



Research in

ISSN : P-2409-0603, E-2409-9325

**AGRICULTURE, LIVESTOCK and FISHERIES**

An Open Access Peer-Reviewed Journal

Open Access

Res. Agric. Livest. Fish.

Research Article

Vol. 6, No. 1, April 2019 : 127-132.

## EFFECTS OF ATROPINE SULPHATE, XYLAZINE HYDROCHLORIDE, KETAMINE HYDROCHLORIDE AND DIAZEPAM IN CATS

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### ARTICLE INFO

### ABSTRACT

**Received**

10 April, 2019

**Accepted**

24 April, 2019

**Online**

30 April, 2019

**Key words:**

Cats

Atropine sulphate,

Xylazine hydrochloride

Ketamine hydrochloride

Diazepam

In this experiment eighteen (18) apparently healthy female cats were assigned in three anesthetic groups to attain the objectives of assess the efficacy and adverse effects of anesthetic agents. The body weight of the cats ranged from 2.5 to 3 kg and 8 to 12 months of age. There were divided into following three groups; A: atropine sulphate (0.04 mg/kg), xylazine hydrochloride (1 mg/kg) and Ketamine hydrochloride (5 mg/kg) body weight intramuscularly, B: xylazine hydrochloride (1 mg/kg) and ketamine hydrochloride (5 mg/kg) body weight intramuscularly and C: ketamine hydrochloride (5 mg/kg) and diazepam (1.4 mg/kg) body weight intramuscularly. The mean of induction period was significantly ( $P<0.05$ ) shorter in Group A and B. Duration of anesthesia, time to first movement there was no difference among these three groups. The induction period was  $2.67\pm0.82$ ,  $3.17\pm0.75$  and  $13\pm2.28$ , Duration of anesthesia was  $34.17\pm2.40$ ,  $39.33\pm1.75$  and  $35.33\pm2.73$ , Time to first movement was  $7.5\pm1.52$ ,  $6.67\pm1.03$  and  $7\pm0.894$ , Time to sternal position was  $10.67\pm1.21$ ,  $10.33\pm1.03$  and  $19.83\pm2.07$ , Time to standing position was  $14.67\pm2.07$ ,  $14.33\pm1.51$  and  $26.22\pm2.61$  respectively in case of Group A, Group B and C. The induction, duration and recovery period from anesthesia was smooth in atropine sulphate-xylazine-ketamine hydrochloride combination. Salivation was found in xylazine-ketamine hydrochloride combination. Vomition observed onset of action and salivation during recovery period in Ketamine hydrochloride-Diazepam combination. From this study it was found that atropine sulphate-xylazine-ketamine hydrochloride does not show any adverse effect on cat and is an identical satisfactory anesthetic combination which will be helpful for performing any surgical interventions for cats.

**To cite this article:** Haque M.M. and N.S. Lucky, 2019. Effects of atropine sulphate, xylazine hydrochloride, ketamine hydrochloride and diazepam in cats. Res. Agric. Livest. Fish. 6 (1): 127-132.



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## INTRODUCTION

Anesthesia is a reversible process which is targeted to produce a convenient, safe, effective, yet inexpensive means of chemical restraint so that medical or surgical procedure may be conducted with minimum stress, pain, discomfort, and toxic side effects to the patients or to the anesthetist (Thurmon et al., 1996 and William et al. 2007). Anesthesia is mandatory for successful surgical procedures with the aim to achieve desirable hypnosis, analgesia and muscle relaxation. General anesthesia is important for carrying out the major operations in small animal practices. An ideal anesthetic regimen for such procedures require, administration of drugs which have minimal cardiopulmonary depressant effects, produce optimum hypnosis and excellent muscle relaxation to ensure rapid and safe recovery.

