DRF-579
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RESEARCH ARTICLE Asian Journal of Dairy and Food Research

# Comparative Study of Xylazine-ketamine and Xylazine-tramadol as General Anesthetic Agents in Cats

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10.18805/ajdfr.DRF-579

## ABSTRACT

**Background:** The appropriate selection and administration of anesthetic agents are paramount for ensuring both the safety and efficacy of surgical and diagnostic procedures in feline patients. This study was designed to evaluate incidence of onset time, efficacy, safety and side effects in using of Xylazine-Ketamine and Xylazine-Tramadol as general anesthetic agents in cats.

**Methods:** Ten adult female and male cats of a parentally health in both group, the experimental animals were divided randomly into two equal groups: five cats for each group: First group (n=5): was given (2%) Xylazine hydrochloride as sedative agent at dose(1) mg/kg I.M followed by I.M injection of 100% Ketamine at dose (20) mg/kg. while, Second group (n=5): was given Xylazine at dose (1) mg/kg I.M followed by I.M injection of (5%) tramadol at dose of (1) mg/kg. The parameters which were used for evaluation included heart and respiratory rates, rectal body temperature. The clinical parameters included induction time, eye reflex, recovery time, muscle relaxation after induction of anesthetic drug. The parameters which were used for evaluation included heart and respiratory rates, rectal body temperature. The clinical parameters included induction time, eye reflex, recovery time, muscle relaxation after induction of anesthetic drug.

**Result:** Physiological parameters showed no-significant changes in both the groups; the induction time started after three to five minutes in first group, while in the second group after five minutes from administration of Xylazine-Tramadol. The recovery was smooth in both the groups, muscle relaxation was excellent in first group and good in second group and was does dependent. The eye reflex was absent in Xylazine-Ketamine group, while in the second group was variable.

**Key wards:** Cats, General anesthesia, Induction time, Ketamine, Muscle relaxation, Tramadol, Xylazine.

## INTRODUCTION

General anesthesia in small animals, particularly cats, is often achieved using ketamine in combination with xylazine due to their synergistic anesthetic and sedative effects (Kumar *et al*., 2018; Kumar *et al*., 2019). Opioid agents such as tramadol hydrochloride (Tramadol HCl) also provide analgesia and muscle relaxation, exhibiting both opioid and non-opioid mechanisms (Ege *et al*., 2018). Tramadol acts on opioid receptors and inhibits serotonin and norepinephrine reuptake, while ketamine and xylazine primarily act through NMDA receptor antagonism and α, -adrenergic agonism, respectively (Robert *et al*., 2013; Danic *et al*., 2017; Ege *et al*., 2018).

Previous studies in ruminants and other animal models have reported that combinations of xylazine with ketamine or other agents (*e.g*., propofol) produce stable anesthetic depth with minimal oxidative stress and predictable cardiovascular effects (Gokalp *et al*., 2020). These findings support further evaluation of alternative drug combinations, including xylazine-tramadol, in feline anesthesia.

This study aimed to compare the anesthetic efficacy, safety and side effects of ketamine-xylazine and ketamine-tramadol combinations in cats, using physical and clinical parameters as evaluation criteria.

## MATERIALS AND METHODS

### Ethical approval

The Ethical Committee of the College of Veterinary Medicine at the University of Fallujah (Approval No. 13, dated 27/05/2025) approved all similarities of methyl-N1-ornithine in *vivo* studies and *in vitro* studies were performed in full conformity with institutional guidelines on the care of experimental animals.

### Animals

A total of 10 adult, apparently healthy male and female cats were used in this experimental study, conducted in 2025 at the College of Veterinary Medicine, University of Fallujah. The animals were housed individually and randomly assigned in equal numbers to two groups:

First group: 2% Xylazine (1) mg/ kg. IM followed by injection of 100% Ketamine at dose of (20) mg/kg.

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**How to cite this article:** Sahep, L.F., Hussein, S.M. and Alhayani, W.A. (2025). Comparative Study of Xylazine-ketamine and Xylazine-tramadol as General Anesthetic Agents in Cats. *Asian Journal of Dairy and Food Research*. 1-5. doi: 10.18805/ajdfr.DRF-579.

**Submitted:** 25-07-2025 **Accepted:** 30-08-2025 **Online:** 06-10-2025

Second group: 5% tramadol at dose of (1) mg/kg. IM followed by injection of 100% Ketamine at dose of (20)mg/kg.

**Experimental design**

After adaptation of all experimental animals they were prepared for general examination at zero time to ensure that all animals are apparently healthy and therafter allotted to two groups of five each. The first group, n=5, was prepared for physical examination (Heart rate, respiratory rate and rectal body temperature) then injected intramuscularly with Xylazine-Ketamine protocol, while the second group n=5 after the same steps physically, injected with Tramadol-Ketamine protocol (Danic *et al*., 2017). All parameters that were measured in this study before, after and during anesthesia for both the groups.

