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Research Article

Effects of Xylazine-Ketamine and Atropine Combinations on Ovariohysterectomy in Local Dogs

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ABSTRACT

Introduction: Ovariohysterectomy in dogs requires safe and effective anesthesia protocols. Nevertheless, the most effective combination and dosage of xylazine and ketamine, with or without adjuncts such as atropine, remain undetermined. The current study aimed to evaluate and compare the effects of xylazine-ketamine and xylazine-ketamine combined with atropine in female dogs undergoing ovariohysterectomy.

Materials and methods: Fifteen mongrel female dogs, aged 2-3 years and weighing 15-20 kilograms, were assigned to three groups of five each. Group A received ketamine-xylazine at a 1:2 volume ratio (1 mL + 2 mL) at 1 mL/10 kg of body weight. Group B received the same xylazine-ketamine mixture with atropine added at 0.04-0.05 mg/kg. Group C received xylazine-ketamine at a 1:1 volume ratio (1 mL xylazine + 1 mL ketamine) at 1 mL/10kg of body weight. All groups received the same diazepam-ketamine maintenance anesthesia intravenously. Physical parameters, including heart rate, respiratory rate, rectal temperature, and oxygen saturation (SpO_2), were recorded every 10 minutes for up to 60 minutes. Blood samples to evaluate hematological parameters, including red blood cell (RBC), white blood cell (WBC), platelets, hemoglobin (Hb), and packed cell volume (PCV), were collected before induction and again 30 minutes after induction.

Results: Heart rate and respiratory rate increased for up to 30 minutes across all treatment groups, with fewer fluctuations observed in Group B. Body temperature initially increased, then decreased, while SpO_2 initially decreased and gradually increased in all treatment groups. Nevertheless, these fluctuations were not statistically significant in Group B compared to the baseline values. No significant changes in WBC, platelet count, or PCV were observed in groups B and C compared with baseline values. The RBC and Hb levels were significantly reduced across all groups compared with baseline.

Conclusion: The present results demonstrated that the xylazine-ketamine-atropine combination provided a more stable anesthetic protocol during ovariohysterectomy in dogs, as the physical parameters indicated safer anesthetic conditions.

1. Introduction

Anesthesia is a temporary state induced by medical procedures that results in unconsciousness, memory loss, pain relief, and muscle relaxation[1]. Different combinations of sedatives and anesthetic medications have been used in animal practice for optimum analgesia during major and minor surgical approaches[2-4]. Along with the anesthetic benefit, the anesthetic medicines may cause anesthesia-related deaths within a few hours of induction[5]. In dogs, the anesthesia-related death rate is 0.6%, and the cardiovascular arrest rate is 1.1%[6]. Cardiorespiratory complications are common hazards during anesthetic practices[7].

In emergency situations such as accidents and animal bites, where sedation should be induced before fasting, ketamine hydrochloride is commonly administered in combination with sedatives and tranquilizers, including xylazine, which prolongs the duration of anesthesia[8]. Xylazine can be used as a sole agent or occasionally in short surgical procedures, as a preanesthetic sedative, or in combination

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with opioid drugs to induce profound sedation[9]. Ketamine may induce excessive salivation and bradycardia in animals, and atropine is employed as a preanesthetic anticholinergic agent[10]. Therefore, in veterinary medicine, alongside xylazine and ketamine, atropine is frequently used to achieve more stable surgical conditions in the protocol[11].

A stable surgical plane refers to maintaining a consistent level of anesthesia or enhancing tissue stability throughout the surgical procedure[12,13]. Veterinarians often perform ovariohysterectomy as a surgical intervention for conditions such as pyometra, uterine tumors, spaying, and other issues related to reproductive tract complications[14]. Given the lack of studies on specific anesthetic combinations in local dog breeds in Nepal, the present study aimed to evaluate the hematological and physiological effects of xylazine-ketamine, with and without atropine, to identify the safest combination for surgical procedures in a local dog breed in Kathmandu, Nepal.

