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Cardiopulmonary and Thermoregulatory Profile of Xylazine-Ketamine Anesthesia Following Preemptive Administration of Nefopam or Tramadol in Himalayan tom cats

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ABSTRACT

Background & aim: This study compared the intra-operative cardiopulmonary and thermoregulatory effects of a xylazine-ketamine anesthetic protocol preceded by preemptive Nefopam or tramadol administration in male Himalayan cats.

Materials and Methods: 24 adult male Himalayan cats were allocated into three groups (n=8): control (xylazine-ketamine alone), tramadol (4 mg/kg preemptive), and Nefopam (2 mg/kg preemptive). Heart rate, systolic/diastolic blood pressure (non-invasively via oscillometry), respiratory rate, peripheral oxygen saturation (SpO_2), and rectal temperature were recorded at 10-minute intervals. Unintubated cats breathed room air spontaneously; anesthetic depth was assessed via pedal withdrawal and palpebral reflexes. No rescue analgesics were administered postoperatively, as preemptive dosing provided sufficient residual analgesia during early recovery, confirmed by stable parameters.

Results: Preemptive analgesia produced distinct cardiopulmonary profiles. The tramadol group developed pronounced bradycardia, with heart rates falling to subnormal levels after 70 minutes. Conversely, the Nefopam group maintained a stable but subnormal heart rate, accompanied by significant hypertension and elevated systolic pressure at multiple time points ($P < 0.05$). The control group showed initial tachycardia with a gradual decline. Nefopam preserved respiratory rates better than tramadol, though both treatment groups experienced transient SpO_2 reductions versus controls, and significant hypothermia developed by 50 minutes (Nefopam) and 60 minutes (tramadol).

Conclusions: Preemptive Nefopam or tramadol combined with xylazine-ketamine produced predictable yet divergent physiological responses in male Himalayan cats. Clinicians should anticipate tramadol-associated bradycardia/hypothermia and Nefopam-associated systemic hypertension when selecting preemptive analgesics, guiding intra-operative monitoring in feline anesthesia.

Introduction

The combination of xylazine and ketamine is widely used in feline anesthesia for its synergistic effects, providing sedation, analgesia, and muscular relaxation [1]. This anesthetic combination has been extensively evaluated across various species, including rabbits, establishing a baseline for its physiological effects [2]. However, this protocol is known to induce significant physiological disturbances, including profound cardiovascular impact and respiratory depression [3]. Understanding and mitigating these effects is paramount for ensuring patient safety during the perioperative period.

The integration of additional analgesic agents, a cornerstone of modern multimodal anesthesia, can further alter this delicate physiological balance. While beneficial for pain management, drugs like opioids or non-opioids can interact with the primary anesthetic agents, leading to complex and sometimes unpredictable changes in hemodynamics and respiratory function. A detailed characterization of these interactions is crucial for safe and effective anesthetic management [4].

This study investigated two such agents. Tramadol, an opioid agonist, is well-established to known to cause bradycardia in several species [5]. Recent comparative studies have further characterized Tramadol's anesthetic interactions and efficacy in other animal models, such as rabbits, highlighting its potent analgesic properties [6]. Nefopam is a non-opioid analgesic whose physiological effects in male Himalayan cats(Toms) are currently uncharacterized, but human and canine studies suggest it may influence blood pressure via its monoaminergic activity [7].

Therefore, the objective of this study was to meticulously characterize and compare the intra-operative cardiopulmonary and thermoregulatory effects of a standard xylazine-ketamine protocol following the preemptive administration of either Nefopam or tramadol in a controlled feline surgical model.

Materials and Methods

Ethical Approval

The local committee of the animal care and use at the College of Veterinary Medicine University of Baghdad provided this ethical approval (number P.G.2271 at 10. Sep.2025).

Animals

Twenty-four adult Himalayan male cats (Toms), deemed healthy upon clinical examination, were included in this prospective study. The cats were housed in individual cages and allowed a two-week acclimatization period. A pre-anesthetic fast of 3–4 hours was implemented [8]. The study protocol and animal handling were conducted in accordance with approved ethical guidelines for animal welfare. The sample size of eight animals per group was selected based on previous comparable feline anesthesia studies utilizing repeated physiological measurements, in which this number has been shown to provide sufficient power to detect clinically meaningful differences in hemodynamic parameters [11].

Experimental Design and Anesthetic Protocol

Animals were randomly allocated to one of three equal groups (n=8).

Control Group (A): The experimental animals were administered an intramuscular (IM) injection of xylazine (0.5 mg/kg B.W.) and ketamine (5 mg/kg B.W.). This specific dose was reduced to a loading dose [9] to evaluate the preemptive analgesic effect, thereby sparing the ketamine dose to prevent respiratory depression.

Tramadol Group (B): Premedicated with tramadol (4 mg/kg B.W., IM) 10 minutes prior to the administration of the same xylazine-ketamine mixture.

Nefopam Group (C): Premedicated with Nefopam (2 mg/kg B.W., IM) 10 minutes prior to the administration of the same xylazine-ketamine mixture.

Following induction, a tibial defect was surgically created (one millimeter drilled pore, 20–30 minutes post preemptive drug injection) in all cats to serve as a standardized surgical stimulus. This standardized orthopedic model aligned with previous methodologies used to assess bone healing and pain management in small animals [10]. No additional postoperative analgesic protocol was administered, as the preemptive analgesic agents (tramadol and Nefopam) were expected to provide adequate

residual analgesia during the immediate recovery period. This design reflects the primary objective of evaluating preemptive analgesia as a standalone perioperative pain management strategy.

