

## Comparative Anesthetic Protocols: Propofol and Thiopental in Xylazine Premedicated Donkeys

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**Abstract:** This study was intended to evaluate the anesthetic quality produced by the Propofol (P) ( $2 \text{ mg kg}^{-1}$ , I.V) and Thiopental (T) ( $10 \text{ mg kg}^{-1}$ , I.V) in 6 donkeys premedicated with Xylazine (X) ( $1 \text{ mg kg}^{-1}$ , I.V). Each donkey was anesthetized 1 time with each dose of P and T, 5 min after X administration in random order at 1 week intervals. Data were collected continuously before premedication and after anesthetic induction at 10, 20 and 30 min (induction time, sleeping time, abolishment of the swallowing reflex period, recumbency period, heart rate and respiratory rate). Quality of induction, recovery, mouth opening, intubation and number of attempts requiring the donkeys to regain the sternal recumbency and standing position were qualitatively and quantitatively assessed. The results revealed the presence of a mild range of differences in the quality of anesthesia between P and T. A significant difference at the level of ( $p < 0.05$ ) was detected between P and T protocols; induction time ( $40.50 \pm 9.36 \text{ sec}$ ) and ( $18.50 \pm 9.14 \text{ sec}$ ), sleeping time ( $12.5 \pm 2.1 \text{ min}$ ) and ( $30.5 \pm 5.42 \text{ min}$ ) and in the abolishment of swallowing reflex ( $9.5 \pm 1.55 \text{ min}$ ) and ( $20.25 \pm 3.47 \text{ min}$ ), respectively. On the other hand, the quality of induction with T provided a smooth and uneventful induction of anesthesia and was greatest in quality than P and animals anesthetized with T required the maximum number of attempts to reach sternal recumbency than P, at  $p < 0.05$ . Clinically, anesthesia by T produced longer narcosis and abolishment of swallowing reflex, rapid induction time, long recumbency period than P. Anesthesia with T produced good and excellent anesthetic protocol for induction of general anesthesia in donkeys when compared with anesthesia by P.

**Key words:** Donkeys, anesthetic protocols, propofol, thiopental, xylazine

### INTRODUCTION

A variety of methods can be used for induction of anesthesia for different sizes and breeds of donkeys exist in the world depending on available drugs, size and condition of the donkey and familiarity with different protocols. Although, very similar to horses, donkeys are not the same. The anesthesia should expect to encounter subtle differences which may affect the anesthetic management. Research data concerning anesthetic regimens in Mammoth asses, mules and horses has proven that donkeys and mules do not respond similarly to horses when anesthetized with the same drugs regimens as was once thought. Physiologically, donkeys are known to have different fluid-balance and partitioning of fluids than do horses. Differences in drug kinetics as well as behavioral differences between donkeys and horses seem to make it difficult to find the optional field anesthetic (Matthews and Van-Dijk, 2004; Mathews *et al.*, 1992, 2002; Maloiy, 1970).

For decades, thiobarbiturates have been used to induce and maintain short term (15-30 min) general

anesthesia in equines (Mama, 2000). Thiopental is a hypnotic anesthetic agent commonly employed and was the first thiobarbiturates to gain popularity as an anesthetic agent for animals (Hall *et al.*, 2003; Lumb and Jones, 1984). Thiopental is classified as a short-acting barbiturate and characterized by rapid onset of the action 30-60 sec and brief duration of anesthesia 10-20 min (Mckelvey and Hollingshead, 2003). Thiopental ( $5 \text{ mg kg}^{-1}$ , I.V) produces a rapid smooth induction, since it does not provide analgesia, it should be used with an effective sedative/opioid premedication. Anesthesia can be maintained for short periods ( $< 25 \text{ min}$ ) with thiopental, but respiration must be carefully monitored, since thiopental may produce apnea (Matthews and Van-Dijk, 2004). The use of intravenous  $\alpha^2$  adrenoceptor agonists (e.g., xylazine) just prior to anesthetic induction reduces the dose required for thiopental anesthesia (Hall *et al.*, 2003).

