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Full Length Article

# Effect of oxygen supplementation on propofol anesthesia in acepromazine/tramadol premedicated dogs

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ABSTRACT

Research in the area of injectable anesthetics in dogs requires mindfulness of ventilation, in order to supply artificial oxygen, which is often achieved with special equipment which may be unaffordable for veterinarians in developing countries. This study evaluated the effect of oxygen supplementation in dogs anesthetized with acepromazine-tramadol-propofol. Six Nigerian indigenous dogs were premedicated with intramuscular injection of acepromazine (0.03 mg/kg) and tramadol (5 mg/kg), followed by induction of anesthesia with propofol (4 mg/kg) IV 20 min later. Maintenance of anesthesia for 2 h was achieved with repeated bolus injections of propofol (2 mg/kg) at 10 min interval and anesthetized dogs breathed oxygen. This experimental trial was repeated a week later without oxygen supply as a control. Anesthetic indices, cardiopulmonary parameters, and rectal temperature were recorded at 10 min intervals for 2 h. Duration of anesthesia, duration of recumbency, time to extubation, and time to standing were not significantly ($P > .05$) different from their respective control values. Mean heart rate progressively decreased from the 60 min interval in both groups of anesthetized dogs. Mean arterial pressure in dogs with supplemented oxygen was similar to the control group. The mean oxygen-haemoglobin saturation was similar in both experimental trials. There was a progressive decrease in rectal temperature from the 60 min interval in both groups of anesthetized dogs. It was concluded that bolus injection of propofol, with and without supplemental oxygen, appeared to be efficacious and relatively safe in acepromazine-tramadol premedicated healthy dogs not undergoing any surgical or diagnostic procedures.

## 1. Introduction

Total intravenous anesthesia (TIVA) involves the use of drugs given solely by repeated or continuous intravenous injection for induction and maintenance of anesthesia [1]. Desirable characteristics of the drugs used for this technique include short duration of action and rapid clearance from the body [2,3]. The use of TIVA for maintaining anesthesia is gaining popularity in small animal anesthesia practice in preference to expensive inhalational agents which also require owning specialized equipment. Injectable anesthetics commonly employed for TIVA in small animals include alfaxalone and propofol [4].

Propofol is a non-barbiturate short acting intravenous agent which has the potential of being used for induction and maintenance of anesthesia [5]. The advantages it has over other CNS depressants which make it suitable for TIVA include; rapid action, excellent hypnosis, good muscle relaxation, a non-cumulative effect, and rapid complete recovery [6].

Premedication is often carried out in small animals practice to calm the animal prior to induction of anesthesia. This sometimes sufficiently allows a procedure such as intravenous catheterization to be carried out. Also, this has been reported to reduce fear and anxiety, and contributing to balanced anesthetic technique by providing extra analgesia, counteracting the side effects of other anesthetic drugs, and contributing to a smooth and quiet recovery [1,7].

The concept of neuroleptanalgesia is gaining popularity for both sedation and analgesia in dogs. This involves the combination of a neuroleptic agent such as acepromazine with a potent opioid analgesic such as tramadol or buprenorphine to reduce the requirement of general anesthesia and facilitate safe physical restraint and anesthetic induction for high risk patients [1,8,9]. Acepromazine is a long acting phenothiazine widely used as a preanesthetic or sedative agent in animals [10]. This drug is characterized by antihistaminic, anticonvulsant, antiarrhythmic, hypotensive, and hypothermic properties [11]. Tramadol may be used to treat post-operative, injury-related, and chronic pain in dogs and cats [12]. It can also be used perioperatively in veterinary anesthesia because it significantly reduces the requirement of

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volatile and injectable anesthetic agents [12,13]. Propofol can be used in a combination with drugs such as acepromazine and opioid analgesics to achieve a balanced anesthesia [14,15].

Regardless of the induction and maintenance method employed, monitoring and support of anesthetized patients are essential. This should begin as early as possible and continued until the animal is fully awake. Such supportive measures include supplemental oxygen, adequate ambient temperature and fluid therapy [1,9]. To date, the impact of supplemental oxygen on propofol anesthesia premedicated with acepromazine-tramadol in dogs has not been reported. Thus, there is a paucity of information on the haemodynamic effects when oxygen is used in combination with this anaesthetic protocol. The aim of this study was to compare the heart rate, respiratory rate, mean arterial pressure, oxygen haemoglobin saturation, and anesthetic indices during propofol anesthesia after premedication with acepromazine and tramadol with and without oxygen supplementation in healthy dogs not undergoing a clinical procedure.

