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Original Article

Efficacy, Safety, and Post-Operative Complications of Three Anesthetic Protocols for Ovariohysterectomy in Rabbits

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ABSTRACT

Introduction: Rabbits are sensitive to anesthesia and prone to perioperative complications, such as cardiorespiratory depression and hypothermia. Choosing a safe, effective anesthetic protocol is essential for surgeries such as ovariohysterectomy. The present study aimed to evaluate and compare the efficacy and safety of three anesthetic protocols, including ketamine, xylazine-ketamine, and diazepam-ketamine, in rabbits undergoing ovariohysterectomy.

Materials and methods: Forty-five young adult female rabbits aged 7-12 months and weighing 0.5-1.9 kg were used in this study. Rabbits were randomly divided into three treatment groups, with 15 rabbits in each group. Each rabbit was considered one biological replicate; therefore, each treatment group had 15 biological replicates. The first group received ketamine at 60 mg/kg of body weight (BW), the second group received xylazine and ketamine (xylazine at 3 mg/kg with ketamine at 35 mg/kg of BW), and the third group received diazepam-ketamine (diazepam at 1.0 mg/kg with ketamine at 25 mg/kg of BW) by intramuscular injection. Anesthetic indices, including onset of loss of righting reflex (OLRR), onset of analgesia (OA), and duration of analgesia (DA), were recorded. Heart rate, respiratory rate, and rectal temperature were measured at 10-minute intervals for 60 minutes. Post-operative complications, including anorexia, hypotension, hypoxemia, hyperthermia, hypothermia, self-trauma, ataxia, delayed recovery, gastrointestinal stasis, bloat, infection, and death, were monitored for 15 days.

Results: Ketamine produced the fastest OLRR at 3.59 ± 0.106 minutes. The xylazine-ketamine group produced the longest DA at 70.60 ± 1.501 minutes. The xylazine-ketamine group demonstrated progressive cardiovascular, respiratory, and thermoregulatory depression, including declining heart rate (171.13 ± 0.52 bpm), reduced respiratory rate (55.53 ± 0.26 bpm), and hypothermia (36.33 ± 0.80 °C). The diazepam-ketamine group demonstrated moderate physiological changes with comparatively stable body temperature (38.5 ± 0.11°C). Anorexia was the most common post-operative complication across all groups. Bloat was most frequent in the ketamine group, followed by the xylazine-ketamine group.

Conclusion: Ketamine was suitable for short procedures requiring rapid induction and relative physiological stability, such as neutering, dental scaling, tooth extraction, and catheterization. Xylazine-ketamine provided prolonged analgesia but required careful cardiovascular, respiratory, and thermal monitoring. Diazepam-ketamine offered a more physiologically balanced response.

1. Introduction

Rabbits are widely used as animal models in biomedical studies and experimental surgery, and have also gained considerable popularity as companion animals[1,2]. Despite their widespread use, safe and effective anaesthetic management in

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rabbits remains a significant clinical challenge. Unlike dogs and cats, rabbits have perioperative mortality rates of 1.39%-4.8% compared to 0.1%-0.2% in dogs and cats, with cardiovascular and respiratory complications being the most frequently reported causes of death[3,4]. Rabbits are prone to life-threatening complications during and after anesthesia, including respiratory arrest, cardiovascular depression, hypothermia, and gastrointestinal (GI) stasis, with cardiorespiratory events accounting for approximately 40% of anesthesia-related deaths[3-5].

Due to the practical limitations of inhalant anesthetic delivery in rabbits, including stress-induced apnoea, breath-holding, and equipment constraints, injectable anesthetic protocols have become increasingly preferred in clinical and experimental research settings[6]. Among injectable protocols, ketamine-based combinations are most widely used. Ketamine, a dissociative anesthetic, produces rapid immobilization but offers limited muscle relaxation and analgesia when used alone[7]. To overcome these limitations, ketamine is commonly combined with either xylazine (an alpha-2 adrenergic agonist) or diazepam (a benzodiazepine)[8].

