RESEARCH ARTICLE

Comparative Anaesthetic Effects of Propofol and Tiletamine-Zolazepam Anaesthetic Agents in Dogs

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Abstract

The study evaluated two different anaesthetic protocols in dogs (n=24) for anaesthetic parameters like dose of anaesthetic agents for induction and maintenance of anaesthesia, quality of sedation, induction, maintenance of anaesthesia and recovery. All the animals were first premedicated with butorphanol @ 0.2 mg/kg b.wt. and xylazine @ 1 mg/kg b.wt., i/m, simultaneously. After 15 min of preanaesthetic medication, induction and maintenance of anaesthesia was achieved by administration of propofol @ 3 mg/kg b.wt., i/v in Group-I (n=12) and tiletamine-zolazepam @ 2 mg/kg b.wt., i/v in Group-II (n=12). Both protocols showed excellent quality of induction and maintenance of anaesthesia in the all animals. Physiological parameters like heart rate, respiration rate, rectal temperature and blood saturation of oxygen altered at different time intervals during the anaesthesia, but remained in normal physiological range. Xylazine and butorphanol preanesthetics showed dose sparing effect on induction and maintenance dose of propofol. Propofol resulted in excellent recovery quality and shorter recovery time compared to tiletamine-zolazepam.

Key words: Butorphanol, Dog, Propofol, Tiletamine-Zolazepam, Xylazine.

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Introduction

An essential component of surgical intervention is anaesthesia, which enables the surgeon to do the process with the greatest degree of accuracy (Muhammad *et al.*, 2009). Balanced anaesthesia provides good intraoperative cardiopulmonary functions, minimise the pain associated with surgery and provides calmer and smooth, coordinated recoveries. For induction of general anaesthesia, intravenous anaesthetic drug is administered as a large bolus and for maintenance of anaesthesia the drug can be administered in continuous lower dosages either by repeated intravenous bolus, constant rate of infusion (CRI) or target-controlled infusion (Tyagi *et al.*, 2020). In recent years, continuous total intravenous anaesthesia (TIVA) has gained popularity in veterinary anaesthesia. TIVA uses a combination of an α-2 agonist with opiods and anaesthetic agents like propofol, tiletamine-zolazepam, which anaesthetize animal by the combination of central nervous system (CNS) depression, muscular relaxation and analgesia. TIVA is a method that utilizes only intravenous anaesthetic drugs to achieve and maintain a desired level of anaesthesia by depressing the CNS (Waelbers *et al.*, 2009). The appropriate selection of pre-anaesthetic drugs can significantly contribute to perioperative analgesia, intraoperative cardiovascular stability and quality of recovery (Murrell, 2016). The use of α -2 agonists in combination with opioids leads to enhancement of the sedative and analgesic effects of α -2 adrenoceptor agonists. The present clinical study was undertaken to compare the clinical efficacy of propofol vs. tiletamine-zolazepam in various surgical cases in dogs.

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Materials and Methods

The present clinical study was carried out during 2022-2023 at the Department of Veterinary Surgery Radiology, College of Veterinary Science and Animal Husbandry, Kamdhenu University, Junagadh, Gujarat (India). The study included a total of 24 dogs that were presented for various surgical conditions

and elective surgeries. The animals were randomly divided into two groups, with twelve animals in each group. All animals were fasted for 12 h and water was withheld for 6 h before anaesthesia. The general status of the animal was evaluated before giving anaesthesia by recording rectal temperature (^{0}F), heart rate (beats/min), respiration rate (breaths/min), blood pressure (mmHg) and saturation of peripheral oxygen (%). All the animals were first premedicated with butorphanol (0.2 mg/kg b.wt., i/m) and xylazine (1 mg/kg b.wt., i/m) simultaneously. After 15 min of preanaesthetic medication, induction of anaesthesia was achieved by administration of propofol (3 mg/kg b.wt., i/v) in Group-I (n=12) and tiletamine-zolazepam (2 mg/kg b.wt., i/v) in Group-II (n=12). Maintenance of anaesthesia was achieved by intravenous administration of propofol (12 mg/kg b.wt.) in Group-I and tiletamine-zolazepam (2 mg/kg b.wt.) in group-II. Induction and maintenance drugs were administered as needed to achieve the desired level of anaesthesia, allowing for accurate measurement of the required dosage of specific anaesthetic agents.