## 2. Materials and methods

### 2.1. Experimental animals

Approval for this study was obtained from the University of Ibadan Animal Care and Use Research Ethical Committee (UI-ACUREC/App/2015/048). Six adult Nigerian indigenous dogs of either sex (3 male, 3 female) were used for this study. The dogs weighed between 7 and 10 kg. They were housed in the kennel of the Department of Veterinary Surgery and Radiology, University of Ibadan and fed a balanced homemade food twice daily.

Fresh water was available free choice in the kennel. The dogs were conditioned for a period of 4 weeks in order to get them familiar with the new environment, new feeding regime, human handling, and observation for any health problem. The dogs were judged to be in a good general health condition based on the complete physical examination findings (absence of ectoparasites, smooth hair coat, absence of any lesion/wound) and minimal blood analysis (packed cell volume and total solids). All findings were within reference limits reported by Khan et al [16] for dogs.

### 2.2. Drugs, equipment, and supplies

The anesthetic drugs used for this study were propofol (Provive®, Claris Life Science Limited, India) supplied as 10 mg/mL of white, oil-in-water emulsion in a vial for intravenous injection, tramadol hydrochloride (Tramed®, Sai Parenteral Put Ltd, India) supplied as 100 mg/2 mL aqueous solution for injection in a 2 mL ampoule, and acepromazine hydrochloride (Acepromazine, Vedco, USA) supplied as 10 mg/mL solution for injection in a 50 mL vial.

The equipment used for this study included; Anesthetic machine, multiparameter veterinary monitor (Cardell 9500 HD Multiparameter monitor, USA), digital thermometer, endotracheal tube (6 mmId), haemostatic forceps, hydraulic operating table with leather mattress, and drip stand.

The supplies used were absorbent cotton wool, methylated spirit, needles (21 and 23 guage)-Agary pharmaceuticals Ltd, syringes (2 mL, 10 mL, 20 mL), IV set, adhesive tape, and infusion fluid (Lactated Ringer's solution).

### 2.3. Study design

This was a 120 min prospective, randomized, blinded, crossover trial, in which each dog received both anesthetic protocols with a washout period of one week between trials. The randomization scheme was generated by using the Web site Randomization.com 〈http://www.randomization.com〉.

### 2.4. Experimental procedure

Prior to the trial, food and water were withheld from the dogs for 12 h. Each dog was premedicated with acepromazine (0.03 mg/kg) and tramadol (5 mg/kg) mixed in the same syringe intramuscularly (IM). Venous access was secured using 21-guage winged needles and general anesthesia was induced with propofol (4 mg/kg) via intravenous route. Endotracheal intubation was done after induction with a 6 mmId cuffed endotracheal tube and connected to the anesthetic machine to breathe pure oxygen from the oxygen flow meter at the rate of 1 L/kg/min flow rate via Bain's circuit (Group A). The patient monitor (Cardell 9500 HD Multiparameter monitor) was attached to monitor all the physiological parameters. Anesthesia was maintained for a period of 120 min by repeated bolus injections of 2 mg/kg propofol at 4 min intervals [6]. Pedal reflex (toe-pinch withdrawal), palpebral reflex and muscle relaxation were evaluated at 2 min intervals throughout the anesthetic period to assess depth of anesthesia for each dog and lactated ringer's solution was administered at 5 mL/kg/h throughout. Following the last two bolus injections of propofol, the dogs were allowed to recover on a padded surface. This trial was repeated a week later with the anesthetized dogs having the endotracheal tube in place but not connected to the anesthetic machine for artificial oxygen supply (control-Group B).

### 2.5. Measurements

Following induction of anesthesia, a multiparameter monitor was attached appropriately to the dog. Heart rate (HR) in beats/min, mean arterial pressure (MAP) in mmHg, respiratory rate (RR) in breath/min, haemoglobin oxygen saturation ($SpO_2$)%, and rectal temperature (RT)˚C were recorded at 10 min intervals over 120 min of anesthesia. The patient monitor (Cardell 9500 HD Multiparameter monitor) was utilized to take all these mentioned physiological parameters.

### 2.6. Calculation of anesthetic indices

The following anesthetic indices were calculated:

Duration of anesthesia: time interval (in minutes) between the disappearance and return of pedal reflex, duration of recumbency: time interval (in minutes) between induced recumbency and assumption of sterna posture, and time to extubation: time interval (in minutes) between the last bolus injection of propofol to the time swallowing reflex was observed for removal of the endotracheal tube, time to standing: time interval (in minutes) between the last bolus injection of propofol and the dog's ability to stand.