The propofol, an alkyl phenol, nonbarbiturate and relatively noncumulative I.V anesthetic agent with rapid onset and recovery and has a neutral pH, which is provided as an oil-in-water emulsion. The clinical efficacy

and safety of propofol in cats and dogs were evaluated in United Kingdom, which produced smooth induction with possibility to maintenance by intermittent injection (Muir *et al.*, 2007; Mckelvey and Hollingshead, 2003; Morgan and Legge, 1989; Watkins *et al.*, 1987). The propofol is a recently introduced as induction agent that may be used as the sole agent for brief procedures or for anesthetic induction before intubation and inhalant anesthesia (Mckelvey and Hollingshead, 2003). Due to these beneficial drug characteristics, its use in the anesthetic management of human being and animal patients is now routine (Mama, 2000). The propofol (2-2.2 mg kg<sup>-1</sup>, I.V) can be used for induction in premedicated horses or miniature donkeys with  $\alpha^2$  adrenoceptor agonists to provide a satisfactory anesthesia with excellent induction, muscle relaxation and smooth recovery (Matthews and Van-Dijk, 2004; Maloiy, 1970; Frias *et al.*, 2003; Matthews and Taylor, 2002; Mama *et al.*, 1996; Nolan and Hall, 1985). Anesthesia in horses by detomedine-propofol is not recommended for surgical procedures if dorsal recumbency is necessary and supplement oxygen is not available (e.g., field anesthesia), (Matthews *et al.*, 1999).

The objective of this study is to evaluate the anesthetic quality produced by propofol (2 mg kg<sup>-1</sup>, I.V) and thiopental (10 mg kg<sup>-1</sup>, I.V) in 6 donkeys premedicated with xylazine (1 mg kg<sup>-1</sup>, I.V).

**MATERIALS AND METHODS**

Six healthy adult from local breed donkeys (2 non pregnant females and four males), aged 2.78±0.65 years (2-3.5 years) and weighing 136.66±32.65 kg (90-180 kg; mean±SD) were used in this study. The animals were housed indoor and kept on straw and grain and had free access to hay and water. The donkeys were premedicated

with xylazine at the dose (1 mg kg<sup>-1</sup>) administered intravenously. Five min later, anesthesia induced with propofol at the dose (2 mg kg<sup>-1</sup>) administered intravenously. The same donkeys, after 1 week intervals, were re-anesthetized with thiopental at the dose (10 mg kg<sup>-1</sup>) administered intravenously, after 5 min of xylazine premedication.

Once the animals were sunken, after induction with P or T, they were placed in right lateral recumbency and blind endotracheal intubations were attempted. Once positioned and secured, they were allowed to breathe fresh air. The animals were kept in right lateral recumbency and did not undergo surgery and were left to recover undisturbed. The endotracheal tube was removed once swallowing reflex returned. Anesthetic induction quality and recovery were evaluated and the average was recorded on a 5-point scale score (Mama *et al.*, 1996): 1 = poor; 2 = marginal; 3 = fair; 4 = good; 5 = excellent (Table 1). The ease of mouth opening and intubation were evaluated and recorded on a 3-point scale score: 1 = difficult, intubation accomplished after third attempt. 2 = moderate, intubation accomplished at second attempt. 3 = easy, intubation accomplished at first attempt. The number of attempts to regain sternal recumbency and standing position were recorded on a 5-point scale score: 1 = 1st attempt, 2 = 2nd attempt, 3 = 3rd attempt, 4 = 4th attempt; 5 = at least 5th attempt required the donkeys to reach to the sternal recumbency or regain the standing position.

The following variables were measured and recorded: Induction time (time from end of injection to sunken and lateral recumbency), sleeping time (from beginning of anesthesia until first head movement), the return of swallowing reflex time (from administration of the induction agent until the swallowing reflex was regained), recumbency period (from administration of the induction agent until the donkeys reached sternal recumbency).

The cardio-pulmonary responses, Heart Rate (HR) and Respiratory Rate (RR) were considered before premedication (base line) and after induction of anesthesia at 10, 20 and 30 min after the injection of both anesthetic protocols.

**Statistical analysis:** The data were expressed as mean±SE. Nonparametric variables were analyses by Fisher Freeman Halton and Wilcoxon tests. The differences between times were analyses with the Student's t-test at level of significant (p<0.05).