Physiological Monitoring and Data Collection

All animals breathed room air spontaneously throughout the procedure; no endotracheal intubation or supplemental oxygen was administered, in order to allow detection of drug-induced respiratory effects under standardized conditions. Arterial blood pressure was measured non-invasively using an oscillometric method via the coccygeal artery. Anesthetic depth was assessed at 10-minute intervals by monitoring pedal withdrawal reflex, palpebral reflex, and jaw tone; no additional doses of anesthetic agents were required during the study period. Rectal temperature was monitored using a digital thermometer. The primary focus of this investigation was the data collected from a multi-parameter monitor (Model BMO210A, BMV Technology Co., Ltd.). Continuous monitoring of hemodynamic and respiratory parameters was performed throughout the anesthetic period. Parameters were recorded at 10-minute intervals and included: heart rate (HR), pulse rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), respiratory rate (RR), peripheral oxygen saturation (SpO_2), and rectal temperature.

Systolic and diastolic blood pressures were measured using the non-invasive oscillometric method. A cuff with a width approximately 40% of the circumference of the antebrachium was used to ensure accuracy, in accordance with established veterinary blood pressure monitoring guidelines for feline patients.

Subjective pain scoring systems were deliberately excluded from this clinical assessment to minimize inter-observer variability and potential bias. Instead, the study relied on objective hemodynamic parameters, such as SBP and heart rate, as indirect indicators of analgesic efficacy and nociceptive response.

All procedures were performed in an indoor surgical facility maintained at an ambient temperature of approximately 22–24°C. No active warming devices were employed during the anesthetic period. The mean duration of the surgical procedure was 9.14 ± 1.16 minutes across all groups. In contrast, the mean durations of surgical anesthesia were 16.00 ± 0.53 minutes in the control group, compared to 51.25 ± 0.81 and 46.25 ± 1.25 minutes in the Tramadol and Nefopam groups, respectively.

Statistical Analysis

Data were analyzed using the Statistical Analysis System (SAS/STAT, version 12.1). Due to the repeated-measures nature of the experimental design, measurements collected from the same animals at multiple time points were analyzed using a Repeated Measures ANOVA to account for within-subject correlation, followed by the Least Significant Difference (LSD) test for post-hoc pairwise comparisons. Results are expressed as mean ± standard error (SE). A P-value of < 0.05 was considered statistically significant [11].

In response to reviewer recommendations and to more rigorously account for the hierarchical structure of the repeated-measures data, a Linear Mixed-Effects Model (LMM) was additionally applied for each physiological parameter using Restricted Maximum Likelihood (REML) estimation. The model specified Group (Control, Tramadol, Nefopam) and Time as fixed effects, a Group × Time interaction term to characterize diverging temporal trajectories across groups, and a random intercept per individual animal to capture between-subject variability. This approach was employed to confirm the robustness of the primary findings and to evaluate the statistical adequacy of the n = 8 per group sample size based on the observed effect sizes across all measured parameters.

Results

Cardiovascular Effects

Heart Rate (HR) and Pulse Rate: The Tramadol group exhibited a progressive and significant decrease in both HR and pulse rate over time, reaching subnormal levels after 70 minutes of anesthesia. In contrast, the Control group showed an initial significant increase in HR, while the Nefopam group maintained a relatively stable, albeit subnormal, heart rate throughout the procedure. Significant differences were observed between the Tramadol group and both

the Control and Nefopam groups at multiple time points (Table 1) (Figure 1).

Table 1: Comparison of heart rate (beats/min) during anesthesia within and among groups (Mean ± SE).

Table 1: Heart Rate (beats/min) — Mean ± SE												
Group	**0 ***	**10 ****	**20**	**30**	**40**	**50**	**60**	**70**	**80**	**90**	**100**	**110**
Control	—	—	219.25 ± 9.69 Bb	219.12 ± 8.71 Bb	210.50 ± 7.39 Bb	202.87 ± 6.52 Ab	199.62 ± 9.30 Ab	196.50 ± 9.24 Ab	195.00 ± 7.62 Ab	190.87 ± 9.24 Ab	189.00 ± 11.56 Ab	185.51 ± 11.99 Ab
Tramadol	—	—	169.62 ± 0.53 Bb	178.12 ± 0.78 Bb	180.62 ± 0.77 Bb	162.25 ± 0.55 Bb	146.75 ± 0.70 Ba	136.25 ± 0.36 Aa	127.12 ± 0.51 Aa	124.25 ± 0.52 Aa	120.25 ± 0.36 Aa	117.75 ± 0.75 Aa
Nefopam	—	—	137.12 ± 2.72 Aa	125.25 ± 3.43 Aa	118.50 ± 4.72 Aa	121.00 ± 10.97 Aa	126.37 ± 13.85 Aa	130.37 ± 14.47 Aa	127.00 ± 7.85 Aa	126.50 ± 8.52 Aa	127.50 ± 8.08 Aa	127.76 ± 8.37 Aa

LSD = 27.78.
* Pre-emptive analgesic injection time.
** Ketamine-Xylazine injection time.
† Bone drilling time.
Different lowercase letters within a column indicate significant differences (P < 0.05). Different uppercase letters within a row indicate significant differences (P < 0.05).
Normal resting HR for cats: 130–260 beats/min [12, 13].

