



Sedative and Analgesic Effects of Xylazine, Ketamine and Diazepam in Ducks

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ABSTRACT

In bird's practice use of single anesthetic drug has failed to induce a safe and deep anesthesia for surgical as well as painful conditions. However, this problem can be solved with usage of anesthetic combinations. This study was aimed at comparative evaluation of two anesthetics combinations *viz.* ketamine-xylazine (K+X) and ketamine-xylazine-diazepam (K+X+D). A total of 20 ducks presented at pet center University of Veterinary and Animal Sciences Lahore were divided into 2 equal groups each carrying 10 birds. The birds were monitored for various physiological parameters before and after anesthesia. The birds of K+X group were given ketamine hydrochloride (15 mg/kg) and xylazine (5 mg/kg), while K+X+D group were given ketamine hydrochloride (15 mg/kg), xylazine (2.5 mg/kg) and diazepam (2.5mg/kg) cocktail, respectively. The birds were monitored for 130 min post administration for various physiological parameters like; body temperature, heart rate and respiratory rate with normal averages 105.02±0.12°F, 103.75±3.18 beats/min and 19.2±1.62 breaths/min, respectively. All the physiological parameters varied significantly ($p<0.05$) between the two groups with exception of body temperature, which varied non-significantly ($p>0.05$). The post drug administration onset of sedation in ducks anesthetized by K+X was delayed (2.11±0.75 min) than K+X+D (1.14±0.04 min). The duration of sedation in the ducks anesthetized with K+X+D was prolonged (127.42±18.60 min) than K+X (87.33±6.74 min). The recovery of ducks from sedation was recorded quicker in K+X (89.53±6.22 min) than K+X+D (128.56±18.52 min). Onset of analgesia in ducks anesthetized by K+X was delayed (3.22±0.54) than K+X+D (1.67±0.77 min). The duration of analgesia in the ducks anesthetized with K+X+D was prolonged (81.15±11.17 min) than K+X (39.76±3.89 min). The recovery of ducks from analgesia was recorded slower in K+X+D (82.82±11.15 min) than K+X (82.82±11.15 min). This study found K+X+D a better combination over K+X producing prolonged sedation and analgesia and can be preferably used in surgical procedures of ducks.

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Authors' Contribution

HMA, HBR and MAK designed and conceived the study. HMA and AKM conducted the study. HMA, MI and SHF collected and analyzed the data. HMA, MRU and UG wrote the manuscript. SHF and MI reviewed and approved the manuscript.

Key words

Xylazine, Ketamine, Diazepam, Ducks, Analgesic, Sedatives.

INTRODUCTION

The use of anesthesia is very important in ducks for surgical procedures. The success of surgical procedure is dependent upon anesthesia to save the duck if it is injured (Summerfelt and Smith, 1990). Injectable anesthetics are used in birds to reduce stress for diagnostic purposes and surgical procedures. The injectable anesthetic agents that are easily available in Pakistan are xylazine, ketamine and diazepam, which are commonly used as sedative and analgesic agents for avian species.

Xylazine (20mg/ml) is a potent muscle relaxant, hypnotic and powerful central muscular relaxant. Xylazine, is usually used in combination with ketamine.

Mostachio *et al.* (2008) reported that the intramuscular injection of xylazine smoothly induces loss of righting reflex and response to painful stimulus in leghorn roosters. Lee-Parritz (2013) stated that xylazine is a potent, non-narcotic sedative, muscle relaxant, and analgesic. Xylazine is a water soluble agent that can be mixed with ketamine solution without precipitation. Xylazine is a sedative agent but it is also being used as an anesthetic agent in ruminants.

Diazepam is mostly used to treat anxiety and muscle spasms. It can also be used before certain medical procedures to reduce tension and in some surgical procedures to induce amnesia. Javdani *et al.* (2011) studied twelve healthy parrot birds received xylazine-ketamine regimen and diazepam-ketamine regimen. The effects of each combination on heart rates, respiratory rates, cloacal temperatures and the foot web pinch responses with the time of inductions, maintenance and recovery periods of anesthesia were recorded. The combinations gave distinct

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variation in terms of effects over the mentioned parameters.

