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ANESTHESIA WITH PROPOFOL IN DOGS – LITERATURE REVIEW

Laura Ver Goltz

Department of Morphology – Universidade Federal do Rio Grande do Sul Porto Alegre - RS http://lattes.cnpq.br/3639378385545865

Lara Lanius

Veterinary Course– Universidade Federal do Rio Grande do Sul Porto Alegre – RS http://lattes.cnpq.br/2532931644043383

Camile Vitória Silva Barreto

Veterinary Course– Universidade Federal do Rio Grande do Sul Porto Alegre - RS http://lattes.cnpq.br/5146863829043025



All content in this magazine is licensed under a Creative Commons Attribution License. Attribution-Non-Commercial-Non-Derivatives 4.0 International (CC BY-NC-ND 4.0). Abstract: Propofol (2,6-diisopropylphenol) a non-barbiturate, hypnotic general is anesthetic that is very practical to use. As an advantage, propofol is a suitable medication for short-term procedures and for anesthetic induction and maintenance. It is possible to administer this drug in repeated doses or continuous infusion, as the residual effect of the drug is minimal. Animals with liver and kidney dysfunction and pregnant females undergoing cesarean section can be safely anesthetized. This medication is highly indicated to replace inhalational anesthesia, as there is no need to purchase equipment and reduces environmental pollution in the anesthetic room. As a disadvantage, propofol is a high-cost drug, intravenous administration is mandatory, it can cause hypotension and is a respiratory depressant, therefore animals with heart disease and hypotension must be carefully anesthetized with this medication, in addition, it can cause pain during administration. injection, myoclonic contraction and muscle movement. Due to these factors and because it is a non-analgesic agent, the use of pre-anesthetic medication such as tranquilizers, sedatives and opioids can minimize some adverse effects. In this work, the objective was to carry out a bibliographic review through books, articles from scientific journals, dissertations and theses on the use of propofol anesthetic in dogs.

Keywords:Anesthetic.Canine.Diisopropylphenol. drug.

INTRODUCTION

Propofol (2,6-diisopropylphenol) is a nonbarbiturate general anesthetic (FANTONI; CORTOPASSI, 2002; MASSONE, 2008). This medication is used on a large scale due to its practicality (FANTONI; CORTOPASSI, 2002) and is used in situations in which the administration of inhalation anesthesia is difficult (FANTONI et al., 2006), not requiring

investment in equipment for inhalation anesthesia and avoiding environmental pollution by anesthetic gases (OLIVEIRA et al., 2007). Propofol is indicated for anesthesia induction and maintenance (FANTONI; CORTOPASSI, 2002), in a single dose for shortterm procedures and for general anesthesia induction, allowing intubation and use of inhalational anesthesia (PADDLEFORD, 2001; FANTONI; CORTOPASSI, 2002). Anesthetic induction with propofol aims to minimize depression of the cardiovascular and respiratory systems, it is safe from the renal and hepatic point of view and is an ultrashort-acting hypnotic (at a dose of 4 to 6 mg/ kg) (FANTONI; CORTOPASSI, 2002).

Propofol appears as a milky white emulsion (FANTONI; CORTOPASSI, 2002; FANTONI et al., 2006; MASSONE, 2008) and does not require dilution. It is a 1% aqueous emulsion, containing 10% soybean oil, 2.25% glycerol and 1.2% purified egg phospholipid, stable at room temperature (PADDLEFORD, 2001; FANTONI et al., 2006).

Propofol's mechanism of action potentiates GABA action on GABAA receptors, acts by inducing chlorine current in the absence of GABA, and exerts a pro-GABAergic action, inhibiting the firing rate of dopaminergic and non-dopaminergic neurons (FANTONI et al., 2006). The rapid onset of propofol action is due to rapid distribution and immediate elevation of its concentration in the central nervous system (PADDLEFORD, 2001).