The quality of sedation and induction were evaluated (Table 1, Table 2). Dose of induction and maintenance anaesthesia were calculated. Quality of maintenance anaesthesia was assessed based on the scoring scale of pedal reflex, palpebral reflex, jaw tone and eyeball position (Table 3) (Singh *et al.,* 2012; Dinesh *et al.,* 2019). Quality and time of recovery (time elapsed in minutes from the cessation of CRI administration up to the return of first righting reflex) (Table 4) were recorded and evaluated.

Table 1: Quality of sedation

Parameters of sedation	Score	Quality
No sedation, alert, open eyes	0	No effect
Mild sedation, mild palpebral reflex, moderate corneal reflex	1	Poor
Moderate sedation, drooping of eyelids, no palpebral reflex, mild corneal reflex	2	Fair
Deep sedation, ventral rotation of eye ball, drooping of eyelids, no palpebral and corneal reflex	3	Good

Table 2: Quality of induction anaesthesia

Parameters of induction	Score	Quality
Obvious excitement, makes attempt to stand, tightly closed jaws, inability to intubate trachea	1	Poor
Mild excitement, slightly prolonged induction, moderate resistance to opening of jaws, longer intubation time	2	Fair
No excitement, mild resistance to opening of jaws, mild reflex response to intubation	3	Good
No resistance to opening of jaws, Easy and quick intubation without any reflex response to intubation	4	Excellent

Table 3: Quality of maintenance anaesthesia

Parameter	Score	Description
Pedal reflex	0 (Unacceptable)	Strong response to pedal reflex
	1 (Poor)	Weak response to pedal reflex
	2 (Fair)	Sluggish and occasional response to pedal reflex
	3 (Good)	Very sluggish response to pedal reflex
	4 (Excellent)	Abolished pedal reflex
Palpebral reflex	0 (Unacceptable)	Strong response to palpebral reflex
	1 (Poor)	Intact but weak palpebral reflex
	2 (Fair)	Intact but weak palpebral reflex
	3 (Good)	Sluggish response to palpebral reflex
	4 (Excellent)	Abolished palpebral reflex
Jaw tone	0 (Unacceptable)	Not allowed to open the jaws and tightly closing jaws
	1 (Poor)	Marked resistance to opening of jaws and closing quickly
	2 (Fair)	Moderate resistance to opening the jaws and close quickly
	3 (Good)	Mild resistance to opening of jaws and close slowly
	4 (Excellent)	No resistance to opening of jaws and jaws remain open
Eyeball position	1 (Poor)	No rotation of the eyeball (Centre position)
	2 (Fair)	Slight downward rotation of the eyeball
	3 (Good)	Moderate downward rotation of the eyeball
	4 (Excellent)	Complete ventromedial rotation of the eyeball

Table 4: Quality of recovery

Parameters of recovery	Score scale	Quality
Excitement, severe ataxia and padding	1	Poor
Some excitement, moderate ataxia and padding	2	Fair
No excitement or struggling and mild ataxia on standing	3	Good
No excitement, no staggering and no ataxia	4	Excellent

The difference between two data sets of two groups were statistically analyzed by using student's 't' test (parametric data) and Mann Whitney test (non-parametric data). The differences between more than two data sets within groups were analyzed by using one-way ANOVA followed by Duncan's Multiple Range Test (DMRT) test (Snedecor and Cochran, 1994).

Results and Discussion

All animals included in the study exhibited stable physiological parameters, including rectal temperature (°F), heart rate (beats/min), respiration rate (breaths/min), blood pressure (mmHg), and peripheral oxygen saturation (%), all within the normal range.

