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Original Article

Anesthetic, Analgesic and Physiological Effects of Intramuscular Xylazine-Ketamine Cocktail Alone or with Tramadol 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.

INTRODUCTION

Injectable agents are very common for induction and/or maintenance of general anesthesia in cats. Alpha$_2$ (α_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 α_2 adrenoreceptor agonist widely used in cats for its sedative, analgesic and muscle relaxant effects [2]. Xylazine is often combined with Ketamine to increase its anesthetic and analgesic effects and to reduce the dose required to induce satisfactory anesthesia. However, administration of xylazine is associated with adverse effects including bradycardia and respiratory depression [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, rigidity and convulsive seizures are centrally mediated. Ketamine produces a dose dependent depression of cardiac function [4]. Tramadol hydrochloride (HCL) is a centrally acting analgesic that is structurally related to codeine and morphine [5]. It acts as a weak m-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 has 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

The current study was approved by the animal studies ethics committee of the faculty of veterinary medicine, New Valley University. (Ref. No. 0003-6-2017). All cats used for the present study were indoor cats, they were housed in one place and received the same treatments.

Twenty healthy adult male domestic cats of Arabian and Egyptian Mau breeds ranging in age from 2-4 years and weighing between 3.0 kg to 4.2 kg were subjects in 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 to the experiment. The first group (XK group) contained 10 cats which 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 participating 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 induction animals were placed in right lateral recumbency, surgically prepared and draped for castration procedure. Eye ointment (Oxypol, EIPICO, Egypt) was used to protect eyes against dryness. Sedation, analgesia and muscle relaxation were recorded and evaluated in each time according to scales in Table 1 And recorded in monitoring sheet. The 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. With the assistance of the owner (non-medical specialized, protocol blinded person), behavioral changes were noted during induction, anesthesia and recovery. Statistical analysis consisted of the Mann-Whitney's test for non-parametric values performed in SPSS v.18. A probability level of 5% ($P < 0.05$) was considered significant. All values are reported as mean ± standard deviation.

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 about three 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. Clonic convulsions were recorded in four cats during induction with XKT combination. One cat of the four and two others of the XKT group showed convulsions during recovery. Convulsions were characterized by rigid open mouth, twitches and rigidity of the four limbs and rigidity of abdominal muscles. Convulsions started suddenly and lasted for seconds. Induction with XKT combination administered intramuscularly in the thigh muscles was also characterized by slow onset in which the animal stands or moves on its fore feet and drag the hind quarter which looks as if it is 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, although induction time was not significantly different between two treatments. Vomiting was recorded in two cases in XK group and convulsions was recorded in six cats of XKT group. Temporary apnea was observed in two cats in XK group during anesthesia stage. No abnormal behavior observed in any of the cats during or after anesthesia. In the XKT group, animals were more conscious during recovery as they make several attempts to raise head and stare, stand with the fore feet or and more frequently vocalize. Ataxia and uncontrolled behavior were rarely observed during recovery in XK group. There was no significant difference in physiological variables between the two different protocols **(Table 3)**. Sedative effect recorded in XK group was significantly high during the first 40 minutes than in XKT group. Cats in XKT group showed significant lower but long-lasting sedative effect. Significant analgesia recorded up to 30 minutes in XK group. During the last 30 minutes, XKT produced more analgesia than XK. Muscle relaxation was significantly higher in XK group allover the time line than XKT. Sedation, analgesia and muscle relaxation scores were recorded in **Table 4**.

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, in consistent with previous reports of Chen [9] and [10]. In contrast, in results reported [10], xylazine-ketamine-tramadol resulted in longer induction period than Tiletamine/

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

Criteria	Score	Observation
Sedation score [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)
Analgesia score [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)
Muscle relaxation score [evaluated by degree of easiness of mouth opening and degree of hind limb flexion]	0 1 2 3	Mouth can't be opened Mouth can open with resistance Mouth opens with little effort 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 2: Induction, anesthesia and recovery periods calculated in minutes.

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

Table 3: Variations in physiological parameters.

Regimen	Rectal temperature (°C)						
	0 min.	10 min.	20 min.	30 min.	40 min.	50 min.	60 min.
XK	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
XKT	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)							
XK	117±10	133±11	129±16	124±12	120±13	114±12	122±13
XKT	118±10	135±10	130±11	125±12	120±11	112±10	119±9
Respiratory rate (B/min)							
XK	22±2	29±8	25±4	23±1	25±2	23±1	23±2
XKT	23±1	30±5	26±4	24±3	24±4	24±2	24±1

Table 4: Sedation, analgesia and muscle relaxation parameters.

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

zolazepam-xylazine-tramadol combination. Recovery period was longer when Xylazine was mixed with ketamine and Tiletamine/zolazepam scored [9], while in the present study the 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 and make it possible to use the XKT combination without anticholinergic premedication. Anesthesia lasted for about 45 minutes in xylazine ketamine group. This result was close to that recorded [10]. Longer anesthesia period was noted in the xylazine-ketamine-tramadol group (49 minutes). Also, it was longer than produced by xylazine-ketamine- tiletamine/zolazepam [9,10].

Sedation was not significantly differed between the two groups all over the duration of the procedure. But, addition of tramadol increased significantly the duration of analgesia. These results were well-matched with using of tramadol in other combinations reported [9] and [10] and supported by the recorded analgesic effect of solely used tramadol reported [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 longer analgesia and a state of balanced anesthesia adequate for short to medium-duration 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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