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Clinical and Hematological Evaluation of The Midazolam, Xylazine and Ketamine as Anesthetic Regime in Donkeys

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Abstract

Aims: The study aimed to evaluate the efficacy of midazolam, xylazine and Ketamine as balance general anesthetic procedure in donkeys.

Methods: Six adult of local breed donkeys were used in current study. The animals were injected via jugular vein with midazolam 0.1 mg/kg of B.W., as premedication and after five minutes of midazolam administration, animals were injected intravenously with xylazine HCl 2% 1.1 mg / Kg of B.W and ketamine 2.2mg/Kg B.W respectively. Physiologic parameters were estimated in zero time as control and in 10, 20, 40, 75 and 120 minutes were including: respiratory rate with heart rate also body temperature was measured in zero time and in 40, 75 and 120 minutes and blood samples were collected at zero, 60, 120 and 180 minutes after anesthesia for findings hematological changes.

Results: A mild decrease in rectal body temperature at 40, 75 minutes after anesthesia with significant difference and increased respiratory rate with substantial difference at 10 and decrease at 20, 40 minutes with significant difference and no significant difference at 75, 120 minutes after anesthesia . The heart rate revealed no significant differences after 10 minute and zero time but show significant difference between zero time and 75, 120 minutes. Hematological tests revealed slight variation with no significant changes in RBCs, WBC, HB and PCV, only WBCs after 180 minute showed a mild significant decrease compared to control values.

Conclusion: the general anesthesia produced by this procedure was effective and had no impact on the physiological parameters in donkeys. It can be applied to this species for both induction and maintenance anesthesia.

Key word: General anesthesia, Midazolam, Xylazine, Ketamine, donkeys.

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Introduction

Donkeys are an important part of the work force in much of the world. Practitioners working with donkeys should understand the difference between donkeys and horses in relation to anesthesia (1). Anesthesia may be divided into two different types: local anesthesia, general anesthesia. Local anesthesia refers to the loss of pain sensation in a specific body area. General anesthesia is a drug-induced state of reversible unconsciousness, in which the animal could not be aroused by noxious stimuli but it does not necessarily mean that the animal does not sense or perceive pain. Surgical anesthesia is a state of general anesthesia that has four components: unconsciousness, amnesia, muscular relaxation, and analgesia (2). There isn't a single anesthetic available right now that can only be used to provide surgical anesthesia, as a result, different drugs are utilized to create different surgical anesthetic components, and this is known as "balanced anesthesia." (3). both injectable and inhalant anesthetic technique can employed in mammals. Although inhalant anesthetic is simpler to use and giving more control of the level of anesthesia, but its application necessitates costly, highly skilled equipment. Injectable anesthesia is often preferred because it can be used without special equipment. (4), various techniques can be employed to induce anesthesia based on the medications that are available and health conditions of the donkey, and familiarity with different practices (5), an ethical and scientific requirement is the appropriate administration of anesthetics and analgesics to research animals. Although anesthetics and analgesics are frequently used in research and veterinary practice for sample collection and surgical treatments, professional judgment is needed to choose the right drugs to prevent cardiovascular and pulmonary harm. (6).

The selection of a suitable agent, use of an acceptable administrative technique, and precise dose are necessary for safe, effective, and reversible anesthesia (7). A benzodiazepines are anticonvulsant, hypnotic, anxiolytic effects, and muscle-relaxant, midazolam has a short half-life benzodiazepines. When administered intravenously, the aqueous solution with low side effect is doesn’t painful on intravenous injection and doesn’t cause thrombophlebitis. (8). It is digested in liver, and in humans, its half-life is significantly shorter than that of diazepam. As a result, its cumulative effects are reduced and recovery is more rapid (9). Due to these qualities, it is utilized for intravenous sedation and "induction of anesthesia in clinical practice (10). The amount and mode of administration of midazolam both affect its sedative and hypnotic effects. (9). Xylazine is a clonidine analog an agonist at the 2 class of adrenergic receptors. It is applied to non-human mammals like cattle, horses and other mammals for sedation, muscle relaxation, anesthesia and analgesia (11). Xylazine and ketamine are frequently used in veterinary anesthesia. (12). A phencyclidine derivative called ketamine

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induces a dissociative anesthesia. (13), since the middle of the 1970s, ketamine used as an anesthetic in equine. At first, ketamine was only used as an induction tool, resulting in forgetfulness, unconsciousness, analgesia, and immobilization. (14). **Therefore, the goal of this study is to evaluate the efficacy of Midazolam, Xylazine and Ketamine together as a general anesthetic procedure in donkeys.**

Materials and Methods

Experimental design:

For this investigation, a total of six healthy native breed donkeys of both sexes were employed with age from one to three years with average weight 120 ± 30 kg. The College of Veterinary Medicine Farm of Diyala University served as the home for the animals. The animals had full access to water and were fed hay and green feed.