The xylazine-ketamine (XK) combination is well established for producing surgical-grade anesthesia in rabbits through a synergistic mechanism. Xylazine enhances sedation and analgesia via central alpha-2 adrenergic activity, while ketamine provides dissociative anesthesia[9,10]. However, XK is associated with significant cardiovascular and respiratory depression, particularly bradycardia and hypoxemia in rabbits[11,12]. The diazepam-ketamine (DK) combination provides effective muscle relaxation and reduces anxiety with potentially less cardiorespiratory compromise; however, its analgesic efficacy remains controversial and is considered insufficient for painful surgical procedures[6,13].

Ovariohysterectomy is one of the most frequently performed elective abdominal surgeries in veterinary practice, particularly in rabbits, where it is used for population control and prevention of uterine diseases such as adenocarcinoma, endometrial hyperplasia, pyometra, and mammary tumors[14,15]. The surgery requires reliable induction of general anesthesia, adequate analgesia, and stable physiological conditions throughout the procedure. Despite numerous studies evaluating individual anesthetic agents in rabbits[16-18], a comprehensive comparison of ketamine, XK, and DK protocols specifically in the context of ovariohysterectomy, including detailed post-operative complication monitoring, remains limited in the literature. The present study aimed to evaluate and compare anesthetic indices in rabbits using K, XK, and DK anesthesia protocols, monitor changes in heart rate, respiratory rate, and rectal temperature during the first 60 minutes of anesthesia, and assess the types and frequencies of post-operative complications associated with each protocol over a 15-day observation period.

2. Materials and Methods

2.1. Ethical approval

All animal procedures were conducted in strict accordance with internationally accepted animal welfare guidelines, including the 3R principles (Replacement, Reduction, and Refinement). The study was approved by the Department of Surgery and Theriogenology, Faculty of Animal Science and Veterinary Medicine, Sher-e-Bangla Agricultural University, Dhaka, Bangladesh. Every effort was undertaken to minimize animal suffering throughout the study.

2.2. Animals

The present study involved 45 young adult female rabbits (*Oryctolagus cuniculus*) aged 7-12 months, weighing 0.5-1.9 kg. Rabbits were purchased from the Katabon Pet Market, New Elephant Road, Dhaka-1205, Bangladesh. The experiment was conducted at the Department of Surgery and Theriogenology, Faculty of Animal Science and Veterinary Medicine, Sher-e-Bangla Agricultural University, Dhaka-1207, from October 2023 to May 2024, including animal procurement, a two-week acclimatization period, staged experimental procedures, postoperative monitoring, and final assessments. The procedures were performed in batches due to facility availability, animal management requirements, and staffing constraints.

2.3. Housing and management

Rabbits were acclimatized for two weeks prior to the start of the experiments under the following housing and feeding conditions. Rabbits were individually housed in clean cages (approximately 60 × 45 × 45 cm) with sufficient space for free movement under controlled environmental conditions at 18-21°C and 55-65% relative humidity. Rabbits were fed green grass, cauliflower, carrots, spinach (*Ipomoea aquatica*), and potato (*Solanum tuberosum*) leaves *ad libitum*, with unrestricted access to clean drinking water[19]. Before the experimental procedures, baseline physiological parameters, including heart rate, respiratory rate, and rectal temperature, were established from all rabbits over the study period from October 2023 to May 2024.

2.4. Anesthetic protocols

The drugs used in this experiment are presented in Table 1. The three anesthetic protocols are described in Table 2. A total of 45 rabbits were randomly divided into three groups of 15. Each group received one protocol administered intramuscularly (IM). The first group received ketamine HCl (G-Ketamine®, 50 mg/mL, Gonosashasthaya Pharma Ltd., Bangladesh) at 60 mg/kg body weight (BW), with maintenance doses of ketamine at 30 mg/kg of BW (half of the induction dose) administered as required (Group K)[20]. The second group received xylazine HCl (Xylazine®, 20 mg/ml, India) at 3 mg/kg BW, administered 30 minutes before ketamine at 35 mg/kg BW IM (Group XK), with ketamine maintained at half the induction dose (17.5 mg/kg BW)[21]. The third group received diazepam (Sedil®, 5 mg/ml, Square Pharmaceuticals, Bangladesh) at 1.0 mg/kg of BW, followed by ketamine at 25 mg/kg BW IM, with maintenance ketamine at half the induction dose (12.5 mg/kg BW) administered 30 minutes after induction (Group

DK)[8]. Animals were fasted for 12 hours prior to anesthesia induction, with free access to water until two hours before the procedure. Each rabbit was weighed immediately before drug administration to ensure accurate dosing.