2. Materials and Methods

2.1. Ethical approval

The present study was approved by the Nepal Veterinary Council (Approval No. Ethical/83/2081-82).

2.2. Animals

The experiment was conducted at the Central Referral Veterinary Hospital (CRVH), Tripureshwor, Kathmandu, Nepal, on 15 clinically healthy female local mongrel dogs weighing 10 to 20 kg, owned by the client, and presented for ovariohysterectomy. The animals were declared healthy by the veterinarian based on body temperature (37.5-39.2°C), heart rate (70-120 bpm), and respiratory rate (10-36 breaths/min), according to the guidelines of the Merks Veterinary Manual Reference Guide[15]. Dogs were kept in quiet, isolated conditions in the holding area of the study location, CRVH, Kathmandu, Nepal, in separate iron cages measuring 1 m × 0.5 m × 0.7 m. Prior to the experiment, all food was withheld for 12 hours and water for 6 hours. The study was conducted from August 2025 to October 2025.

2.3. Study design

Fifteen dogs were randomly allocated into three experimental treatment groups, each comprising five dogs. The medicines administered included xylazine 2% (20 mg/mL, Interchemie, Holland), ketamine 50 mg/mL (National Healthcare, Nepal), and atropine 0.60 mg/mL (National Healthcare, Nepal).

All dogs received a xylazine-ketamine mixture through an intravenous (IV) catheter placed in the cephalic vein using an 18-gauge needle. The mixture was prepared in a single syringe, and the dose (mL/kg body weight) was calculated individually based on each dog's weight.

Group A received xylazine and ketamine in a 1:2 ratio (1 mL xylazine + 2 mL ketamine), administered at 1 mL per 10 kg body weight. Group B received the same 1:2 xylazine-ketamine mixture at 1 mL per 10 kg, along with 1 mL atropine (National Healthcare, Nepal), administered intravenously in a separate syringe. The atropine dose (mg/kg) was calculated based on each dog's body weight. Group C received xylazine and ketamine in a 1:1 ratio (1 mL xylazine + 1 mL ketamine), administered at 1 mL/10 kg body weight[16]. Anesthesia was maintained in all groups using IV diazepam (5 mg/mL, Neon Laboratories Limited, India) and ketamine (50 mg/mL, National Healthcare, Nepal) in a 1:2 ratio. The surgical intervention was identical for all dogs and was not considered an experimental variable, as all groups were treated equally.

2.4. Surgical procedure

The ovariohysterectomy was performed by giving a midline (linea alba) incision of about 5- 6 cm starting from the umbilicus so that the surgeon could have direct access to the uterine horn and could pull the ovarian pedicle easily. The surgical approach was followed as described by Bencharif et al.[17].

2.5. Parameters and data collection

The physiological vital parameters, including temperature, heart rate, and respiratory rate, were recorded at the start of anesthesia induction and at 10, 20, 30, 40, 50, and 60 minutes thereafter. These measurements were obtained utilizing a digital thermometer (Misppro 2X Veterinary Digital Thermometer, Misppro, USA), a stethoscope (Best Care, China), and visual observation of thoracic excursions during respiration. Visual observation of respiration was performed for 1 minute at 10-minute intervals. The physiological parameters measured at the start of anesthesia (time = 0 minutes) were considered the baseline values. Oxygen saturation (SpO_2) was monitored using the Patient Monitor (G3D, General Meditech, China). Blood samples (3 mL) were collected aseptically from the cephalic vein at two time points, before anesthetic administration and 30 minutes after administration, and were immediately transferred into EDTA tubes for hematological analysis. Hematological profiles, comprising hemoglobin concentration (Hb), red blood cell (RBC) count, white blood cell (WBC) count, platelet count, and packed cell volume (PCV), were determined using a fully automated hematology analyzer (XL-180, ERBA, Germany). The pedal reflex, which was graded on a scale of 0 to 3 with 0 indicating no limb withdrawal and 3 indicating a quick withdrawal, and the palpebral reflex, rated on a scale of 1 to 4 with 1 denoting no change or a sharp blink in the reflex, 2 indicating a moderate reflex, 3 representing a slow response, and 4 indicating an absence of reaction, were utilized for clinical monitoring of anesthetic depth during anesthesia in accordance with the protocol established by Ibrahim[18].