### 2.7. Statistical analysis

Data were analyzed as mean ± standard error mean (SEM). Anesthetic indices (The means of duration of anesthesia, duration of recumbency, time to extubation and standing) were compared with control values using students' T-test for paired data. Two-way ANOVA for repeated measures was used to compare the differences within and between groups, followed as appropriate by the Duncan test when a significant difference was indicated. A value of $P < .05$ was considered statistically significant in all cases.

## 3. Results

In each experimental dog, the intramuscular (IM) administration of acepromazine (0.03 mg/kg) combined with tramadol (5 mg/kg) produced moderate sedation characterized by drowsiness, calmness, and lack of resistance to handling and manipulation. The degree of sedation obtained facilitated the establishment of venous access with an appropriately sized winged needle. Induction of anaesthesia with propofol (4 mg/kg) was smooth and rapid (30–40 s) in all dogs. Attainment of

**Table 1**
Anesthetic indices of dogs anesthetized with acepromazine-tramadol-propofol with and without supplemental oxygen.

| Anesthetic index | Group A (n = 6) | Group B (n = 6) |
|---|---|---|
| Duration of anesthesia (min) | 127.3 ± 1.3 | 126.0 ± 2.1 |
| Duration of recumbency (min) | 131.3 ± 0.8 | 129.9 ± 0.3 |
| Time to extubation (min) | 12.8 ± 0.5 | 11.0 ± 0.2 |
| Time to standing (min) | 3.0 ± 0.1 | 3.8 ± 0.4 |

jaw relaxation and suppression of pharyngeal reflexes allowed easy passage of the endotracheal tube. The induction and recovery time were uneventful.

### 3.1. Anesthetic indices

Table 1 shows the anaesthetic indices in dogs on acepromazine-tramadol-propofol with and without supplemental oxygen. There were no significant alterations ($P > .05$) observed in the anesthetic indices of dogs in the two protocols.

### 3.2. Cardiovascular parameters

Mean heart rate (HR) and mean arterial pressure (MAP) responses of dogs anesthetized with acepromazine-tramadol-propofol are shown in Table 2. In dogs breathing oxygen, mean heart rate were not significantly different when compared to the control group (B). From the 60 min interval, mean HR progressively and significantly ($P < .05$) decreased from the 10-minute interval time point.

There were no significant ($P > .05$) differences in MAP between the supplemental oxygen group (Group A) and group B over time as shown in Table 2.

### 3.3. Respiratory parameters

Table 3 shows the Mean RR and $SpO_2$ responses of the anesthetized dogs. Mean RR was significantly ($P < .05$) higher in dogs breathing pure oxygen than that of the control (Group B) at multiple time points.

In dogs breathing supplemental oxygen, mean $SpO_2$ was similar to that in dogs breathing room air (control). There was no significant ($P > .05$) difference between the two groups.

### 3.4. Rectal temperature values

Mean RT responses of both anesthetic protocols are shown in Table 4. The rectal temperature values recorded for both groups were similar, however, at around the 60 min interval RT progressively decreased ($P < .05$) from the initial values obtained at the 10 min interval in both groups.

**Table 2**
Mean heart rates and mean arterial blood pressure responses of dogs to acepromazine-tramadol-propofol anesthesia with and without supplemental oxygen.

| Time interval (min) | Heart rated (beat/min) | | Mean arterial pressure (mmHg) | |
|---|---|---|---|---|
| | Group A | Group B | Group A | Group B |
| 10 | 118.7 ± 11.3 | 114.8 ± 9.1 | 61.8 ± 3.0 | 72.8 ± 7.0 |
| 20 | 116.2 ± 8.9 | 107.2 ± 10.1 | 76.2 ± 2.5 | 76.7 ± 6.4 |
| 30 | 114.8 ± 9.3 | 109.8 ± 9.3 | 80.7 ± 2.5 | 73.3 ± 6.1 |
| 40 | 140.0 ± 10.2 | 105.5 ± 9.5 | 72.8 ± 4.0 | 71.8 ± 5.8 |
| 50 | 99.3 ± 8.3 | 112.5 ± 10.0 | 71.0 ± 4.6 | 84.5 ± 6.7 |
| 60 | 92.0 ± 7.4 | 101.8 ± 8.7 | 75.6 ± 2.7 | 81.5 ± 3.9 |
| 70 | 92.2 ± 7.9[a] | 101.8 ± 10.7 | 78.0 ± 5.5 | 81.5 ± 3.9 |
| 80 | 89.8 ± 4.7[a] | 88.7 ± 7.8[a] | 70.3 ± 6.4 | 85.8 ± 3.0 |
| 90 | 92.7 ± 8.7[a] | 87.0 ± 9.0[a] | 74.2 ± 4.8 | 73.0 ± 8.6 |
| 100 | 85.0 ± 6.1[a] | 90.8 ± 10.6[a] | 70.8 ± 5.5 | 72.8 ± 6.6 |
| 110 | 85.5 ± 7.1[a] | 86.7 ± 9.1[a] | 69.5 ± 3.0 | 80.3 ± 4.9 |
| 120 | 86.2 ± 8.5[a] | 89.7 ± 9.3[a] | 66.0 ± 3.3 | 81.3 ± 4.3 |

