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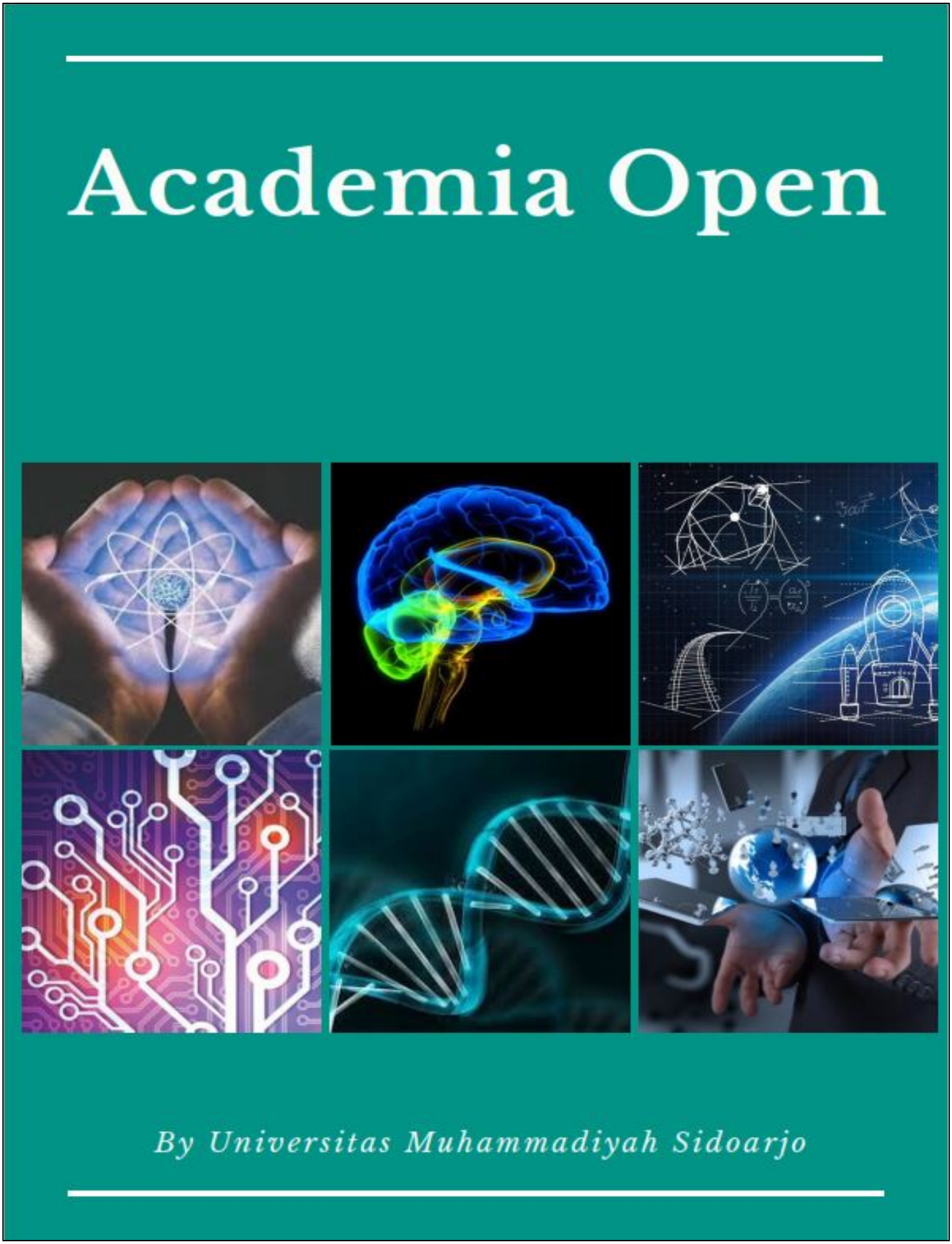

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Xylazine-Ketamine Outperforms Diazepam-Ketamine in Rabbit Anesthesia