2.6. Statistical analysis

The data were presented in a Microsoft Excel (version 2019) sheet and analyzed as mean ± SD using GraphPad Prism 10 free trial version (GraphPad Software, USA). For physical parameters, One-Way Analysis of Variance (ANOVA) at a 95% confidence level, followed by Tukey's multiple comparison test, was used to compare means between groups at different time points ($p < 0.05$). For hematological parameters, a paired t-test (Student's t-distribution) at a 95% confidence level was used to compare means between groups before and 30 minutes after administration of the drug combination, with p-values less than 0.05.

3. Results

The experiment was conducted to determine the effects of different combinations of xylazine and ketamine on physiological and hematological parameters in dogs and to

compare these effects. The pedal reflex and palpebral reflex were used for clinical anesthetic monitoring in all experimental groups. After 5 minutes of induction, dogs in all groups showed no pedal reflex (grade 0) and gradually started responding after 10 minutes; quick withdrawal (grade 3) was seen after 60 minutes of induction. Similarly, the palpebral reflex demonstrated that dogs in all experimental groups had no eye reflex (grade 4) after 5 minutes of induction and gradually started to respond (grade 4 to grade 2), with a sharp blink (grade 1) after 60 minutes of induction.

3.1. Physiological parameters

The heart rate increased rapidly following induction, reaching its peak at 30 minutes in groups B (140.60 ± 6.66 beats/minute) and C (130.20 ± 9.98 beats/minute), before gradually approaching baseline values by 60 minutes (108.80 ± 6.38 beats/minute and 109.60 ± 4.83 beats/minute, respectively; Figure 1A). At 30 minutes, heart rate in Group B was significantly higher than in Group C ($p < 0.05$), and both groups exhibited significantly higher rates than Group A (83.60 ± 8.76 beats/minute; $p < 0.05$). Throughout the monitoring period, Group A consistently had the lowest heart rate, with a significant decrease below baseline observed at 40-60 minutes ($p < 0.05$; Table 1). Temperature decreased in all treatment groups over the 60-minute period. The most pronounced reduction in temperature was observed in Group A, from 38.97 ± 0.77°C to 36.94 ± 1.26°C, followed by Group B (from 38.94 ± 0.27°C to 38.03 ± 1.56°C) and Group C (from 39.36 ± 0.05°C to 38.65 ± 0.16°C). At baseline (0 min), Group C (39.36 ± 0.05°C) had a significantly higher temperature than groups A (38.97 ± 0.77°C) and B (38.94 ± 0.27°C; $p < 0.05$). At 30 minutes and later, Group A exhibited the lowest temperature (37.75 ± 0.22°C), which was significantly lower than Group C at 30 minutes (38.76 ± 0.44°C) and significantly lower than both groups B and C at 60 minutes (36.94 ± 1.26°C versus 38.03 ± 1.56°C and 38.65 ± 0.16°C, respectively; $p < 0.05$; Figure 1B; Table 1). All groups exhibited an initial increase in respiratory rate following anesthesia. Respiratory rate increased significantly in Groups A and B, peaking at 30 minutes (29.60 ± 0.55 and 27.20 ± 1.10 breaths/min, respectively) compared with baseline values ($p < 0.05$). In contrast, respiratory rate in Group C ranged from 25.40 ± 1.52 to 26.80 ± 0.84 breaths/min and did not differ significantly from baseline ($p > 0.05$). Inter-group comparisons revealed that at 20 minutes, Group A (28.20 ± 0.55 breaths/min) had a significantly higher respiratory rate than groups B (26.00 ± 1.22 breaths/min) and C (26.60 ± 0.55 breaths/min; $p < 0.05$). By 60 minutes, Group A (23.60 ± 1.14 breaths/min) demonstrated a significant decline below baseline and was significantly lower than groups B (25.00 ± 0.71 breaths/min) and C (25.60 ± 1.14 breaths/min; $p < 0.05$; Table 1). The SpO_2 initially decreased across all treatment groups and gradually increased toward baseline by the end of the experiment (Figure 1D). The most pronounced decrease in SpO_2 occurred at 30 minutes in Group A (84.20 ± 2.17%), which was significantly lower than in groups B (91.20 ± 2.68%) and C (89.40 ± 1.34%; $p < 0.05$). The SpO_2 fluctuated significantly in groups A and C compared with baseline values ($p < 0.05$), whereas Group B demonstrated no significant deviation throughout the monitoring period ($p > 0.05$). At 60 minutes, all groups recovered toward baseline levels, with Group C (93.40 ± 1.14%) indicating a significantly higher SpO_2 than Group A (92.00 ± 0.71%) and Group B (92.40 ± 2.07%; $p < 0.05$; Table 1).

