Vol. 10(7), pp. 180-184, July 2018
DOI: 10.5897/JVMAH2018.0682
Article Number: AAF495957576
ISSN: 2141-2529
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Journal of Veterinary Medicine and Animal Health

Full Length Research Paper

Anaesthetic and cardiopulmonary parameters of dogs administered propofol-acepromazine-butorphanol or propofol-acepromazine-buprenorphine anaesthesia

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Received 28 March, 2018: Accepted 13 June, 2018

The efficacy and safety of premedication with acepromazine-butorphanol or acepromazine-buprenorphine combination were compared in dogs anaesthetized with propofol using total intravenous anaesthesia. Six mature Nigerian indigenous dogs were randomly assigned to 1 of 2 premedication groups: Group 1 (acepromazine, 0.03 mg/kg, IM; butorphanol, 0.4 mg/kg, IM), or 2 (acepromazine, 0.03 mg/kg, IM; buprenorphine, 0.02 mg/kg, IM); propofol was administered using bolus injection method of total intravenous anaesthesia (TIVA); cardiopulmonary parameters of anaesthetized dogs were recorded at 20 min intervals for 2 h. The results of this study showed that significant alterations ($p>0.05$) were not observed in the anaesthetic indices of dogs on the two protocols. However, significant increase ($p<0.05$) was observed in the heart rate of dogs anaesthetized with ACE-BUP-PRO compared with those anaesthetized with ACE-BUT-PRO at all time intervals of 20 to 120 min after the induction of anaesthesia. The mean arterial blood pressure decreased significantly ($p<0.05$) in dogs anaesthetized with ACE-BUP-PRO at 40 and 120 min post anaesthetic induction, compared with dogs anaesthetized with ACE-BUT-PRO. Likewise, the respiratory rate of dogs anaesthetized with ACE-BUP-PRO decreased significantly ($p<0.05$) at 60, 100 and 120 min post anaesthetic induction. Haemoglobin-oxygen saturation and rectal temperature were not significantly at variance in dogs on the two anaesthetic protocols. In conclusion, either butorphanol or buprenorphine can be used in combination with acepromazine for premedication of dogs for routine surgical and diagnostic procedures. However, caution is advised with the use of buprenorphine in dogs with pre-existing cardiac disease or hypertension.

Key words: Propofol, acepromazine, butorphanol, buprenorphine, total intravenous anaesthesia (TIVA), dogs.

INTRODUCTION

Propofol is an alkyphenol anaesthetic agent widely used for total intravenous anaesthesia (TIVA). The administration of propofol usually is accompanied by smooth and rapid induction of anaesthesia and short

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recovery times (Adetunji et al., 2002). Smooth inductions and short recovery times are peculiar characteristics of propofol which qualifies it to be used as a constant rate infusion for maintenance of anaesthesia (Aoki et al., 2017).

Despite the widespread use of propofol for total intravenous anaesthesia (TIVA) in dogs (Kumar et al., 2014), the drug has no potent antinociceptive activity when used alone (Quandt, 2013). Therefore, propofol is not recommended as the sole agent for maintenance of surgical anaesthesia, as it does not prevent haemodynamic responses to noxious stimulation except at high doses, which are invariably accompanied by considerable cardiopulmonary depression (Alipour et al., 2014).

Neuroleptanalgesia is a state of profound sedation and analgesia produced by co-administration of a neuroleptic agent such as acepromazine and an opioid such as butorphanol or buprenorphine (Poller et al., 2013, Chang et al., 2014). The neurolept acepromazine has a relatively low toxicity and potentiates the analgesic effect of an opioid (Quandt, 2013). Butorphanol and buprenorphine are both partial agonists that produce short and long duration of analgesia respectively and are widely used as premedication in small animals (Izer et al., 2014). Till date, the comparative effects of both neuroleptanalgesics have not been reported in propofol-anaesthetized dogs.

Thus, these drugs are used without adequate information that may be associated with the haemodynamic disturbances when used as premedicants with propofol. The aim of this study, therefore, was to compare the efficacy and safety of TIVA with propofol in dogs premedicated with either acepromazine-butorphanol or acepromazine-buprenorphine without the confounding effects of a surgical procedure.

