



ISSN: 2456-2912

NAAS Rating (2026): 4.61

VET 2026; 11(6): 238-241

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www.veterinarypaper.com

Received: 14-03-2026

Accepted: 18-04-2026

D Kusuma Latha

PG Scholar, Department of
Veterinary Surgery and
Radiology, CVSc Proddatur,
Andhra Pradesh, India

P Vidya Sagar

Assistant Professor and Head,
Department of Veterinary
Surgery and Radiology, CVSc
Proddatur, Andhra Pradesh,
India

N Sumiran

Assistant professor, Department
of Veterinary Surgery and
Radiology, CVSc Proddatur,
Andhra Pradesh, India

B Supriya

Associate Professor and Head,
Department of Veterinary
Anatomy, CVSc Proddatur,
Andhra Pradesh, India

Corresponding Author:

D Kusuma Latha

PG Scholar, Department of
Veterinary Surgery and
Radiology, CVSc Proddatur,
Andhra Pradesh, India

Physiological and cardiopulmonary effects of Tiletamine–Zolazepam–Ketamine–Xylazine (TKX) combination as an induction agent for ovariohysterectomy under isoflurane maintenance anaesthesia in dogs

D Kusuma Latha, P Vidya Sagar, N Sumiran and B Supriya

DOI: <https://www.doi.org/10.22271/veterinary.2026.v11.i6d.3534>

Abstract

The present study evaluated the physiological and cardiopulmonary effects of the tiletamine–zolazepam–ketamine–xylazine (TKX) combination as an induction agent for ovariohysterectomy under isoflurane maintenance anaesthesia in six clinically healthy, non-pregnant and non-oestrous female dogs. Physiological and cardiopulmonary parameters were monitored at predetermined intervals throughout the anaesthetic period. Following induction, heart rate increased significantly, whereas respiratory rate decreased significantly. Rectal temperature showed a non-significant decline, while peripheral oxygen saturation (SpO₂) remained stable at values above 98% during anaesthesia. Mean arterial pressure decreased significantly during the maintenance phase. The TKX–isoflurane protocol provided smooth induction and satisfactory maintenance of anaesthesia with minimal physiological and cardiopulmonary disturbances, indicating its safety and efficacy for ovariohysterectomy in dogs.

Keywords: Tiletamine–Zolazepam–Ketamine–Xylazine (TKX), ovariohysterectomy, physiological, cardiopulmonary

Introduction

Balanced anaesthesia is an essential approach in veterinary practice that combines different anaesthetic drugs and techniques to provide hypnosis, analgesia, muscle relaxation and physiological stability while minimizing adverse effects (Muir and Hubbell, 2014) ^[16].

Tiletamine–zolazepam is a combination, consisting of equal proportions of tiletamine hydrochloride and zolazepam hydrochloride (Nam *et al.*, 2013) ^[17]. The pharmacological actions of these two drugs are complementary, with tiletamine producing dissociative anaesthesia, analgesia, and immobilization, while zolazepam, a benzodiazepine derivative, provides muscle relaxation and tranquilization (Saikumar *et al.*, 2023) ^[23]. Owing to these combined effects, the tiletamine–zolazepam combination is widely used as a pre-anaesthetic agent, for induction prior to inhalational anaesthesia, and for producing general anaesthesia during diagnostic procedures as well as minor and major surgical interventions (Pawson and Forsyth, 2008; Nam *et al.*, 2013) ^[19, 17]. α_2 -agonists are commonly combined with dissociative anaesthetics to improve anaesthetic quality, recovery and counteract undesirable excitatory effects, thereby facilitating balanced anaesthesia in dogs (Gomez Villamandos *et al.*, 2013; Mahantesh *et al.*, 2024) ^[6, 14]. Present study was undertaken to evaluate the physiological and cardio pulmonary effects of tiletamine-zolazepam-ketamine-xylazine anesthetic combination in dogs.

Materials and Methods

Approval for the anaesthetic study was obtained from the Institutional Animal Ethics Committee, College of Veterinary Science, Proddatur (Approval No. 11-CVScPdtr/IAEC/2025

dated 16.09.2025). Six healthy non-oestrous, non-pregnant bitches of varying age group presented for ovariohysterectomy were selected for anaesthetic study and subjected to preanesthetic screening including clinical and haemato-biochemical examination.

