# Assessment of clinical anesthesia and cardiopulmonary effects of propofol in detomidine premedicated donkeys

**Howaida M. Abu-Ahmed**

Department of Surgery, Faculty of Veterinary Medicine, Alexandria University, Egypt

**Abstract**

This study was carried out to evaluate the anesthetic quality and cardiopulmonary effects of propofol in detomidine premedicated donkeys underwent castration. Seven clinically healthy donkeys were used; each one was used in two trials with one week interval. The donkeys in both trials were sedated by slow i.v injection of 0.04 mg/kg detomidine, 10 minutes later the anesthesia was induced by slow i.v injection of 2 mg/kg propofol. The donkeys were allowed to recover without surgery in the first trial. One week later the same donkeys were used for the second trial where after induction the anesthesia was maintained for 30 minutes by i.v infusion of 0.1 mg/kg/min. propofol. The infusion started 10 minutes post detomidine/propofol induction to accomplish castration. During anesthesia, induction and recovery scores, sleeping and recovery times, respiratory and heart rates and blood gases were assessed. Propofol resulted in rapid induction (20-23 seconds) and smooth recovery with total recumbency period of $29.5 \pm 3.29$ and $100 \pm 10.24$ minutes in the first and second trial, respectively. Respiratory rate was significantly reduced with significant increase in $PCO_2$ in both trials. Thus, i.v injection of 2mg/kg propofol in detomidine pre-medicated donkeys provided rapid, excellent induction and smooth recovery. Maintenance of anesthesia with propofol infusion provided adequate sedation, analgesia and muscle relaxation for castration in donkeys with transient cardiopulmonary changes.

**Keywords:** Castration, detomidine, propofol, cardiopulmonary, donkeys

## Introduction

Donkeys are known to have different fluid balance and partitioning of fluid than do horses. Difference in drug kinetics as well as behavioral difference between donkeys and horses seems to make it difficult to extrapolate the results of horses in donkeys for optimal field anesthesia (Maloiy, 1970; Mathews et al., 1997). An increased risk with anesthesia could be related to the cardiopulmonary depressant effect of inhalation anesthesia in equine than small animals and human (Luna et al., 1996). Total intravenous anesthesia is now a clinically accepted technique of veterinary anesthesia especially for short acting, non-cumulative anesthetic agents (Hughes and Nalon, 1999). Propofol is a popular anesthetic induction agent widely used in veterinary practice to produces a fast and smooth induction of anesthesia (Watkins et al., 1987) and it was characterized by a virtual lack of any cumulative effect and had a rapid recovery after administration either by repeated bolus injection or by continuous infusion (Adetunji et al., 2002). Administration of propofol by the continuous infusion rate for maintenance of anesthesia resulted in stable cardiopulmonary effects in

**\*Corresponding author:** Howaida M. Abu-Ahmed, PhD, Alexandria Veterinary Medicine, Edfina, P.O. 22758, Egypt; Email:Howaida_maf@yahoo.com

donkeys (Naddaf et al., 2014). Detomidine is an $\alpha_2$ agonist which has potent sedative and analgesic properties (England and Clarke, 1996). Premedication with either xylazine or detomidine improve the quality of anesthesia produced by a single bolus of propofol (Mathews et al., 1999). The objective of the present study was to evaluate the anesthetic quality and cardiopulmonary effects of propofol in detomidine pre-medicated donkeys underwent castration.

## Materials and Methods

### Donkeys

Seven apparently healthy male donkeys aged 3-5 years and weighing 150-170 kg were used in this study. All experimental techniques were reviewed and approved by Institutional Animal Use and Care Committee at Faculty of Veterinary Medicine, Alexandria University- Egypt.

### Study design

Two trials were performed in this study. The donkeys in both trials were fasted for 12 hours and sedated by slow i.v injection of 0.04 mg/kg detomidine (Domosedan, Farmos-Orion Co.,Finland). Ten minutes later the anesthesia was induced by slow i.v injection of 2 mg/kg propofol (Diprivan, ICI-Zeneca pharmaceuticals, UK Ltd), then the donkeys were allowed to recover without surgery in the first trial. One week later the donkeys were premedicated and anesthetized as mentioned before .The anesthesia was maintained for 30 minutes by i.v infusion of 0.1mg/kg/min. propofol diluted in 5% dextrose solution in a ratio of 1:4, respectively (Ismail et al., 2010). The infusion started 10 minutes post detomidine/propofol induction. In this trial the donkeys were controlled in lateral recumbency and castration was performed as usual during infusion.