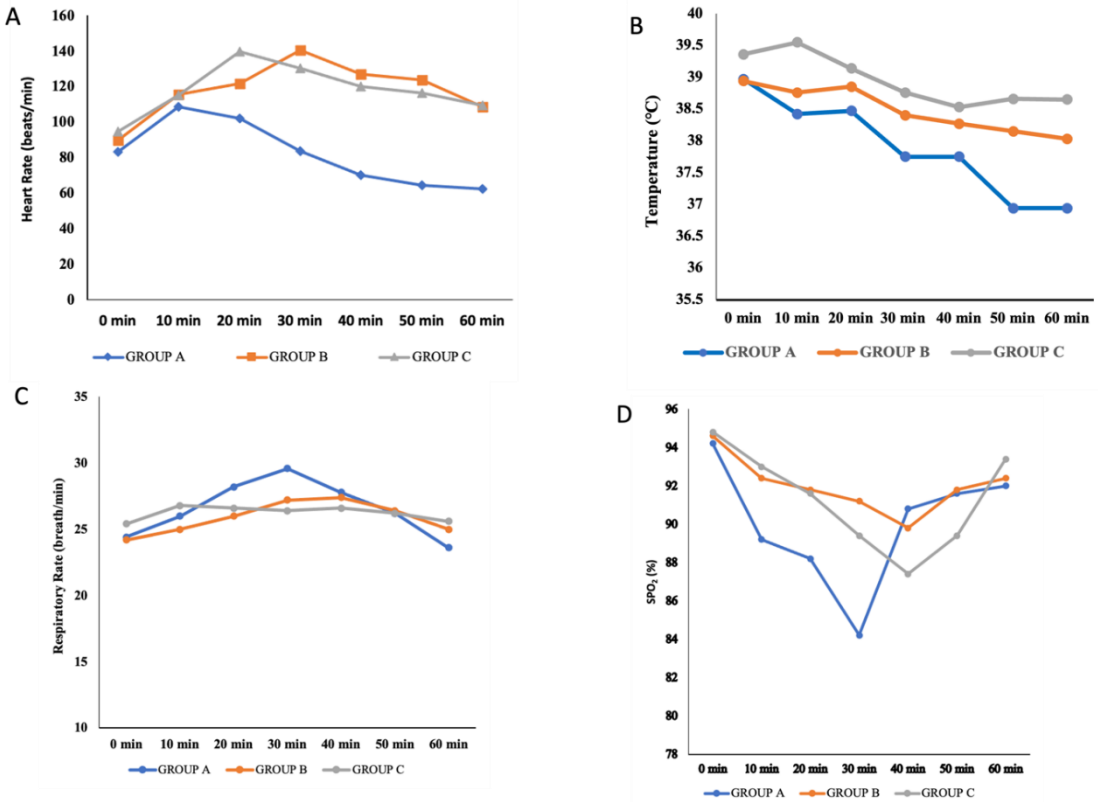

Figure 1. Mean physiological effects of xylazine-ketamine and xylazine-ketamine-atropine combinations in female dogs. **A**: Heart rate, **B**: Body temperature, **C**: Respiratory rate, **D**: Oxygen saturation (SpO_2) following administration of the anesthetic combinations.