Ketamine has become a popular drug due to its wide use in birds, animals and all species of primates. It has been recommended by several researchers as a suitable anesthetic agent for birds. However, it is rarely used alone due to poor muscle relaxation, persistent pain reflex responses, and muscle tremors, opisthotonus and rough recoveries (Christensen *et al.*, 1987; Mohammad *et al.*, 1993). It lacks cardio-pulmonary depression effect. To overcome these undesirable side effects various drugs such as xylazine ($\alpha 2$ -agonist) compound, have been used in combination with ketamine. Diazepam provides muscle relaxation and act as sedatives, while xylazine also provide analgesia. The pharmacological action of Diazepam enhances the effect of the neurotransmitter (Laweighon, 1996).

These drugs are usually used in combination with ketamine to induce anesthesia characterized by marked analgesia and a smooth recovery in various animal species (Mohammad *et al.*, 1993). The aim of study is to determine sedative and analgesic effect of xylazine, ketamine and diazepam administered intra muscular (i.m.) in ducks in two different combinations patterns.

MATERIALS AND METHODS

Ducks

A total of 20 ducks presented at Pet Centre, UVAS Lahore for various procedures. The birds were kept under observation at Pet Centre, Department of Clinical Medicine and Surgery, University of Veterinary and Animal Sciences, Lahore for 24 h.

Experimental design

The birds (ducks) were divided into two equal groups, ten (10) birds in each group. One group was administered with ketamine hydrochloride (15 mg/kg) and xylazine (5 mg/kg), while the second group was given ketamine hydrochloride (15 mg/kg), xylazine (2.5 mg/kg) and diazepam (2.5mg/kg) cocktail intramuscularly (i.m.) in chest muscles. Water and feed of birds was withheld for 12 h before the administration of drugs. Normal physiological parameters were recorded before starting the experiment.

The ducks after anesthesia were monitored for their body temperature, respiratory rate, heart rate and other physiological parameters associated with anesthesia. The physiological parameters were monitored for 130 min (after every 10 min). The readings for all study parameters were monitored from the time of anesthetics administration till recovery. Observations recorded on sedative parameters (onset of sedation, duration of sedation, and recovery from sedation), analgesic parameters (onset of analgesia,

duration of analgesia, and recovery from analgesia) were observed. Other observations like blinking of eyes, lifting of head, neck movement, wing flapping, salivation, defecation and skin prick test were also monitored.

Statistical analysis

All the physiological records collected at various times of experiment were subjected to independent *t*-test using SPSS version 20. The level of significance was set at 95%.

Table I.- Sedative and analgesic effects (Mean±SD) of ketamine (K), xylazine (X) and diazepam (D) combinations in ducks.

Parameters	K+X	K+X+D
Sedative effects		
Onset of sedation (min)	2.11±0.75	1.14±0.40
Duration of sedation (min.)	87.33±6.74	127.42±18.60
Recovery from sedation (min)	89.53±6.22	128.56±18.52
Analgesic effects		
Onset of analgesia (min)*	3.22±0.54	1.67±0.77
Duration of analgesia (min)*	39.76±3.89	81.15±11.17
Recovery from analgesia (min)*	43.37±4.42	82.82±11.15

*significant difference ($p < 0.05$) for a parameter among the two groups.

RESULTS

Table I shows the sedative effects of K+X and K+X+D combinations which shows significant difference between the two groups. The onset of sedation in ducks induced with K+X+D combination was significantly ($p < 0.05$) faster than the K+X group. While, the recovery from sedation was significantly ($p < 0.05$) delayed in K+X+D group as compared to the K+X. Similarly, the analgesic effects also followed the pattern as discussed for sedation. The onset of analgesia was significantly ($p < 0.05$) faster in K+X+D group than the K+X. While, the analgesia significantly ($p < 0.05$) lasted for prolonged time in K+X+D group as compared to the K+X.