### Clinical assessments

As given in table 1, the quality of anesthetic induction and recovery was evaluated and scored based on the scales 1 (worse) to 5 (best) as previously described by (Bettschart-Wolfenberger et al., 2002). Induction time (time from end of injection to sunken and lateral recumbency), sleeping time/anesthetic time (time from beginning of anesthesia until first head movement), recumbency period (time from administration until reached sternal recumbency), standing time (interval between assumptions of sternal recumbency to animals' ability to stand) and recovery time (time interval from the end of propofol injection in 1st trial and cessation of propofol infusion in 2nd trial to animal's ability to stand) were recorded. In addition, heart and respiratory rates were recorded before premedication and 10, 20, 30, 40, 70 and 100 minutes

after premedication. Arterial blood samples were collected in a heparinized tube from the facial artery via a catheter just before induction of anesthesia then every 15 minutes. The tubes were capped and placed in an ice water bath and the samples were analyzed within 20 minutes of collection for determination of blood gases ($PO_2$, $PCO_2$, and $TCO_2$) electrolytes ($Na^+$, $Ca^+$, $K^+$ and $HCO_3$).

### Statistical analysis

Arterial blood gases were analyzed by descriptive statistical methods. Heart rates and respiratory rates were analyzed and summarized as mean ± SD using analysis ANOVA for repeated measures. In order to detect differences to pre-anesthetic values Dunnett's post test was performed (SAS, 2002).

## Results

Induction of anesthesia with propofol was smooth with adequate muscle relaxation and its score varied from good (score 4) to excellent (score 5). Only one donkey in the first trial showed fair induction with paddling and head shaking for few seconds. Recumbency occurred at 20 ± 4.25 and 23 ± 5.30 seconds after end of the injection in the 1st and the 2nd trial, respectively. The mean sleeping time in the 1st trial was 15.30 ± 3.55 minutes. The mean sleeping time in second trial (including surgery time) was 63.30 ± 6.30 minutes. Induction of anesthesia with propofol was satisfactory for donkey's castration and accompanied with good muscle relaxation and absence of movement in response to surgery. The time required for castration varied from 19 to 25 minutes. Recovery was smooth and good (score 4) in all animals. The mean recumbency period was 29.5 ± 3.29 and 100.00 ± 10.24 minutes in 1st and 2nd trial, respectively. Recovery time lasted for 34.10 ± 3.11 and 74.00 ± 5.50 minutes in 1st and 2nd trial, respectively (Table 2).

Mean heart and respiratory rates decreased significantly post detomidine injection. Propofol injection resulted in an increase in heart rate above the pre induction value while respiratory rate continued to decrease significantly till 40 minutes post induction but remained within the physiological limit. Apnea was not recorded in the present study (Tables 3 and 4). PH didn't change significantly throughout the experiment. $PO_2$ was significantly decreased post propofol injection till 45 minutes then increased again to reach the pre-injection value by the end of the experiment. On the other hand $PCO_2$ was significantly increased and never returned to the pre-injection value until the end of the experiment. Propofol resulted in significant decrease in $Na^+$ and $k^+$ without significant effect on $Ca^+$ (Table 5and 6).

**Table 1: Induction and recovery scores according to Bettschart-Wolfenberger et al. (2002)**

|  | Score | Description |
|---|---|---|
| Induction | 1 | Very poor, un predictable fall of the animal, the animal being injured |
|  | 2 | Poor, attaining recumbency unpredictably, but no injuries |
|  | 3 | Fair, animal slowly attains sternal recumbency, marked paddling of limbs or shaking of head |
|  | 4 | Good, animal slowly attains recumbency, only slight paddling of limbs or head shaking |
|  | 5 | E excellent, recumbency achieved slowly and smoothly, no paddling or head shaking |
| Recovery | 1 | Very poor, bad recovery with high risk of injury |
|  | 2 | Poor, more than one attempt to stand, animal is excited |
|  | 3 | Good, 1 attempt to stand, animal stays calm |
|  | 4 | Good, 1 attempt to stand, some ataxia |
|  | 5 | Excellent, 1 attempt to stand, minimal or no ataxia |

**Table 2: Induction, sleeping, recumbency, recovery and standing times in donkeys under detomidine/ propofol anesthesia**

|  | Induction (Sec) | Sleeping (min) | Recumbancy (min) | Standing (min) | Recovery (min) |
|---|---|---|---|---|---|
| 1st trial | 20.00±4.25 | 15.30±3.55 | 29.50±3.29 | 5±1.55 | 34.10±3.11 |
| 2nd trial | 23.00±5.30 | 63.30±6.30 | 100.00±10.24 | 14±3.14 | 74.00±5.50 |