Food and water were withheld for 12 hours and 6 hours respectively prior to anaesthetic trial. All the animals were pre-medicated with inj. Atropine sulphate at the dose rate of 0.02 mg/kg body weight intramuscularly, 5mins prior to induction of anaesthesia

Induction was carried out by administration of Inj. Tiletamine-Zolazepam at a dose rate of 2.5 mg/kg body weight, Inj. Ketamine hydrochloride at a dose rate of 2.5 mg/kg body weight and Inj. Xylazine at a dose rate of 0.5 mg/kg body weight mixture (TKX) in a single syringe intravenously to the effect. Anaesthesia was maintained with isoflurane inhalant anaesthesia.

Physiological and cardiopulmonary parameters were recorded throughout the anaesthetic period in all dogs. Heart rate, respiratory rate, and rectal temperature were recorded before and immediately after induction, subsequently at 15-minute time intervals during anaesthetic maintenance and after recovery. Peripheral oxygen saturation (SpO₂) and mean arterial pressure (MAP) were measured at 15-minute time intervals during maintenance anaesthesia and after recovery using a multiparameter vital signs monitor.

Statistical analysis

The data generated during the study were analysed using SPSS software version 22.0. comparison of mean values within each treatment group before and after drug administration were carried out using the paired t-test. The effects of treatment and various time intervals during the anaesthetic period were assessed using repeated measures analysis of variance (ANOVA) under the general linear model. P-value of ≤ 0.05 was considered statistically significant, whereas a P-value of ≤ 0.01 was considered highly significant.

Results and Discussion

Withholding of food and water for 12 hours and 6 hours respectively prior to induction anaesthesia was found effective in preventing vomiting in all the dogs (Tiwari *et al.* (2024) [25]. In the present study, excessive salivation was not observed in all the animals. Administration of atropine sulphate as pre-anaesthetic (0.02 mg/kg) was effective in controlling excessive salivation. Present findings were in accordance with Alvaides *et al.* (2008) [1]. Induction with Tiletamine-Zolazepam-Ketamine-Xylazine mixture found to be adequate and facilitated smooth induction, good muscle relaxation with easy endotracheal intubation. This concurred with the reports of Chen *et al.* (2005) and Koli *et al.* (2021) [9].

A significant decrease ($P \leq 0.05$) in respiratory rate was

observed following induction in all the animals. Present findings were in accordance with the observations of Beck *et al.* (2025) [3]. Tiletamine is well known to produce transient respiratory depression after induction and give rise to apneustic breathing pattern (Pereira *et al.* 2019) [20]. The decrease in respiratory rate immediately after induction might be attributed to depressant action of anaesthetic agents on pulmonary function, as reported by Kwon *et al.* (2003) [10]. However, a highly significant ($P \leq 0.01$) decrease in respiratory rate observed during isoflurane inhalant anaesthesia at 30th minute. Similar findings were reported by Galloway *et al.* (2004) [5], who observed dose-dependent respiratory depression during maintenance of isoflurane anaesthesia.

There was a significant ($P \leq 0.05$) increase in heart rate following induction in all the animals. Findings were in accordance with Chen *et al.* (2005) who reported that increase in heart rate after induction might be attributed to the combined sympathetic stimulating effect of tiletamine and the vagolytic effect of atropine. In the present study, a highly significant ($P \leq 0.01$) decrease in heart rate was observed at the 30th and 45th minute of maintenance anaesthesia, which might be attributed to the dose-dependent cardiovascular depressant action of isoflurane. Similar findings were reported by Galloway *et al.* (2004) [5] and Sousa *et al.* (2008) [24].

Rectal temperature showed a non-significant decrease following induction. Present observations were in accordance with Li *et al.* (2015) [12]. The decrease in rectal temperature might be attributed to decreased metabolic rate and central nervous system depression caused by the anaesthetic agents, as reported by Lu *et al.* (2013). A significant ($P \leq 0.05$) decrease in rectal temperature was noticed at 30th minute during the maintenance period compared to pre-induction values. Li *et al.* (2015) [12] reported that decrease in rectal temperature might be due to the heat loss associated with cold inhaled anaesthetic gas, abdominal lavage and laparotomy procedures.

