INTERNATIONAL JOURNAL OF SCIENCE AND NATURE

www.scienceandnature.org

EFFECT OF KETOPROFEN AND PHENOBARBITAL ON SOME PHYSIOLOGICAL PARAMETERS IN EQUINE MODEL

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ABSTRACT
The purpose of this study was to compare experimentally the effect of using Ketoprofen or Phenobarbital sodium injection as a preanesthetic agents with total intravenous anesthesia (TIVA) infusion of Xylazine-ketamine mixture as a general anesthetic protocol in donkeys on some physiological parameters. Results concerning physiological parameters showed a significant changes in heart rate, respiratory rate and rectal body temperature, which start mainly after, time 20 minutes in all groups and within each one of them.

KEYWORDS: Ketoprofen, Phenobarbital sodium, heart rate, respiratory rate, rectal body temperature.

INTRODUCTION

A standout amongst the most prevalent anesthesia administrations utilized is the ketamine/xylazine mixture[1]. This combination produces anesthesia in horses, with minimal cardiovascular effects and smooth recovery. Disadvantages are lack of muscle relaxation and a short, fairly unpredictable, duration of anesthesia[2]. Although the administration of xylazine and ketamine may be repeated to prolong anesthesia, a drug combination requiring single injections and producing a longer duration of anesthesia would be more useful[3], so good pre-anesthetic work-up and patient stabilization prior to induction along with an anesthetic protocol designed to minimize the adverse effects of the drugs on the patient's existing physiologic problems are imperative to ensure a safe and favorable outcome to any anesthetic event[4]**.** Therefore, this study aimed to compare between Ketoprofen and Phenobarbital effects on some physiological parameters in equine model.

MATERIALS & METHODS

This study was designed using 10 clinically healthy male donkeys weighing (81.20 ±6.36) kg. and aged (9.40 ± 1.12) months; they were divided randomly into two groups: First group was given 2.2 mg/kg B. Wt. Ketoprofen (Isofenal®) IM as preanesthetic followed by I.M injection of 0.5 mg/kg B. Wt. Xylazine and after 10 minutes induction done by I.V injection of 2.2 mg/kg B. Wt. Ketamine then maintenance done by TIVA infusion of 0.8 ml Xylazine: 100ml Normal saline pluse1ml ketamine: 100 ml normal saline (as a mixture) for one hour; while second group was given 20 mg/kg B. Wt. Phenobarbital IV as preanesthetic followed by I.M injection of 0.5 mg/kg B. Wt. Xylazine and after 10 minutes induction was done by I.V injection of 2.2 mg/kg B. Wt. Ketamine then maintenance done by TIVA infusion of 0.8 ml Xylazine:100ml Normal saline pluse1ml ketamine: 100 ml normal saline (as a mixture)for one hour [5]. Clinical observation includes: HR, RR, and Rectal body temperature; were recorded before, during and after anaesthesia in which these parameters were estimated prior to anesthesia and each 20 minutes till TIVA infusion stopped in the following intervals (20; 40 and 60) minutes: 1-Heart rate :(beats /minutes) by auscultation using a stethoscope). 2-Respiratory rate: (breath /min) was counted by (Movement of the chest and abdominal muscle); and 3-Rectal temperature (°C): (was recorded by a digital thermometer).

Statistical analysis was performed using SPSS-21 (Statistical Packages for Social Sciences- version 21)[6]. Data were analyzed using Two way ANOVA and Least significant differences (LSD) post hoc test was performed (multiple comparisons), to assess significant difference among means. Also independent t test was used to assess the significant difference between two groups. $P < 0.05$ was considered statistically significant.

RESULTS & DISCUSSION

The results concerning heart rate showed significant changes within each group. In which P1 recorded obvious decrease at time 20 minutes (38.40 ±0.74) which last till the end of the experiment, while P2 showed significant decrease at time 40 minute (32.20 ±1.35), although this decrease start from time 20 minutes and last till the end of the experiment. Between P1 and P2 there were significant changes at time 40 minutes in which P2 (32.20 ±1.35) record significant decrease in comparison with P1 (35.80 ±0.58) (Table 1, Figure 1). It is well known that regular heart rate ensures constant oxygen supply to vital organs and can also be used to assess anaesthetic depth and analgesia [7]. Decrease of heart rate was obvious at time 40 minute in P2 (32.20 ±1.35) in comparison with P1 at the same time, this result could be due to the effects of phenobarbital which used primary before Xylazine – ketamine for general anesthesia. this decrease agree with[8], who mention that Xylazine caused atrioventricular

block, slightly decreased heart rate, and significant decreases in cardiac index and stroke volume. Hypertension was seen initially, but then blood pressure decreased with most treatments. These results also agree with[9]. Who mentioned that Ketamine could produce indirect cardiovascular stimulation and minimally sensitize the heart to catecholamine leading to induce arrhythmias [10].

