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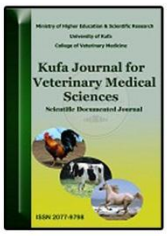

Effect of Use Two General Anesthetic Regimes on Some Clinical and Biochemical Parameters in Donkeys

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Abstract:

The present study was assigned to investigate the effect of use two general anesthetic regimes (Tramadol, Ketamine and Xylazine) and (Diazepam, Ketamine and Xylazine) on some clinical and biochemical parameters in donkeys. Eight adult local breed donkeys weighting between (90- 160 kg) were used in this study. Donkeys were divided equally into two groups (T+K+X)and (D+K+X) .

Group(T+K+X): Four donkeys used to induction of general anesthesia by intravenous administration of the following drugs: Tramadol hydrochloride (5mg /Kg B.W.), Ketamine (2.2 mg/kg B.W) and Xylazine (1.1 mg/kg B.W). Group (D+K+X): Four donkeys used to induction of general anesthesia was made by administration of the same drugs in the same dose as in group (T+K+X) except Tramadol that was replaced by Diazepam(0.11 mg/kg B.W).

Data were collected immediately before intravenous administration of premedication (control data) and continuously after administration of anesthetics. Parameters included clinical measures: heart rate and rectal temperature, at time of 5,10,15,20,25,30, and 60 minutes. The biochemical examination (AST and ALT) estimated at the times zero, 25 minutes and 3 days.

The results revealed that significant differences in the means of heart rate between groups (T+K+X)and(D+K+X) the heart rate was increase in (D+K+X) group in compare with(T+K+X) group . as well as was significant differences in the means of heart rate within(T+K+X) groups , it was gradually increased at times 5 and 10 minute then return close to control value at 15,20,25,30 and 60 minute while in (D+K+X) the means of heart rat were increased at all times in compared with zero time. There were significant differences in rectal body temperature between two groups , the means of rectal temperature were significantly increased in (D+K+X) group at 10,15 and 60 minutes . In addition there were gradual decreases in the rectal temperature within group at time 10, 15, 20, 25, 30 and 60 minutes in(T+K+X) while it was increased at 20 and 25 then stayed within normal values in other group. There were no significant differences in the mean values of AST between two groups. AST mean was elevated significantly at Day 3 in (T+K+X) but it was decreased at time 25 minutes in(D+K+X). The results also showed significant increase in ALT value in (T+K+X) group in compare with (D+K+X) group at time 25 minutes but it was completely inversed at Day 3. At time 25 minutes ALT was increased significantly in (T+K+X) then decreased at Day 3 while it was decreased at times 25 minutes and Day 3 in (D+K+X).

تأثير استخدام نظامين للتخدير العام على بعض المؤشرات السريرية والكيموحيوية في الحمير

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الخلاصة:

صممت الدراسة الحالية لمعرفة تأثير استخدام نوعين من أنظمة التخدير العام هما نظام (ترامادول، كيتامين والزيلازين) ونظام (ديازيبام، كيتاميين والزيلازين) على بعض المؤشرات السريرية والكيموحيوية في الحمير.استخدمت ثمانية حمير من السلالة المحلية يتراوح وزنها من(90-160) حيث قسمت إلى مجموعتين متساويتين(T+K+x)و(D+K+X).

مجموعة(T+K+X): استخدمت فيها أربعة حمير لإحداث التخدير العام بواسطة حقن الأدوية التالية وريدياً :ترامادول هيدروكلورايد (5ملغم/كغم من وزن الجسم) وكيتامين (2.2ملغم/كغم من وزن الجسم) والزايلازين (1.1ملغم/كغم من وزن الجسم).

مجموعة(D+K+X) وفيها استخدمت اربعة حمير لإحداث التخدير العام بإعطاء نفس أدوية وجرع المجموعة السابقة ماعدا الترامادول حيث استبدل بالديازيبام(0.11ملغم/كغم من وزن الجسم).

سجلت البيانات مباشرة قبل الحقن الوريدي(بيانات السيطرة) واستمر تسجيل البيانات بعد أعطاء المخدرات العامة . مقاييس التجربة شملت المقاييس السريرية (معدل ضربات القلب ودرجة حرارة الجسم) 60,30,25,20,15,10,5 دقيقة .الاختبارات الكيميوحيوية (ALT و AST) قيست في الأوقات صفر، 25 دقيقة و3 أيام.