Saturation peripheral oxygen (SpO₂) concentration recorded during maintenance anaesthesia was stable and there was no significant difference SpO₂ within the groups, relatively higher values observed during the isoflurane maintenance anaesthesia. This might be attributed to 100% oxygen supplementation during isoflurane maintenance anaesthesia. This was in accordance with the observation of Patel *et al.* (2022) [18] and Manjusha *et al.* (2023) [15] who reported SpO₂ values above 98%.

Mean arterial blood pressure values showed a progressive and statistically significant decrease throughout the maintenance period of anaesthesia. Present findings were in line with observations of Galloway *et al.* (2004) [5] and Lemke (2004) [11]. The reduction in mean arterial pressure might be attributed to the depressant effect of isoflurane on myocardial contractility along with its arterial and venous vasodilatory actions (Bayan *et al.* 2024) [2].

Table 1: Mean ($\pm$ SE) heart rate (beats/min), respiratory rate (breaths/min) and rectal temperature (OF) during different stages of anaesthesia

Parameter	Before induction	After induction	During maintenance of anaesthesia				After recovery
			0th min	15th min	30th min	45th min	
Heart rate	118.50 $\pm$ 2.27 ^B	139.33 $\pm$ 1.83 ^A	139.00 $\pm$ 1.71 ^a	136.83 $\pm$ 1.64 ^b	131.50 $\pm$ 1.60 ^c	128.33 $\pm$ 1.17 ^c	120.50 $\pm$ 1.25
Respiratory rate	23.83 $\pm$ 0.60 ^A	19.50 $\pm$ 0.42 ^B	18.50 $\pm$ 0.42 ^a	18.50 $\pm$ 0.42 ^a	16.66 $\pm$ 0.33 ^b	16.00 $\pm$ 0.25 ^b	21.66 $\pm$ 0.84
Rectal temperature	101.9 $\pm$ 0.06 ^A	101.1 $\pm$ 0.17 ^A	100.98 $\pm$ 0.17 ^a	100.00 $\pm$ 0.19 ^{ab}	99.45 $\pm$ 0.14 ^c	99.01 $\pm$ 0.31 ^{bc}	101.88 $\pm$ 0.03

Table 2: Mean ($\pm$ SE) saturation of peripheral oxygen (%) and mean arterial blood pressure (mm Hg) during maintenance of anaesthesia

Parameter	During maintenance of anaesthesia			
	0 th minute	15 th minute	30 th minute	45 th minute
Saturation of peripheral oxygen (SpO ₂) (%)	97.16 $\pm$ 0.54 ^a	97.50 $\pm$ 0.56 ^a	98.00 $\pm$ 0.51 ^a	98.00 $\pm$ 0.51 ^a
Mean arterial blood pressure (MAP) (mm Hg)	117.66 $\pm$ 0.88 ^a	110.50 $\pm$ 0.99 ^b	103.66 $\pm$ 0.88 ^c	99.66 $\pm$ 0.88 ^d

Conclusion

In the present study, Tiletamine–Zolazepam–Ketamine–Xylazine anaesthetic protocol resulted in smooth and rapid induction, adequate muscle relaxation. The physiological and cardiopulmonary parameters evaluated throughout the anaesthetic period remained within normal physiological limits in all animals. Although variations in these parameters were observed, they were transient and did not result in any clinically significant adverse effects. The findings of the present investigation indicate that the anaesthetic protocol employed was safe, effective, and well tolerated in dogs.

Conflict of Interest

Not available

Financial Support

Not available

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How to Cite This Article

Latha DK, Sagar PV, Sumiran N, Supriya B. Physiological and cardiopulmonary effects of Tiletamine–Zolazepam-Ketamine-Xylazine (TKX) combination as an induction agent for ovariohysterectomy under isoflurane maintenance anaesthesia in dogs. International Journal of Veterinary Sciences and Animal Husbandry. 2026;11(6):238-241.

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