**RESULTS**

Quality of induction of anesthesia with propofol (2 mg kg<sup>-1</sup>) revealed that most donkeys showed good

Table 1: Scoring system of responses associated with anesthetic induction and recovery (Mama *et al.*, 1996)

Score	Induction	Recovery
5	Smooth timely collapse to lateral recumbency, good muscle relaxation	Single coordinated effort to stand with minimal to no ataxia
4	Smooth transition to lateral recumbency, minor facial or limb movements	Single attempt to stand with some ataxia
3	A slight delay in time to lateral recumbency with increased (compared with 4) muscular rigidity or limb movement	Quiet recovery with >1 attempts to stand
2	Increased muscular activity prior to and during the transition from standing to lateral recumbency	Uncoordinated attempts to stand with or without minor injury (e.g., superficial laceration)
1	Vigorous struggling, paddling limb motions, increased coordinated muscle activity during the transition to lateral recumbency	Multiple, uncoordinated attempts resulting in major or life-threatening injury (e.g., broken limb)

Table 2: Quality of induction and recovery (score 1-5; poor-excellent), mouth opening and intubation (score 1-3; difficult-easy) and number of attempts to regain sternal recumbency and standing position in 6 donkeys premedicated with xylazine (1 mg kg<sup>-1</sup>, I.V) and intravenous anesthesia with either propofol (2 mg kg<sup>-1</sup>) or thiopental (10 mg kg<sup>-1</sup>)

Score		-----Propofol (2 mg kg <sup>-1</sup> )-----						-----Thiopental (10 mg kg <sup>-1</sup> )-----					
Quality		1	2	3	4	5	X	1	2	3	4	5	X
Induction	No.	0	0	1	4	1	4.0	0	0	0	1	5	4.8
	%	0.0	0.0	16.7	66.7	16.6	a	0.0	0.0	0.0	16.7	83.3	b
Recovery	No.	0	0	1	3	2	4.0	0	1	2	2	1	3.5
	%	0.0	0.0	16.7	50.0	33.3	a	0.0	33.3	33.3	33.3	16.7	a
Quality		1	2	3	4	5	X	1	2	3	4	5	X
Mouth opening	No.	0		2	4		2.7	0		0	6		3.0
	%	0.0		33.3	66.7		a	0.0		0.0	100		a
Intubation	No.	1		1	4		2.5	0		0	6		3.0
	%	16.7		16.7	66.7		a	0.0		0.0	100		a
No. of attempts		1	2	3	4	5	X	1	2	3	4	5	X
Sternal recumbency	No.	4	2	0	0	0	1.3	0	1	2	2	1	3.5
	%	66.7	33.3	0.0	0.0	0.0	a	0.0	16.7	33.3	33.3	16.7	b
Standing position	No.	4	1	1	0	0	1.5	4	1	1	0	0	1.5
	%	66.7	16.7	16.7	0.0	0.0	a	66.7	16.7	16.7	0.0	0.0	a

X = Mean value; the different letters horizontally mean significant difference between propofol and thiopental in quality of induction and number of attempts required to regain sternal recumbency, at p<0.05 using fisher freeman halton and wilcoxon tests

induction (66.7%), which was smooth, calm and gradual and the induction time was 40.50±9.36 sec and sleeping time lasted for 12.50±2.10 min with good muscle relaxation. The pattern of recovery was smooth with single coordinated to stand and minimal to no ataxia as illustrated in Table 2, which shows those 2 donkeys scored excellent recovery (33.3%) and three have good recovery (50%). The quality of mouth opening was easy (score 3) and endotracheal tube could be inserted in 4 donkeys (66.7%) with first attempt.

- Xylazine 2 %, CEVA Animal health, France.
- Propofol 1% emulsion, Diprivan®, Astrazeneca and Macclesfred, UK.
- Thiopental, Intraval Sodium 5%, May and Baker LTD, Dagenham, England.

Swallowing reflex abolished time lasted for 9.50±1.55 min and recumbency period was 28.75±10.48 min. And 4 donkeys (66.7%) with P anesthesia needed one attempts for regaining the sternal recumbency and standing position (score 1), as illustrated in Table 2 and 3. Anesthesia with P clinically produced increase in the H.R. and decrease in the R.R., but it did not represent any significant difference from their base line at p<0.05, as shown in Table 4.