The parameters which were used for evaluations are:

1. Physical parameters that measured before and during administration of anesthesia that includes:

A. Heart rate.
B. Respiratory rate.
C. Rectal body temperature.

2. Clinical parameters which were recorded during administration of anesthesia:

A. Induction time.
B. Muscle relaxation.
C. Eye reflex.
D. Recovery time.

**Parameters measurement**

**Clinical parameters**

**Measuring induction time as per** (Mohammed, 2011).

Muscle relaxation is based on flexion and extension of limbs with showing of score card of muscle relaxation (Table 1), (Thakur *et al*., 2011).

**Eye reflexes**

The vital reflexes of eye were as following:

A. Corneal by touching it using finger.(presence+, Absence -, variable±)
B. Palpebral by touching the media canthus.(presence+, Absence-, variable ±).
C. Eye ball movement (presence +, Absence -, variable ±).

**Recovery time**

The recovery was observed from the time of reappearance of the reflex until complete consciousness if it was smooth, staggering and difficult in standing .Table (2) show score card for quality of recovery time.

**Statistical analysis**

The Statistical Package of Social Sciences-SPSS (2019) program was used to detect the effect of difference groups in study parameters. T-test was used to significant compare between means. Chi-Square test was used to significant compare between percentage of this study.

## RESULTS AND DISCUSSION

**Results of physical parameters**

Results of heart rate that recorded before anesthesia in first group (57.20±5.80 beat minute) was increased to 63.80±3.32 beat minute after anesthesia, while in second group the heart rate before anesthesia was 56.20±6.21 beat minute and become 53.80±1.85 beat minute after anesthesia, the data revealed no significant changes in both group (Table 3).

As everyone knows, the normal heart rate guarantees constant oxygen supply to the vital organs and can also be utilized to estimate the depth of anesthesia and analgesia (Yamashita *et al*., 2000), it is quite understandable why

**Table 1:** Score card for quality of muscle relaxation.

| Score | Quality | Character |
|---|---|---|
| 1 | Poor | Rigidity in muscles of neck, head and limbs |
| 2 | Moderate | Partial relaxation of head, neck and limb muscles |
| 3 | Good | Adequate muscle relaxation of surgical procedure. |
| 4 | Excellent | Complete relaxation. |

**Table 2:** Score card for recovery time.

| Score | Quality | Character |
|---|---|---|
| 1 | Excellent | Cat capable of standing at first attempt |
| 2 | Very good | Cat remain calm and needed two attempts to stand |
| 3 | Good | Cat remained calm but needed more than two attempts to stand |
| 4 | Poor | Excitement during recovery, danger of injury and needed more than two attempts to stand |
| 5 | Very poor | Sever excitement during recovery with injury |

**Table 3:** Values of heart rate (beat/minute) under two protocols of general anesthesia.

| Group | Before anesthesia | After anesthesia | T-test (P-value) |
|---|---|---|---|
| Xylazine-ketamine | 57.20±5.80 | 63.80±3.32 | 7.219 NS (0.286) |
| Xylazine-tramadol | 56.20±6.21 | 53.80±1.85 | 6.542 NS (0.737) |
| T-test (P-value) | 9.605 NS (0.909) | 8.774 * (0.3030) | - |

with first group, there was the spurring up of the heart rate after anesthesia which can be attributed to development of the atrioventricular block due to the systemic effect of Xylazine together with ketamine that acts as the increase of the heart index and stroke volume agreeing with Stamford (1995); Kumar *et al*., (2018). In second group the heart rate lowers after the use of Xylazine withTtramadol because combination of these drugs may trigger bradycardia and cardiac output and impair ionic activity in the heart, this finding is in support with Ismail *et al*. (2010) who stated that there was a reduction in the central sympathetic outflow in addition to the alpha-2 adrenergic agonist, thus, outcome was decrease in heart rate but without significance at the dosage used.

**Respiratory rate**

Result of Respiratory rate R.R in first group before anesthesia (36.20±5.39 breath minute) was decreased to 27.20±5.59 breath minute after anesthesia, while in the second group the R.R (35.80±5.30 breath minute) was decreased to 28.20±1.53 breath minute after administration of Xylazine with Tramadol. There were no significant changes recorded between each group (Table 4). The results agree with Lee (2006), which expected due to respiratory depression effect was secondary to central nervous system depression produce by alpha2- adrenoreceptors stimulation that some time tend to produce severe laryngeo-spasm, broncho-spasm and cough.

**Rectal body temperature**

The results of rectal body temperature in first group before anesthesia was (38.10±0.48)°C which decreased to 37.64±0.51°C after anesthesia, while in second group the temperature before anesthesia was 39.00±0.54°C also decreased to 38.00±1.52°C after administration of Xylazine with Tramadol. No significant changes recorded in each group (Table 5).

