

# Clinical Anesthetic, Sedative and Analgesic Effects and Physiological Changes After Xylazine-Ketamine-Tramadol Cocktail Administration in Cats Undergoing Orchiectomy

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## Abstract

Twenty adult male Egyptian local breed client owned cats were divided into two equal groups and anesthetized using two different Ketamine based protocols. The first group received a mixture of Xylazine and Ketamine (XK) in a single syringe administered intramuscular. The other group received Xylazine-Ketamine-Tramadol mixture (XKT) in the same syringe. Non-significant variations in physiological parameters, induction, anesthesia or recovery periods were detected. Post-operative sedation and analgesia significantly increased in the XKT group. Seizures like convulsions were noticed during induction and recovery in XKT group. Anesthesia and recovery periods were slightly prolonged in the same group than in XK group. In conclusion, addition of tramadol in a dose of 2mg/kg to Xylazine-Ketamine combination didn't depress the cardiopulmonary functions hence didn't require further addition of anticholinergic premedication, produced adequate sedation and post-operative analgesia and slightly prolong the anesthesia duration.

**Keywords:** Anesthesia; Cat; Ketamine; Tramadol; Xylazine

## Introduction

Injectable agents are very common for induction and/ or maintenance of general anesthesia in cats. Alpha<sub>2</sub> ( $\alpha_2$ ) adrenoceptor agonist-ketamine combination is one of the most common injectable anesthetic protocols for achieving general anesthesia in cats [1]. Xylazine hydrochloride is an  $\alpha_2$  adrenoreceptor agonist widely used in cats for its sedative, analgesic and muscle relaxant effects [2]. Xylazine combined with Ketamine to increase its anesthetic and analgesic effects and to reduce the dose required to induce satisfactory anesthesia. However, its use is associated with adverse effects including bradycardia and respiratory depression [2,3]. Ketamine hydrochloride is a dissociative anesthetic with central sympathomimetic activity when used alone it tends to poor muscle relaxation and persistent pain reflex. The muscle twitching and rigidity and convulsive seizures are centrally mediated. Ketamine produces a dose dependent depression of cardiac function [4]. Tramadol hydrochloride is a centrally acting analgesic that is structurally related to codeine and morphine [5]. It acts as a weak

$\mu$ -opioid agonist coupled with inhibition of synaptic reuptake of serotonin and norepinephrine, achieving spinal modulation of pain and preventing impulses reaching the brain [6]. It had been used in several species, including cats [7,8]. The concept and idea of the current anesthetic protocol has been discussed in the veterinary field. However, it may be useful to accumulate the real clinical case data for this anesthesia method. The other concept of the recent study was to determine if addition of tramadol hydrochloride to xylazine-ketamine combination have superior analgesia and anesthesia property or if they were similar.

## Materials and Methods

Twenty adult healthy male cats (aged from 2-4 years and weighting from 3-4.200 kg) were participated this clinical study. Cats were caught with assistance of the owner and weighted with an electronic scale. Essential physiological parameters such as rectal temperature, heart rate and respiratory rate were collected and documented for each cat in a separate monitoring sheet. Cats were randomly allocated in two groups. Food was withheld 8 hours and water two hours' prior the experiment. The first group

(XK group) contained 10 cats received xylazine (Xylaz, Farvet, Holland) and ketamine (ketamine 100, Pantex, Holland) 1 mg/kg and 10 mg/kg respectively mixed in a single syringe and injected intramuscularly. The other group (XKT group) contained 10 cats and received a combination of xylazine 1mg/kg, ketamine 10 mg/kg and tramadol 2mg/kg (Tramal 100, GRUNENTHAL, Germany) mixed in a single syringe and administered by intramuscular route. All participated cats underwent open surgical castration.