Table 1. Medication information used on rabbits during the study

Medicines (trade name)	Active ingredients	Company and country
Xylazine Hcl®	Xylazine HCl (20 mg/ml)	Xylazine, India
G-ketamine®	Ketamine HCl (50 mg/ml)	Gonosashasthaya Pharma Ltd, Bangladesh
Sedil	Diazepam (5 mg/ml)	Square Pharmaceuticals, Bangladesh
Trizone	Ceftriaxone (100 mg/ml)	Acme Laboratories, Bangladesh
Melvet	Meloxicam (5 mg/ ml)	Acme Laboratories, Bangladesh

Table 2. Anesthetic medicine combinations and maintenance doses in 7–12-month-old rabbits for ovariohysterectomy

Group	Induction	Maintenance	Justification
Group K	Ketamine HCl at 60 mg/kg of body weight	Half a dose of induction (Ketamine HCl 30 mg/kg BW)	Ketamine was used alone to assess the baseline anesthetic effects without additional sedatives or analgesics. Although ketamine lacks strong analgesic properties, this protocol was included to evaluate its safety and stability.
Group XK	Xylazine HCl at 3 mg/kg + Ketamine at 35 mg/kg of body weight	Half a dose of induction (Ketamine HCl 17.5 mg/kg BW)	Xylazine provided sedation and analgesia, whereas ketamine induced anesthesia. The dose was chosen within clinically acceptable ranges.
Group DK	Ketamine HCl at 25 mg/kg + Diazepam At 1.0 mg/kg of body weight	Half a dose of induction (Ketamine HCl 12.5 mg/kg BW)	Diazepam was used as a muscle relaxant and sedative to complement ketamine's anesthetic effects, aiming to assess its impact on cardiorespiratory stability.

2.5. Anesthetic indices

The following anesthetic indices were recorded according to the method described by Oguntoye and Oke[8]. The onset of loss of righting reflex (OLRR) was defined as the time elapsed in minutes from the administration of the ketamine injection until the animal lost its ability to maintain the righting reflex. The onset of analgesia (OA) was recorded as the time in minutes from ketamine injection until the pedal withdrawal reflex was absent in both hind limbs, which was evaluated by applying pressure to the hind paw using hemostatic forceps closed to the first ratchet. The duration of analgesia (DA) was determined as the total time in minutes between the disappearance and subsequent return of the pedal withdrawal reflex in either hind limb, which was assessed by hind paw pinching performed at two-minute intervals[8].

2.6. Physiological parameter monitoring

Heart rate (beats per minute) was measured by placing a stethoscope over the second to fifth intercostal spaces on the left. Respiratory rate (breaths per minute) was determined by counting the number of chest inflations and deflations. Rectal temperature (RT, °C) was measured using a digital clinical thermometer. These three parameters were recorded at baseline (0 min) and every 10 minutes for 60 minutes after administration of three anesthetic protocols[22].

2.7. Surgical procedure

Following anesthetic induction, each rabbit was placed in right lateral recumbency on a cushioned surgical table. Ovariohysterectomy was performed under aseptic conditions using standard surgical techniques by a trained veterinary surgeon[23].

2.8. Post-operative care

The surgical site was cleaned with sterile gauze and dusted with Sulphanilamide BP powder (Sumid-Vet® powder, Square Pharmaceuticals, Bangladesh). Ceftriaxone sodium (Trizone Vet®, 100 mg/mL, Acme Laboratories Ltd., Bangladesh) was administered intravenously at 0.1 mg/kg of BW once daily for seven days. Meloxicam (Melvet®, 5 mg/mL, Acme Laboratories Ltd., Bangladesh) was administered subcutaneously at 0.2 mg/kg BW once daily for three days[24]. Sutures were removed on post-operative day 15. Each rabbit was monitored daily for 15 days post-surgery. The following complications were recorded, including anorexia, GI stasis, bloat, infection, self-trauma, ataxia, hypotension, hypertension, hypoxemia, hypothermia, and delayed recovery.