Xylazine-Ketamin Mengungguli Diazepam-Ketamin dalam Anestesi Kelinci

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Abstract

Background: Limited research on the effects of ketamine combinations on rabbit anesthesia underscores the need for safe and effective injectable methods. **Specific Background:** This study compares the efficacy and safety of two anesthetic combinations—xylazine-ketamine and diazepam-ketamine —in rabbits to address this gap. **Knowledge Gap:** Ketamine combinations are commonly used in rabbits, but there is limited data on their effects on analgesic properties and anesthesia duration. **Aims:** The study assesses the onset of righting reflex loss, analgesia duration, recumbency duration, and standing attempts in rabbits treated with XK and DK. **Results:** Ten healthy rabbits were administered XK (5 mg xylazine and 10 mg ketamine per kg) or DK (1 mg diazepam and 30 mg ketamine per kg) intramuscularly. The study found no significant difference in OLRR between the groups. Only XK produced significant analgesia (OA: 4.5±0.2 min, DA: 45.1±1.9 min), while DK showed no analgesic effect. DR and ATS were significantly shorter in XK (56.1±3.1 min and 7.3±0.7 min) compared to DK (121.1±7.5 min and 25.3±1.2 min). **Novelty:** The study compares XK and DK in rabbits, finding XK provides superior analgesia and faster recovery times, while DK is ineffective for pain management. **Implications:** The study indicates that XK is more effective for analgesic procedures, while DK is recommended for painful treatments with additional analgesics.

Highlights:

1. XK Provides Analgesia: Only Xylazine-Ketamine offers significant pain relief.
2. Shorter Recovery Time: XK results in quicker recovery compared to DK.
3. DK Needs Supplement: Diazepam-Ketamine requires additional analgesics for pain management.

Keywords: Anesthesia, Xylazine-Ketamine, Diazepam-Ketamine, Rabbits, Analgesia

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Introduction

When studying the effects of various surgical techniques, rabbits are commonly utilized as test subjects. Given that inhalant anaesthetic administration devices might present practical problems in rabbits, intubation of volatile anesthetic drugs can be overly complicated, time-consuming, and prone to producing apnea. These considerations highlight the need for a safe, simple, and injectable method that provides adequate depth of anesthesia for rabbits without sacrificing quality or recovery, all without requiring extremely complex equipment [1]. There are a number of injectable anesthetics that have been tried on rabbits, ketamine is among them. This drug is widely used in the fields of veterinary and human medicine to put patients to sleep during surgeries by reducing the amount of calcium influx into neurons and depressing the central nervous system (CNS). However, when given to rabbits as a single anesthetic, ketamine can induce skeletal muscle convulsions, deprived analgesic reflex response, and a traumatic recovery [2]. To enhance the anesthetic effects of ketamine in rabbits, we combined it with xylazine, an alpha 2 receptor agonist that acts by stimulating presynaptic adrenergic receptors, resulting in reduced catecholamine release from nerve endings. In addition to its extensive usage as a pre-anesthetic to provide balanced anesthesia in many animals, xylazine is a powerful analgesic and muscle relaxant compared to related anesthetic drugs [3]. Diazepam was also utilized for these purposes. Rabbits are at least seven times more likely to die from anesthesia-related causes than either dogs or cats, while being the third most often anesthetized species [4]. Despite the widespread use of both groups of ketamine drugs, little research has been conducted on their effectiveness or safety in rabbits.

By administering two doses of the xylazine-ketamine (XK) and the diazepam-ketamine (DK) intramuscularly (im) to rabbits, the objective of this study was to determine whether or not these two combinations were safe and efficacious.

Methods

Experimental animals

Ten adult male rabbits, all of whom seemed to be in good health, considering 1.6 ± 0.2kg (mean ± sem). Each pair of rabbits was placed in cages at the College of Veterinary Medicine- University of Basrah, and each animal was carefully examined for general health issues before the experiment began. The animals were given a diet of green grass and clean water to drink. The study was conducted after obtaining approval from the Ethical Committee with BCVM regulations of the Veterinary Medicine College, Basrah University.

Study protocol

There were two groups of anesthesia given to the ten rabbits at random. Anesthesia was administered using either the xylazine-ketamine (XK) or diazepam-ketamine (DK) procedures. The rabbits were first given xylazine as a premedication of (20 mg/ml) from Alfasan in Woerden, The Netherlands), at a dosage of 5 mg/kg body weight [5]. But the other group, they were given diazepam (5 mg/ml) from Roche products Ltd in Welywn Garden City, U.K., at a dosage of 1 mg/kg body weight. Each group underwent anesthesia for thirty minutes following premedication. Ketamine (Ketamine Fresenius ®, Fresenius Kabi, Austria; 50 mg/ml) was giving at a dosage rate of 10 mg/kg if xylazine (XK) was premedicated, and 30 mg/kg if diazepam (DK) was premedicated [6]. Each and every medication was injected intramuscularly.

The analgesic effect was evaluated by monitoring the pedal withdrawal response right after anesthesia was induced. At 2-minute intervals, the rabbits' rear feet were pinches using a couple of hemostatic forceps close to the initial ratchet. We timed how long it took for the rabbits to stop retracting their hind limbs in reaction to the pinch, in other words, when they lost their pedal reflex. At intervals of two minutes, the rabbit's paws were pinched until it began to retract its hind legs in reaction. This duration was noted as the period when the pedal reflex returned. The anesthetized rabbits were put on a padded hardwood table in right lateral recumbency once they lost their righting reflex. [7].