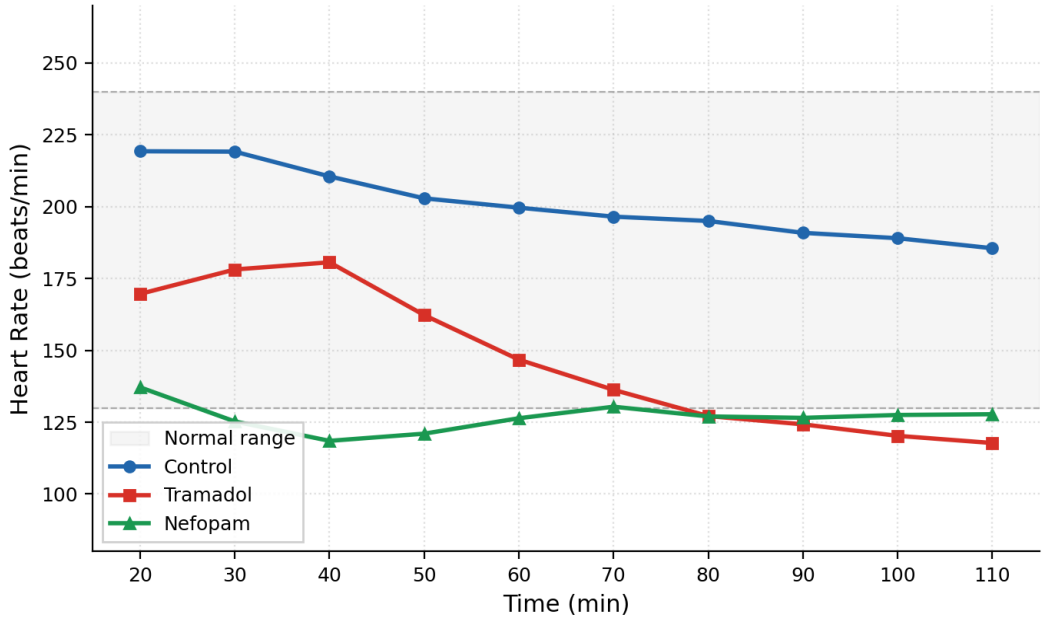

Figure 1: Comparison of heart rate (beats/min) during anesthesia within and among groups

Arterial Blood Pressure: The Nefopam group developed a significant hypertensive response, with systolic blood pressure (SBP) values being significantly higher than other groups at multiple time points. The Tramadol group also showed a significant increase in SBP, particularly between 60 and 90 minutes. Diastolic blood pressure (DBP) was significantly higher in the Tramadol group compared to the Control group from 30 to 90 minutes, with values exceeding the normal range at 70 and 80 minutes. The Control group experienced periods of DBP below the normal range (Tables 2 & 3) (Figures 2&3).

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Table 2: Comparison of systolic blood pressure (mmHg) during anesthesia within and among groups (Mean ± SE).

Table 2: Systolic Blood Pressure (mmHg) — Mean ± SE												
Group	**0 ***	**10 ****	**20**	**30**	**40**	**50**	**60**	**70**	**80**	**90**	**100**	**110**
Control	—	—	130.37 ± 13.10 Ba	113.62 ± 9.69 Aa	112.75 ± 13.41 Aa	116.37 ± 11.69 Aba	126.87 ± 9.20 Ba	116.87 ± 12.81 Aa	137.75 ± 7.22 Ba	137.62 ± 5.05 Ba	128.12 ± 8.22 Ba	126.11 ± 6.26 Ba
Tramadol	—	—	113.12 ± 2.27 Aa	121.37 ± 0.99 Aa	124.37 ± 1.41 Aa	121.37 ± 1.71 Aa	133.87 ± 0.93 Aa	155.25 ± 1.39 Bb	149.25 ± 1.53 Ba	144.00 ± 1.36 Ab	122.25 ± 0.90 Aa	115.37 ± 1.71 Aa
Nefopam	—	—	148.00 ± 5.20 Bb	149.75 ± 5.06 Bb	139.37 ± 4.78 Ab	147.00 ± 5.02 Bb	143.12 ± 4.67 Aa	125.12 ± 5.93 Aa	138.50 ± 4.17 Aa	141.00 ± 4.13 Aa	140.75 ± 4.53 Ab	141.65 ± 3.81 Ab

LSD = 18.10.
* Pre-emptive analgesic injection time.
** Ketamine-Xylazine injection time.
Different lowercase letters within a column and different uppercase letters within a row indicate significant differences ($P < 0.05$).
Normal SBP in cats: 110–160 mmHg [14, 15, 16, 17].

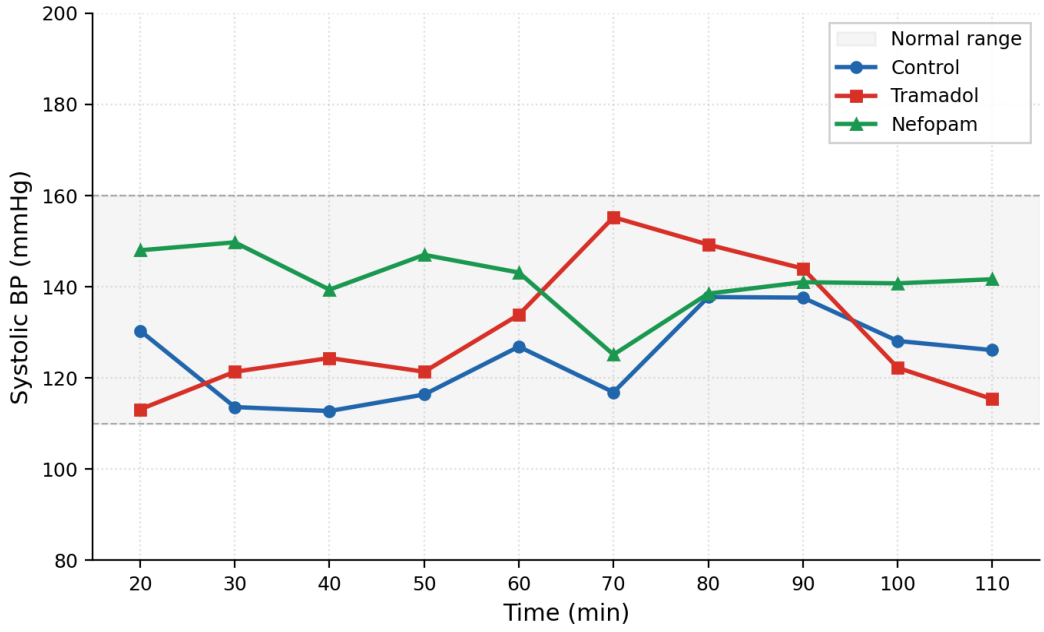

Figure 2: Comparison of systolic blood pressure (mmHg) during anesthesia within and among groups

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Table 3: Comparison of diastolic blood pressure (mmHg) during anesthesia within and among groups (Mean ± SE).