2.9. Statistical analysis

Data were expressed as Mean ± standard error of the Mean (SEM) for 15 rabbits per group. One-way analysis of variance (ANOVA) was used to compare OLRR, OA, and DA among the three groups, followed by Tukey's post-hoc test for pairwise comparisons. Differences were considered statistically significant at a p-value less than 5 % ($p < 0.05$).

3. Results

3.1. Anesthetic indices

The OLRR, OA, and DA for the three groups were summarized in Table 3. The fastest OLRR was observed in Group K (3.59 ± 0.106 min), followed by Group XK (3.99 ± 0.164 min) and Group DK (5.17 ± 0.127 min), with statistically significant differences among all groups ($p < 0.05$). The OA was the shortest in the Group K (3.96 ± 0.060 min) and longest in the Group XK (6.92 ± 0.136 min). The Group XK exhibited the longest DA (70.60 ± 1.501 min), significantly greater than Group K (53.13 ± 0.735 min) and Group DK (47.46 ± 0.716 min; $p < 0.05$).

Table 3. Onset of loss of righting reflex, onset of analgesia, and duration of analgesia in rabbits that received different anesthetic medications

Criteria	K	XK	DK
Onset of loss of righting reflex (min)	3.59 ± 0.106[a]	3.99 ± 0.164[b]	5.17 ± 0.127[c]
Onset of analgesia (min)	3.96 ± 0.060[a]	6.92 ± 0.136[c]	5.98 ± 0.038[b]
Duration of analgesia (min)	53.13 ± 0.735[b]	70.60 ± 1.501[c]	47.46 ± 0.716[a]

K: Rabbits received ketamine HCl at 60 mg/kg of body weight, XK: Rabbits received xyazine HCL at 3 mg/kg + ketamine at 35 mg/kg of body weight, DK: Rabbits received ketamine HCl at 25 mg/kg + diazepam at 1.0 mg/kg of body weight. Data are presented as Mean ± SEM. Each group contained 15 rabbits. [a,b,c] Mean different superscript letters demonstrated significant differences in a row among groups at $p < 0.05$.

3.2. Heart and respiratory rates

Heart rate and respiratory rate data were presented in Table 4. At baseline (0 min), Group XK had the highest mean heart rate (250.40 ± 1.37 bpm), followed by Group DK (192.67 ± 0.81 bpm) and Group K (149.47 ± 0.47 bpm). In Group XK, heart rate declined progressively, reaching 171.13 ± 0.52 bpm at 60 minutes. Heart rate in groups K and DK remained relatively stable throughout the observation period, whereas it decreased in Group XK. Group K consistently recorded the highest respiratory rate, starting at 171.29 ± 0.79 breaths/min and remaining elevated (173.07 ± 0.54 breaths/min) at 60 minutes. Group XK demonstrated a marked and progressive decline in respiratory rate relative to baseline, decreasing from 124.6 ± 0.89 breaths/min to 65.20 ± 0.28 breaths/min at 60 minutes. Group DK demonstrated a moderate and stable respiratory rate value (99.10 ± 0.40) throughout the observation period compared to groups XK and K.

3.3. Rectal temperature

Body temperature data were presented in Table 5. Baseline temperatures were 38.00°C for Group K, 38.00°C for Group XK, and 39.0°C for Group DK. Compared with their respective baseline values[16], Group K indicated minimal fluctuation, with a slight dip at 10 minutes (37.20°C) and recovery to 38.93°C by 60 minutes. Group XK demonstrated a progressive decline, reaching a minimum of 36.33°C at 50 minutes, before a mild recovery to 38.07°C at 60 minutes, suggesting a notable hypothermic effect. Group DK exhibited moderate fluctuations, with a trough at 40 minutes (37.5°C) and a return to baseline at 60 minutes (39.0°C).