Atropine is a plant alkaloid that has been used extensively in most animal species. The use of anticholinergic agents is controversial and their efficacy varies greatly with species (Wixson et al., 1987). This agent normally used as premedicants with other anesthetic drugs in veterinary practices to prevent or minimize the vagal effects that may induce bradycardia. Prevention of bradycardia is particularly important during lengthy surgical and experimental procedures involving the laboratory animals (Wixson et al., 1987). These drugs reduce potential smooth muscles spasms, gastrointestinal motility and secretion, salivation, animal respiratory secretion during anaesthesia and surgical manipulations (Thurmon, Tranquilli, Benson, 1996, Vangs, Sondore, 2008). Ketamine, as dissociative anesthetic agents have the potential to revolutionize the anesthetic management of the dogs and cats (Deyoung et al., 2000). The dissociative state produced by these agents is characterized by muscle rigidity and the presence of many reflexes (e.g. swallowing, laryngeal, corneal, palpebral and conjunctival reflexes), which are normally absent when other general anesthetic agents are used. Recently, research findings indicated that dissociative agents do not act by depression, but rather by excitation of central nervous system. These agents are largely excreted intact by the kidney and partially metabolized by the liver with renal excretion of metabolites (Deyoung et al., 2000). Ketamine hydrochloride is a congener of phencyclidine, is unique dissociative general anesthetic, which causes less cardiovascular depression and can be administered by intramuscular or intravenous route without appreciable tissue irritation (Lanning and Harmel, 2005). Ketamine hydrochloride produces a state of dissociative anesthesia and it causes the patient to feel dissociated from the environment during induction (Vangs, Sondore, 2008). Xylazine hydrochloride, an alpha-2 agonist used in animal experiments, which hinders nerve conduction in the central nervous system leading to relaxation of striated muscles. Xylazine hydrochloride can be inhaled or administered intravenously, intramuscularly, subcutaneously, or orally either by itself or in conjunction with other anesthetics, such as ketamine, barbiturate, chloral hydrate, and halothane in order to provide reliable anesthesia effects (Reyes et al., 2012). As a veterinary anesthetic, xylazine hydrochloride is typically only administered once for intended effect before or during surgical procedures (Greene and Thurmon, 2008). The sedative and analgesic effects of xylazine are related to central nervous system depression. Xylazine's muscle relaxant effect inhibits the transmission of neural impulses in the central nervous system. Diazepam is a potent hypnotic-sedative that causes muscle relaxation. It is a long-acting drug as it is metabolized slowly, and it has relatively weaker cardiovascular effects as compared to other sedative drugs (Durrani et al., 2008). Diazepam is a benzodiazepine tranquilizer and has the property to produce muscular relaxation, sleep and analgesia (Balaci and Andreescu, 2001). Diazepam is often used in general anaesthesia for its sedative, tranquilizing and muscle relaxant and anticonvulsant effects (Purvins, 1994). Drugs in this class act directly on the brain and are central nervous system depressants. Diazepam is a potent anticonvulsant, sedative and muscle relaxant and has been used as a premedicant particularly prior to dissociative anesthesia to reduce the muscular tremors (Hall and Clarke, 2009). It is considered relatively safe preoperative sedative for patients with underlying cardiac or metabolic diseases because it causes minimum cardiopulmonary side effects and provides good muscle relaxation. Therefore, the study was designed to evaluate the suitability of atropine sulphate-xylazine-ketamine hydrochloride, xylazine-ketamine hydrochloride and diazepam-ketamine hydrochloride combination for surgical procedures to investigate the effects of premedication and anesthetic agent's combination and to examine the aptness for short and long duration of these combinations in cats.

## MATERIALS AND METHODS

A total of eighteen apparently healthy female cats to investigate the effect of anesthetic, premedicant and sedative agent combination. The body weight of the cats ranged from 2.5 to 3 kg and 8-12 months of age. Cats were collected from Sylhet Agricultural University campus and surrounding local area like Baluchor, Sylhet. The experiment was conducted from 1st January to 5th April 2015 at Professor Moshleh Uddin Ahmed Chowdhury Veterinary Teaching Hospital and Surgery and Theriogenology Department, Veterinary, Animal and Biomedical Sciences Faculty, Sylhet Agricultural University, Sylhet. The cats were fasted overnight prior to introducing of anesthesia. The experimental cats were divided into following three groups and allocated with the different anesthetic agents:

**Group A:** Six cats were administered with atropine sulphate-xylazine-ketamine hydrochloride combination with the dose rate of 0.04 mg/kg, 5 mg/kg and 1 mg/kg body weight, respectively at intramuscularly.