Table 3: Diastolic Blood Pressure (mmHg) — Mean ± SE												
Group	**0 ***	**10 ****	**20**	**30**	**40**	**50**	**60**	**70**	**80**	**90**	**100**	**110**
Control	—	—	78.37 ± 12.30 Aa	67.62 ± 12.76 Aa	67.87 ± 11.24 Aa	63.37 ± 10.12 Aa	68.12 ± 11.66 Aa	67.00 ± 11.64 Aa	81.50 ± 10.91 Aa	83.87 ± 7.21 Ba	79.37 ± 6.04 Aa	77.42 ± 6.79 Aa
Tramadol	—	—	89.50 ± 2.79 Aa	94.87 ± 2.28 Bb	95.75 ± 2.51 Bb	87.25 ± 1.48 Ab	99.37 ± 4.20 ABb	125.50 ± 1.41 Bb	120.50 ± 1.08 Bb	107.87 ± 2.16 ABb	85.75 ± 1.27 Aa	72.00 ± 0.80 Aa
Nefopam	—	—	96.87 ± 7.14 Aa	94.37 ± 6.76 Ab	89.00 ± 5.90 Ab	89.25 ± 7.20 Ab	87.87 ± 6.21 Aa	89.00 ± 7.43 Ab	82.12 ± 5.18 Aa	84.37 ± 5.92 Aa	97.16 ± 8.50 Aa	98.23 ± 8.95 Ab

LSD = 20.42.
* Pre-emptive analgesic injection time.
** Ketamine-Xylazine injection time
Different lowercase letters within a column and different uppercase letters within a row indicate significant differences ($P < 0.05$).
Normal DBP in cats: 73–101 mmHg [14, 15, 16, 17, 18].

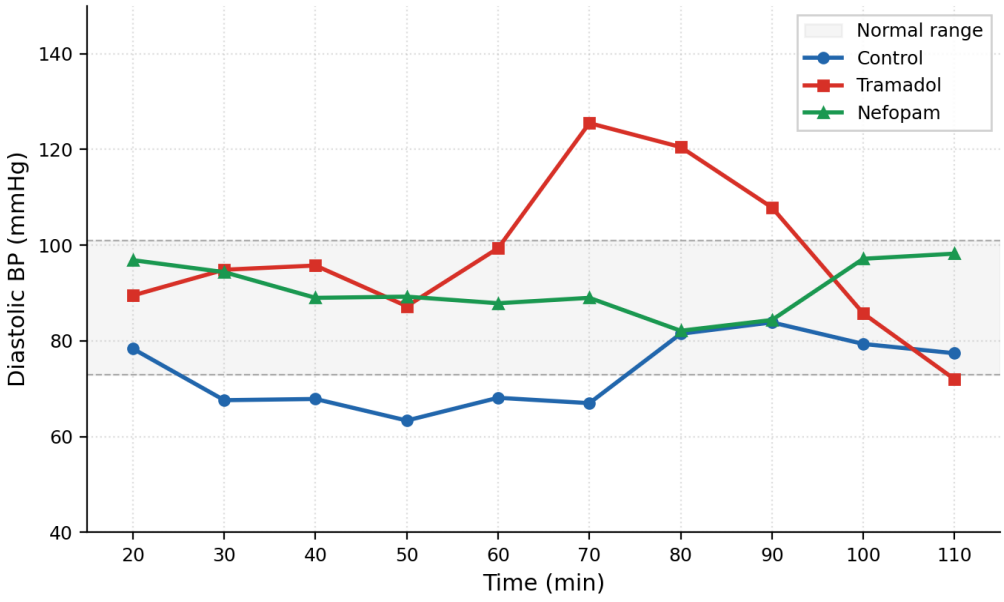

Figure 3: Comparison of diastolic blood pressure (mmHg) during anesthesia within and among groups

Respiratory and Oxygenation Effects

Respiratory rate was significantly higher in the Nefopam group at 60 and 70 minutes compared to its baseline. The Control group maintained a higher respiratory rate than the Tramadol group at several time points. The Tramadol group experienced a significant decrease in SpO_2 levels, particularly between 30 and 50 minutes. While the Nefopam group also showed low SpO_2 levels, they were significantly higher than the Tramadol group between 40 and 60 minutes (Table 4&5)(Figure 4&5).

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Table 4: Comparison of respiratory rate (breaths/min) during anesthesia within and among groups (Mean ± SE).