Table 1. Effects of xylazine-ketamine and xylazine-ketamine-atropine combinations on physiological parameters in dogs

parameters	Heart rate (beats/minutes)			Temperature (°C)			Respiratory rate (breaths/minute)			SPO_2 (%)		
Time interval	Group A	Group B	Group C	Group A	Group B	Group C	Group A	Group B	Group C	Group A	Group B	Group C
0 minutes	83.20 ± 5.02^{a}	89.80 ± 5.40^{a}	94.60 ± 5.32^{a}	38.97 ± 0.77^{b}	38.94 ± 0.27^{b}	39.36 ± 0.05^{a}	24.40 ± 1.52^{a}	24.20 ± 0.84^{a}	25.40 ± 1.52^{a}	94.20 ± 1.48^{a}	94.60 ± 1.52^{a}	94.80 ± 1.64^{a}
10 minutes	108.60 ± 6.31^{b}	115.40 ± 6.19^{a}	115.00 ± 10.61^{a}	38.97 ± 0.82^{ab}	38.76 ± 0.93^{ab}	39.55 ± 0.27^{a}	26.00 ± 0.84^{a}	25.00 ± 0.71^{b}	26.80 ± 0.84^{a}	89.20 ± 1.10^{c}	92.40 ± 2.07^{a}	93.00 ± 1.87^{a}
20 minutes	102.00 ± 2.74^{c}	121.80 ± 4.09^{b}	139.60 ± 8.82^{a}	38.47 ± 0.49^{b}	38.85 ± 0.88^{b}	39.14 ± 0.22^{a}	28.20 ± 0.55^{a}	26.00 ± 1.22^{b}	26.60 ± 0.55^{b}	88.20 ± 1.10^{b}	91.80 ± 2.59^{a}	91.60 ± 1.67^{a}
30 minutes	83.60 ± 8.76^{c}	140.60 ± 6.66^{a}	130.20 ± 9.98^{b}	37.75 ± 0.22^{c}	38.40 ± 1.26^{b}	38.76 ± 0.44^{a}	29.60 ± 0.55^{a}	27.20 ± 1.10^{b}	26.40 ± 0.55^{c}	84.20 ± 2.17^{c}	91.20 ± 2.68^{a}	89.40 ± 1.34^{b}
40 minutes	70.20 ± 7.46^{c}	127.00 ± 5.92^{df}	120.20 ± 7.33^{bc}	37.75 ± 0.79^{a}	38.27 ± 1.33^{a}	38.53 ± 0.88^{a}	27.80 ± 1.52^{a}	27.40 ± 0.55^{a}	26.60 ± 1.52^{ab}	90.80 ± 1.64^{a}	89.80 ± 5.22^{ab}	87.40 ± 2.19^{b}
50 minutes	64.40 ± 5.90^{c}	123.60 ± 3.51^{a}	116.40 ± 6.43^{b}	36.94 ± 1.37^{a}	38.15 ± 1.34^{a}	38.66 ± 0.27^{a}	26.20 ± 1.48^{a}	26.40 ± 0.55^{a}	26.20 ± 1.48a	91.60 ± 0.55^{a}	91.80 ± 2.59^{a}	89.40 ± 1.82^{b}
60 minutes	62.60 ± 4.93^{b}	108.80 ± 6.38^{a}	109.60 ± 4.83^{a}	36.94 ± 1.26^{b}	38.03 ± 1.56^{a}	38.65 ± 0.16^{a}	23.60 ± 1.14^{b}	25.00 ± 0.71^{a}	25.60 ± 1.14^{a}	92.00 ± 0.71^{b}	92.40 ± 2.07^{b}	93.40 ± 1.14^{a}

Group A: Xylazine and ketamine in a 1:2 ratio, Group B: Xylazine and ketamine in a 1:2 ratio with the addition of atropine, Group C: Xylazine and ketamine in a 1:1 ratio. ^{a,b,c} Mean different superscript letters within the same row and for each factor differ significantly from each other ($p < 0.05$). Data are presented as mean ± SD.