**Group B:** Six cats were administered intramuscularly with xylazine-ketamine hydrochloride at the dose rate of 1 mg/kg and 5 mg/kg body weight.

**Group C:** Six cats were used to inject with diazepam-ketamine hydrochloride at the dose rate of 1.4 mg/kg and 5 mg/kg body weight intramuscularly.

The anesthetic period was recorded carefully, monitoring the different reflexes and observing conditions of the cats. The period prolonging from time of injection up to the onset of recumbency was mentioned as the period of induction. The recovery period lengthens from the stage of reappearance of consciousness up to the stage when the cats stand on feet.

## STATISTICAL ANALYSIS

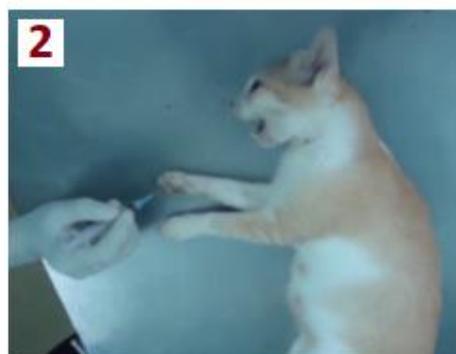
The data generated from this experiment were entered in Microsoft Excel worksheet, organized and processed for further analysis. Analysis was performed with the help of the ANOVA.

## RESULTS

The longest induction period ( $13 \pm 2.28$  min) was observed in case of Diazepam-Ketamine hydrochloride combination (group C) at the dose rate of 1.4 mg/kg and 5 mg/kg body weight. The shortest induction period ( $2.67 \pm 0.82$  min) was observed in group A, at the dose rate of 0.04 mg/kg, 1 mg/kg and 5 mg/kg body weight with atrophine-xylazine-ketamine hydrochloride combination (Table 1). The longest duration of anesthesia ( $39.33 \pm 1.75$  min) was recorded with xylazine-ketamine hydrochloride combination (group B) at the dose rate of 1 mg/kg and 5 mg/kg body weight. While the shortest duration ( $34.17 \pm 2.40$  min) of anesthesia was observed at the dose rate 0.04 mg/kg, 1 mg/kg and 5 mg/kg body weight with atrophine-xylazine-Ketamine hydrochloride combination (Table 1). The longest duration of time to first movement ( $7.5 \pm 0.894$  min) was recorded with atrophine-xylazine-Ketamine hydrochloride combination at the dose rate 0.04 mg/kg, 1 mg/kg and 5 mg/kg body weight. While the shortest duration ( $6.67 \pm 1.03$  min) was recorded with ketammine-xylazine hydrochloride combination at the dose rate 5 mg/kg and 1 mg/kg body weight (Table 1). The longest duration ( $19.83 \pm 2.07$  min) of time to sternal position was recorded with Diazepam-Ketamine hydrochloride combination at the dose rate of 1.4 mg/kg and 5 mg/kg body weight. While the shortest duration ( $10.33 \pm 1.03$  min) was recorded with xylazine-ketammine hydrochloride combination at the dose rate of 1 mg/kg and 5 mg/kg body weight (Table 1). The longest duration ( $26.22 \pm 2.61$  min) of time to standing position was recorded with Diazepam-Ketamine hydrochloride combination at the dose rate of 1.4 mg/kg and 5 mg/kg body weight. While the shortest duration ( $14.33 \pm 1.51$  min) was recorded with xylazine-ketammine hydrochloride combination at the dose rate of 1 mg/kg and 5 mg/kg body weight (Table 1). The induction of anesthesia produced by group A and B was found fast and smoothly as compared to group C.