Table 4: Respiratory Rate (breaths/min) — Mean ± SE												
Group	**0 ***	**10 ****	**20**	**30**	**40**	**50**	**60**	**70**	**80**	**90**	**100**	**110**
Control	—	—	42.50 ± 5.10 Ab	42.87 ± 6.13 Aa	42.87 ± 7.35 Aa	40.75 ± 5.65 Aa	39.25 ± 5.23 Ab	38.62 ± 4.29 Ab	36.87 ± 2.88 Aa	38.62 ± 2.42 Ab	40.10 ± 2.31 Ab	40.47 ± 2.15 Aa
Tramadol	—	—	37.62 ± 0.32 Ba	39.25 ± 0.25 Ba	36.00 ± 0.80 Ba	31.62 ± 0.41 Aa	28.50 ± 0.37 Aa	27.25 ± 0.45 Aa	28.00 ± 0.46 Aa	28.37 ± 0.46 Aa	29.12 ± 0.39 Aa	37.50 ± 0.53 Ba
Nefopam	—	—	31.25 ± 0.83 Aa	35.25 ± 1.42 Aa	40.00 ± 1.51 Aa	38.87 ± 1.10 Aa	46.25 ± 8.08 Bb	43.37 ± 6.27 Bb	36.53 ± 2.44 Aa	38.56 ± 2.52 Ab	39.12 ± 2.22 Ab	39.75 ± 2.70 Aa

LSD = 9.62.
* Pre-emptive analgesic injection time.
** Ketamine-Xylazine injection time.
Different lowercase letters within a column and different uppercase letters within a row indicate significant differences (P < 0.05).
Normal respiratory rate in cats: 16–40 breaths/min [19].

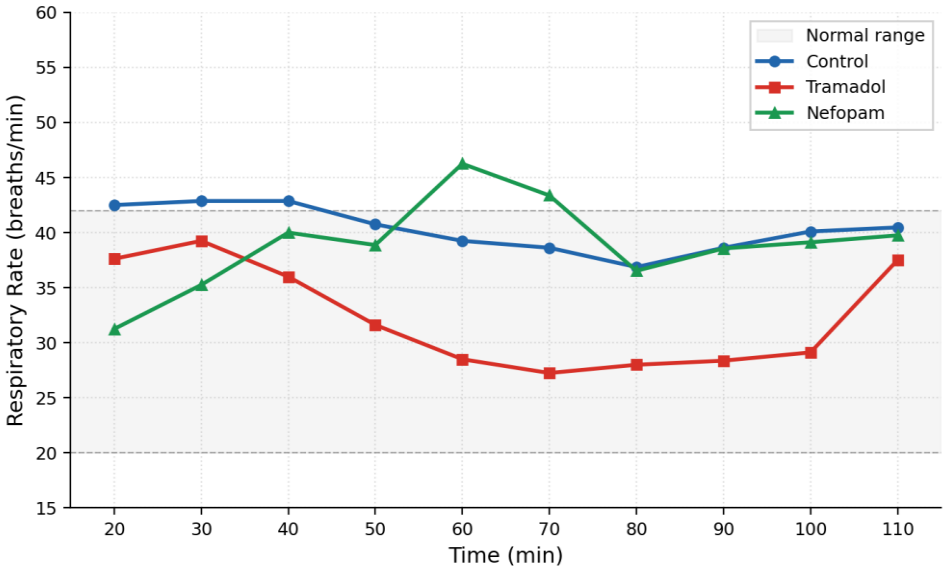

Figure 4: Comparison of respiratory rate (breaths/min) during anesthesia within and among groups

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Table 5: Comparison of the means ±SD of SpO2, % percentage during anesthesia within and among the experimental groups

Table5: SpO2Table5: SpO2 (%) — Mean ± SD (%) — Mean ± SD												
Group	**0 ***	**10 ****	**20**	**30**	**40**	**50**	**60**	**70**	**80**	**90**	**100**	**110**
Control	—	—	B96.62 ±1.13 Bb	94.87 ±2.24 Bb	B94.75 ±1.03 Bb	B95.00 ±1.00 Bb	90.87 ±2.45 Ab	92.75 ±1.38 Ab	89.12 ±4.15 Aa	90.68 ±2.46 Aa	93.38 ±0.77 Ab	B93.84 ±1.20 Ab
Tramadol	—	—	B91.87 ±0.51 Ab	88.00 ±0.84 ABa	A76.50 ±0.98 Aa	79.62 ±0.26 Aa	81.75 ±0.64 ABa	87.87 ±0.63 Ba	88.00 ±0.37 Ba	89.50 ±0.46 Ba	90.50 ±0.59 Ba	89.12 ±0.44 Ba
Nefopam	—	—	A85.62 ±1.71 Aa	A85.25 ±2.05 Aa	87.25 ±1.25 Ab	B89.62 ±0.99 Bb	91.25 ±0.70 Bb	91.87 ±0.29 Ba	88.12 ±1.64 Aa	87.41 ±1.32 Aa	88.51 ±1.70 Aa	89.87 ±1.23 Aa

LSD = 4.09
* Pre emptive injection time.
** Ketamine +Xylazine mixture injection time.
✦ Pore drilling (pain induction) time.
(P<0.05)
Normal SpO_2 level is 94-98% .[20];[21]