MATERIALS AND METHODS

Animals

This study was carried out with the approval of University of Ibadan Animal Care and Use Research Ethics Committee (UI-ACUREC/App/2015/002). Six adult Nigerian indigenous dogs comprising 4 intact male and 2 intact, non-pregnant, non-lactating females were used for the study. Apparently healthy dogs were purchased from a local dog market in Ibadan. They were clinically observed for ectoparasites, overt signs of anaemia and infection (inflamed lymph nodes), and the heart rate, pulse rate and respiratory rate were recorded before the commencement of the study. Their body weight ranged between 10 and 13 kg. They were housed in a standard animal house at the faculty of veterinary medicine, University of Ibadan.

The dogs were fed ad libitum once daily on a home-made, rice-based diet with fish and meat offal supplements. Fresh drinking water was made available free choice at all times. Before the experiments of the trials, the dogs were allowed three weeks to get accustomed to their new environment, feeding regime and constant human handling. They were judged to be healthy (American Society of Anaesthesiologists physical status classification 1 or 2) on the basis of complete physical examination and minimal blood analysis (packed cell, volume and total solids). All findings were within reference limits (Khan et al., 2011) for dogs.

Study design

This study was a randomized, blinded, cross-over trials, in which each dog received the two regimens of premedication with a washout period of 7 days between treatments. Dogs were randomly allocated into the two treatments; the randomization scheme was generated by using the Web site Randomization.com ⟨http://www.randomization.com⟩.

Experimental procedure

Food was withheld from the dog the night before the trial but water was allowed up to the time of premedication. The dog was weighed for the purpose of drug dose determination. Syringe containing a neuroleptic - opioid mixture was prepared by one person that was not involved in the trial. The drug mixtures were prepared as follows:

1. 0.03 mg kg^{-1}acepromazine (Plegial 10 mg mL^{-1}, Pharmaxim Sweden AB, Sweden) and 0.4 mg kg^{-1}butorphanol tartarate (Torbugesic 10 mg ml^{-1}, Forte Dodge, Iowa 50501, USA)
2. 0.03 mg kg^{-1}acepromazine (Plegial 10 mg mL^{-1}, Pharmaxim Sweden AB, Sweden) and 0.2 mg Kg^{-1} buprenorphine hydrochloride (Temgesic 0.3 $mgmL^{-1}$, ReckiH Benckiser Healthcare, UK)

Each drug mixture was administered intramuscularly (IM) in the pelvic limb. After 15 min of drug administration, sedation was scored by another person using a numeric descriptive scale (NSP) as follows:

0: No sedation
1: Mild sedation, ataxic, ambulatory
2: Moderate sedation, sternal recumbency, cervical tone present
4: Deep sedation, sternal recumbency, lift up head sporadically
5: Very deep sedation, lateral recumbency.

After obtaining sedation scores of the unrestrained and undisturbed dog, cephalic venous access was then secured using a 21G winged needle and an intravenous administration of 5% dextrose in water at an infusion rate of 5 $mLKg^{-1}h^{-1}$ was begun. Twenty minutes after premedication intravenous anaesthesia was induced with 4 mg kg^{-1}propofol (Propofol-lipuro 10 $mg.mL^{-1}$, FresiusKabi, Halfway House, South Africa) administered by hand over approximately 2 min at a rate of approximately 0.25 mg Kg^{-1} every 1.5 s. The end point was an absence of head, jaw and tongue movements and a jaw tone sufficiently reduced to allow intubation of the trachea with a cuffed 6 mm1D endotracheal tube immediately after tracheal intubation, the anaesthetised dog was placed in left lateral recumbency and a multiparameter physiological monitor (Cardell 9500 HD) was attached. Anaesthesia was maintained for 2 h with repeat bolus injections of 2 mg Kg^{-1} propofol at 5-minute interval (Adetunji et al., 2002). Anti-nociception was assessed at 2-minute intervals using a toe-pinch pedal withdrawal reflex response to haemostatic forceps closed to one ratchet.