**Figure 1.** The figure shows an anaesthetized cat;



**Figure 2.** The figure shows the depth of anesthesia was monitored by pinching a needle on the paw

**Table 1.** Induction, duration, time to first movement, time to sternal position and time to standing position of anesthetic combinations

Groups	Combination	On set of Action (min)	Duration of Anesthesia (min)	Time to first Movement (min)	Time to Sternal Position (min)	Time to Standing Position (min)
A	Atrophine Sulphate-Xylazine-Ketamine HCL	2.67±0.82	34.17±2.40	7.5±1.52	10.67±1.21	14.67±2.07
B	Xylazine HCL-Ketamine HCL	3.17±0.75	39.33±1.75	6.67±1.03	10.33±1.03	14.33±1.51
C	Diazepam-Ketamine HCL	13±2.28	35.33±2.73	7±0.894	19.83±2.07	26.22±2.61
P-value		0.01**	0.83	0.67	0.01**	0.01**

## DISCUSSION

Clinical anesthetic trial was conducted in present study with the pre anesthetic, sedative and anesthetic combinations. The similar result also observed by Nesgash et al., 2016. The anesthetic parameters: induction time, duration of anesthesia, time for sternal recumbency, time for unassisted standing in munities recorded during the study was presented by them. The result of the present study was in line with the findings of Azizpour and Hassani (2012). The slow induction of anesthesia result in group C was similar to the reports of the earlier studies in sheep (Ozkhan et al., 2010). When Ketamine and Diazepam used together, they have a synergistic effect resulting in a smooth recovery and better muscle relaxation and their efficacy is enhanced which was in line of agreement with Sumitra et al. (2004) conducted a research on male Wistar rats. Duration of anesthesia, time to first movement for Group A, Group B and Group C was found, which was contradictory to the previous study observed in the study of birds by Durrani et al., 2008. This might be due to dose and species difference as compared to the previous study.

In the present study, smooth recoveries were observed significantly in group A (Atropine, Ketamin and xylazine hydrochloride) than group B and C. Durrani et al., 2008 and Mahmud et al., 2014 were observed smooth recoveries with the administration of Diazepam-Ketamine anesthesia. The longest recovery period was observed in the birds of Diazepam-Ketamine anesthesia, which was desirable since Diazepam could augment Ketamine's anesthetic effects decreasing its effects; thus, it provided necessary depth and duration

of anesthesia for the comfortable completion of surgeries (Mahmud et al., 2014). Diazepam and Ketamine induced a synergistic action producing a deep analgesia for long duration. Similar observations were also reported in pigeons using ketamine-diazepam (Durrani et al., 2008 and Lumeij et al., 2003). This result is in line with the present study in which the duration of recovery of group C was significantly longer than group A and group B. Although Diazepam is an initial cause of salivation, but the loss of spontaneous swallowing and the loss of spontaneous tongue reflex occurred during this study might be the cause of salivation observed after recovery as a result of Diazepam injection.

## CONCLUSION

The results of the present study concluded that atropine sulphate-xylazine and ketamine hydrochloride combination is useful and a very satisfactory anesthetic protocol for excellent induction, adequate muscle relaxation, satisfactory duration of anesthesia and smooth recovery in cats. Prolonged induction and recovery of anesthesia with some complications like salivation and vomiting were found in Ketamine hydrochloride-diazepam combination. No cats were died during anesthesia or after recovery from anesthesia. All drug combinations can be safe for surgical operation if used appropriately. However, further studies are required to evaluate the effects on duration of anesthesia and cardiopulmonary function of these drug combinations in detail which will be helpful for performing any surgical operation.

## CONFLICT OF INTEREST

The author does not have any conflict of interest.

## ACKNOWLEDGEMENT

The authors are grateful to the authority and all concerned technical staffs of the Department of Surgery and Theriogenology, Faculty of Veterinary, Animal and Biomedical Sciences, Sylhet Agricultural University, Sylhet, Department of Medicine and Surgery, Faculty of Veterinary and Animal Sciences, Chittagong Veterinary and Animal Sciences University, Chittagong, Bangladesh for efforts in providing data for this study. The authors are also acknowledged with thanks and gratefulness to the authority of Professor Mosleh Uddin Ahmed Chowdhury Veterinary Teaching Hospital, Sylhet Agricultural University, Sylhet.

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