The cost of the medication is a little high, but it has better anesthetic quality than barbiturates (PADDLEFORD, 2001; FANTONI; CORTOPASSI, 2002). In addition, propofol can be used in high-risk patients with a safety margin higher than other inducing agents, and can be safely used in healthy, elderly patients (FANTONI; CORTOPASSI, 2002), nephropathy and liver disease (MASSONE, 2008), due to propofol having low nephrotoxicity and hepatotoxicity (FANTONI; CORTOPASSI, 2002), fact evidenced by the absence of alteration in the hepatic function (alanine aminotransferase – ALT; aspartate aminotransferase – AST) and renal (urea and creatinine) (FANTONI et al., 2006).For Fantoni et al. (2006) the use of propofol must be avoided in patients with compromised cardiovascular function, geriatric and hypovoemic patients.

Propofol is obligatorily used intravenously (IV) and can be used in continuous injection, through an infusion pump or equipment, in repeated doses (bolus) or in target-controlled infusion (PADDLEFORD, 2001; FANTONI et al., 2006; OLIVEIRA et al., 2007). The choice of the appropriate anesthetic protocol varies according to the general state of the patient (FANTONI; CORTOPASSI, 2002). The amount of medication needed depends on the pre-anesthetic medication (PAM) used and the type of surgery to be performed (PADDLEFORD, 2001). The dose for dogs indicated by Massone (2008) and Fantoni and Cortopassi (2002) is 5 mg/kg. The dose can vary from 2 to 8 mg/kg (IV), according to the MPA employed, as the potentiation synergism may be lower when using a tranquilizer, but may be greater when associating an opioid (FANTONI; CORTOPASSI, 2002). Fantoni et al. (2006) indicate a dose of 5 to 7 mg/kg (IV), but with the use of MPA, this dose can be reduced by 30 to 40%, and the maintenance dose by continuous infusion is 0.4 mg/kg per minute (min). According to Paddleford (2001) the effective dose for induction of anesthesia in dogs that did not receive MPA is 6.6 to 8.8 mg/ kg and with tranquilizing, sedative or opioid MPA the dose is reduced to 2.2 to 4.4 mg /kg. Propofol is most frequently used associated with ketamine and lidocaine (OLIVEIRA et al., 2007). Propofol must be administered slowly over 60 to 90 seconds until the desired anesthetic level is achieved and to prevent short-term apnea from occurring due to propofol induction (PADDLEFORD, 2001).

Anesthesia with propofol does not produce analgesia (FANTONI et al., 2006; MASSONE, 2008) and the degree of muscle relaxation is moderate (FANTONI et al., 2006). This medication can cause, as an adverse effect, depression of the cardiovascular and respiratory systems, of blood pressure (PADDLEFORD, 2001; FANTONI; CORTOPASSI, 2002; FANTONI et al., 2006) and of myocardial contractility (PADDLEFORD, 2001). Because of this, these parameters require careful monitoring (PADDLEFORD, 2001). Propofol, as well as atropine, xylazine and thiopental, can cause relaxation of the esophageal sphincter causing vomiting (FANTONI; CORTOPASSI, 2002).

Injection pain may occur when propofol is injected into a small-caliber vein and does not cause tissue damage if administered outside the vein (PADDLEFORD, 2001; FANTONI et al., 2006). indicates the administration in larger caliber veins, such as the cephalic vein, being possible to opt for the association with lidocaine to reduce the pain in the initial moment of the application (MANNARINO, 2002).

The clearance distribution and of propofol are fast because it is very lipophilic, biotransformed quickly through being glucuronization and sulfoxidation (FANTONI et al., 2006). Propofol is metabolized both hepaticly and extrahepatically, and other organs such as the lung and kidney are also involved in the metabolism. Plasma elimination exceeds hepatic blood flow and after 30 minutes, less than 20% of the dose can be recovered as unchanged compound (PADDLEFORD, 2001). The metabolites are excreted through the urine (PADDLEFORD, 2001; FANTONI et al., 2006).