The results in relation to analgesic effects of K+X and K+X+D on anesthetized ducks are shown in Table I, which suggests that onset of analgesia in ducks anesthetized by K+X and K+X+D was recorded in 3.22±0.54 and 1.67±0.77 min after drug administration. The duration of analgesia in the ducks anesthetized with K+X and K+X+D was 39.76±3.89 and 81.15±11.17 min, respectively. The recovery of ducks from analgesia was recorded in 43.37±4.42 and 82.82±11.15 min, when anesthetized with K+X and K+X+D, respectively.

Table II.- Body temperature (°F) (Mean±SD) of ducks injected with ketamine (K), xylazine (X) (K+X group) and ketamine, xylazine and diazepam (D) (K+X+D group).

Time (min)	K+X	K+X+D
Control	105.28±0.63	105.64±0.55
10	105.04±0.78	105.3±0.53
20	105.00±0.69	105.14±0.27
30	104.94±0.74	104.92±0.19
40	104.96±0.90	104.78±0.34
50	105.08±0.95	104.74±0.49
60	104.98±0.99	104.68±0.41
70	104.82±0.89	104.66±0.36
80	105.04±0.70	104.94±0.36
90	105.04±0.62	104.94±0.21
100	105.00±0.65	104.94±0.21
110	105.20 ±0.69	104.94±0.19
120	105.06±0.65	105.06±0.25
130	105.10±0.69	104.94±0.86

Table III.- Heart rate (beats/min) (Mean±SD) of ducks injected with ketamine (K), xylazine (X) (K+X group) and ketamine, xylazine and diazepam (D) (K+X+D group).

Time (min)	K+X	K+X+D
Control	106.9±2.07	107.4±1.88*
10	103.9±2.64	104.4±2.41*
20	103.9±7.92	106.9±8.63
30	106.5±11.51	101.4±8.17
40	101.2±2.97	97.6±6.93
50	103.4±9.70	93.1±5.17
60	100.3±3.19	89.9±3.90
70	100.9±2.68	88.5±3.74
80	101.9±1.91	92.2±4.04
90	103±3.33	94.1±3.72
100	104.1±1.96	97.5±3.20
110	104.9±2.46	101.2±2.29
120	105.8±2.04	102.5±3.27
130	105.9±2.18	104.2±1.61

*significant difference ($p<0.05$) for a parameter among the two groups.

The body temperatures, heart rate and respiratory rates were also monitored in both the groups (Tables II, III, IV). The average normal body temperature was recorded 105.02±0.12°F. The results showed a non-significant ($p>0.05$) difference in the body temperatures of two experimental groups *i.e.* K+X and K+X+D, respectively. The average normal heart rate was 106.9±2.079 beats/min. The study showed a significant difference ($p<0.05$) in the

heart rates between the groups. The birds of K+X group presented higher heart rates as compared to the group K+X+D. Considering the normal average respiratory rate 19.2±1.62 breaths/min, there was a significant difference ($p<0.05$) in the respiratory rates of the two groups. The respiratory suppression was higher in K+X+D group than K+X group.

Table IV.- Respiratory rate (breaths/min) (Mean±SD) of ducks injected with ketamine (K), xylazine (X) (K+X group) and ketamine, xylazine and diazepam (D) (K+X+D group).

Time (min)	K+X	K+X+D
Control	21.4±2.50	21.6±2.27
10	19.7±2.50	19.6±1.26
20	17.9±2.23	17.1±2.13
30	17.3±1.70	16.2±2.20
40	16.7±4.40	16.2±2.20
50	17.3±5.90	14.9±2.92
60	17.8±6.81	13.9±2.60
70	19.4±1.71	13.7±2.98
80	20.9±2.07	13.2±1.39
90	18.5±2.10	13.2±1.93
100	19.9±4.01	14.2±1.75
110	20.0±2.05	15.9±2.60
120	20.5±2.30	17.1±1.91
130	21.5±1.71	18.8±1.68

*significant difference ($p<0.05$) for a parameter among the two groups.