3.2. Hematological parameters

The effects of different anesthetic combinations on hematological parameters, including RBC, WBC, Hb, platelets, and PCV, are illustrated in Table 2 and Figure 2. All hematological parameters were decreased 30 minutes after induction in all the experimental groups. The RBC and Hb levels decreased significantly in all treatment groups after 30 minutes of induction ($p < 0.05$). Group A demonstrated a significant decrease in WBC (17.14 ± 0.37 109/L), platelets (164.60 ± 3.03 109/L), and PCV (41.24 ± 1.13%) after 30 minutes of induction compared with pre-induction values ($p < 0.05$).

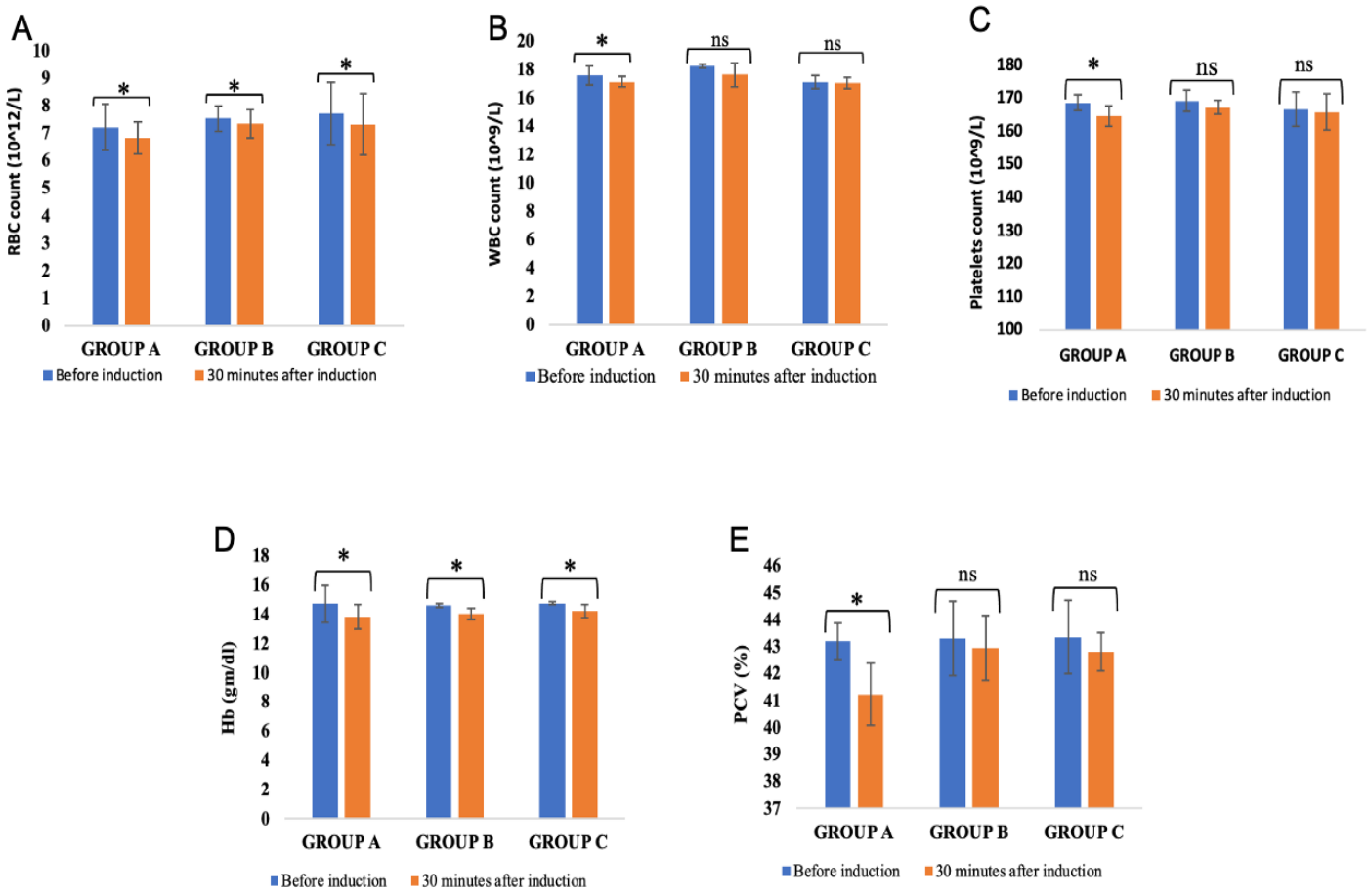

Figure 2. Hematological effects of xylazine-ketamine and xylazine-ketamine-atropine combinations in female dogs. **A**: Red blood cell count, **B**: White blood cell count, **C**: Platelet count, **D**: Hemoglobin concentration, **E**: Packed cell volume. Data are presented as mean ± SD. Group A: Xylazine and ketamine in a 1:2 ratio, Group B: Xylazine and ketamine in a 1:2 ratio with the addition of atropine, Group C: Xylazine and ketamine in a 1:1 ratio. Data are presented as mean ± SD.

Table 2. Effects of xylazine-ketamine and xylazine-ketamine-atropine combinations on hematological parameters in female dogs