The anesthesia produced by T (10 mg kg<sup>-1</sup>) was characterized by rapid induction (18.50±9.14 sec), with smooth and excellent quality of induction (score 5) in 5 donkeys (83.3%), as illustrated in Table 2 and 3. The pattern of anesthesia was characterized by good muscle relaxation and narcosis with a sleeping time for about 30.5±5.42 min. Recovery was excellent in 1, good in 2 and acceptable in 2 donkeys. Most of the animals revealed

Table 3: The induction, sleeping, return of swallowing reflex and recumbency time in 6 donkeys anesthetized with P or T

Variable	Induction (sec)	Sleeping (min)	Swallowing reflex (min)	Recumbency (min)
Propofol (2 mg kg <sup>-1</sup> )	40.50±9.36	12.50±2.10	9.50±1.55	28.75±10.48
Thiopental (10 mg kg <sup>-1</sup> )	18.50±9.14*	30.50±5.42*	20.25±3.47*	35.5±10.53*

The value significantly different from the Propofol value (in induction, sleeping time and in swallowing reflex), at p<0.05; The data were expressed as mean±SE

score 3 (33.3%) and score 4 (33.3%) for quality of recovery with this protocol and the pattern of recovery was quiet and most of the animals needed single attempt to stand. All animals have easy of mouth opening and the endotracheal intubation accomplished at first attempts (score 3). The abolishment of swallowing reflex period was 20.25±3.47 min. Whereas, the animals required 3 or 4 attempts to regain sternal recumbency and the recumbency period was 35.5±10.53 min and regaining of standing position with thiopental anesthesia was from the first attempts (score 1) in 4 donkeys (66.7%), as shown in Table 2 and 3. Anesthesia with T produced decrease H.R. and R.R. clinically, but this did not represent significant difference from its base line at p<0.05 and animals showed apnea for 23.7±6.8 sec and then the respirations returned to all animals, as shown in Table 4.

The quality of induction with T anesthesia provided a smooth and uneventful induction of anesthesia and was greatest in quality than propofol and animals anesthetized with thiopental required the maximum number of attempts to reach sternal recumbency than propofol, at p<0.05. No significant differences were assessed between the 2 protocols in the quality of recovery, ease of mouth opening, endotracheal intubation and number of attempts required for regaining of standing position, at p<0.05.

Table 4: The heart rate and respiratory rate in 6 donkeys anesthetized with propofol (2 mg kg<sup>-1</sup>) and thiopental (10 mg kg<sup>-1</sup>)

Variable	Propofol (2 mg kg <sup>-1</sup> )				Thiopental (10 mg kg <sup>-1</sup> )				
	Before (min)	10 (min)	20 (min)	30 (min)	Before (min)	10 (min)	20 (min)	30 (min)	Apnea (sec)
R.R	26.0±4.76	23.50±3.30	22.0±3.30	23.25±1.10	28.0±4.89	23.0±5.50	22.0±3.46	22.0±3.36	23.7±6.8*
H.R.	42.50±2.2	44.50±5.3	52.0±5.88	60.50±8.57	56.0±9.38	52.0±4.76	50.0±2.5	47.5±4.50	

\*Apnea occurs only in thiopental anesthesia; The data were expressed as mean±SE

Whereas, the student's t-test showed that the induction time in T anesthesia was shorter than P anesthesia, sleeping time during anesthesia with T was better and longer than P and the swallowing reflex was abolished with T for a longer period than with P, at p<0.05. But it did not represent any significant difference in the recumbency period between P and T.