a = ($P < .05$) within groups.
b = ($P < .05$) between groups.

**Table 3**
Respiratory rate and haemoglobin-oxygen saturation responses of dogs anesthetized with acepromazine-tramadol-propofol anesthesia with and without supplemental oxygen.

| Time interval (min) | Respiratory rate (Breath/min) | | Haemoglobin-$O_2$ saturation (%) | |
|---|---|---|---|---|
| | Group A | Group B | Group A | Group B |
| 10 | 26.2 ± 3.1 | 34.6.0 ± 6.0[b] | 92.5 ± 1.7 | 95.2 ± 1.6 |
| 20 | 24.2 ± 1.4 | 26.3 ± 3.3 | 92.3 ± 1.1 | 93.3 ± 1.6 |
| 30 | 24.3 ± 2.3 | 27.2 ± 3.3 | 93.2 ± 1.1 | 94.2 ± 1.1 |
| 40 | 26.0 ± 3.6 | 31.7 ± 5.6[b] | 92.7 ± 1.0 | 94.3 ± 1.3 |
| 50 | 22.0 ± 2.0 | 33.2 ± 5.3[b] | 94.5 ± 1.6 | 93.7 ± 2.0 |
| 60 | 24.3 ± 1.9 | 27.2 ± 5.3 | 93.7 ± 2.6 | 93.5 ± 2.0 |
| 70 | 26.0 ± 1.5 | 23.3 ± 3.3 | 91.7 ± 2.1 | 93.0 ± 2.0 |
| 80 | 28.7 ± 2.8 | 33.5 ± 4.0[b] | 92.3 ± 1.7 | 93.2 ± 1.1 |
| 90 | 25.8 ± 3.0 | 27.2 ± 3.5 | 93.2 ± 1.7 | 95.5 ± 1.1 |
| 100 | 21.2 ± 5.4 | 27.8 ± 2.2 | 92.0 ± 1.8 | 95.2 ± 0.9 |
| 110 | 25.8 ± 3.8 | 29.7 ± 4.1 | 94.8 ± 1.1 | 95.5 ± 1.2 |
| 120 | 23.0 ± 3.1 | 25.5 ± 2.3 | 95.2 ± 0.9 | 95.0 ± 1.3 |

a = ($P < .05$) within the groups.
b = ($P < .05$) between the groups.

**Table 4**
Rectal temperature of dogs anesthetized with acepromazine-tramadol-propofol with and without supplemental oxygen.

| Time interval (min) | Rectal temperature (C) | |
|---|---|---|
| | Group A | Group B |
| 10 | 37.8 ± 0.2 | 37.6 ± 0.2 |
| 20 | 37.7 ± 0.2 | 37.4 ± 0.2 |
| 30 | 37.5 ± 0.2 | 37.1 ± 0.3 |
| 40 | 37.4 ± 0.2 | 37.0 ± 0.2 |
| 50 | 37.2 ± 0.2 | 36.8 ± 0.3 |
| 60 | 37.0 ± 0.2 | 36.7 ± 0.2 |
| 70 | 36.7 ± 0.2[a] | 36.6 ± 0.1 |
| 80 | 36.5 ± 0.2[a] | 36.5 ± 0.1[a] |
| 90 | 36.5 ± 0.2[a] | 36.4 ± 0.1[a] |
| 100 | 36.4 ± 0.2[a] | 36.3 ± 0.1[a] |
| 110 | 36.2 ± 0.2[a] | 36.1 ± 0.2[a] |
| 120 | 36.3 ± 0.3[a] | 36.1 ± 0.1[a] |

a = $P < .05$ within groups.
b = $P < .05$ between groups.