Anesthetic recovery is calm, fast (FANTONI; CORTOPASSI, 2002) and free

of excitement and side effects, since no cumulative effect is observed even when subsequent doses are applied (PADDLEFORD, 2001; FANTONI; CORTOPASSI, 2002; MASSONE, 2008). Fantoni et al. (2006) say that excitatory phenomena are not observed when sedatives are used in MPA. Even when anesthesia is prolonged, recovery occurs in the same period of time as after a single dose administration, gait being quickly regained and almost devoid of motor incoordination.

DEVELOPMENT

Intravenous general anesthesia with propofol has advantages such as practicality of use, is indicated for short and medium duration procedures, causes less hepatotoxicity, lack of pollution in operating rooms and does not expose the surgical team to gases exhaled by inhalation anesthesia equipment that can cause mood swings, diabetes mellitus, liver cirrhosis and genetic mutations (MOREIRA; SILVA, 2008).

It is important that the anesthetic induction is fast and allows easy intubation of the animal. This happens with the use of ultrashort-term hypnotic agents, such as propofol, causing minimal cardiovascular depression and rapid and peaceful recovery (FANTONI; CORTOPASSI, 2002).

Massone (2008) and Fantoni and Cortopassi (2002) indicate an average dose of 5 mg/kg for dogs when pre-treated with 1 mg/kg of levomepromazine to produce an anesthetic period of 10 to 15 minutes. This dose may cause mild hypotension and tachycardia, but it does not alter the blood gas or hematological values, when compared to the baseline values. of discomfort. According to Paddleford (2001), a dose of propofol provides 10 minutes of anesthesia with complete recovery in 20 to 30 minutes.

The authors Moreira and Silva (2008) indicate rates of propofol for dogs from 0.15

to 0.4 mg/kg/min in continuous infusion and from 0.5 to 2 mg/kg in infusion with intermittent bolus, but these doses can change according to MPA and the association with sedatives and analgesics.

Fantoni and Cortopassi (2002) say that propofol causes significant cardiovascular depression after induction when using low (1.5 mg/kg) and high (2.5 mg/kg) doses. However, they comment that propofol does not have a standard effect on heart rate (HR), because tachycardia, bradycardia and HR maintenance were observed with the use of this medication, however, for Fantoni et al. (2006) the cardiac index is not markedly affected. According to Paddleford (2001) propofol is not exactly arrhythmogenic, however it exacerbates the arrhythmogenicity of catecholamines. According to Oliveira et al. (2007) the isolated use of propofol in continuous infusion causes greater respiratory depression, but when associated with analgesic agents it is possible to reduce the infusion rate, minimizing side effects.

The authors Carareto et al. (2007) analyzed HR variability in 12 adult dogs anesthetized with continuous infusion of propofol and different doses of sufentanil. The animals received as MPA 0.05 mg/kg, IV of acepromazine maleate, were induced with 5 mg/kg, IV of propofol and maintained with propofol at 0.2 mg/kg/min, IV, associated with sufentanil citrate at 0.025, 0.5 and 0.1 µg/kg/ min for 120 minutes. There was no significant variation in HR variability and a marked reduction in HR, the latter being considered as a dose-dependent effect of propofol in stimulating parasympathetic tonus and of sufentanil in increasing vagal activity.

Using similar medications, authors Hatschbach et al. (2008) performed a study comparing target infusion techniques controlled by an infusion pump (induction: 3.5 μ g/ml; maintenance: 1.5 μ g/ml, IV) and fixed rate continuous infusion (induction: 5 mg/ml). kg; maintenance: 0.2 mg/kg, IV) in 20 bitches to ovariosalpingohysterectomy submitted (OSH). min). The occurrence of bradycardia, mild hypotension, hemogasometric and respiratory stability, good myorelaxation and hypnosis was more evident with continuous infusion. The two protocols and the anesthetic doses were effective for performing the surgery, however in the target-controlled anesthesia technique there was less anesthetic consumption and the recovery periods were faster. The association of propofol with remifentanil provides good myorelaxation and good hypnosis, but due to bradycardia and hypotension, the animal must be constantly monitored.