### DISCUSSION

Propofol anesthesia in a dose 2 mg kg<sup>-1</sup>, in the present study produced an increase in heart rate and decrease in respiratory rate, although that was not significantly different from base line and this has been revealed by other studies in horses, which found that the effect of propofol (2-8 mg kg<sup>-1</sup>) in cardiovascular system produces little change in heart rate, dose dependent, decrease in arterial blood pressure result in hypotension and respiratory depression was manifested by decrease in respiratory rate, as well as xylazine reduced the respiratory rate and co-administration of either propofol or thiopental decreased it further (Muir *et al.*, 2007; Nolan and Hall, 1985; Mama *et al.*, 1996). The propofol in our study produced a rapid onset 40.5±9.36 sec, short duration of action (sleeping time) 12.5±2.10 min, recumbency period 28.75±10.48 min, very smooth and calm recovery and these were improved and agreement with results of previous studies (Nolan and Hall, 1985; Nolan and Hall, 1984; Aguiar *et al.*, 1993) in equine, whose found that intravenous injection of propofol (2 mg kg<sup>-1</sup>, I.V) was adequate for induction of anesthesia and proved a satisfactory technique when given 5 min after I.V administration of alpha<sub>2</sub>-adrenoceptor agonists and the anesthesia appears to last for approximately 10 min, with recovery to standing within 30 min. All these are referred to the very lipophilic characteristics of the propofol and its rapid uptake by the vessel rich groups (organs) such as the brain, heart, liver and kidney, but is very quickly redistributed to muscle and fat and is subsequently metabolized and relatively rapid biotransformation by the liver leading to rapid clearing from the body by hepatic and extra hepatic metabolism compared with thiopental (Mckelvey and Hollingshead, 2003; Muir *et al.*, 2007; Bettschart-Wolfensberger *et al.*, 2005).

Intravenous injection of thiopental sodium 10 mg kg<sup>-1</sup>, in the present study caused cardio respiratory depression and this result agrees with other observations used thiopental in a dose (6-12 mg kg<sup>-1</sup>, I.V) in horses (Muir *et al.*, 2007). Others found that intravenous administration of the thiopental produce an increase in heart rate and the initial toxic effect of this anesthetic agent is the marked depression of the respiratory center, both rate and amplitude are affected (Rawling and Kolata, 1983; Lumb and Jones, 1984; Muir *et al.*, 2007). Whereas, in the present study there was a decrease in the respiratory rate after 10, 20 and 30 min of injection of thiopental, but it were not significantly different from the base line. The injection of thiopental in the current study also caused apnea (23.7±6.8 sec) and this was mentioned in other studies as a characteristic sign of the thiopental injection in horses, which showed that apnea is more common after rapid intravenous injection of thiopental (Muir *et al.*, 2007). Induction of anesthesia using thiopental (5-6 mg kg<sup>-1</sup>, I.V) in premedicated horses with suitable tranquilizer usually followed by slow irregular respirations and sometimes brief periods of apnea (up to 1 or 2 min) (Lumb and Jones, 1984).

On the other hand, the rapid induction of thiopental alone in horses induced a moderate tachycardia, slight reduction in mean arterial blood pressure and a short period of respiratory depression (Tavernor and Less, 1970). Others found that sedation with promazine 0.25 mg 1b<sup>-1</sup> followed by rapid intravenous injection of thiopental 3.74 mg 1b<sup>-1</sup> in horses produce a mean duration of surgical anesthesia of (6.5 min) and a recovery period (to standing) of (45.8 min) (Jones *et al.*, 1960). The quality of recovery from anesthesia is almost always good in all donkeys with each anesthetic protocol. Donkeys in the present study, which were anesthetized with thiopental required the maximum number of attempts to reach sternal recumbency than propofol (p<0.05); this is due to redistribution of ultra short-acting barbiturates (thiopental) which rely on redistribution to lean body tissues (muscle) for their duration of action, whereas the accumulation of drug in muscle tissue corresponded to the approximate duration of thiopental anesthesia and concentrated in muscle and skin after thiopental injection (Muir *et al.*, 2007). Generally, donkeys will remain in

sternal recumbency until they are quite able to stand unassisted and it is generally impossible to make a donkey get up before it is ready (Matthews *et al.*, 2002). Therefore, most donkeys (66.6%) in each anesthetic protocols of this study can regain to the standing position from the first attempt.

### CONCLUSION

This study confirmed that intravenous injection of thiopental sodium in a dose 10 mg kg<sup>-1</sup> in xylazine premedicated donkeys produced an excellent induction quality with rapid onset time for about 18.5±9.36 sec, mean duration of sleeping time 30.5±5.42 min and abolishment of swallowing reflex for a period of 20.25±3.47 min. All these values made the thiopental an excellent anesthetic protocol for induction of general anesthesia than propofol 2 mg kg<sup>-1</sup> in donkeys.

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