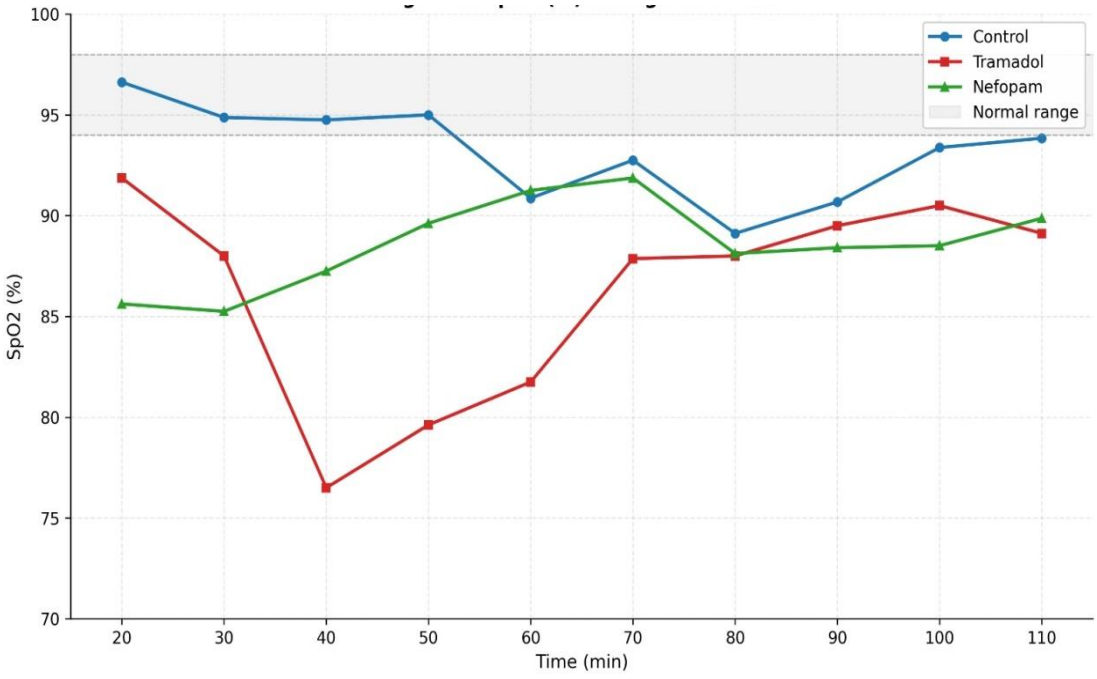

Figure 5: Comparison of SpO2, % percentage during anesthesia within and among groups

Thermoregulatory Effects

The Tramadol group developed significant hypothermia, with rectal temperature decreasing progressively and reaching subnormal levels after 60 minutes of anesthesia. The Nefopam group also showed a significant decrease in temperature, but values began to recover towards the end of the procedure. The Control group maintained a more stable, though slightly low, body temperature throughout (Table 6).

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Table 6: Comparison of rectal body temperature (°C) during anesthesia within and among groups (Mean ± SE).

Table 6: Rectal Body Temperature (°C) — Mean ± SE												
Group	**0 ***	**10 ****	**20**	**30**	**40**	**50**	**60**	**70**	**80**	**90**	**100**	**110**
Control	—	—	36.15 ± 0.35 Aa	36.12 ± 0.46 Aa	36.07 ± 0.28 Aa	35.97 ± 0.28 Aa	36.11 ± 0.29 Aa	36.12 ± 0.36 Aa	36.47 ± 0.49 Ab	36.22 ± 0.61 Aa	36.17 ± 0.53 Aa	36.47 ± 0.30 Ab
Tramadol	—	—	38.15 ± 0.09 Bb	37.71 ± 0.06 Bb	37.30 ± 0.08 Bb	37.13 ± 0.15 Bb	36.26 ± 0.11 Aa	35.73 ± 0.21 Aa	35.50 ± 0.14 Aa	35.76 ± 0.24 Aa	35.87 ± 0.33 Aa	35.57 ± 0.37 Aa
Nefopam	—	—	37.42 ± 0.15 Bb	37.05 ± 0.11 Bb	36.72 ± 0.13 Ba	36.21 ± 0.16 Aa	35.58 ± 0.35 Aa	36.06 ± 0.25 Aa	36.39 ± 0.17 Bb	36.45 ± 0.13 Ba	36.53 ± 0.12 Ba	36.64 ± 0.13 Bb

LSD = 0.80.
* Pre-emptive analgesic injection time.
** Ketamine-Xylazine injection time.
Different lowercase letters within a column and different uppercase letters within a row indicate significant differences ($P < 0.05$).
Normal rectal temperature in cats: 36.6–39.1°C [22].

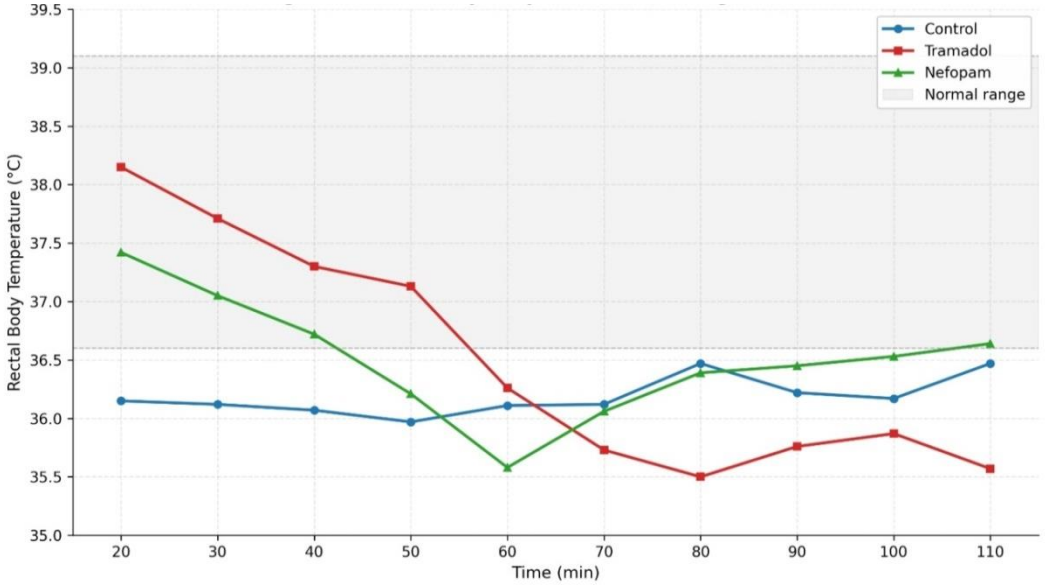

Figure 6: Comparison of rectal body temperature (°C)during anesthesia within and among groups

Discussion

The present study found that the addition of preemptive tramadol or Nefopam to a xylazine-ketamine protocol produced distinct and clinically relevant alterations in cardiopulmonary and thermoregulatory parameters in Himalayan tom cats.