For Fantoni et al. (2006) there is depression in the respiratory system, transient apnea after administration, decrease in minute volume and respiratory rate (RR) with increase in arterial partial pressure of carbon dioxide (PaCO2) and decrease in arterial partial pressure of oxygen (PaO2), these effects being directly proportional to the dose administered, the speed of application of the drug, the MPA used and the presence of hyperventilation and hyperoxia.

Propofol reduce myocardial may contractility in healthy dogs. In a study with 8 dogs anesthetized with continuous infusion of propofol (0.7 mg/kg/min) under spontaneous ventilation, it was concluded that different fractions of inspired oxygen (FiO2) do not affect echocardiographic parameters, structure and hemodynamics, cardiac function (LOPES et al., 2009). Regarding the effect of different FiO2 on the respiratory dynamics, it was noticed that the oximetry values (SpO2) were lower in the lowest FiO2 (= 0.21) and the PaO2 varied according to the fraction of oxygen supplied, concluding that the supply of oxygen to 100%, 80% and 21% must be avoided, because they cause damage to the respiratory system of dogs under this anesthesia (LOPES et al., 2007). And regarding the effect of different FiO2 on the bispectral index (BIS), it was observed that the higher the FiO2, the higher the PaO2 and PaCO2 and no differences were observed in the variables related to the BIS, concluding that these are not affected by the different FiO2 (LOPES et al., 2008).

The BIS is correlated with the degree of hypnosis in patients during anesthesia (NISHIMORI et al., 2007), demonstrating the action of the drug in the central nervous system (LOPES et al., 2008).

Nishimori et al. (2007) studied BIS in 32 anesthetized dogs with increasing (from 0.4 to 0.8 mg/kg/min) and decreasing (from 0.8 to 0.4 mg/kg/min) infusions of propofol with or without nitrous oxide (N2O), and concluded that both increasing and decreasing infusions of propofol and N2O or oxygen reduced BIS and promoted cardiovascular depression in a dose-dependent manner. BIS values were more adequate at a dose of 0.6 mg/kg/min of propofol and with higher doses of propofol, HR parameters, mean systolic arterial pressure (MAP) and cardiac index were lower, demonstrating that lower doses of propofol are used with greater safety.

Fantoni and Cortopassi (2002) consider that the association of propofol with isofluorane in dogs is similar to epidural anesthesia with regard to maternal safety and fetal viability. Paddleford (2001) and Fantoni et al. (2006) explain that propofol crosses the placental barrier, but does not cause teratogenic effects or significant depression that makes fetuses unfeasible. Neonates of mothers anesthetized for cesarean section with this medication are born depressed, the degree of depression being dose-dependent. In one study, Gabas et al. (2006) evaluated the effects on neonates caused by the anesthetic that mothers received during caesarean section compared to normal delivery. Six normal deliveries and six cesarean sections were performed. Bitches undergoing caesarean section were given acepromazine (0.05 mg/kg, IV) as MPA, induced with propofol (5 mg/kg, IV) and maintained on sevoflurane. Greater respiratory and neurological depression were observed and there were no cardiocirculatory changes in pups born by cesarean section compared to those born by normal delivery, however the anesthetic protocol employed did not compromise the viability and health of pups and mothers, being considered safe in pregnant bitches.

In another study with scores and their neonates, the effects of anesthesia-inducing drugs such as propofol (4.7 mg/kg, IV), etomidate (1.54 mg/kg, IV) and thiopental (9.82 mg/kg, IV) and epidural anesthesia with lidocaine followed by induction. 20 female dogs separated into 4 groups were used.

All received midazolam (0.22 mg/kg, IM) of MPA and anesthetic maintenance with halothane (initial concentration of 3V%). All anesthetic protocols were adequate for the mothers with minimal systemic effects and for the pups, the protocol that used epidural anesthesia and maintenance with halothane in the mothers was superior to those that used injectable agents in the anesthetic induction, and the neonates in the propofol group were the best. second group with the best result, where at ten minutes of life the puppies did not need more special care (LAVOR et al., 2004).

