

**ANESTHESIA IN XYLAZINE PREMEDICATED DONKEYS WITH  
KETAMINE AND KETAMINE-PROPOFOL MIXTURE:  
A COMPARATIVE STUDY**

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**ABSTRACT**

This study was conducted to evaluate the anesthetic quality produced by ketamine hydrochloride (K) (3 mg/kg, I.V.) and ketamine-propofol (K-P) mixture (2 mg/kg-1 mg/kg, I.V., respectively) in six donkeys premedicated with xylazine (X), (1 mg/kg, I.V.). Each donkey was anesthetized one time with each dose of (K) and (K-P), five minutes after (X) administration, in random order at (1) week intervals. The anesthetic parameters; induction and sleeping time, abolishment of the swallowing reflex, recumbency period, cardiopulmonary responses, were qualitatively and quantitatively assessed.

The results revealed presence of significant difference ( $p < 0.05$ ) in the induction and sleeping time between (K) and (K-P) protocols. Neither the swallowing reflex, nor recumbency period represented statistical difference between (K) and (K-P) protocols. But clinically, anesthesia with (K-P) produced shorter and smoother recovery to recumbency than with (K), and the swallowing reflex was abolished while persisted with (K) anesthesia. The excellent anesthesia produced with K-P was characterized by smooth, calm, gradual and free of excitement induction ( $23.75 \pm 1.75$  sec), good narcosis ( $22.50 \pm 3.57$  minutes) and muscle relaxation. The swallowing reflex was abolished for ( $15.75 \pm 5.61$  minutes). The recumbency period was characteristically smooth and featured by its rapidness ( $10.50 \pm 2.62$  minutes). While on the other hand, induction of anesthesia with (K) protocol was characterized by rough, slow and excitement ( $56.25 \pm 8.44$  sec), muscle rigidity, and persistence of the swallowing reflex (not disappeared or slightly disappeared). The shorter sleeping time ( $10.5 \pm 0.95$  minutes) and the longer recumbency ( $14.75 \pm 2.28$  minutes) periods that was associated with violent convulsion and excitement, were clinically an obvious associate with (K) anesthesia. The intubations with (K-P) anesthetic protocol was easily performed, but was difficult or failed during (K) anesthesia.

In conclusion, anesthesia with (K-P) protocol produced an excellent anesthetic mixture for induction of general anesthesia in donkeys, and up to our knowledge this the first report on the use of this mixture for total intravenous anesthesia in donkeys.