Quality of Sedation

The median value of sedation quality was 4.000±0.00 in both the groups. Sedation score was observed good in all the animals of both the groups. No significant difference in sedation quality was observed between the groups. Following the administration of preanaesthetics, all animals in the study exhibited common signs such as ataxia, drooping of eyelids, ventral rotation of eyeball, sleepiness, and assuming positions of sternal recumbency and lateral recumbency. In all animals of both groups, no any sign of nausea and vomition was observed. However, Sahoo *et al.* (2018) reported nausea in one dog after 5 min of xylazine administration. Xylazine (alpha-2 agonists) combination with butorphanol (opioid agonist-antagonist) produce profound muscle relaxation as animal came in to lateral recumbency in present study.

Dose and Quality of Induction Anaesthesia

The mean ± SE value of induction dose rate (mg/kg) was 1.90±0.08 in group I and 1.96 ±0.06 in group II. Statistical analysis showed significant decrease in induction dose rate of propofol in group I compared to initially kept dose rate 3 mg/kg. It might be suggesting that the premedication with xylazine and butorphanol may have contributed to a dose-sparing effect on propofol. In Group II, the decrease in induction dose rate of tiletamine-zolazepam was found to be negligible than control dose 2 mg/kg. This finding suggests that the initially chosen lower dose of tiletamine-zolazepam was effective in achieving the desired results without the need for further adjustments.

The median value of induction quality was 4.00±0.00 in both the groups. No significant difference of induction quality was observed between the groups. Apnea, a temporary suspension of breathing, was observed in 2 out of 12 dogs during the induction phase when propofol was administered in group I. This occurrence was consistent with the known effects of propofol, which can cause a transient suppression of respiratory centre (Smith *et al.,* 1993). Similar finding was observed by Bufalari *et al.* (1997) with propofol induction in dogs.

In Group II, one dog displayed an apneustic respiratory pattern characterized by deep breathing followed by a brief pause lasting a few seconds. This might be due to reason that administration of the tiletamine-zolazepam combination results in temporary respiratory depression shortly after intravenous administration. Furthermore, it can induce an apneustic respiratory pattern characterized by deep breathing with irregular frequency and prolonged pauses (Berry, 2015).

Dose and Quality of Maintenance Anaesthesia

The mean ± SE values of CRI maintenance dose rate (mg/kg/h) were 10.11 ± 0.52 and 2.66±0.12 in group I and II, respectively. Group I exhibited a statistically significant decrease in the dose rate of propofol for maintenance compared to initially kept maintenance dose (12 mg/kg/h), indicating a dose sparing effect of the premedication with xylazine and butorphanol. However, Chandrakala *et al.* (2017) used 18 mg/kg/h dose rate of propofol CRI in xylazine- butorphanol premedicated dogs. The sedative effects of xylazine and the analgesic effects of butorphanol can lead to a decreased requirement for propofol to achieve and maintain the desired level of anaesthesia.

Group II showed a significant increase in the dose rate of tiletamine-zolazepam for maintenance compared to initially kept maintenance dose (2 mg/kg/h). In Group II, the maintenance dose of anaesthesia was set at 2 mg/kg/h but dose required in this particular study was found to be 2.66±0.12 mg/kg/h. This indicates that, on average, a slightly higher dose was needed to maintain the desired depth of anaesthesia throughout the surgical period in this group. The findings of this study align with the research conducted by Pereira *et al.* (2019), which also indicated that a maintenance dose of 2 mg/kg/h of tiletamine-zolazepam, when combined with acepromazine premedication, may not be sufficient to achieve a surgical plane of anaesthesia.

Quality of maintenance anaesthesia was assessed based on the scoring scale of pedal reflex, palpebral reflex, jaw tone and eyeball position at different time intervals.