According to Fantoni and Cortopassi (2002), the use of propofol in anesthetic induction or maintenance may cause a decrease in blood pressure, due to depressant effects on the myocardium and arterial and venous vasodilation. However, this reduction is less intense than that triggered by thiopental. Propofol promotes an effect on intracellular calcium homeostasis during systole and diastole, but these changes cause very little change in myocardial contractility. For Fantoni et al. (2006) systemic hypotension occurs due to the reduction of peripheral vascular resistance in a more accentuated way than thiopental in similar doses. According to Paddleford (2001) primary hypotension results from arterial and venous vasodilation.

Delirium and dysphoria may occur during recovery from anesthesia due to passing through stage II anesthetics, as propofol is an anesthetic with rapid elimination. The nonuse of tranquilizers in MPA can also be a cause (FANTONI; CORTOPASSI, 2002).

Myoclonic twitching, tremors, and muscle movement may occur during induction and maintenance of anesthesia with propofol. This muscle reaction occurs because of the carrier agent used by propofol, but the use of tranquilizers, sedatives and opioids such as MPA can reduce the occurrence of these symptoms (PADDLEFORD, 2001). Ferreira et al., 2008 observed three cases of adverse reactions (myoclonus, opisthotome and prolonged apnea), during anesthetic procedures in dogs with no previous history of neurological disorders, when using propofol from the same batch and within the validity period. All animals had received morphine as MPA, a drug that could influence the bioavailability of propofol, but when changing the drug batch, there were no more adverse effects.

Continuous infusion of propofol has good hemodynamics, minimal effects on liver function, rapid anesthetic induction and recovery, few adverse effects, and absence of excitatory effects when sedatives are used in APM. During continuous infusion, this drug has constant plasmatic concentration, because as the anesthetic undergoes redistribution and metabolization, a new supply of drug is being performed (MOREIRA; SILVA, 2008). In the respiratory system, it can cause transient apnea after administration (being directly related to the speed of propofol administration, which can cause depression in the respiratory centers) (FERRO et al., 2005; MOREIRA; SILVA, 2008), decrease in the minute volume (MV), respiratory rate (RR) and PaO2 and increase in PaCO2 pressure (MOREIRA; SILVA, 2008).

The authors Ferro et al. (2005) compared in 24 dogs the administration of different doses of propofol in continuous infusion (0.2, 0.4 and 0.8 mg/kg/min). Systolic (SBP), diastolic (DBP) and MAP blood pressure had a greater reduction (30.6%, 52.7% and 38.4%, respectively) in the 0.8 mg/kg/min infusion, which may have been caused by the decrease in peripheral vascular resistance and the decreases in SBP, DBP, MAP, RR and rectal temperature (TR) were dependent on the infusion dose of the drug. HR remained within the range considered physiological in all groups. The 0.4 mg/kg/min infusion group had a smaller reduction in MAP (26.3%) and no increase in HR, a fact explained by FERRO et al. (2005) that propofol does not change the sensitivity of baroreceptors or the number of muscarinic receptors. The reduction in TR was around 1.4°C, explained by the decrease in the basal metabolism rate and by the arterial and venous vasodilation caused by the drug. About 8.33% of the animals had muscle tremors in the head and limbs.

Campos et al. (2009) reported the association of continuous propofol infusion with epidural block in a dog submitted to femoral head resection. APM was performed with acepromazine (0.05 mg/kg) associated with tramadol (2 mg/kg, intramuscularly – IM), induction was with propofol (4 mg/kg, IV) and maintenance with continuous infusion of propofol (0.3 mg/kg/min, IV). Epidural anesthesia was associated with lidocaine (3 mg/kg), bipuvacaine (0.5 mg/kg) and morphine (0.1 mg/kg). HR, RR, SpO2,

TR and SBP parameters were monitored. It was concluded that the anesthetic protocol was safe and did not cause major changes in the parameters, remaining within the values considered physiological, did not depress the respiratory system and the patient remained in spontaneous breathing.