**Table 3: Mean heart rate before and after detomidine/propofol anesthesia in donkeys**

|  | -5 | 10 | 20 | 30 | 40 | 70 | 100 |
|---|---|---|---|---|---|---|---|
| 1st trial | 50±5.10[a] | 40±4.12[c] | 44±4.11[b] | 47±4.17[b] | 49±4.22[a] | 50±5.22[a] | 51±5.23[a] |
| 2nd trial | 45±4.55[a] | 37±3.17[c] | 39±3.19[b] | 42±4.22[a] | 44±4.14[a] | 45±5.14[a] | 46±4.16[a] |

Means within the same row superscripted with different letters are significantly different (P<0.05)

**Table 4: Mean respiratory rate before and after detomidine/propofol anesthesia in donkeys**

|  | -5 | 10 | 20 | 30 | 40 | 70 | 100 |
|---|---|---|---|---|---|---|---|
| 1st trial | 25±4.15[a] | 16±3.13[b] | 10±2.11[b] | 13±3.19[b] | 14±3.14[b] | 19±4.18[a] | 22±3.15[a] |
| 2nd trial | 27±5.15[a] | 20±4.18[b] | 15±3.44[b] | 14±3.12[b] | 12±3.17[b] | 18±4.19[a] | 24±5.19[a] |

Means within the same row superscripted with different letters are significantly different (P<0.05)

**Table 5: Mean arterial PH, $CO_2$, $O_2$, $HCO_3$, $TCO_2$, $Na^+$, $K^+$, $Ca^+$ before and after induction of propofol anesthesia in donkeys**

| Parameter | -5 | 15 | 30 | 45 |
|---|---|---|---|---|
| pH | 7.30±1.33[a] | 7.17±2.33[c] | 7.25±1.44[b] | 7.29±1.33[a] |
| $PaO_2$(mmHg) | 91.7±3.44[a] | 86.80±4.55[b] | 90.90±3.99[a] | 91.50±5.66[a] |
| $PaCO_2$(mmHg) | 38.5±3.55[c] | 45.60±4.26[a] | 40.0±4.33[b] | 39.0±3.55[bc] |
| $HCO_3$(mEq/l) | 22.50±2.55[b] | 23.80±3.25[a] | 23.0±3.22[a] | 22.30±2.33[b] |
| T $CO_2$(mEq/l) | 23.00±2.33b[c] | 25.00±3.55[a] | 24.80±4.38[a] | 22.90±3.45[c] |
| $Na^+$(mEq/l) | 135±5.26[a] | 130±5.26[c] | 131±6.33[c] | 133±3.88[b] |
| $K^+$(mEq/l) | 3.90±1.22[a] | 3.0±1.33[c] | 3.60±1.26[b] | 3.80±1.23[a] |
| $Ca^+$(mg/dl) | 9.80±2.88[a] | 9.70±2.23[b] | 9.80±2.38[a] | 9.70±2.71[b] |

Means within the same row superscripted with different letters are significantly different (P<0.05)

**Table 6: Mean arterial PH, $CO_2$, $O_2$, $HCO_3$, $TCO_2$, $Na^+$, $K^+$, $Ca^+$ before and after induction and maintenance of propofol anesthesia in donkeys**

| Parameter | -5 | 15 | 30 | 45 | 60 | 75 |
|---|---|---|---|---|---|---|
| pH | 7.38±2.80[a] | 7.24±2.40[c] | 7.23±2.33[c] | 7.30±2.33[b] | 7.30±2.33b | 7.39±2.34[a] |
| $PaO_2$(mmHg) | 91.90±8.20[a] | 87.0±7.34[b] | 88.0±8.33[b] | 88.20±8.22[b] | 90.70±7.99[a] | 91.00±9.35[a] |
| $PaCO_2$(mmHg) | 38.70±3.87[e] | 55.70±5.77[b] | 56.00±6.54[a] | 57.90±5.59[a] | 51.90±5.69[c] | 41.20±4.59[d] |
| $HCO_3$(mEq/l) | 22.70±4.27[b] | 24.00±4.22[a] | 24.90±4.39[a] | 25.70±5.27[a] | 25.60±5.60[a] | 23.60±3.44[b] |
| T $CO_2$(mEq/l) | 23.80±3.38[c] | 25.70±5.22[b] | 26.40±6.22[ab] | 27.30±5.24[a] | 27.10±5.24[a] | 26.90±5.24[ab] |
| $Na^+$(mEq/l) | 138±3.14[a] | 133±8.14[b] | 131±8.15[c] | 132±8.15b[c] | 138±9.24[a] | 139±8.52[a] |
| $K^+$(mEq/l) | 3.70±1.37[a] | 3.10±1.34[c] | 3.30±2.33[b] | 3.40±2.34[ab] | 3.60±2.35[a] | 3.60±2.37[a] |
| $Ca^+$(mg/dl) | 9.60±3.44[a] | 9.50±3.55[ab] | 9.40±3.14[b] | 9.70±3.17[a] | 9.50±3.15[ab] | 9.50±3.17[ab] |

Means within the same row superscripted with different letters are significantly different (P<0.05).