Table 4. Heart and respiratory rates of the rabbits at different times after receiving different anesthetic medications

Time (minute)	Heart rate (Beats per minute)			Respiratory rate (Breaths per minute)		
	K	XK	DK	K	XK	DK
0	149.47 ± 0.47	250.40 ± 1.37	192.67 ± 0.81	171.29 ± 0.79	124.6 ± 0.89	97.25 ± 1.52
10	169.73 ± 0.54	236.80 ± 0.88	203.13 ± 0.49	117.07 ± 1.25	66.4 ± 0.27	75.69 ± 0.73
20	151.13 ± 0.60	210.60 ± 0.62	190.73 ± 0.48	145.07 ± 0.88	63.33 ± 0.54	75.69 ± 0.48
30	165.20 ± 0.78	172.33 ± 1.11	195.27 ± 0.33	157.07 ± 0.72	55.53 ± 0.26	83.69 ± 0.074
40	175.27 ± 0.45	185.53 ± 0.77	204.20 ± 0.24	160.07 ± 1.08	60.67 ± 0.27	95.25 ± 0.57
50	163.73 ± 0.56	175.67 ± 0.72	199.80 ± 0.33	167.00 ± 0.48	67.13 ± 0.35	95.25 ± 0.61
60	156.47 ± 0.47	171.13 ± 0.52	189.20 ± 0.34	173.07 ± 0.54	65.20 ± 0.28	122.50 ± 0.64

K: Rabbits received ketamine HCl at 60 mg/kg of body weight, XK: Rabbits received xyazine HCL at 3 mg/kg + ketamine at 35 mg/kg of body weight, DK: Rabbits received ketamine HCl at 25 mg/kg + diazepam at 1.0 mg/kg of body weight. Data are presented as Mean ± SEM.

Table 5. Body temperature of the rabbit at different times after receiving different anesthetic medications

Time (minute)	Body temperature (°C)		
	K	XK	DK
0	38.00 ± 0.00	38.00 ± 0.00	39.0 ± 0.00
10	37.20 ± 0.17	38.30 ± 0.45	38.4 ± 0.30
20	38.06 ± 0.16	38.00 ± 0.00	38.8 ± 0.15
30	38.27 ± 0.14	37.47 ± 0.50	39.0 ± 0.20
40	38.40 ± 0.12	36.87 ± 0.60	37.5 ± 0.15
50	37.07 ± 0.07	36.33 ± 0.80	39.5 ± 0.17
60	38.93 ± 0.11	38.07 ± 0.50	39.0 ± 0.30

K: Rabbits received ketamine HCl at 60 mg/kg of body weight, XK: Rabbits received xyazine HCL at 3 mg/kg + ketamine at 35 mg/kg of body weight, DK: Rabbits received ketamine HCl at 25 mg/kg + diazepam at 1.0 mg/kg of body weight. Data are presented as Mean ± SEM.

3.4. Post-operative complications

The post-operative complications recorded in Group K are shown in Figure 1, while those for Group XK and Group DK are presented in figures 2 and 3, respectively. Anorexia and bloat were each observed in 100% of rabbits in Group K. Delayed recovery occurred in 33.33% of cases. GI stasis was observed in 20% of rabbits, secondary infection due to self-trauma in 13.33%, and hyperthermia and hypothermia each in 6.67%. Anorexia occurred in 100% of rabbits in Group XK. Bloat was recorded in 66.67% of cases. Delayed recovery and GI stasis were noted in 13.33% and 20% of rabbits, respectively. Self-trauma and hypotension were observed in a minority of cases in Group XK. In Group DK, all

monitored rabbits exhibited anorexia and bloat at a frequency of 100%, while GI stasis was observed in 20% of rabbits. Hyperthermia, hypothermia, and infection were recorded less frequently, affecting 6.67%, 6.67%, and 13.33% of rabbits, respectively. Self-trauma was noted in 13.30% of rabbits.