The time of administration was marked as (time 0), physiological variables were collected within 10 minutes' interval (10 m, 20 m, 30 m, 40 m, 50 m and 60 m). after immobilization

animals were placed in right lateral recumbency, surgically prepared and draped for castration procedure. Eye ointment (Oxypol, EIPICO, Egypt) was used to protect eye against dryness. Sedation, analgesia, muscle relaxation, vomiting, excitement and apnea were recorded and evaluated in each time according to scales in Table 1. And recorded in monitoring sheet. Monitoring sheet is written in time lined manner. Induction time of anesthesia, time to elapse stage of anesthesia, duration of anesthesia, duration of analgesia and recovery times were recorded. Statistical analysis was performed using SPSS v.18 and Mann-Whitney's test for non-parametric values.

Criteria	Score	Observation
<b>Sedation score</b> [evaluated by degree of immobilization, calmness, disappearance of reflexes and consciousness]	0	No sedation (animal moves around and all reflexes present)
	1	Mild sedation (sternal recumbency but alert and all reflexes present)
	2	Moderate sedation (sternal recumbency, head dropped, salivation, start vomiting and not respond to stimuli)
	3	Profound sedation (easily laid in lateral recumbency, no movement and not respond to stimuli)
<b>Analgesia score</b> [evaluated via needle break at whole body and sensitive areas as interdigital space and scrotum]	0	No analgesia [poor] (refuse handling/ completely aroused)
	1	Mild analgesia (respond violently to stimuli)
	2	Moderate analgesia (respond to pin break stimuli on highly sensitive only)
	3	Profound analgesia [excellent] (not respond to pin break stimuli all over the body)
<b>Muscle relaxation score</b> [evaluated by degree of easiness of mouth opening and degree of hind limb flexion]	0	Mouth can't be opened
	1	Mouth can open with resistance
	2	Mouth opens with little effort
	3	Mouth opens and limb moves without resistance.
Criteria	Reference	Observation
Rectal temperature	38.1-39.2°	Measured by electronic thermometer
Heart rate	120-140	Measured at the ventrolateral aspect of the thorax by stethoscope in one minute.
Respiratory rate	16-40	Measured by thoracic and abdominal movements in one minute.

**Table 1:** The criteria used to evaluate the anesthetic effect in both (XK) and (XKT) groups.

## Results

After intramuscular administration, cats showed signs of dissociative anesthesia characterized by open eye, mydriasis, mouth movement and licking of the nose. Cats in both groups became laterally recumbent within five to eight minutes. Recovery in XK group was characterized by slow movements of the eyes, twitching of the ears and attempts to lift the head and to stand on the fore feet. Colonic convulsions were recorded in four cats during induction with XKT combination. One cat of the four and two others showed convulsions during recovery. Convulsions

were characterized by rigid open mouth, twitches and rigidity of the four limbs and rigidity of abdominal muscles. Induction with XKT combination administered intramuscular in the thigh muscles was also characterized by slow onset, animal stands or moves on its fore feet and drag the hind quarter which looks like paralyzed. Induction, anesthesia and recovery times are illustrated in Table 2. Anesthesia and recovery times were significantly longer using XKT combination compared to XK mixture; induction time was not significantly different between two treatments. Vomiting was recorded in two cases in XK group, excitement was recorded in six cats of XKT group, temporary apnea was observed in two cats

in XK group during anesthesia stage. Abnormal behavior was not observed in any of the cats during or after anesthesia. In the XKT group, animals were more conscious during recovery. They make several attempts to raise head and steer, stand with the fore feet or vocalize. Ataxia and uncontrolled manners were rarely observed during recovery in XK group. There was no significant difference in physiological variables between the two different protocols (Table 3). Sedation, analgesia and muscle relaxation scores were recorded in Table 4.