## تخدير الحمير المهدئة بالزايلازين، بالكيتامين و بمزيج الكيتامين-بروبوفول: دراسة مقارنة

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### الخلاصة

في هذه الدراسة تم تقييم خصائص التخدير بالكيتامين (3 ملغم/كغم، بالحقن الوريدي) أو بمزيج الكيتامين-بروبوفول (2 ملغم/كغم-1 ملغم/كغم، بالحقن الوريدي) في ستة حمير تم تهدئتها مسبقا بالزايلازين (1 ملغم/كغم، بالحقن الوريدي). تم تخدير كل حمير التجربة بعد تهدئتها مسبقا وقبل 5 دقائق بالزايلازين، عشوائيا بالدوائن وبالمتعاقب، بعد ترك مدة لا تقل عن سبعة أيام مابين العلاج بالمخدرين. وتم اختبار كفاءة الدوائن في تخدير الحمير كما ونوعا وفق المعايير التالية: زمن أحداث التخدير والنوم؛ فقدان منعكس البلع؛ زمن الرقاد (الجنبي و القصي)؛ وأثرهما على الجهازين القلبي-الرئوي. بينت النتائج وجود فرق معنوي بين المخدرين في زمن أحداث التخدير والنوم، في حين لم يشاهد مثل ذلك الفرق في فقدان منعكس البلع وزمن الرقاد. لكن المشاهدة السريرية للتخدير بالكيتامين-بروبوفول أوضح بأن الأفاقة كانت أقصر وأكثر سلاسة من تلك الناجمة عن التخدير بالكيتامين. كما أن منعكس البلع كان قد تم إبطاله في التخدير بالمزيج، في حين بقي مستمرا في التخدير بالكيتامين. أحدث مزيج الكيتامين-بروبوفول تخديرا ممتازا، تميز بحدوثه بشكل سلس وهادئ ومتعاقب وخالي من التشنجات ( $1.75 \pm 23.75$  ثانية)، ونوم جيد ( $3.57 \pm 22.5$  دقيقة)، وأرخاء جيد للعضلات. وتم إبطال منعكس البلع لمدة ( $5.6 \pm 15.75$  دقيقة). أما الرقاد فقد أمتاز بسلاسته وسرعة أنقضائه ( $2.62 \pm 10.5$  دقيقة). أمتازت صفات أحداث التخدير بالكيتامين؛ بالعاصف والبطيء والمتشنج ( $8.44 \pm 56.25$  ثانية)، وبصلابة العضلات وبعدم إبطال منعكس البلع (حيث أنه أما أن لم يبطل تماما أو تم إبطاله جزئيا). وكما كان زمن النوم أقصر ( $0.5 \pm 10.5$  دقيقة) وفترة الرقاد أطول ( $2.28 \pm 14.75$  دقيقة) والذي صاحبه تشنجات عنيفة، وهذه كلها كانت صفات سريرية ملازمة للتخدير بالكيتامين. كانت عملية تنبيب الرغامي أثناء التخدير بمزيج الكيتامين-بروبوفول سهلة للغاية، وصعبة جدا أثناء التخدير بالكيتامين.

ونستنتج من كل ماضى بأن مزيج الكيتامين-بروبوفول مخدر ممتاز في الحمير وطبقا لمعلوماتنا يعتبر هذا التقرير الأول في استخدام هذا المزيج للتخدير الكامل بالوريد في الحمير.

### INTRODUCTION

The dissociative drug, ketamine [dl-2-(o-chlorophenyl)-2-(methylamino) cyclohexanone hydrochloride] (1), have an undesirable central nervous system excitatory property during their use in equines (2). Ketamine (ketalar®, vetalar®) can be used in donkeys and mules for short procedures at (2-3 mg/kg); however increase ketamine above (3.3 mg/kg) has been associated with rough recoveries (3 and 4). It produce profound analgesia without muscle relaxation and tonic-clonic spasms of limb muscles may occurred even in the absence of surgical or other

stimulation. The difficulty in assessing the degree of unconsciousness coupled with poor muscle relaxation produced by the drug make it doubtful whether ketamine should ever be used alone for surgical operations (1).

Propofol; 2, 6 diisopropyl phenol, is a new ultra short acting, rapidly metabolized intravenous anesthetic agent. The drug characterized by a virtual lack of any cumulative effect and by rapid recovery after its administration in bolus doses or by continuous infusion and it has action without excitatory side effects (1, 5, and 6). Propofol is an intravenous anesthetic agent with a desirable pharmacokinetic profile in horse, i.e., rapid onset of action, short duration of anesthesia and prompt recovery, even following continuous infusion or supplementary dose administration. Smooth anesthetic induction is obtainable when propofol is combined with a tranquillizer (1, 6). Studies with horses have demonstrated that, when used in combination with alpha-2 adrenergic agonists, propofol has the same effects in horse as those observed in other species (6), and may have advantages over ketamine (2). Pre-medication with either xylazine or detomidine improved the quality of anesthesia produced by a single bolus of propofol (2, 7).

The aim of the present work was to determine the anesthetic interaction effects of intravenous mixture of propofol with ketamine at the dose rate of 1 mg/kg and 2 mg/kg, respectively in xylazine premedicated donkeys and comparing these responses to the undesired side effects produced by ketamine anesthesia alone.