## 4. Discussion

The results of the present study showed that TIVA with repeated bolus injections of propofol following premedication with the intramuscular administration of acepromazine combined with tramadol, with or without supplemental oxygen, was efficacious and relatively safe in healthy dogs not undergoing any clinical procedure.

The use of propofol alone for TIVA has been widely reported in dogs [17–19]. Despite its widespread use, however, it has been reported in humans and mice that antinociception is limited or not present at all when propofol is used [20,21]. Therefore, propofol is not recommended as a single agent for anesthetic maintenance for major surgical procedures. This is because this agent does not prevent haemodynamic responses to noxious stimulation unless in high doses to produce deep anesthesia. These haemodynamic responses are invariably accompanied by considerable cardiovascular depression [19,22,23]. For this reason, propofol was administered in this study following premedication with acepromazine-opioid combination [24]. The duration of anesthesia of more than 2 h obtained in this study (Table1) is consistent with long-acting acepromazine and tramadol components of the

neuroleptanalgesia premedicants.

During general anesthesia, a major aim is to maintain tissue perfusion and oxygenation. Since it is rarely possible to measure tissue perfusion directly, blood pressure and blood lactate can be measured, inferences are then made about tissue perfusion and the adequacy of oxygen delivery to tissues. Nonetheless, the optimal tissue oxygen delivery depends upon the cardiac output and arterial oxygen content [25]. Hypotension is one of the most common anesthetic complications observed in even healthy, young veterinary patients [26]. Hypotension is defined as a MAP < 60 mmHg [27]. In this study, mean arterial pressure ranged from 66.0 ± 3.3 to 86.7 ± 0.2 mmHg (Table 2) and no hypotension developed in both the treated and control groups of anesthetized dogs. This is a positive result considering the hypotensive potential of acepromazine and propofol used in this study. Acepromazine can contribute to hypotension during general anesthesia by causing a decrease in arterial blood pressure due to its alpha-antagonism and resultant vasodilation and hypotension [28,29]. Likewise, propofol at therapeutic doses causes significant decreases in HR and MAP, as well as a direct ionotropic effect [30] leading to hypotension. The administration of lactated Ringer's solution at 5 mL/kg/h in the course of anesthesia contributed to maintaining normotension in the face of anesthetic-induced vasodilation.

The lack of a difference in oxygen haemoglobin concentrations between the two groups of experimental dogs (Table 3) is interesting. This implies that healthy dogs used in this experiment were able to maintain oxygenation with or without supplementation. However, anesthetized dogs with respiratory diseases are most likely to benefit from such oxygen supplementation.

It is noteworthy that after about 1 h in the course of the anesthesia, the mean HR progressively decreased in both the treated and control groups of anesthetized dogs (Table 2). The cause of such slowing of HR could be due to entering a deeper plane of anesthesia. This may not be observed in a patient undergoing a procedure due to surgical stimulation. However, it is interesting to note that the decreases in mean HR coincided with progressive decreases in mean RT (Table 4). Therefore, the tendency of bradycardia might be resulted from cooling of the cardiac pace-maker (sino-atrial node) by the falling body temperature. Nonetheless, despite the decreases in mean HR, the MAP and oxygen delivery to tissues appeared to be well maintained during the course of anesthesia.

In this study, the mean RT began to fall after about an hour in the course of anesthesia (Table 4). This is surprising in view of the fact that most of the factors that predispose to a fall in body temperature during anesthesia were not present. These include low ambient temperature, excessive clipping of the operative site and use of copious alcohol during surgical preparation, and exposure of visceral surfaces. The observed fall in mean RT in this study might be related to the administration of unwarmed intravenous lactated Ringer's solution and inspiration of cold, dry gases (room air and oxygen). In view of the consequences of body temperature variations during anesthesia, it would be advisable to place a circulating warm blanket underneath the anesthetized dog to maintain normothermia.

## 5. Conclusions

In conclusion, TIVA with repeated bolus injections of propofol, with or without supplemental oxygen appeared to be efficacious and relatively safe in acepromazine-tramadol premedicated dogs not undergoing any clinical procedure. The only cause for concern was the potential development of hypothermia. Further studies are recommended to assess these anesthetic protocols in dogs undergoing operative or diagnostic procedures.

## Competing interests

I hereby declare that the authors of this research work have no conflict of interest of any kind.

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