Drugs: the Animals received midazolam (Mezolam, Sun Pharmaceutical Industries Ltd, India) as premedication at 0.1mg/kg of BW, after 5 minutes was administered with a xylazine HCL (Xyl-M2, VMD, Belgium 2%) and ketamine (Ketamine, 10g in 50 ml, Fabrique par pharmaceuticals, Holland) for initiation the anesthesia at 1.1mg/kg and 2.2 mg/kg of B.W. respectively (15, 16).

Methods: Prior to anesthesia, the animals were fasted for 12 hrs. and they had free access to water. The animals were placed in operation room of large animals in surgery and obstetrical department for injection anesthetic drugs and were observed the physiological parameters. The physiological parameters of this regime were evaluated by collocated data of respiratory rate, heart rate, temperature and blood samples from each animal undergo experimental prior to injection of any drugs as (zero minutes), as well as in 10, 20, 45, 75, and 120 minutes for respiratory and heart rates, while body temperature was recorded in zero time and after 40, 75, and 120 minutes after anesthesia.

For the homological test, the blood samples were taken at zero time, 60, 120, and 180 minutes of anesthesia. Samples were taken in a commercial EDTA tube, and analysis complete blood counts conducted immediately after collection.

Statistical analysis:

The Kolmogorov-Smirnov test for normal distribution was performed on all the numerical data using SPSS version 20 from IBM Corporation in New York, USA. To establish the statistical significance between before and after induction, use the Student t-test. One-way ANOVA and Tukey and Duncan post hoc tests were used to evaluate statistical differences between samples collected at different times when the probability threshold was P 0.05. (17).

Results

The assortment of midazolam, xylazine and ketamine was provided clinically good general anesthesia without hematological side effects. Induction of anesthesia were smooth without excitation or apnea, and it did not require additional dose to achieve optimal anesthesia. Induction of anesthesia

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was characterized by signs of falling of the head, dropping of the lip, abduction of the legs, profound ataxia, continuous snoring, and negative responses to painful stimuli. The fall was painless and was over in three and a half to one minutes without any injuries. The duration of the anesthetic was very uniform, resulting in total unconsciousness, good analgesia, good muscle relaxation, absence of all reflexes, and a negative responses to noxious or painful stimuli((pin break in coronary band) and paddling and stiffness of limbs stopped.. This protocol of anesthetic agent effectively induced general anesthesia in all donkeys within (22 ± 3.8) minutes, resulting in very good muscle relaxation, full unconsciousness, and the absence of reflexes. Additionally, the duration of anesthesia by utilizing this regimen is longer than if using ketamine and xylazine alone. The recovery was welled, free of convulsions, struggling, and the return of limb movement, but the animal was still in a lateral recumbent position (7± 2.8) minutes then the animal tries to raise its head while remaining quiet after this time the animal returned to sternal position and getup standing position. Because they have a longer half-life than ketamine and no animals in this experimental trained to recline after standing, midazolam and xylazine were utilized in this regime to cause smooth recovery.

The respiratory rate was increased after the injection of anesthetic drugs. Tachypnea may be recognized to stressful and excitement of the animal; these singularities by elevation in the respiratory rate when compared with normal 19±1.8±. Additionally, there were notable variations from prior times to the point of recovery (Table 1).

The statistical analysis of heart rate found significant differences between control time and 10, 20, 40, and 75 minutes at the level of (P0.05) following anesthesia. The temperature showed a considerable reduction at the level of P0.05; it continued to fall for another time until 75 minutes before increasing at 120 minutes but persisted below normal.

Hematological testing showed no statistically significant difference between total RBC levels at 60 and 120 minutes following anesthesia and zero minutes (table 2). The level of packed cells volume did not significantly change over the course of the study, nor did the hemoglobin value. Additionally, there was no significant difference between the total white blood cell count at 60 and 120 minutes after anesthesia and at zero minutes, but there was a significant decline at 180 minutes.

Table 1: Effect of (6) donkeys' physiological parameters during a general anesthetic regimen caused by midazolam, xylazine, and ketamine.