بينت نتائج الدراسة الحالية وجود اختلافات معنوية في معدل ضربات القلب بين المجموعتين (T+K+X) و(D+K+X) حيث ارتفعت في مجموعة(D+K+X) مقارنة بمجموعة (T+K+X) اضافة الى ذلك كان هنالك اختلافات معنوية ضمن المجموعة(T+K+X) حيث ارتفعت تدريجيا في الاوقات 5و10 دقيقة ثم عادت الى قيمة السيطرة في الاوقات 10 و 60 دقيقة غير ان مجموعة(D+K+X) اظهرت ارتفاع في معدل ضربات القلب في كل اوقات بالتجربة مقارنه بوقت الصفر.

أظهرت النتائج أيضا اختلافات معنويه في درجة حرارة الجسم بين المجموعتين حيث ارتفعت في مجموعة(D+K+X) مقارنة بالمجموعة الاخرى في الاوقات 15,10 و60 دقيقة، اضافة الى ذلك كان هنالك انخفاضا معنويا تدريجيا في درجة حرارة الجسم ضمن المجموعة في الاوقات 30,25,20,15,10 و 60 دقيقة في مجموعة (T+K+X) غير انها كانت مرتفعة عند الاوقات 20 و 25 دقيقة عادت ضمن القيم الطبيعية ضمن المجموعتين.

اظهر التحليل الاحصائي عدم وجود فروقا معنوية في معدلات انزيمAST بين المجموعتين غير ان معدلات AST ارتفعت في اليوم 3 في مجموعة (T+K+X) لكنها انخفضت عند الوقت 25 دقيقة في مجموعة (D+K+X) . واضهرت النتائج ايظا ارتفاعا معنويا في قيمة ALT في مجموعة (T+K+X) مقارنة مع مجموعة (D+K+X) عند الوقت 25 دقيقة غير انها انعكست تماما في اليوم الثالث . عند الوقت 25 دقيقة ارتفع انزيم ALT في مجموعة (T+K+X) ثم انخفض في اليوم 3 غير انه انخفض عند الوقت 25 دقيقة واليوم 3 في مجموعة (D+K+X).

Introduction:

Equine practitioners are often required to perform surgical procedures under field conditions and although these surgical procedures are often similar to those performed in a hospital setting, management of general anesthesia may be quite different (1).

There is no available anaesthetic drug which can provide proper anesthesia alone now a day. Therefore, combinations of sedatives and other anesthetics have been widely used in animal practice .The anesthetic combination should congregate different characteristics, having adequate sedation and a deep unconsciousness state, without greatly changing the patient's physiologic parameters (2). General anesthesia is needed for certain surgical procedures, which are otherwise cannot be performed under regional and local anesthesia (3).

In the last 15 years the greatest interest and emphasis for equine field anesthesia have been on various combinations of an alpha2-adrenergic agonist sedative/analgesic with a phencyclidine (4). Cardiopulmonary investigations involving such combinations have been

published and have shown favorable responses compared to the previous barbiturate-based anesthetic regimes (5). Xylazine/ketamine was the first reported combination of this type and remains the standard field anesthetic technique in North America (6). Is an α2-adrenoceptor agonist sedative with a much higher interspecies variability in effect (7). It is commonly used in veterinary medicine as nonnarcotic sedative for analgesia and muscle relaxation. First synthesized in Germany in 1962 for use as an antihypertensive agent, it was found to have potent sedative effects (8).

Tramadol, an atypical centrally acting analgesic with opoid and nonopoid like properties (9) of the aminocyclohexanol group (10), structurally related to codeine and Abstract morphine, consists of two enantiomers, both of which contribute to analgesic activity via different mechanisms (11).

Tramadol inhibits norepinephrine reuptake, enhancing inhibitory effects on pain transmission in the spinal cord. The complementary and synergistic actions of the two enantiomers improve the analgesic efficacy and tolerability profile of the racemate (12). Diazepam (Valium) is a benzodiazepine (BDZ) derivative; has an established role in human and veterinary anaesthesia regimen (13). It is the drug of choice for all varieties of status epilepticus (14). Diazepam was synthesized in 1961 by Steinbach and Reader in New Jersey, and first used in the treatment of anxiety states (15). It is widely used as a sedative, hypnotic, and anti-anxiety drug. (16).

This study was conducted to compare between effects of two general anesthetic regimes on some clinical and biochemical parameters in donkeys.

Materials and Methods:

This study was carried out on eight adult clinically healthy donkeys weighing from (90- 160 kg), they were divided randomly and equally into two groups and each donkey was anesthetized with each drug combination. The following two drug combinations were studied:

Group **(T/K/X):** Four donkeys was injection with a single dose of tramadol HCL intravenously (5 mg/kg b.w.) followed after 5 min with a single intravenous injection of ketamine (2.2 mg/kg b.w.) and xylazine (1.1 mg/kg b.w.) in the same syringe.