TABLE 1: shows (Mean± SE) for effect of different anesthetic protocols on heart rate (beat/minute)

Time/minutes / Groups	0	20	40	60
P1	A46.20 ± 0.80a	B38.40 ± 0.74a	B35.80 ± 0.58a	B39.20 ± 0.48a
P2	A46.75 ± 0.75a	B40.80 ± 1.35a	C32.20 ± 1.35b	B37.00 ± 1.91a
LSD	3.441			

Means with different small letter in the same column significantly different (P<0.05) (between two groups)
Means with different capital letter in the same raw significantly different (P<0.05) (within group)
P1: ketoprofen – Xylazine – Ketamine + Xylazine-Ketamine
P2: Phenobarbital – Xylazine –Ketamine + Xylazine – Ketamine

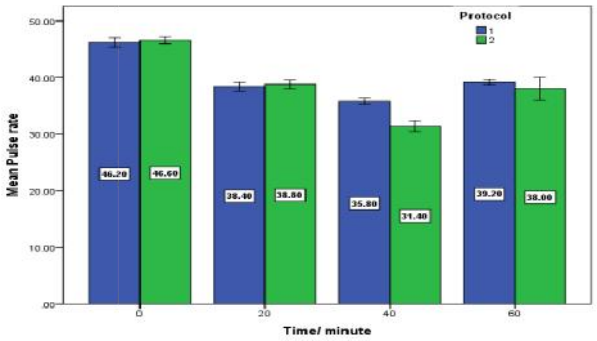

FIGURE 1: shows Mean ± SE of different anesthetic protocols effects on Heart rate (beat/minute)
Blue column: PI (ketoprofen – Xylazine – Ketamine + Xylazine-Ketamine)
Green column: P2 (Phenobarbital – Xylazine –Ketamine + Xylazine – Ketamine)

Our result in both protocols showed a significant changes in heart rate within each group start from time 20 till end of experiment Table (1), these result agree with[11], who refer that combination of Xylazine -ketamine could cause bradycardia, the positive chronotropic effect of ketamine temporarily counter balanced the bradycardia effect of the alpha-2 agonist in which xylazine administration lead to decrease in myocardial contractility and cardiac output [12-15], so these results agree with Ismail *et al*. [16] who revealed that addition of alpha-2 adrenergic agonist induces a reduction in central sympathetic outflow, which tends to decrease heart rate, so marked bradycardia commonly occurs, and the heart rate decreases, arterial blood pressure also declines Although respiratory rate showed significant changes within each groups (P1 and P2) but it was mostly obvious decrease at time 40 minutes. In both groups PI (12.40 ±0.40); and P2 (11.60 ±0.74); while between groups there was no significant changes (Table 2 and Figure 2).

The result of respiratory rate showed a decrease in both protocols start from time 20 and was mostly obvious at time 40 minute in P1 and P2 (12.40 ±0.40;11.60 ±0.74) respectively which can be noticed in (table 2).This decrease in respiratory rate in P2 agree with Kharbanda *et al*.[17] who mentioned that the decrease of respiratory rate was expected due to using Phenobarbital which belong to Barbiturate group which some time tend to produce severe respiratory depression, apnea, laryngospasm, bronchospasm, and cough, particularly during rapid intravenous administration , while obvious decrease at time 40 minutes in both protocols agree with Lankveld *et al*., [18] who used ketamine in horse; and agree with Adams and Werner[19]who confirm that Ketamine produce only mild respiratory depression. Also these results agree with Sinclair [20] who sustain that respiratory depression occurs secondary to the C.N.S depression produced by alpha 2-adrenoreceptor stimulation.

TABLE 2: shows Mean± SE of different anesthetic protocols effects on respiratory rate (breath/minute)

Time/minutes / Groups	0	20	40	60
P1	A17.60 ±0.74a	B14.80 ±0.48a	C12.40 ±0.40a	B15.60 ±0.74a
P2	A17.50 ±0.95a	B14.80 ±0.49a	C11.60 ±0.74a	B14.00 ±1.15a
LSD	2.2592			

Means with different small letter in the same column significantly different (P<0.05) (between two groups)
Means with different capital letter in the same raw significantly different (P<0.05) (within group)
P1: ketoprofen – Xylazine – Ketamine + Xylazine-Ketamine
P2: Phenobarbital – Xylazine –Ketamine + Xylazine – Ketamine