#### **MATERIALS AND METHODS**

Six adult young (aged from 2-4 years) donkeys from both sexes were used in this study. The animals were ranging in weight from (50 to 170 kg). The donkeys were housed indoor kept on straw and grain, and had free access to water. The donkeys were premedicated with xylazine (X), (Xylazine 2%; Ceva Animal Health, France) at the dose (1 mg/ kg) administered intravenously into the jugular vein. Five minutes later, anesthesia was induced with ketamine hydrochloride (Ketamine BP 50, Holden Medical, Netherlands) at the dose (3 mg/kg) administered intravenously into the jugular vein. The same donkeys, after 7-10 days interval, were re-anesthetized with (K-P) (Propofol; Diprivan®; AstraZeneca, Macclesfield, UK; 1% emulsion) mixture at the dose (2 mg/kg-1 mg/kg, I.V., respectively), after 5 minutes of (X) premedication, also intravenously via the same jugular vein.

Once the animals were sunken, after induction with (K) or (K-P), they were placed on right lateral recumbency and 'blind' endotracheal intubations were attempted. Once positioned and secured, they were allowed to breathe fresh air. The animals were kept on lateral recumbency and did not undergo surgery and were left to recover undisturbed. The endotracheal tube was removed once swallowing reflex returned. The quality of anesthesia with both protocol was assessed by an expert anesthetist and the following parameters was monitored; the time of the induction (from end of injection to sunken and lateral recumbency); quality of induction; sleeping time (from beginning of anesthesia until first head movement); return of swallowing reflex (duration of the abolishment of swallowing reflex from disappear to appear); recovery periods from anesthesia was determined by achievement of the periods from the time of head movement to sternal recumbency period until the animal could stand unaided; the quality of

recovery and the quality of plane of anesthesia was determined by the assessment to the degree of muscle relaxation, and the incidence of side effects. The cardiopulmonary responses (heart rate and respiratory rates), were considered before premedication and after induction of anesthesia at (10) minutes intervals.

The data was analyzed statistically by using in depended (T) test at level of significant ( $p < 0.05$ ).

### RESULTS

The obtained clinical results and the analyzed statistical data for the scored parameters for this study as shown in Table (1) were as follow:

The quality of anesthesia produced by (K) at dose (3 mg/kg) after (X) premedication (1 mg/kg) referred as; rough and slow induction associated with a moderate excitement ( $56.25 \pm 8.44$  sec). After induction, the animals show muscle rigidity, and irregular cardiopulmonary responses. The orotracheal intubation was very difficult (or failed, in 4 cases), due to locked jaws as a result of the rigidity of the masseter muscles of the jaws. The swallowing reflex persists and narcosis was poor to light during anesthesia. The sleeping time was ( $10.5 \pm 0.95$ ) minutes and recumbency period was ( $14.75 \pm 2.28$ ) minutes. Recovery with (K) protocols was characterized by rough and some violent awake with excitement in nature. Although a clinically increased cardiopulmonary (HR & RR) parameters during anesthesia with (K) was observed, but did not represent significant difference statistically. While, on the other hand, the quality of anesthesia produced by (K-P) mixture at dose (2mg/kg-1mg/kg) produced excellent induction characterized by rapid, smooth and free of excitement ( $23.75 \pm 1.75$  seconds). The statistical analysis by the use of Student's -t test, show that; both, the induction and sleeping time, during anesthesia with (K-P) was better than (K) at  $p < 0.05$ , but no significant difference was represented in the recumbency period between (K) and (K-P). The orotracheal intubations were easily performed in all (K-P) anesthetized animals and the quality of anesthesia after induction was characterized by good muscle relaxation and narcosis. The swallowing reflex was abolished and its duration lasted for about ( $15.75 \pm 5.61$  minutes). The duration of sleeping time lasted for a mean ( $22.50 \pm 3.57$ ) minutes, which was longer than with (K), ( $p < 0.05$ ). The recumbency period was ( $10.50 \pm 2.62$ ) minutes. The pattern of recovery was very smooth and its period was as twice as that caused by (K) ( $10.50 \pm 2.62$  minutes).