Kattri *et al.* (2013) stated that anesthesia induced hypothermia and in both protocols the reduction of body temperature during general anesthesia might be explained by the effects of anesthetic agent on body temperature regulating process. Where the administration of Xylazine caused the suppressions of thermo regularity mechanisms and the possibility of either hypothermia or hyperthermia had occurred based on the effect of such drug on thermo regularity center in the brain. Ketamine can either reduce the amount of heat produced or increments heat loss (Fahime *et al*., 1973). The cause of this decline through release of monoamines in the anterior hypothalamus is because the noradrenaline declines as well as the 5-hydroxyleptamine alleviate normal body temperatures within the body. Similar decreases in temperature have been observed in ruminants under xylazine-ketamine anesthesia (Kumar *et al*., 2018; Gokalp *et al*., 2020).

**Clinical parameters**

**Induction time**

The anesthetic time for the first group was 8.8 : 32.25, which was significantly faster than second group (11.2 :11.8) and this result agree with Luo and Sugiyama (2000) who mention that the gamma-amino butyric-acid (GABA) receptor in central nervous system (CNS) are thought to be a potential target site of action for a variety of general anesthetics. Extensive studies have shown that the differences in induction time between both group that may be interfere with high lipid solubility that is shown in the first group lead to increase of absorption and decrease of duration time especially with administration of Xylazine-Ketamine, while in second group that Xylazine with Tramadol characterized by low lipid solubility lead to increase of induction time, but with increase in duration more than first group (Table 6).

**Muscle relaxation**

The satisfactory muscle relaxation in the first group could be as a result of the action of Xylazine on muscle relaxant that accrues by the inhibition of the transmission of the neural impulses in the CNS (Table 6). It is an open secret that ketamine induces tonic-clonic muscle activity in anticipation

**Table 4:** Values of respiratory rate (breath/minute) under two protocols of general anesthesia.

| Group | Before anesthesia | After anesthesia | T-test (P-value) |
|---|---|---|---|
| Xylazine-ketamine | 36.20±5.39 | 27.20±5.59 | 7.366 * (0.0412) |
| Xylazine-tramadol | 35.80±5.30 | 28.20±1.53 | 7.152 * (0.0379) |
| T-test (P-value) | 7.437 NS (0.959) | 7.383 NS (0.867) | |

**Table 5:** Values of rectal body temperature (°C) under two protocols of general anesthesia.

| Group | Before anesthesia | After anesthesia | T-test (P-value) |
|---|---|---|---|
| Xylazine-ketamine | 38.10±0.48 | 37.64±0.51 | 2.076 NS (0.661) |
| Xylazine-tramadol | 39.00±0.54 | 38.00±1.52 | 1.859 NS (0.820) |
| T-test (P-value) | 1.686 NS (0.253) | 2.692 NS (0.827) | - |

**Table 6:** Clinical parameters under two protocols of general anesthesia.

| Group | Induction time | Anesthesia time | Recovery time | Muscle relaxation | Eye reflex |
|---|---|---|---|---|---|
| Ketamine-xylazine | 8.8 : 32.25 | 5.4 : 15.6 | Very good | Excellent | Absent |
| Ketamine-tramadol | 11.2 : 11.8 | 7.25 : 25.4 | Good | Good | Variable |

of sensor inputs to higher centers of the CNS and therefore the combination of this protocol played a crucial role to exclude muscle rigidity that takes place when ketamine alone is used (Delehant *et al*., 2003). In second group which was deemed as satisfactory in surgical procedure where no reflexes were noted after injection of tramadol with Xylazine as the direct result of Xylazine touching the neural transmitter of the muscle in all parts of the body providing the richness in inhibition of impulse in the CNS which is deep and long lasting compared to first group due to synergistic effect of tramadol and Xylazine.

### Eye reflex

Eye reflex_(reflex on cornea and palpebral) in the first group was absent, whereas in the second group the results were variable (Table 6). The eye movement in general are either categorized as gaze stabilizing or gaze shift mechanism that ensures that the eye focus on the object of interest remains in the field of vision when the subject of that object is moving around, the mechanism thus rendering to the eye an involuntary motion.Elevated depth of anesthesia can usually inhibit eye movement but not always (Nair *et al*., 2011).

### Recovery time

Recovery time of first group was very good and in the second group good (Table 6) that begin after reappearances of first reflex or excitement, which agrees with Matthews and Tylor (2002), who detected that cats hardly develop hysteria as it relates to anything, so the outcomes of anesthesia are nearly peaceful and tranquil. A cat is just never made to get up and it is usually not possible to get it up before it wants.

## CONCLUSION

According to the results which were proven in this study, beside little references about the effect of anesthetic agents, we concluded that the Xylazine-ketamine is better suited for procedure requiring strong sedation and muscle relaxation, but carries higher risk of cardiovascular and respiratory depression. The second group of Xylazine-Tramadol is preferable when analgesia is the primary aim, especially in cats with cardiovascular or respiratory depression.The first group yielded excellent muscle relaxation and rapid induction with fast recovery; while second group gave smooth prolonged induction, good analgesia with satisfactory muscle relaxation.

### Conflict of interest

The authors declare that there are no conflicts of interest regarding the publication of this article. No funding or sponsorship influenced the design of the study, data collection, analysis, decision to publish or preparation of the manuscript.

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