Calculations

1. Onset of analgesia: Time interval (in minutes) between the initial bolus injection of propofol to disappearance of pedal reflex induced with artery forceps closed to the first ratchet.
2. Duration of analgesia: Time interval (in minutes) between the disappearance and return of the pedal reflex.

Table 1. Anaesthetic indices for ACE-BUT-PRO and ACE-BUP-PRO trials.

Anaesthetic index	ACE-BUT-PRO (minute)	ACE-BUP-PRO (minute)
Induction time	4.3 ± 0.2	4.3 ± 0.6
Duration of analgesia	124.0 ± 1.4	121.6 ± 1.1
Duration of recumbency	139.8 ±6.9	134.3 ± 1.4
Time to standing	7.8 ± 2.6	5.0 ± 1.8

3. Duration of recumbency: time interval (in minutes) between acepromazine-buprenorphine or acepromazine-butorphanol induced recumbency and the dog's assumption of the sternal posture.
4. Extubation time: Time interval (in minutes) between the last bolus injection of propofol and the time of extubation.
5. Recovery time: Time interval (in minutes) between the last bolus injection of propofol and the dog's ability to stand
6. Induction dose: Quantity in milligrams of general propofol used for induction of anaesthesia.
7. Duration of analgesia: Time interval (in minutes) between loss of pedal reflex and return of pedal reflex.
8. Duration of recumbency: Time interval (in minutes) between assumption of standing posture and assumption of sternal posture.

Measurements

Heart rate (HR), respiratory rate (f_R), haemoglobin oxygen saturation (SpO_2), mean arterial blood pressure (MAP), and rectal temperature (RT) were measured immediately after induction of anaesthesia and during the course of maintenance of anaesthesia at 20 min intervals over a period of 120 min. This was considered as the cost critical period of anaesthesia. The variables were monitored to access relative safety of six total intravenous regimens under study. The patient monitor (Cardell 9500 HD Multiparameter monitor) was utilized to take all these mentioned physiological parameters.

Data analysis

All calculated and measured variables are expressed as mean ± SEM (Standard error mean) of six dogs. The means of duration of analgesia, duration of recumbency for total intravenously administered drug was compared in both instance of premedication using student t-test when a significant difference was indicated.

The mean values of the physiological variables (HR, RR, SP, MAP, SpO_2 and RT) were compared using analysis of variance (ANOVA) for repeated measures followed as appropriate by Duncan test when a significant difference was indicated. A value of $p<0.05$ was considered statistically significant for all the comparisons.

RESULTS

Anaesthetic indices

The anaesthetic indices of dogs administered ACE-BUT-PRO AND ACE-BUP-PRO anaesthesia are presented in Table 1. Significant alterations ($p>0.05$) were not observed in the anaesthetic indices of dogs on the two protocols.

Cardiopulmonary parameters

The cardiopulmonary parameters of dogs administered ACE-BUT-PRO and ACE-BUP-PRO anaesthesia are presented in Table 2. Significant increase ($p<0.05$) was observed in the heart rate of dogs anaesthetized with ACE-BUP-PRO compared with those anaesthetized with ACE-BUT-PRO at all time intervals of 20 to 120 min after the induction of anaesthesia. However, the mean arterial blood pressure decreased significantly ($p<0.05$) in dogs anaesthetized with ACE-BUP-PRO at 40 and 120 min post anaesthetic induction, compared with dogs anaesthetized with ACE-BUT-PRO. Likewise, the respiratory rate of dogs anaesthetized with ACE-BUP-PRO decreased significantly ($p<0.05$) at 60, 100 and 120 min post anaesthetic induction. Haemoglobin-oxygen saturation and rectal temperature were not significantly at variance in dogs on the two anaesthetic protocols.