Calculated anaesthetic indices

A number of anesthetic indices were computed based on the following parameters [3]:

a) The onset of loss of righting reflex (OLRR): is how much time, measured in minutes, that elapses among the administration of ketamine to the rabbit and the beginning of the loss of the righting reflex.

b) Onset of analgesia (OA): time interval (in minutes) between the ketamine injection and the anesthetized rabbit's loss of the pedal withdrawal reflex in both hind limbs.

c) Analgesia duration (DA): a measure of the amount of time, measured in minutes, that occurs when an anesthetic rabbit's pedal withdrawal reflex in either its hind limbs is temporarily lost and then gained back.

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d) The duration at recumbency (DR): is the time in minutes it takes for the anesthetized rabbit from loss of righting reflex until assume a sternal posture.

e) Attempt to stand (ATS): is the amount of time (in minutes) that passes between the anesthetized rabbit assuming a sternal position and standing.

Analysis of data

The recorded information was computed using the means ± standard error of means (sem) of ten rabbits. One way ANOVA was used to compare the means of OA, DA, DR, ATS, and OLRR for XK and DK. For each comparison, a value of $P < 0.05$ was deemed statistically significant. [8].

Result and Discussion

Table 1 displays the anesthetic indices for the two medication combinations. There was no significant difference in OLRR between the two medication combinations. DK showed no discernible analgesic effect, whereas XK showed OA of 4.5±0.2min and DA of 45.1±1.9 min.With XK values of 56.1±3.1 and 7.3±0.7, respectively, DR and ATS were much shorter ($P < 0.05$) than with DK values of 121.1±7.5 and 25.3±1.2 minutes.

Table 1: Anesthetic lists of rabbits given intramuscular ketamine after being premedicated with injectable xylazinea and diazepamb

Groups receiving therapy		Index
XK	DK	
3.3±0.2	2.2±0.0	OLRR(min)
4.5±0.2	NA	OA(min)
45.1±1.9	NA	DA(min)
56.1±3.1	121.1±7.5	DR(min)
7.3±0.7	25.3±1.2	ATS(min)

Table 1.

The results were presented as the means ± SEM of ten rabbits.

a- 5 mg/kg xylazine, then 10 mg/kg ketamine 30 minutes afterward

b- Administer 1 mg/kg diazepam first, and then 30 min later, 30 mg/kg ketamine.

OLRR- the onset of loss righting reflex.

OA- Onset of analgesia

DA- Duration of analgesia

DR- Duration at recumbency

ATS- Attempts to stand

NA- Not applicable

*P<0.05

In research involving two medication combinations, analgesia was only achieved by XK. The antinociceptive effect of XK does not qualify as only to the given ketamine, as it failed to provide any discernible analgesic effect when combined with diazepam, even at greater doses of xylazine (30 mg/kg) compared to (10 mg/kg). Without a doubt, the analgesic effects of ketamine were enhanced by the addition of xylazine to the medication combination.

Consistent with previous research, we found that XK produced analgesia in our study [3,9,10]. On the other hand, some researchers found no analgesia in any of the rabbits they tested, even when administered xylazine-ketamine at doses higher than those used in our research [11], and others found analgesia in a small number of rabbits for a brief time [12].

Xylazine-ketamine combinations in the other research experiments with rabbits provided only slight analgesia, with higher doses of xylazine-ketamine still showing increased pain levels. This could be due to the fact that the rabbits

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used in these experiments vary in terms of the breed or bloodline. It is to note that due to the fact that their reactions to anesthetics arguably show many degrees of differences even between individuals, and strains as well in respect to sexes [13].

The fact that XK produced anesthesia in our trial suggests that, in actual clinical settings, only XK is helpful for painful operations. However, by adding certain analgesics to painful treatments, it would also be able to expand the use of DK.

The results of the study/studies which we discussed show, outweighed the absence of analgesia with DK combination. Due to the lack of sufficient analgesia for the surgery, DK only provided enough sedation and muscle relaxants but they were eventually found to be insufficient [9].

Finding extended durations of recumbency with both DK and XK is intriguing. This result could be partially explained by the fact that DK received larger ketamine dosages (30 mg/kg) than did XK (10 mg/kg). The longer period of recumbency may have also been caused by the diazepam's extended effects on muscular relaxation and the experimental rabbits' lack of surgical stimulation

Conclusion

We found that while both of the ketamine medication combinations resulted in unconsciousness and immobilization, only XK offered further analgesia. For unpleasant operations, only XK may be helpful. If certain analgesic compounds are added to DK, it could be feasible to expand its usage to painful operations.

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