Group **(D/K/X):** Four donkeys was injection with a single dose of diazepam intravenously (0.11 mg/kg b.w.) followed after 5 min with a single intravenous injection of ketamine (2.2 mg/kg b.w.) and xylazine (1.1 mg/kg b.w.) in the same syringe.

The animals were maintained in individual cages under normal environment including climate, management and feeding.

Two months prior to initiate the experiment, the administration of any medication was stopped. Twelve hours before each experiment, the animals withheld from food and water. Under aseptic conditions an intravenous injection using 18- gauge mm needle syringe in the jugular vein for administration of anesthetics drugs and for collection of blood samples.

Tramadol Hydrochloride Neodol® the ampoule contains 2ml (100mg/2ml), Ibn Hayyan Pharm-Homs-Syria. **Diazepam** Diazepam 10® the ampoule contains2 ml (10mg/2ml), Aleppo-Pharmaceutical Industries, Aleppo-Syria.

Ketamine Hydrochloride Ketamine® (10%) Vial contains 10 ml Vet. Injection, kepro pharmaceuticals, Holland. **Xylazine Hydrochloride** Xylazine 2%® Vial contains 50ml (20mg/1ml), Ceva Saute animal, Spain.

Rectal temperature (°C):rectal body temperature was measured by putting the thermometer (electron thermometer) in the rectum of animal.

Heart rate:(beats / minutes) was measured by stethoscope.

The mean values of these parameters were considered as base-line values or control (zero time values). The same above parameter, mentioned were taken at 5, 10, 15, 20, 25, 30and 60 minutes .

The blood samples were collected via jugular vein puncturing with18 G needle at times zero, 25 minutes and 3 days . The blood in the plain tubes was allowed to form serum at room temperature and centrifuged at 1500rpm for 3-5 minutes(17) after the serum was harvested and stored at -20^0C until analysis. The biochemical tests were done in Central Research Unit of Veterinary Medicine of Basrah University by using Chemistry auto analyzer made in Germany by Human Star Company serial no. 20628 the machine has 54 wells which are numbered from 1 to 54, the samples deposited in each specific wells. The reagent was put in special container beside the wells. The serum biochemical parameters estimated by this instrument were Aspartate aminotransferase (AST), Alanine aminotransferase (ALT).

Statistical Analysis:

Data were analyzed statistically by using Complete Randomized Design (C.R.D.) in factorial experiment.We used SPSS program (2008) (18) to study different between and times by used Duncan Multiple Test (19).

Results and Discussion:

The results revealed that significant differences in the means of heart rate between groups (T+K+X)and(D+K+X) the heart rate was increase in (D+K+X) group in compare with(T+K+X) group , as well as was significant differences in the means of heart rate within(T+K+X) groups , it was gradually increased at times 5 and 10 minute then return close to zero time at 15,20,25,30 and 60 minute while in (D+K+X) the means of heart rat were increased at all times in compared with zero time (table 1).

These results agreed with the result of other researches that attributed to the effect of α-2 agonist drugs which causes depression of heart rate that lead to arrhythmogenic include sinoatrial block first and second atrioventricular (AV) block, bradycardia, and sinus arrhythmia. Bradycardia occurred after administration of the anα-2 agonist drugs (20 and 21). In time 5 minute, of the experiment the heart rate increased due to the ketamine effect on cardiovascular stimulating properties. Wong and Jenkins, (1974) (22) revealed that ketamine causes high blood pressure, tachycardia and increased cardiac output are primarily sympathomimetic actions as a result of stimulation of the central sympathetic nervous system.

Table (1) Effect on the heart rate (beat/minute) in groups (T+K+X) and (D+K+X).

Groups	Times minutes							
	Zero	5	10	15	20	25	30	60
T+K+X	**B b 42.75 ±1.83**	**A b 45.75 ±2.25**	**A b 46.00 ±1.41**	**B b 42.75 ±2.05**	**B b 40.25 ±2.10**	**B b 40.25 ±2.10**	**B b 40.00 ±2.16**	**B b 40.50 ±1.94**
D+K+X	**C a 48.00 ±0.80**	**B a 52.25 ±1.03**	**A a 54.75 ±2.36**	**A a 56.25 ±2.25**	**A a 56.00 ±3.16**	**A a 55.00 ±2.38**	**B a 53.75 ±1.03**	**B a 51.50 ±0.96**

- Different capital litters referred to the significant differences between times at ($P \leq 0.05$).
- Different small litters referred to the significant differences between treatment (groups) at ($P \leq 0.05$).

There were significant differences in rectal body temperature between two groups, the means of rectal temperature were significantly increased in (D+K+X) group at 10,15 and 60 minutes. In addition there were gradual decreases in the rectal temperature within group at time 10, 15, 20, 25, 30 and 60 minutes in(T+K+X) while it was increased at 20 and 25 then stayed within normal values in two groups(Table 2).

