), electrocardiogram, and rectal thermometer. Systolic blood pressure was measured with a portable vascular Doppler DL330 (Delta Life, São José dos Campos, SP, Brazil) and a size 3 cuff. There were no complications, and at the end of the procedure, the patient was stable, with parameters within normal limits and rapidly recovering from anesthesia. Morphine 0.10 mg/kg/IM (Dimorf®, Cristália, Itapira, SP, Brazil) was administered as rescue analgesia. After the procedure, the patient was clinically evaluated, and her parameters were monitored in the postoperative period. As she did not present abdominal pain, her posture, ear position,
and facial expression were normal, and her vital parameters remained stable, she was discharged from the hospital.

**Graph 1.** Profile of vital parameters assessed in the preoperative, intraoperative, and postoperative periods of a 3-year-old, mixed-breed female dog undergoing ovariohysterectomy, who presented a Seizure-Like episode after anesthetic induction with propofol. The parameters were measured and recorded every 5 minutes during anesthesia and anesthetic recovery.

**DISCUSSION**

According to some studies, although considered rare, the seizure-like reaction is well-documented in human medicine. It is characterized by involuntary and arrhythmic contractions of the thoracic limbs after the administration of propofol (Schramm & Orser, 2002; Cosetino & Torres, 2012). In veterinary medicine, however, there is a scarcity of works on this pathology. This study identified only one case during three years of evaluation of canine patients sedated or anesthetized with propofol, showing a low incidence rate (0.02%) and associated with healthy and young patients.

In the reported case, the patient did not present any noteworthy alterations in the anamnesis, with no evidence or indication of neurological alteration that could trigger some type of crisis. It is described by Borgeat (1997) that this seizure-like phenomenon
is mostly not of epileptic origin, but rather at the muscular level, manifesting as rigid
extension of the thoracic limbs, myoclonus, opisthotonos, dystonia, and involuntary
mandibular movements. The patient in question presented only one crisis, as in other
existing reports in the literature (Walder et al., 2002; Cokay-Abut et al., 2018; Rocha et
al., 2020;), with an approximate duration of five minutes.

Although classified as ASA I, meaning a healthy animal without organic
alterations (Schwam et al., 1982), the described patient manifested a seizure-like
phenomenon after propofol administration during induction. This uncommon reaction can
occur as a result of the antagonism of glycine receptors located in subcortical structures
(Cokay-Abut et al., 2018).

Glycine, a non-essential amino acid, plays important roles in the central nervous
system. According to Johnson & Ascher (1987), it acts as a co-agonist in cerebral
excitatory transmission, activating N-methyl-D-aspartate (NMDA) receptors, and as a
neurotransmitter in inhibitory synapses of the brainstem and spinal cord (Siegel et al.,
1989). Borgeat (1997) describes propofol as a drug that can act as an antagonist or agonist
of glycine, depending on the dose. At higher doses, such as during anesthetic
maintenance, it exerts an agonist effect on glycine, while at lower doses, such as during
induction and anesthetic recovery, it exerts an antagonist effect. In the case in question,
propofol was used only in anesthetic induction at a relatively low and single dose, which
may have contributed to the occurrence of the uncommon excitatory reaction.

The antagonism between propofol and glycine can lead to the conversion of
glycine into glutamate, which in large quantities can cause neuroexcitatory symptoms
(Hickey et al., 2005). This antagonism can occur due to changes in the animal's
consciousness state, with cerebral excitement acting as a promoter of these phenomena,
or in response to instability in propofol plasma concentration, with changes in drug levels
in brain tissue and blood (Walder et al., 2002). This instability in plasma concentration
may have been a cause of the phenomenon observed in the described case, where propofol
was administered as a bolus in a small quantity, without maintaining a constant
pharmacological stability that would be achieved through continuous infusion.

Other theories suggest that the seizure-like phenomenon may occur due to
stimulation of subcortical dopaminergic areas (Borgeat, 1997) or to the toxicity of some
metabolite derived from the drug itself (Van Den Berg et al., 2001). Patel et al. (2004)
also suggest that propofol may interact with the endocannabinoid system, resulting in this
adverse reaction.
Cattai et al. (2015) described treatment methods for the seizure-like phenomenon, using isoflurane associated with neuromuscular blockers such as atracurium or rocuronium, in addition to intravenous lidocaine. The treatments were able to interrupt the signs of the phenomenon, but there was a need for additional doses of rocuronium, and lidocaine presented fewer hemodynamic effects.

On the other hand, Davies (1991) cited the use of Diazepam as a treatment method, but it did not completely cease the seizure-like phenomenon in all cases. This differs from the treatment used in the present study, where none of the above-described medications were used to terminate the alteration.

In the described case, in order to interrupt the seizure-like reaction, ketamine, an NMDA receptor antagonist known for its potential in preventing seizures (Huntsman et al., 2010), was administered. NMDA receptors are linked to calcium channels and late excitatory postsynaptic potentials, blocking the ion channel and leading to muscle relaxation (Valadão, 2019).

After intravenous administration of ketamine, the animal presented muscle relaxation, without signs of myoclonus, rigid extension of the thoracic limbs, or paddling movements, demonstrating the efficacy of ketamine in combating this adverse reaction caused by propofol.

Based on the observed case, it is possible to infer that the seizure-like reaction can be confused with other syndromes, such as the second stage of Guedel's plan, where the animal also presents excitement and involuntary movements, but not restricted only to the thoracic limbs (Guedel, 1951). However, further studies are needed on this alteration, as it may be impactful for professionals who are not familiar with the phenomenon.

CONCLUSION

In conclusion, seizure-like reactions are a reality in veterinary surgical centers, despite their low incidence. The administration of ketamine is an effective option to interrupt the crisis, allowing for the safe continuation of the procedure. However, further studies on this condition are needed, as it can be confused with other syndromes and impact the appropriate treatment if not correctly recognized.
ACKNOWLEDGMENTS

We would like to express our gratitude to the Universidade de Uberaba (UNIUBE), FAPEMIG, and CAPES for funding the study, granting scholarships, and providing the infrastructure that made our research project possible. The financial support and facilities played a significant role in the success of our work. We sincerely appreciate this essential partnership for advancing knowledge.

REFERENCES