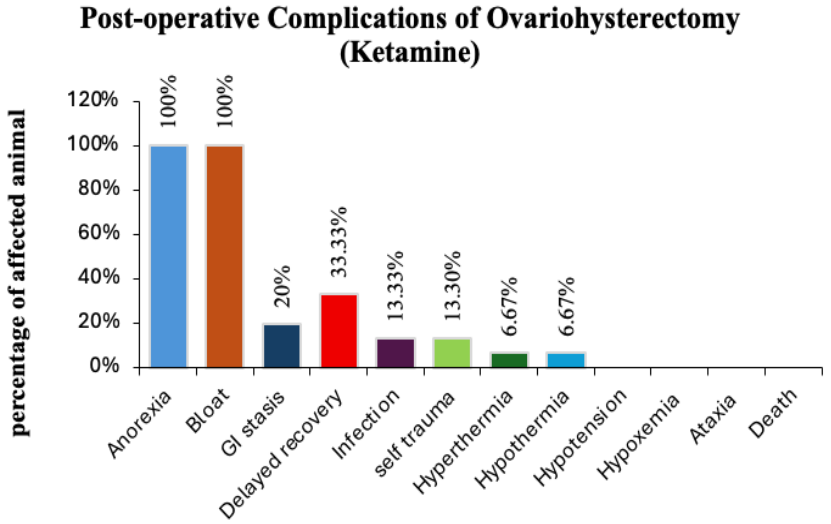

Figure 1. Post-operative complications in rabbits with intramuscularly administered ketamine through ovariohysterectomy

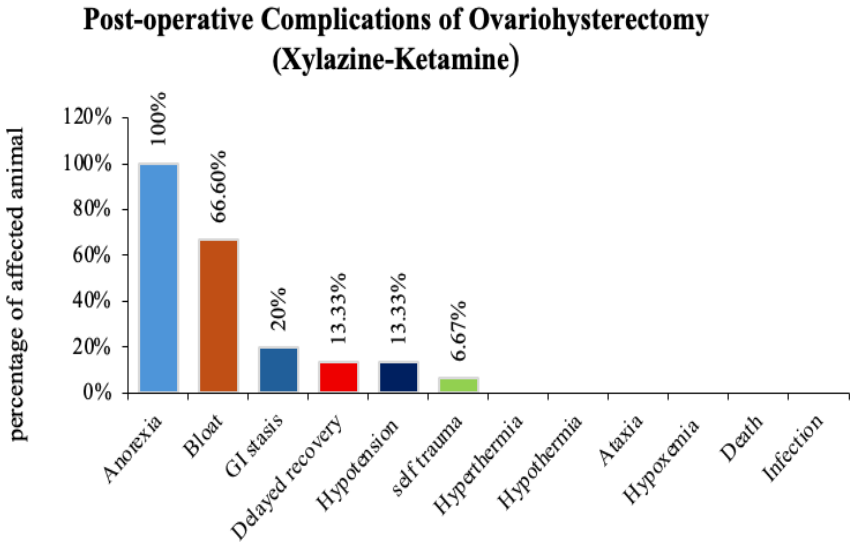

Figure 2. Post-operative complications in rabbits with intramuscularly administered xylazine-ketamine combination through ovariohysterectomy

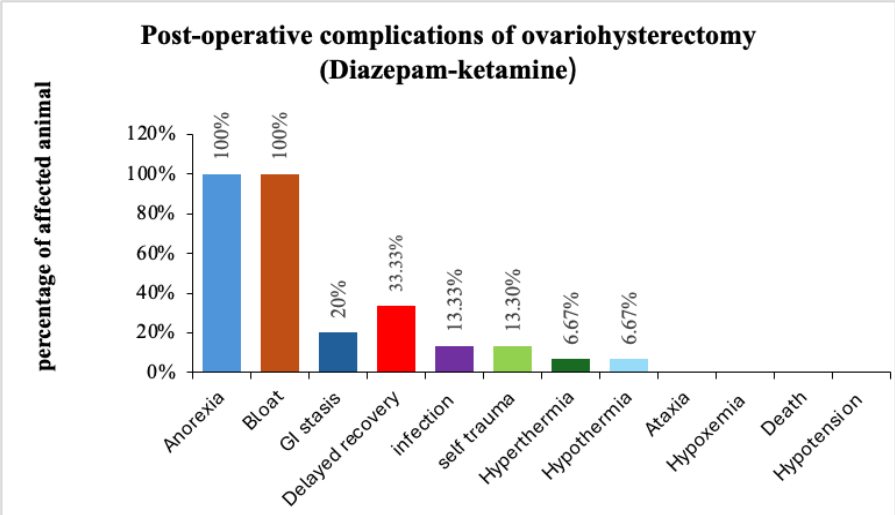

Figure 3. Post-operative complications in rabbits with intramuscularly administered diazepam-ketamine combination through ovariohysterectomy

4. Discussion

The present findings demonstrated that each anesthetic protocol had distinct pharmacological advantages and clinical limitations, underscoring the importance of selecting a protocol based on the nature of the procedure, including its duration, invasiveness, and anticipated hemodynamic stress. Additionally, the individual patient's clinical status, encompassing comorbidities, age, and baseline cardiovascular and respiratory function, should be carefully considered when selecting an appropriate anesthetic protocol.