Hematological parameters	Treatment groups	Before induction	30 minutes after induction	p-value
RBC (10^{12}/L)	Group A	7.22 ± 0.84[a]	6.82 ± 0.58[b]	P = 0.028
	Group B	7.54 ± 0.47[a]	7.33 ± 0.51[b]	P = 0.002
	Group C	7.72 ± 1.14[a]	7.32 ± 1.13[b]	P < 0.001
WBC (10^9/L)	Group A	17.62 ± 0.66[a]	17.14 ± 0.37[b]	P = 0.020
	Group B	18.27 ± 0.14[a]	17.63 ± 0.83[a]	P = 0.215
	Group C	17.14 ± 0.48[a]	17.07 ± 0.41[a]	P = 0.070
Platelets (10^9/L)	Group A	168.60 ± 2.30[a]	164.60 ± 3.03[b]	P = 0.047
	Group B	169.20 ± 3.27[a]	167.20 ± 2.17[a]	P = 0.108
	Group C	166.60 ± 5.18[a]	165.80 ± 5.50[a]	P = 0.751
Hb (mg/dL)	Group A	14.72 ± 1.26[a]	13.84 ± 0.84[b]	P = 0.010
	Group B	14.62 ± 0.11[a]	14.02 ± 0.38[b]	P = 0.008
	Group C	14.78 ± 0.11[a]	14.22 ± 0.44[b]	P = 0.018
PCV (%)	Group A	43.20 ± 0.67[a]	41.24 ± 1.13[b]	P = 0.028
	Group B	43.30 ± 1.39[a]	42.96 ± 1.19[a]	P = 0.058
	Group C	43.36 ± 1.35[a]	42.82 ± 0.70[a]	p = 0.159

[a, b] Mean values with different superscript letters differ significantly within the same row ($p < 0.05$). Group A: Xylazine and ketamine in a 1:2 ratio, Group B: Xylazine and ketamine in a 1:2 ratio with the addition of atropine, Group C: Xylazine and ketamine in a 1:1 ratio. Data are presented as mean ± SD.