Anesthesia with the mixture of (K-P) maintained the heart and respiratory rates clinically. Both, RR and HR did not represent significant difference at  $p < 0.05$  with this anesthetic protocol (Table 2).

Table 1: Summary of induction, sleeping, swallowing, and recumbency periods in six donkeys induced with ketamine (K) or ketamine-propofol mixture (K-P).

Variables	Induction time (seconds)	Sleeping time (minutes)	Swallowing reflex time (minutes)	Recumbency period (minutes)
(K) (3 mg/kg)	$56.25 \pm 8.44$ sec	$10.5 \pm 0.95$ m.	**	$14.75 \pm 2.28$ m.
(K-P) (2 mg/kg -1 mg/kg)	$23.75 \pm 1.75$ sec *	$22.50 \pm 3.57$ m. *	$15.75 \pm 5.61$ m.	$10.50 \pm 2.62$ m.

\* Data significance at  $p < 0.05$ : \*\* Swallowing reflex still present

Table 2: Summary of heart rate (HR) and respiratory rate (RR) in six donkeys induced with ketamine (K) or ketamine-propofol mixture (K-P).

Variables	(K)				(K-P)			
	Before injection (0-time)	10 min	20 min	30 min	Before injection (0-time)	10 min	20 min	30 min
H.R.	50.50±5	53±6	51±6	60±8	45.50±3	46±2	56± 4	54± 6
R.R.	25± 5	32.5±7	30.5 ± 6	30 ± 2	21.50±1	20±0	21.50± 3	18.5 ±1

### DISCUSSION

According to the results obtained from this study, injection of (K) intravenously to the donkeys premedicated with (X) induced a slow and rough induction associated with excitement. This finding could be due to the undesirable effect of ketamine on the central nervous system as an excitatory properties and the induction of anesthesia with ketamine alone is unsatisfactory as muscle tone is extreme, spontaneous and virtually continuous (1, 2). While the addition of propofol with ketamine, which produced a homogenized mixture proper for intravenous injection, was found to beneficial. Hence by improving the quality of anesthesia; as induction become calm, smooth and rapid. This was due to the excellent ultra short acting beneficial effect of propofol as an anesthetic agent having rapid onset of action. Additionally, the mixture likes to exert synergistic effect (5, 7-9). The mixture of (K-P) was made the orotracheal intubations very easy, while in (K), the orotracheal intubations was extremely difficult; time consuming and needs a good physical efforts, otherwise failed. Off course this condition is due to the well known side effect of ketamine that cause muscle rigidity which lead to closure of the jaws (1, 7-9).

The quality of anesthesia in (K-P) greatly improved the undesirable quality of anesthesia in (K) which was characterized by poor narcosis with short duration of action and muscle rigidity. The finding is in agreement with these reported by (9-11), where the rapid distribution of ketamine from brain to other tissue may account for its short action. The analgesia is not accompanied by central nervous depression and hypnosis but what appear to be a state of catalepsy. Analgesia appears very early and was representing shortly following loss of consciousness. The specific effect will vary with the species of animals that generally ocular, oral and swallowing reflex are present also muscle tone increase (10 and 11).

The recovery patterns from (K-P) anesthesia were characterized by its smooth, rapid and free of excitement features. This finding is in agreement with that found by (8 and 12) who stated the use of propofol and ketamine together for maintenance of anesthesia in ponies anesthetized for castration with detomidine

premedication. Others had also evaluated ketamine and propofol mixtures; and reported very good operations and quite recoveries from anesthesia. They referred the smooth recoveries to the effect of propofol, and they judged it as a reason for the improvement in that concern. In opposite, recoveries from ketamine were undesirable and this known to be due to tonic-colonic spasm effect of ketamine, which may occasionally occur and the rigidity of muscle remain during the peak effect of the drug with gradual subsidence during the recovery period (1, 10, and 13)