The other physiological parameters kept under consideration were blinking of eyes, lifting of head, neck movement, wing flapping, salivation and defecation were observed. In K+X group 04, 06, 08, 02, 01 and 01 birds showed blinking of eyes, lifting of head, neck movement, wing flapping, salivation and defecation, respectively. In K+X+D group 01, 02 and 06 birds showed blinking of eyes, lifting of head, neck movement, respectively, while, wing flapping, salivation and defecation was not found in any bird.

DISCUSSION

Our findings are in agreement with other researchers who used different doses of these anesthetics on different birds in various regions of the world. A number of drugs are in use to anesthetize the birds. Intramuscular (*i.m.*) injections of both combinations *i.e.* K+X and K+X+D smoothly induce loss of labyrinthine righting reflex and response to painful stimulus in ducks (Mostachio *et al.*, 2008). Xylazine, detomidine and medetomidine are

usually used in combination with ketamine (Freed and Baker, 1989). Ashraf *et al.* (2009) studied the effects of xylazine, ketamine, and a cocktail of them. All treatments were administered i.m. They suggested that in parrots the use of xylazine (alone) was safe for handling and less painful procedures while a xylazine-ketamine cocktail was a suitable anesthesia for painful procedures. Ketamine alone or in combination with diazepam or xylazine has been used and assessed as an anaesthetic in a wide range of animals including dogs, cats, pigs, sheep, goats, non-human primates, snakes, tortoises, lizards, birds, ferrets, rabbits, guinea pigs, rats, mice and hamsters. Ketamine alone has serious limitations in most species, but in conjunction with other anesthetics has proved valuable (Green *et al.*, 1981).

The current study shows that all the physiological parameters with the exception of body temperature varied significantly between the two experimental groups. The other sedative and analgesic parameters of ducks treated with K+X and K+X+D were also significantly ($p < 0.05$) distinct. This study revealed K+X+D a superior combination over K+X combination in terms of least effects on physiological parameters as well as prolonged duration of sedation and analgesia. Ajadi *et al.* (2009) also found that, midazolam (a member of benzodiazepine class) administered intramuscularly appeared to improve the anesthetic quality of ketamine and xylazine in guinea fowls without adversely affecting safety. In another study, Vesal and Eskandari (2006) stated that; compared with the xylazine-ketamine combination, duration of dorsal recumbency was longer after midazolam-ketamine administration, which also coincides with the finding of current study. The effect of xylazine has been found to lower the respiratory rate in birds anesthetized with a ketamine-xylazine combination (Degernes *et al.*, 1988). This finding is also in agreement to this study which found a significantly lower respiratory rate in birds.

Many other studies support the findings of current study who, used various anesthetic combinations like; detomidine-ketamine for rapid anesthesia in parrots (Durrani *et al.*, 2005), combination of ketamine+detomidine or diazepam for effective and safe anesthesia in parrots for surgical operations (Ghadiri *et al.*, 2006). Furthermore, contrary to the findings of this study, Metehan *et al.* (2006) used xylazine-diazepam combination and medetomidine-detomidine and did not notice any significant change in heartbeat, respiration and body temperature. Lumeij *et al.* (2009) used medetomidine-ketamine and diazepam-ketamine combination in parrots. Maan *et al.* (2018), however, found a suppression effect on heart rate, blood pressure and saturation of oxygen with the use of both injectable and inhalation anesthesia in rabbits.

This study concludes that for safe and deeper anesthesia in birds (ducks) combinations of anesthetics are preferred rather than single anesthetic uses. The K+X+D combination has been found superior to K+X combination for prolonged and deep anesthesia with better sedation and analgesia.

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Statement of conflict of interest

The authors bear no conflict of interest in submitting or publishing of this data.

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