The evaluation of the sample size (n = 8) revealed that it was sufficient to characterize the primary physiological trajectories observed, particularly for Heart Rate and Body Temperature where the differences were most pronounced. However, it is acknowledged that parameters with high biological variability, such as Systolic Blood Pressure, may benefit from larger cohorts

in future studies to further enhance statistical reliability.

The most profound cardiovascular effect was the progressive bradycardia observed in the Tramadol group. This finding was consistent with literature describing the opioid-mediated increase in parasympathetic tone [5, 23]. Of note, xylazine itself is a potent alpha-2 adrenoceptor agonist that independently induces bradycardia; the additive interaction between alpha-2 agonism and opioid-mediated parasympathetic tone likely accounts for the pronounced heart rate depression observed in the Tramadol group [1]. In contrast, the Nefopam group developed a pronounced hypertensive response. While this finding aligns with nefopam's known monoaminergic mechanism of inhibiting norepinephrine reuptake [7, 24], alternative explanations cannot be entirely excluded. Specifically, the observed SBP elevation may also reflect an insufficient analgesic depth in response to the surgical stimulus, as nociception-driven sympathetic activation is a recognized cause of intraoperative hypertension [4]. Since analgesic efficacy was not directly assessed in this study, the relative contribution of pharmacodynamic drug effect versus nociceptive response to the hypertensive profile remains an important limitation to acknowledge. Future studies incorporating validated pain scoring tools would help delineate these mechanisms.

The profound bradycardia observed in the Tramadol group likely reflects an additive interaction between two mechanistically distinct pathways. Xylazine, as an alpha-2 adrenergic agonist, independently reduces heart rate in cats through centrally mediated sympatholysis [1, 25]. Tramadol, through its opioid-mediated enhancement of vagal tone, provides an additional parasympathetic impetus for cardiac slowing. The convergence of these two mechanisms produced the progressive and pronounced bradycardia uniquely observed in this group beyond 70 minutes of anesthesia.

The observed elevation in Systolic Blood Pressure (SBP) within the Nefopam group is primarily a reflection of the drug's established sympathomimetic profile rather than a manifestation of inadequate analgesia. This hemodynamic response is driven by the inhibition of norepinephrine, serotonin, and dopamine reuptake [26], which increases adrenergic tone — a phenomenon clinically documented in humans [27] and experimentally confirmed in feline models [28, 29]. Such cardiovascular responses in felines mirror human findings due to the highly conserved nature of monoaminergic signaling pathways across mammalian species [30]. In the present study, these effects were likely potentiated by a synergistic interaction with ketamine [4]. Importantly, the non-linear biphasic trajectory of DBP in the Tramadol group identified by the LMM suggests that the linear model may underestimate the true interaction effect; the incorporation of a quadratic time term is therefore recommended for future analyses of this parameter.

To ensure an objective, data-driven assessment and eliminate potential observer bias, behavioral pain scoring systems were intentionally excluded from the current methodology. Nevertheless, the stability of other vital signs confirms that adequate antinociception was achieved. Thus, the observed hypertensive response should be interpreted as a predictable pharmacodynamic consequence of Nefopam's mechanism of action rather than a clinical indicator of pain [31].

From a respiratory standpoint, the maintenance or slight increase in respiratory rate in the Nefopam group was a notable advantage, as it suggested a lack of the respiratory depression commonly associated with opioids [32]. Although periods of oxygen desaturation were observed in both preemptive groups, the effects were more pronounced with tramadol, consistent with its central depressant effects.

Thermoregulatory stability was also differentially affected. The significant hypothermia that developed in the Tramadol group is a common and clinically important side effect of many anesthetic combinations that include opioids and alpha-2 agonists [1]. It is important to acknowledge, however, that the observed temperature decline across all groups may have been further influenced by environmental factors, including the ambient room temperature and the duration of the procedure, neither of which were actively controlled for in this study. The absence of active warming devices represents a limitation that may have contributed to the overall hypothermic

trend observed, independent of drug effects [8]. Nevertheless, the LMM-derived slope analysis — revealing a Tramadol-associated decline rate of −0.298°C per 10 minutes versus −0.066°C in the Nefopam group and +0.034°C in the Control — provides robust quantitative evidence that the temperature depression in the Tramadol group represents a genuine and clinically significant pharmacological effect beyond environmental confounders. The more stable temperature profile in the Nefopam group may therefore represent a clinical benefit, reducing the risk of hypothermia-related complications [33].

The clinical implications of these findings are direct. Clinicians opting for preemptive tramadol with this protocol should be prepared to actively manage bradycardia and provide robust thermal support. Conversely, when using preemptive Nefopam, vigilance for and potential management of systemic hypertension are warranted. In conclusion, this detailed physiological characterization revealed that while preemptive analgesics were beneficial, they were not physiologically inert. Understanding the specific cardiopulmonary and thermoregulatory profiles induced by different analgesic agents is essential for tailoring anesthetic monitoring, anticipating complications, and ensuring patient safety in feline anesthesia.

Conclusions

The present study concluded that the integration of preemptive tramadol or Nefopam into a xylazine-ketamine anesthetic protocol significantly modulates the physiological response in male Himalayan cats(Toms), producing distinct and divergent clinical profiles.