4. Discussion

The present findings indicated that including atropine with xylazine-ketamine was associated with higher heart rates and reduced SpO_2 fluctuations than in the other groups. Furthermore, all administered combinations resulted in notable reductions in RBC and Hb levels. The rapid increase in heart rate observed in the present experiment may be due to the dose-dependent tachycardic effects of ketamine, consistent with previous reports[19]. The current findings related to the effects of ketamine were similar to those of Gebremedhin[20] but contrasted with those of Yohannes et al.[19], who observed a non-significant reduction in heart rate following anesthesia. Previous studies indicated that anticholinergics can prevent the bradyarrhythmia associated with an alpha-2 agonist[21,22] and can result in initial tachycardia[21]. Therefore, the increase in heart rate following the administration of the xylazine-ketamine combination with atropine may be attributed to the vagolytic property of atropine[23]. The reduction in body temperature observed in the current study following the administration of anesthesia may be attributable to the blockade of the hypothalamic thermoregulatory center[24]. The decreases in temperature after administration of the xylazine-ketamine combination observed in the present study were similar to the findings of Gebremedhin et al.[24] and Abdel-Hady et al.[25] in dogs using xylazine and ketamine as intravenous anesthesia. Additionally, Yohannes et al.[19] reported a decrease in temperature after ketamine anesthesia in a local breed of dogs. Unlike many anesthetic medications, ketamine has been shown to have cumulative effects on heart rate, blood pressure, and respiratory rate, resulting from heightened sympathetic activation[26], which may explain the initial increase in the dog's respiratory rate in the present study. The present study observed no notable change in respiratory rate in the group that received xylazine and ketamine in a 1:1 ratio. This result may reflect a dose-dependent effect, as the ketamine dose in the group receiving xylazine and ketamine at a 1:1 ratio was lower than in the groups receiving xylazine and ketamine at a 2:1 ratio or receiving atropine. The respiratory rate findings were consistent with those of Abdel-Hady et al.[25], who reported an initial increase in respiratory rate in dogs after using xylazine-ketamine as anesthetic drugs. This finding contrasted with those of Ibrahim[18], who recorded a notable decrease in respiratory rate in dogs while using ketamine-xylazine at a constant infusion rate. The initial drop in SPO_2 in experimental dogs could be related to the anesthetic drugs' suppression of the lungs' ventilatory function[27]. Abdel-Hady et al.[25] and Kamal et al.[28] reported similar findings, including an initial drop in SpO_2 in dogs after anesthesia. Furthermore, the vasoconstrictive properties of xylazine and ketamine may result in decreased pulse oximeter readings[4].

During anesthesia, the analysis of blood cells outside the bloodstream could explain the observed decreases in RBCs, WBCs, Hb, platelets, and PCV between the pre- and post-induction samples[25]. The current findings were consistent with those of Kamal et al.[28], who reported decreases in different hematological parameters after induction in dogs using xylazine-ketamine. Moreover, Rubio et al.[29] supported the finding of the present study who also found the decrease in different hematological parameters in dogs after induction of anesthesia while doing ovariohysterectomy. The spleen is generally known as the organ capable of sequestering blood cells like RBCs, WBCs, and Platelets[30], and when anesthetic agents cause the relaxation of the spleen's blood vessels, it can lead to a decrease in the concentration of circulating blood cells in the peripheral blood or an increase in the spleen's reserve pool[31].

5. Conclusion

The present findings demonstrated that xylazine and ketamine combined with atropine provided a comparatively more stable anesthetic condition during ovariohysterectomy. Further investigation is suggested to find the combination effect of xylazine and ketamine with and without atropine on other hematological and biochemical parameters.

Declarations

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Authors' contributions

All authors contributed to the study's conception and design, as well as to finalizing the research and manuscript. The research was conceptualized by Manish Gautam. Swastika Sapkota, Manish Gautam, and Arjun Aryal designed and finalized the methodology. Data collection, data curation, investigation, and original draft writing were conducted by Swastika Sapkota. Data analysis and validation were undertaken by Manish Gautam and Swastika Sapkota. Draft review and editing were performed by Manish Gautam and Arjun Aryal. The resourcing of the research and supervision were managed by Arjun Aryal. All authors have read and approved the final edition of the manuscript.

Availability of data and materials

The raw data set and materials will be made accessible by the corresponding author upon a reasonable request.

Competing interests

The authors declare no conflict of interest in the present study

Ethical considerations

All data presented in this study are original findings and were not retrieved or manipulated from elsewhere, and the authors take full responsibility for the data originality before submission and during the peer review process. The authors have observed all ethical considerations, including plagiarism checks. The study has not been concurrently submitted to any other journal. Additionally, the manuscript was composed without the assistance of any AI tools.

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