## Discussion

Total intravenous anesthesia has several advantages for veterinary anesthetists because it is relatively easy to manage and doesn't require expensive apparatus for delivery; furthermore it avoids the pollution of the operation theater and environment with traces of inhalation agents (Wagner and Hellyer, 2000). Induction of anesthesia after propofol injection was rapid and smooth without unusual reaction and with

rapid smooth recovery; these characteristics are clearly related to the high lipid solubility of propofol that results in rapid blood/brain equilibrium and hence rapid onset of action (Langley and Keel, 1988). Only one donkey in the first trial showed fair induction characterized by paddling and head shaking for few seconds which could be attributed to rapid injection of the propofol so it was injected slowly in other donkeys all over the experiment. Rapid recovery after propofol administration either by repeated bolus or by continuous infusion was reported. This is due to the rapid metabolism and lack of cumulative effect of propofol. Similar finding was previously recorded in dogs (Hall and Chambers, 1987), in horses (Mathews and van-Dijk, 2004) and donkeys (Abd-Almaseeh, 2008). Propofol as a hypnotic has no reported intrinsic analgesic properties (Hall and Clarke, 1991), so donkeys in this study were pre-medicated with 0.04mg/kg detomidine due to its sedative and analgesic properties produced by its binding with α2 receptors in brain stem and spinal cord (Lamont and Tranquilli, 2002). Sleeping time in the $1^{st}$ trial was 15.30±3.55 minutes; hence propofol infusion in the $2^{nd}$ trial started 10 minutes post induction. Induction of anesthesia with detomidine/propofol resulted in total period of recumbency of 29.5 ± 3.29 minutes. This result agrees with that reported by (Nalon and Chambers, 1989) in ponies with detomidine/propofol induction. Total intravenous anesthesia with propofol had provided satisfactory anesthesia for carotid artery translocation (Umar et al., 2006) and abdominal surgery in horses (Mathews et al., 1999). Propofol at the dose of 2mg/kg produced satisfactory anesthesia and immobilization for castration in donkeys with a total sleeping period of 63.30 ± 6.30 minutes and recovery period of 74.00 ± 5.50 minutes after 30 minutes propofol infusion period. In this respect, Nalon and Hall (1985) previously reported 24 minutes recovery time after xylazine/propofol induction followed by propofol infusion for 60 minutes. This longer recovery time in the current study might be related to longer duration of action of detomidine than xylazine (Mathews et al., 1999). The reduction of respiratory rate in this study may be attributed to depression of central respiratory drive and ventilator response to arterial $O_2$ tension (Goodman et al., 1987). The $PaCO_2$ tension was significantly increased throughout the experiment. Hypo-ventilation and hypoxemia during detomidine/propofol anesthesia in horses was detected by Mathews et al. (1999), who suggested that the initial decrease in respiratory rate and increase of $PaCO_2$ may be related to bolus of propofol for induction of anesthesia or to hoisting and positioning in dorsal recumbency. The significant increase in the heart rate in this investigation was agreed with Abd-Almaseeh (2008) in donkeys, Umar et al. (2006) in horses and Adetunji et al. (2002) in dogs.

Propofol may be associated with an increase in sympathetic tone (Mama et al., 1996). It has been reported that propofol reversed bradycardia, sinoatrial and atrioventricular block produced by α2 agonists (Frias et al., 2003). Apnea was not recorded in the current study that may be due to slow injection of propofol, as observed in dogs (Mathews and van-Dijk, 2004; Sams et al., 2008). Although $PO_2$ appeared to be significantly decreased from the statistical point of view but it was clinically accepted as it was still within the physiological limit, the same result was observed by Naddaf et al. (2014). The reduction in the $PO_2$ occurred as a result of hypoventilation and perfusion abnormalities caused by anesthesia induced recumbency, pulmonary shunting and diffusion abnormalities (Robinson, 1991).

## Conclusion

Intravenous injection of 2mg/kg propofol in detomidine premedicated donkeys provided a rapid excellent induction and smooth recovery with short period of recumbency. Maintenance of anesthesia by propofol infusion provided adequate sedation, analgesia and muscle relaxation for castration in donkeys with transient cardiopulmonary changes.

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