While both agents enhanced the multimodal anesthetic approach, they imposed specific challenges on the patient's homeostatic balance. Preemptive tramadol administration is associated with a profound, time-dependent bradycardia and significant hypothermia necessitating vigilant heart rate monitoring and robust thermal support during prolonged procedures. In contrast, preemptive Nefopam tended to maintain a more stable heart rate and respiratory profile but triggered a pronounced hypertensive response, likely due to its monoaminergic activity, which requires careful blood pressure management.

Furthermore, the observed reductions in oxygen saturation in both analgesic groups highlight the need for supplemental oxygen when combining these agents with xylazine-ketamine. These findings collectively emphasize that analgesic selection should be guided not only by efficacy, but also by the patient's physiological status, with monitoring and supportive care tailored to the specific hemodynamic and thermoregulatory profile of each agent. Future studies employing larger sample sizes, particularly for blood pressure endpoints, where the current n = 8 was demonstrated to be insufficient, and formal a priori power calculations are recommended to further confirm and extend these findings.

Conflict of Interest Statement

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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المؤشرات القلبية الرئوية والتنظيم الحراري لبروتوكول التخدير بمزيج الزيلازين-كيتامين عقب التسكين الاستباقي بالنيفوبام أو الترامادول في ذكور قطط الهيمالايا

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الملخص

االهدف: قارنت هذه الدراسة التأثيرات القلبية الرئوية والتنظيمية الحرارية (أثناء الجراحة) لبروتوكول التخدير بـ (الزايلازين-كيتامين) عند سبقه بالإعطاء الاستباقي لـ (نيفوبام) أو (الترامادول) في ذكور قطط الهيمالايا.

المواد والطرق: تم تقسيم 24 من ذكور قطط الهيمالايا البالغة إلى ثلاث مجموعات متساوية (8 قطط في كل مجموعة): المجموعة الضابطة (خضعت لبروتوكول الزايلازين-كيتامين فقط)، مجموعة الترامادول (حُقنت بالترامادول بجرعة 4 مجم/كجم كعلاج استباقي)، ومجموعة النيفوبام (حُقنت بالنيفوبام بجرعة 2 مجم/كجم كعلاج استباقي). وعلى فترات زمنية منتظمة كل 10 دقائق، تم تسجيل المؤشرات الحيوية التالية: معدل ضربات القلب، ضغط الدم الانقباضي والانبساطي، معدل التنفس، نسبة تشبع الأكسجين في الدم (SpO2)، ودرجة حرارة المستقيم. خضعت القطط للتخدير دون إدخال أنبوب تنفسي (أنبوبة رغامية)، وكانت تتنفس هواء الغرفة تلقائياً. كما جرى تقييم عمق التخدير من خلال مراقبة استجابة القطط لمنعكس سحب القدم (عند الضغط عليها) والمنعكس الجفني (رمش العين). ولم تتلقَّ القطط أي مسكنات إضافية بعد العملية؛ نظراً لأن الجرعات الاستباقية التي حُقنت بها قبل الجراحة وفرت مفعولاً مسكناً ممتداً وكافياً خلال مرحلة التعافي المبكرة، وهو ما أكده استقرار مؤشراتها الحيوية.

النتائج: أظهر استخدام التسكين الاستباقي تأثيرات واضحة ومتفاوتة على وظائف القلب والرئتين بين المجموعات؛ حيث عانت مجموعة الترامادول من تباطؤ شديد وملحوظ في معدل ضربات القلب، إذ انخفضت المؤشرات عن المعدل الطبيعي بعد مرور 70 دقيقة من التخدير. وفي المقابل، حافظت مجموعة النيفوبام على معدل ضربات قلب مستقر (رغم كونه أقل من الطبيعي)، ولكن صاحب ذلك ارتفاع ملحوظ في ضغط الدم العام والضغط الانقباضي في فترات زمنية متعددة ($P < 0.05$). أما المجموعة الضابطة فقد أظهرت تسارعاً أولياً في ضربات القلب، أعقبه انخفاض تدريجي بمرور الوقت. من جانب آخر، حافظ النيفوبام على استقرار معدل التنفس بشكل أفضل من الترامادول، برغم أن كلتا المجموعتين (الترامادول والنيفوبام) شهدتا انخفاضاً مؤقتاً في نسبة تشبع الأكسجين (SpO2) مقارنة بالمجموعة الضابطة. كما أظهرت النتائج انخفاضاً حاداً في درجة حرارة الجسم (خطر الهبوط الحراري) بدأ بعد 50 دقيقة في مجموعة النيفوبام، وبعد 60 دقيقة في مجموعة الترامادول.

الاستنتاجات: أدى دمج النيفوبام أو الترامادول كمسكنات استباقية مع بروتوكول (الزايلازين-كيتامين) إلى استجابات فسيولوجية متوقعة ولكنها متباينة (مختلفة) في ذكور قطط الهيمالايا. وبناءً على ذلك، يجب على الأطباء البيطريين عند اختيار المسكن الاستباقي أخذ الحيطة وتوقع حدوث تباطؤ في ضربات القلب وانخفاض في درجة حرارة الجسم عند استخدام الترامادول، أو حدوث ارتفاع في ضغط الدم الشرياني عند استخدام النيفوبام؛ مما يسهم في توجيه وتحسين عملية مراقبة العلامات الحيوية للقطط بدقة أثناء فترة التخدير والجراحة.

الكلمات المفتاحية: التسكين الاستباقي، التخدير في قطط هيمالايا، مراقبة المؤشرات القلبية الرئوية، النيفوبام، الترامادول، التنظيم الحراري.