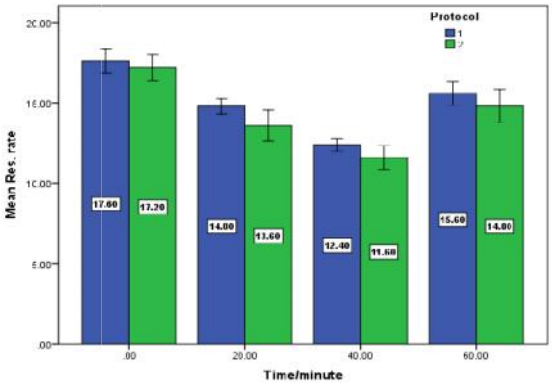

FIGURE 2: shows Mean ±SE of different anesthetic protocols effects on Respiratory rate (breath/minute)
Blue column: PI (ketoprofen – Xylazine – Ketamine + Xylazine-Ketamine)
Green column: P2 (Phenobarbital – Xylazine –Ketamine + Xylazine – Ketamine)

Rectal body temperature showed significant changes within each groups (P1 and P2) especially at time 40 minutes, in which PI and P2 record significant decrease (36.62±0.13); (36.70±0.09) respectively; while between groups there was no significant changes (Table 3 and Figure 3).

TABLE 3: shows Mean± SE of different anesthetic protocols effects on rectal body temperature / ºC

Time/minutes / Groups	0	20	40	60
P1	A 37.42 ±0.14a	A 37.20 ±0.10a	B 36.62 ±0.13a	AB 36.92 ±0.04a
P2	A37.30 ±0.14a	A37.36 ±0.16a	B36.70 ±0.09a	B36.78 ±0.10a
LSD	0.3564			

Means with different small letter in the same column significantly different (P<0.05) (between two groups)
Means with different capital letter in the same raw significantly different (P<0.05) (within group)
P1: ketoprofen – Xylazine – Ketamine + Xylazine-Ketamine.
P2: Phenobarbital – Xylazine –Ketamine + Xylazine – Ketamine.

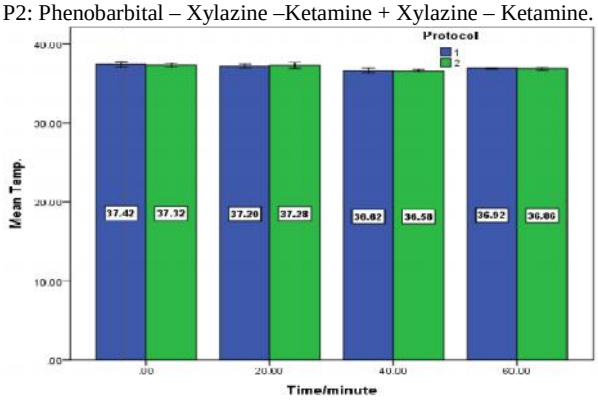

FIGURE 3: shows (Mean± SE) for effect of different anesthetic protocols on rectal body temperature / ºC
Blue column: PI (ketoprofen – Xylazine – Ketamine + Xylazine-Ketamine).
Green column: P2 (Phenobarbital – Xylazine –Ketamine + Xylazine – Ketamine).

According to Schmitz *et al.*[7] Anaesthesia often leads to hypothermia. In both protocols there was a significant decrease in rectal body temperature (P1 (36.62 ±0.13) and P2 (36.70 ±0.09)) as shown in Table (3). These results concur with van Praag[21]who confirm that anesthesia and surgery commonly cause substantial thermal perturbations. In which occurring of hypothermia during general anesthesia could be due to influence of anaesthetic agents on the body temperature mechanisms. In which use of Xylazine leads to depress thermoregulatory mechanisms and either hypothermia or hyperthermia is a possibility depending on ambient air temperature [22] while ketamine may be decrease heat production and (or) increase heat loss [23]. The reason of this decrease could be explained as Fahim *et al.* [24] mentioned that hypothermia during anesthesia could be due to release of monoamines in the anterior hypothalamus, since the noradrenaline lowers and 5-hydroxytryptamine (5-HT) raises the body temperature, when acting on the anterior hypothalamus. Or as Khattri *et al.*[25] mentioned that hypothermia might be attributed to a decrease in the skeletal muscle tone, reduced metabolic rate and muscle relaxation along with depression of thermoregulatory centers. The decrease in temperature in P2 at 40 minutes does not agree with Sant'Anna *et al.* [26] who mentioned that phenobarbital could be used in treatment of some patient undergoing hypothermia

treatment although phenobarbital may modify core temperature profile during the induction phase due to its effect on brain metabolic rate (BMR) and thermogenesis. So our opinion is depend mainly on the effect of xylazine and ketamine effects since neither phenobarbital nor ketoprofen affect body temperature severely wither increase or decrease.

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