In a study, the authors Gasparini et al. (2009) compared total intravenous anesthesia using propofol with its use associated with ketamine, in continuous infusion in 12 bitches submitted to OSH. MPA was performed with atropine (0.05 mg/kg, subcutaneously, SC) and xylazine (1 mg/kg, IM). In one group, six bitches were induced with propofol (5 mg/kg, IV) and maintained with continuous infusion of propofol (0.4 mg/kg/min) and in the other group, another six bitches were induced with propofol (3, 5 mg/kg, IV) associated with ketamine (1 mg/kg, IV) and maintained with continuous infusion with the same drugs at a dose of 0.28 and 0.06 mg/kg/ min (IV), respectively. A reduction in blood pressure was observed in the first group; reduction in TR, hypercapnia and respiratory acidosis in both groups; increase in PaO2, bicarbonate and glucose in the second group. It was concluded that both protocols were safe and sufficient for surgical anesthesia of OSH, however the quality of anesthesia was superior in the animals of the second group, since there was a need to increase the speed of propofol infusion to 0.34 mg/kg/ min compared to the 0.6 mg/kg/min increment of the first group. Considerable respiratory depression occurred in both groups, requiring assisted or controlled ventilation.

The association of propofol and ketamine in continuous infusion was also performed by Almeida et al. (2008), who compared the anesthetic maintenance of propofol (0.4 mg/ kg/min) and racemic ketamine (0.2 mg/kg/ min) with propofol (0.4 mg/kg/min) and levorotatory ketamine in 12 bitches. As a result, there was an increase in HR, without electrocardiographic changes, a reduction in RR, a decrease in SBP, MAP and DBP and the presence of hypoventilation and hypoxia, in both groups. In some animals, analgesia did not occur or was discreet, showing that both protocols were safe, but there was not enough analgesia to perform a surgical procedure, and must be used with caution in patients with heart disease and with the need for oxygen during the supplementation procedure (ALMEIDA et al., 2008). The increase in HR in patients undergoing continuous infusion of propofol may be a consequence of the reduction in blood pressure caused by the drug or may be directly linked to the speed of propofol administration (MOREIRA; SILVA, 2008).

The association of continuous infusion of propofol (induction: 10 mg/kg, IV; maintenance: 0.7 mg/kg/min) with tramadol (induction: 2 mg/kg; maintenance: 0.5 mg/kg/h) does not causes alteration in the ventilometric, cardiovascular, electrocardiographic and BIS parameters, however it caused a reduction in TR, red blood cell count, hemoglobin, hematocrit, total leukocyte count and lymphocytes, concluding that this protocol did not cause alteration in the cardiorespiratory parameters, however it must be used with caution in immunosuppressed animals (COSTA, 2009).

Propofol can be used in continuous infusion (0.985 mg/kg/min) together with lidocaine, which may lead to less depression, greater cardiovascular resistance and mild acidosis.

The use of lidocaine potentiates analgesia and hypnosis, increases the recovery period, decreases cardiovascular depression and propofol infusion rate (administered alone at a dose of 1.25 mg/kg/min) (MANNARINO, 2002).

Lopes (2009) compared the continuous infusion of propofol (0.8 mg/kg/min) and thiopental (0.5 mg/kg/min) in 20 dogs with pulmonary hypertension and concluded that the continuous infusion of thiopental produces greater stability of respiratory and blood gas parameters, as it attenuates vasoconstriction and bronchoconstriction caused by pulmonary hypertension. However, anesthesia with propofol maintained the higher HR.

CONCLUSION

It is concluded that propofol is a drug used for anesthetic induction and maintenance in *bolus* or continuous infusion, which can be used safely both in healthy patients and in patients with liver disease, kidney disease, parturients and their neonates, but it is an expensive medication and requires its intravenous administration.

The doses indicated in the literature are quite variable due to the MPA used, the speed of administration and the use of anesthetic associations, which requires the use of anesthetic monitoring for anesthesia to be performed with greater safety. Therefore, the results obtained in the various scientific works regarding propofol correspond to those indicated in the literature.

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