4.1. Anesthetic indices

The fastest OLRR was observed in rabbits that received ketamine only, consistent with ketamine's high lipid solubility, which enables rapid central nervous system (CNS) penetration and a rapid dissociative induction. A similar finding was reported by Schmid et al.[5], who noted that ketamine-based protocols without sedative premedication consistently produced faster OLRR than combinations of medicines in rabbits. The XK combination produced the longest DA compared to the K and DK combinations. Group XK demonstrated the longest DA among the three protocols. The extended analgesic duration observed with the XK combination reflects the synergistic pharmacodynamic interaction between xylazine and ketamine. Specifically, xylazine acts as a central alpha-2 adrenergic agonist, inhibiting norepinephrine release at presynaptic terminals and activating descending pain-modulating pathways. Consequently, this action prolongs the analgesic effect of the ketamine[25]. These results were consistent with the findings of Abduljaleel[26], who similarly reported a longer analgesic duration with the XK combination compared to the DK combination in rabbits. The shortest DA was recorded in rabbits that received the DK combination. Diazepam has limited intrinsic analgesic activity, and its potential to accelerate the redistribution of ketamine from the CNS may further reduce analgesic duration[8]. Multiple studies have confirmed that the DK combination provided inadequate analgesia for painful surgical procedures and should therefore be used with caution in ovariohysterectomy or other procedures requiring prolonged pain control[26].

4.2. Heart and respiratory rates

The elevated baseline heart rate observed in rabbits receiving the XK combination was attributable to xylazine's biphasic cardiovascular effects. This effect was characterized by an initial transient sympathomimetic phase, followed by central sympathoinhibition, leading to progressively slower heart rate, peripheral vasoconstriction, and higher arterial pressure. These findings were consistent with a previous report in rabbits that received XK combination anesthesia[27]. The subsequent progressive decline in heart rate to 171.13 ± 0.52 bpm at 60 minutes was consistent with the pharmacological mechanism of xylazine and has been reported in previous studies that administered XK combination in rabbits within comparable dose ranges[5,6]. The marked decline in respiratory rate in the rabbits that received XK combination, from 124.6 ± 0.89 breaths/min at baseline to 65.20 ± 0.28 breaths/min at 60 minutes, reflected the well-documented respiratory depressant effect of xylazine through central alpha-2 adrenergic stimulation[3]. The current findings underscore the importance of accurate respiratory monitoring and the use of supplemental oxygen when the XK combination is employed in rabbit surgical procedures. The group that received ketamine maintained the highest and most stable respiratory rate throughout the observation period, consistent with ketamine's sympathomimetic properties, which sustain central respiratory effects[28]. The rabbits that received the DK combination demonstrated moderate and stable cardiorespiratory parameters throughout the study, indicating that diazepam's anxiolytic and mild central depressant effects help to moderate, rather than worsen, ketamine's cardiovascular stimulation[5].

4.3. Rectal temperature

The rabbits that received the XK combination demonstrated a progressive decline in rectal temperature, reaching a minimum of 36.33°C at 50 minutes. This hypothermic response was attributed to xylazine's inhibition of the hypothalamic thermoregulatory center, which reduced metabolic heat production and impaired peripheral vasoconstriction[26]. The mild recovery from 36.33°C to 38.07°C at 60 minutes likely reflected a decline in plasma xylazine concentrations at that time point. Xylazine-induced hypothermia has been consistently reported in laboratory rabbits and can be clinically important, particularly in low-weight animals or cold environments[4]. Active thermal support, including warm water bottles, heating pads, or insulated recovery areas, is strongly recommended when using the XK combination. The rabbits that received only ketamine maintained near-baseline temperatures throughout, with only a transient dip at 10 minutes (37.20°C), followed by recovery to 38.93°C at 60 minutes, reflecting ketamine's sympathomimetic effects that sustain cardiovascular output and metabolic heat generation. The rabbits that received the DK combination exhibited moderate fluctuations, with the lowest rectal temperature recorded at 40 minutes (37.5°C) and returned to baseline (39.0°C) by 60 minutes, suggesting that diazepam at 1.0 mg/kg of BW combined with ketamine at 25 mg/kg of BW did not substantially impair thermoregulation.