Pedal reflex and Palpebral reflex

The median ± SD values of the pedal reflex and palpebral reflex were consistently recorded as 4.00±0.00 (excellent) throughout the entire observation period during the maintenance of anaesthesia in both groups. No significant difference was observed between groups at any time of observations. Similarly, Chandrakala (2015) and Pusp (2022) also found complete abolished pedal reflex and palpebral reflex during entire period of maintenance anaesthesia on propofol. Naryal (2020) also found abolished pedal reflex and absence of palpebral reflex immediately after induction with propofol. Nam *et al.* (2013) found sluggish pedal reflex in tiletamine-zolazepam anaesthesia. Propofol lacks intrinsic analgesic property, but butorphanol and xylazine provided sufficient analgesia. The absence of the palpebral reflex in Group II, where tiletamine was used, may be attributed to the synergistic effects of zolazepam, xylazine, and butorphanol which induce deep sedation and muscle relaxation, including the eyelid muscles.

Jaw tone and Eyeball position

The median ± SD values of the jaw tone and eyeball position were consistently recorded as 4.00±0.00 (excellent) throughout the entire observation period during the maintenance of

anaesthesia in both groups. Similar finding on jaw tone was observed by Chandrakala (2015) with xylazine-butorphanol preanaesthetics on propofol induction and maintenance of anaesthesia in dogs. Pereira *et al.* (2019) also reported abolished jaw tone in most of cases of tiletamine-zolazepam anaesthesia in dogs. Before administration of preanaesthetics, eyeball was centrally located in all animals in both groups. After induction of anaesthesia and during maintenance period, complete ventromedial rotation of eyeball was observed in all animals of both groups. Naryal (2020) observed ventro-medial eyeball rotation immediately after induction and throughout maintenance anaesthesia in all animals. Salve *et al.* (2022) also found that tiletamine-zolazepam produced excellent quality of maintenance anaesthesia with adequate analgesia and muscle relaxation without remarkable side effects.

Recovery Time and Quality

The mean ± SE value of recovery time was 24.66±1.20 min in group I and 71.33±1.44 min in group II. Group I showed statistically significant decrease in recovery time compared to group II. Similarly, Bufalari *et al.* (1997) recorded recovery time of 21.07±6.25 min in propofol anaesthesia with butorphanol premedication in dogs. Group I also showed rapid recovery as compared to group II, which might be due to rapid metabolism and clearance of propofol from the body, allowing for a smooth and relatively quick recovery from anaesthesia (Kundu, 2001). Longer recovery time of 71.33±1.44 min observed in group II concurred with Salve *et al.* (2022), who observed it as 78.83±10.08 min with xylazine-tiletamine-zolazepam anaesthesia in dogs. Slower recovery process in group II might be due to fact that tiletamine has a longer elimination half-life compared to propofol.

Quality of recovery was found excellent with score value of 4.00±0.00 in group I and 3.16±0.23 in group II, which showed significant difference between the groups. In animals of group I, no excitement, no staggering and very mild ataxia was observed with less time of recovery compared to group II indicating excellent quality of recovery. Similarly, Andreoni and Hughes (2009) and Pusp (2021) reported smooth and uneventful recovery without excitement after propofol anaesthesia.

In Group II, all the animals showed longer recovery time and also during the recovery phase, two animals exhibited signs of excitement, moderate ataxia and vocalization, while six animals showed no excitement or struggling with mild ataxia and four animals showed no excitement, no ataxia. Lu *et al.* (2014) also reported mild ataxia and vocalization in recovery from tiletamine-zolazepam anaesthesia. However, Nam *et al.* (2013) reported smooth recovery from tiletamine-zolazepam anaesthesia.

Conclusions

In both groups, propofol and tiletamine-zolazepam anaesthetics produced excellent quality of induction and maintenance anaesthesia in dogs with xylazine and butorphanol premedication. Xylazine and butorphanol preanesthetics provided excellent quality of sedation in both groups and showed dose sparing effect on induction and maintenance dose of propofol. Propofol group had a recovery time one-third shorter than the tiletamine-zolazepam group and achieved a superior quality of recovery. Both anaesthetic protocols provided sufficient depth and excellent quality of anaesthesia in all animals without altering physiological responses, but propofol was better in terms of recovery time compared to tiletamine-zolazepam.

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