Regimen	Induction	Anesthesia*	Recovery
<b>Xylazine-Ketamine (XK)</b>	3.25±0.24	45.16±8.77	11.26±5.64
<b>Xylazine-Ketamine-Tramadol (XKT)</b>	3.54±0.18	49.48±11.46	9.19±2.89

**Table 2:** Induction, anesthesia and recovery periods calculated in minutes.

Regimen	Rectal temperature (°C)						
	0 min.	10 min.	20 min.	30 min.	40 min.	50 min.	60 min.
<b>XK</b>	38.9±0.45	38.7±0.1	38.6±0.2	38.5±0.4	38.1±0.1	37.9±0.4	37.8±0.2
<b>XKT</b>	38.8±0.53	38.6±0.4	38.4±0.2	38.1±0.2	37.9±0.2	37.8±0.5	37.9±0.3
Heart rate (B/min)							
<b>XK</b>	117±10	133±11	129±16	124±12	120±13	114±12	122±13
<b>XKT</b>	118±10	135±10	130±11	125±12	120±11	112±10	119±9
Respiratory rate (B/min)							
<b>XK</b>	22±2	29±8	25±4	23±1	25±2	23±1	23±2
<b>XKT</b>	23±1	30±5	26±4	24±3	24±4	24±2	24±1

**Table 3:** Variations in physiological parameters.

Regimen	Sedation						
	0 min.	10 min.	20 min.	30 min.	40 min.	50 min.	60 min.
<b>XK</b>	0	2±6	2.2±0.45	1.9±0.27	1.7±0.66	1.1±0.42	0.35±0.71
<b>XKT</b>	0	1.9±2	2±0.66	1.7±0.61	1.5±0.54	1.4±0.44	1.1±0.45
Analgesia							
<b>XK</b>	0	2.9±0.25	3±0.36	2.8±0.54	2.2±0.71	1.8±0.32	0.5±0.45
<b>XKT</b>	0	2.6±0.45	2.8±0.45	2.7±0.21	2.5±0.14	2.5±0.01	1.8±0.96
Muscle relaxation							
<b>XK</b>	0	3±0.45	3±0.11	3±0.64	2.8±0.11	2.7±0.96	1.75±0.75
<b>XKT</b>	0	2.8±0.56	3±0.55	2.7±0.51	2.5±0.50	1.75±0.87	0.9±0.54

**Table 4:** Sedation, analgesia and muscle relaxation parameters.

## Discussion

Both Xylazine-Ketamine and Xylazine-Ketamine-Tramadol cocktails produced adequate general anesthesia for the procedures. Non-significant differences were detected in induction time for both groups. The induction time average was about 3 minutes, likewise previous reports of Chen and Chee (2005) and Li et al. (2013) [9,10]. In contrast to results reported by Li et al. (2013) [10], xylazine-ketamine-tramadol resulted in longer induction period than Tiletamine/zolazepam-xylazine-tramadol combination. Recovery period was longer when Xylazine was mixed with ketamine and Tiletamine/zolazepam scored by Chen and Chee (2005) [9], while, in the present study recovery period was very short and scored about 10 minutes. The former result is most likely due to the excitatory effect of both tramadol and ketamine. Physiological parameters didn't score any significant variation between the two groups, which suggests that tramadol

produces little or no cardiopulmonary depressing effect that make it possible to use the combination without anticholinergic premedication. Anesthesia lasted for about 45 minutes in xylazine ketamine group. This result was close to that recorded by Li et al. (2013) [10]. Longer anesthesia period was noted in the xylazine-ketamine-tramadol group. Also, it was longer than produced by xylazine-ketamine- tiletamine/zolazepam Chen and Chee (2005) and Li et al. (2013) [9,10].

Sedation was not significantly differed between the two groups. But, addition of tramadol increased significantly the duration of analgesia. These results were well-matched with using of tramadol in other combinations reported by Chen and Chee (2005) and Li et al. (2013) [9,10] and also supported by the recorded analgesic effect of solely used tramadol reported by [11]. Muscle tremors and convulsions were recorded preoperatively in 4 cats and postoperatively in 3 cats, this is likely to be due to

presentation of serotonin like effect of both tramadol and ketamine during induction and recovery [12,13]. The present study showed that xylazine-ketamine combination associated with tramadol caused adequate immobilization characterized by rapid induction, adequate analgesia and a state of balanced anesthesia sufficient for short to medium surgical procedure with a single complication which is convulsion or seizures that may arise in some cases. Regarding this result, further studies on using other sedative-muscle relaxing anti-convulsant agents like diazepam or midazolam may be tested for controlling this complication.

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