The increase in HR and RR during ketamine anesthesia was resembled to those observed by others (1 and 14). Intravenous injection of ketamine has been reported to produce arise in HR with arrhythmias associated with mild respiratory depression, and in clinical practice this is usually manifested by increased RR which does not compensate for decreased tidal volume. The maintenance in the degree of HR during (K-P) anesthesia and RR resembled to the observation by (15) in horses undergoing total intravenous anesthesia with propofol or ketamine-medetomidine-propofol combination, HR and arterial blood pressure were maintained within acceptable limits.

In conclusion, anesthesia with (K-P) mixture protocol produced an excellent anesthetic mixture for induction of general anesthesia in donkeys, and up to our knowledge this the first report on the use of this mixture for total intravenous anesthesia in donkeys.

#### **REFERENCES**

1. Hall LW, Clarke KW, Trim CM. *Veterinary Anesthesia* 10<sup>th</sup> edition. W.B. Saunders, Edinburgh 2003; pp: 247-313.
2. Mama KR. *Anesthetic management of the horse: intravenous anesthesia*. Ithaca, N. Y. ([www.ivis.org](http://www.ivis.org)) 2000. A 060 41000.
3. Matthews DG, Cross FH. Hematologic values of burros from birth to maturity: cellular elements of peripheral blood. *Am J Vet Res* 1969; 30: 1921-1927.
4. Trawford A. anesthesia in the field (including field castration) in proceeding of the donkey: a unique equidae 2000: 25-30.
5. Frias AF, Marsico F, Gomez de, Seguray IA, Nascimento PR, Nascimento AJr, Soares JH, Almosny NR. Evaluation of different doses of propofol in xylazine pre-medicated horses. *Veterinary Anesthesia and Analgesia*, 2003, 30, 193-201.
6. Aguiar AJA, Hussni CA, Luna SPL, *et al.* Propofol compared with propofol/guaiphenesin after detomidine premedication for equine surgery. *J Vet Anaesthesia* 1993; 20: 26-28.
7. Mama KR, Stefey EP, Pascoe PJ. Evaluation of propofol for general anesthesia in pre-medicated horses. *Am J Vet Res* 1996; 57: 512-516.
8. Nolan AM, Chambers JP. The use of propofol as an induction agent after detomidine premedication in ponies. *J Assoc Vet Anesth* 1989; 16: 30-32.
9. Lumb WV, Jones EF. *Veterinary Anesthesia*; Lea and Febiger, Philadelphia USA 1973; pp: 322-323.
10. Corssen G, Domino EF. Dissociative anesthesia: further pharmacologic studies and first clinical experience with the phencyclidine derivative CI-581-Anesth. *Analgesia (Cleveland)* 1966; pp: 45-29.

11. Matorras AA, Felipe MAN. Selection of induction on the use of CI-58 and observation on 198 cases. In progress in Anesthesiology. Proceeding of the 4<sup>th</sup> World Congress of Anesthesiologists, London 1968; pp: 1000.
12. Flaherty D, Reid J, Welsh E. A pharmacodynamic study of propofol or propofol and ketamine infusion in ponies undergoing surgery. *Res Vet Sce* 1997; 62: 179-184.
13. Commons M. Clinical experiences with ketamine hydrochloride as an intramuscular general anesthetic in cat. *Vet Med Small Animal Clinic* 1970; 65: 1151.
14. Soma LR. Preanesthetic Medication. In: Text book of veterinary anesthesia. The Williams and Wilkins Company, Philadelphia, USA 1977; pp: 147-150.
15. Umar MA, Yamashita K, Kushiro T, Muir WW. Evaluation of total intravenous anesthesia with propofol or ketamine-medetomidine-propofol combination in horses. *J Am Vet Med Assoc* 2006;15; 228 (8):1221-1227.