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Parameter	Times (Minutes)					
	Zero	10	20	40	75	120
Heart rate	45±2.4	54.6±3.1*	32.6±3.1 *	50.6±2.7 *	40.5±1.8 *	43±1.8
Respiratory	19±1.8	27±1.9 *	12.5±2.2 *	15.1±2.1*	17.5±2.2	18±2.1
Temperature	37.2± 0.4	-	-	36±0.2*	36±0.5 *	36±0.9

* indicate significant difference, $p < 0.05$ between Zero and other times.

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Table 2: Effect of (6) donkeys' hematological parameters under a general anesthetic regimen caused by midazolam, xylazine, and ketamine

Parameter	Times (minutes)			
	Zero	60 min	120 min	180 min
WBC	7325±829.5	300±111.62	305±109.54	7230±92.15*
RBC	6117±954.6	733±1082.6	997±1103.2	6092±1034.2
PCV	32±5.3	30.4±4.	30.1±7.	31.2±1.8
Hb	9.8±1.7	9.4±1.6	9.3±2.0	9.6±3.0

* indicate significant difference at $p < 0.05$ between Zero and other times.

Discussion

Numerous investigations on medication combinations for inducing balanced anesthesia for use in human and animal medicine have been published (18), the combination of xylazine, ketamine, and midazolam as premedications produced clinically effective general anesthesia without hematological side effects. It also generated good muscle relaxation, total unconsciousness, and the absence of reflexes. Moreover, the duration of anesthesia by utilizing this regimen is longer than if using ketamine and xylazine alone. This could be because of the synergistic CNS inhibitory effects of the combination caused by the profound sedative effects of midazolam, xylazine, and ketamine (19). The recovery was smooth, free of convulsions, struggling, and the resumption of limb movement, but the animal was still lying on its side and trying to raise its head while remaining silent. After this, the animal returned to its sternal position and stood up. Because they have a longer half-life than ketamine, the medications in this regimen, midazolam and xylazine caused a smooth recovery when given together. (19, 20).

The respiratory rate was increased after the injection of anesthetic drugs, this result was smaller to other study (21). The animal's enthusiasm during IV administration of anesthetic medications and the animal's increased respiratory rate at 10 minutes after

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midazolam-ketamine injection may be related to the animal's anxiety during first stage and second stage of general anesthesia. While alpha-2 agonist drugs like xylazine, also effect of midazolam, and ketamine cause respiratory depression, the stability of the respiratory rate between 40 and 120 minutes after drug administration may be caused by adrenergic neuron in the medullary respiratory center. (22). On the other hand this result disagreed with other researchers(23), who reported drop in respiration as a result of using xylazine and ketamine for maintained anesthesia in donkeys at different durations of time, also Domino *et al*., (24) found that midazolam which causes respiratory depression due to depression of the CNS.

The heart rate results showed significant differences at the level of (P0.05) between control time and 10, 20, 40, and 75 minutes, as well as between 120 and control time. The findings were being a significant increase in 10 and 40 min. with a significant decrease in 20 and 75 min. with no sig. difference in 120 minute these in line with those of other studies that linked the action of -2 agonist medications to a reduction in heart rate and bradycardia (25; 26), also this result differs with (16, 27)In statement indicated to the heart rate gradually returning to normal due to ketamine's reversible effects on the effects of xylazine and midazolam, which is consistent with our study. When the anesthetic was applied for 40, 75 minutes, and at zero time, the rectal temperature significantly varied, this result agree with (28) who found that the ketamine/xylazine combination had a strong hypothermic impact in donkeys and that similar findings were seen in other research. (29, 30).

Hematological changes were discovered, and RBC counts in the 60, 120, and 180 minutes following anesthesia compared to the zero-minute period showed no significant difference (31). The total white blood cell count did not differ significantly between 60 and 120 and 180 minutes after anesthesia, but it did differ significantly between 60 and 120 minutes and 180 minutes after anesthesia in comparison to zero minutes during the study. The hemoglobin value also showed a slight decrease but no significant changes. This agree with (32) and another result of Kilic, 2008 (26) and Mion and Villevieille, 2013 (33). These alterations may be attributed to a transient decrease in PCV, HB, and WBC to the accumulation of circulating blood cells in the spleen and a switch from extravascular to intravascular fluid to maintain animals' normal cardiac output (34). Furthermore, the WBC decreased as a result of acute stress and corticosteroid induced changes following administration of the anesthetic drugs (35, 36).

conclusion, the general anesthesia produced by this procedure was effective and had no impact on the physiological parameters in donkeys. It can be applied to this species for both induction and maintenance anesthesia.

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