4.4. Post-operative complications

All rabbits exhibited anorexia after the procedure, which was expected due to the GI sensitivity of rabbits to surgical stress, pain, and the residual influence of anesthetic agents on gut motility. This post-operative inappetence was closely associated with GI stasis, a condition driven by stress-induced catecholamine release and pain-mediated suppression of normal enteric reflexes[3]. These findings highlighted the practical importance of initiating nutritional support early in the recovery period, including syringe feeding and the use of gut motility promoters, irrespective of the anesthetic protocol used[29]. The 100% incidence of

bloat in rabbits that received only ketamine was higher than the 66.67% observed in rabbits that received a XK combination. This effect could be attributed to ketamine's lack of anxiolytic premedication, which leads to heightened post-operative stress, aerophagia, and gas accumulation in the GI tract. Bloat and GI stasis were considered serious post-operative complications in rabbits that can quickly develop into life-threatening obstructions when unmanaged[4]. The rabbits that received the DK combination exhibited the broadest complication profile, with anorexia, GI stasis, bloat, hypotension, infection, and delayed recovery collectively recorded across rabbits. Despite its cardiovascular stabilizing properties, diazepam has limited analgesic efficacy, which may lead to inadequate post-operative pain control and predispose rabbits to pain-mediated GI dysfunction, autonomic instability, and prolonged sedation[8,27]. Delayed recovery in the rabbits that received ketamine only (33.33%) reflected the prolonged redistribution and hepatic metabolism of ketamine when administered without sedative premedication, consistent with the findings of Marietta et al.[30]. The low incidence of wound infection and self-trauma across all groups reflected the effectiveness of the prophylactic ceftriaxone and meloxicam treatment protocols employed. However, the absence of microbiological culture data represented a limitation, as specific causative pathogens could not be identified.

Several limitations should be acknowledged. First, the sample size of 15 rabbits per group, though comparable to published studies in this field, limited the statistical power to detect smaller between-group differences. Second, the study was conducted at a single institution with a specific weight range (0.5-1.9 kg) and breed, potentially limiting the generalisability of the findings to other rabbit populations. Third, pulse oximetry and capnography were not employed due to equipment constraints, limiting precise assessment of oxygenation and ventilation. Future studies should incorporate these monitoring modalities alongside larger, multi-breed sample sizes and multimodal anesthetic protocols to further optimize surgical safety in rabbits.

5. Conclusion

The present study demonstrated that ketamine alone was best suited for short-duration procedures due to its rapid induction and cardiorespiratory stability in rabbits, whereas the xylazine-ketamine combination was preferable for prolonged surgeries owing to its extended analgesic duration, albeit requiring close cardiovascular and thermal monitoring. The diazepam-ketamine protocol offered physiological balance but exhibited limited analgesia and a broad post-operative complication profile, warranting further refinement. Protocol selection should be guided by procedure duration, animal condition, and available monitoring facilities. However, the single-institution study design, moderate sample size, and absence of advanced monitoring tools such as pulse oximetry and capnography should be taken into account when interpreting the current study's results. Future studies incorporating multimodal anesthetic approaches, objective monitoring tools, and culture and sensitivity data are recommended to further improve anesthetic safety and better characterize post-operative infection profiles in rabbits.

Declarations

Acknowledgments

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Authors' contributions

Sadia Islam conceptualized the study, performed the surgical procedures and experimental activities, collected and analyzed data, and wrote and prepared the original manuscript. Md Anowarul Haque designed the study protocol, contributed to data analysis, and critically revised the manuscript. Md Rashedul Islam provided principal supervision throughout the study, contributed to the methodology and project administration, and gave final approval of the manuscript for submission. All authors have read and approved the last edition of the manuscript.

Availability of data and materials

The data that support the findings of the present study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare no conflict of interest.

Ethical considerations

The authors confirmed that this manuscript is original, free from plagiarism, and complies with all relevant ethical and publication guidelines. The authors used Grammarly only for language editing, grammar correction, and sentence restructuring. No AI-assisted tool was used to generate scientific content, data, results, or interpretations. All authors took full responsibility for the final edition of the manuscript.

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