In the normal animal, body heat is unevenly distributed with the core temperature being 2–4°C higher than the peripheral. These results agreed with the other researchers England and Clark, (1996) (23); Freeman and England, (2000) (24) who found that decreased in body temperature during general anesthesia due to reduced basal metabolic rate and muscle activity and probably the result of the effect of α-2 adrenoceptors drugs which causes depression of hypothalamic thermoregulatory center. Ketamine and other dissociative anesthetics which cause hypothermia by releasing monoamines responsible for centrally mediated hypothermia by inhibiting endogenous release of norepinephrine (25 and 26).Also hypothermia may develop in animals anaesthetized in a cool environment by exposure to cold operating room conditions, administration of unwarned I.V. fluid contributes substantially to the decrease in body temperature (27).

Decrease in temperature of 1–3 ° C below normal has been demonstrated to provide substantial protection against cerebral ischemia and hypoxemia in anaesthetized animals (27 and 28).

The results agree with the results of Ketamine and other dissociative anesthetics which cause hypothermia by releasing monoamines responsible for centrally mediated hypothermia by inhibiting endogenous release of norepinephrine (29). The body temperature showed significant decrease and this decrease was evidenced by shivering of all animals of this group, this is similar to the finding of (30) in donkeys.

Table (2) Effect on body temperature (c^{o}) in groups (T+K+X) and (D+K+X).

Groups	Times minutes							
	Zero	5	10	15	20	25	30	60
T+K+X	**A a 37.48 ±0.24**	**A a 37.04 ±0.32**	**B b 35.82 ±0.43**	**B b 35.10 ±0.64**	**B a 35.00 ±0.83**	**B a 35.45 ±0.82**	**B a 35.69 ±0.81**	**B b 35.53 ±0.80**
D+K+X	**A b 36.95 ±0.32**	**A b 36.61 ±0.53**	**A a 36.92 ±0.27**	**A a 36.82 ±0.24**	**B a 35.67 ±0.46**	**B a 35.65 ±0.29**	**AB a 36.05 ±0.51**	**A a 36.33 ±0.50**

- Different capital litters referred to the significant differences between times at (P≤0.05).
- Different small litters referred to the significant differences between treatment (groups) at (P≤0.05).

There were no significant differences in the mean values of AST between two groups. AST mean was elevated significantly at Day 3 in (T+K+X) but it was decreased at time 25 minutes in(D+K+X) (table 3). The table four showed significant increase in ALT value in (T+K+X) group in compare with (D+K+X) group at time 25 minutes but it was completely inversed at Day 3. At time 25 minutes ALT was increased significantly in (T+K+X) then decreased at

Day 3 while it was decreased at times 25 minutes and Day 3 in (D+K+X).

Aspartate aminotransferase is present in most tissue and increases with muscle injury especially cardiac muscle, as well as hepatocellular injury, also present in kidney, pancreas and erythrocytes. Thus AST assay should be run in conjunction with other enzymes assay, especially ALT when evaluating liver function. Increased ALT with normal to mildly elevated AST may indicate reversible liver damage. Marked elevation in ALT and AST indicate hepatocellular necrosis. Increased AST with normal ALT may indicate that the source of AST is not the liver (31 and 32).Thus AST has also been used as a cardiac marker (33).

Results of ALT (Table 3), showed no significant difference in the mean values of the ALT enzyme between groups, the enzyme level within normal range in all-time of experiment. This test is using to detect liver injuries and long-term liver disease. Highly elevated levels may indicate active hepatitis from any cause, including virus, drug or toxin. Some prescription and over-the-counter medications can cause an increase in ALT levels. ALT levels can be dramatically affected by shock, low blood pressure or any other condition that deprives the liver of blood and oxygen (34).

Table (3) Effect on AST and ALT in groups (T+K+X) and (D+K+X).

Enzymes	Groups	Times		
		Zero	25 min.	3Days
AST	**T+K+X**	**B a 202.30 ±2.77**	**A a 215.92 ±3.91**	**B a 203.78 ±2.87**
	D+K+X	**B a 204.05 ±2.67**	**A a 215.24 ±4.98**	**A a 213.34 ±4.33**
ALT	**T+K+X**	**B a 33.60 ±6.21**	**A a 42.98 ±7.66**	**C b 15.55 ±2.84**
	D+K+X	**A a 33.93 ±3.90**	**B b 22.88 ±5.20**	**B a 23.76 ±6.28**

- Different capital litters referred to the significant differences between times at ($P \leq 0.05$).
- Different small litters referred to the significant differences between treatment (groups) at ($P \leq 0.05$).

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