DISCUSSION

Premedication is often carried out in practice to alleviate fear and anxiety, to reduce the induction and maintenance dose of general anaesthesia, to provide extra analgesia when necessary, to counteract the side effects of other drugs, and to ensure an uneventful induction and recovery from anaesthesia (Hedenqvist et al., 2013). Anaesthetic indices and physiological parameters are monitored in patients under general anaesthesia periodically or continuously to warn, advice or to instruct on a patient's condition (Alam et al., 2014). In this study, the mean induction time, duration of analgesia, duration of recumbency and time to standing with both groups of anaesthetic protocols (ACE-BUT-PRO and ACE-BUP-PRO) were similar. Moreover, long duration recumbency and smooth recovery was achieved with both anaesthetic protocols. Therefore, where applicable, the two opioids, BUP or BUT, possess beneficial effects and may be used for premedication in dogs to alleviate common complications of propofol-induced general anaesthesia. However, the observation of significantly higher heart rate with BUP may be interpreted as a need to exercise caution with the use of this premedicant as there may be inherent arrhythmogenic complications in some patients. Total

Table 2. Cardiopulmonary parameters of dogs anaesthetized with propofol following premedication with either acepromazine-butorphanol (ACE-BUT) or acepromazine-buprenorphine (ACE-BUP).

Variable	Time interval (min) after anaesthetic induction					
	20	40	60	80	100	120
Heart rate (beats/minute)						
ACE-BUT	107.7±8.4	104.8±10.4	103.7±9.3	102.3±10.3	105.2±8.0	106.0±7.0
ACE-BUP	143.0± 9.0*	137.0±11.6*	126.3±13.0*	123.3±12.2*	128.2±17.7*	127.5±15.0*
Mean arterial blood pressure (mmHg)						
ACE-BUT	71.0±6.0	73.7±4.4	70.0±3.9	70.0±3.4	76.2±4.1	78.8±5.1
ACE-BUP	68.5±4.4	65.0±6.5#	71.0±6.3	72.3±4.8	72.0±4.8	70.0±5.7#
Respiratory rate (breath/minute)						
ACE-BUT	22.2±1.9	21.5±3.2	24.8±3.7	24.2±3.3	26.2±3.5	21.5±1.5
ACE-BUP	20.5±3.0	18.0±3.4	18.8±2.0#	22.0±2.0	17.0±1.7#	15.7±1.7#
Haemoglobin-oxygen saturation (%)						
ACE-BUT	92.2±1.0	92.7±0.6	93.2±0.5	93.5±0.9	93.0±1.3	93.3±1.0
ACE-BUP	94.5±1.0	94.5±0.9	94.5±1.0	93.8±1.1	94.2±1.0	95.5±1.0
Rectal temperature (°C)						
ACE-BUT	37.2±0.2	36.9±0.2	36.4±0.1	36.2±0.1	36.0±0.1	35.7±0.2
ACE-BUP	37.2±0.3	37.0±0.3	36.8±0.3	36.7±0.3	36.5±0.3	36.4±0.3

intravenous anaesthesia (TIVA) is generally accomplished by repeat bolus injection or continuous rate infusion via infusion pump. Repeat bolus injections can be administered based on the patient response or at regular interval depending on the drug half-life (Bergmann et al., 2013). In this study, since the published half-life of propofol is 5 to 10 min, repeat bolus was adopted every 5 min throughout the anaesthetic period. Intravenous (IV) fluids are routinely administered during anaesthesia to maintain venous access as well as circulating blood volume, cardiac output and blood pressure (Sasai et al., 2014). The various types of intravenous fluids used include crystalloid, colloid and whole blood. Dextrose saline (5%) was used for this study as previously reported by Sriganesh et al. (2017). Although IV fluid is usually administered at the rate of 10 ml/kg/h during anaesthesia and surgery, a rate of 5 ml/kg/h was used in this study because abdomen or thorax were not entered.

Patients under general anaesthesia need to be endotracheally intubated to maintain open airway, to protect the airway from reflux gastric content and to connect the patient to anaesthetic machine (Krausz et al., 2015). In this study, endotracheal intubation was done after induction with propofol to maintain patent airway. Anaesthetic indices and physiological parameters are monitored generally in patients under general anaesthesia periodically or continuously to warn, advice or to instruct on a patient's condition (Alam et al., 2014). In this study, they were monitored non-invasively without surgical procedure. The quality of the recovery in this study was judged to be good to excellent.

It is concluded that either butorphanol or buprenorphine can be used in combination with acepromazine for premedication of dogs for routine surgical and diagnostic procedures. However, caution is advised with the use of buprenorphine in dogs with pre-existing cardiac disease or hypertension.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

REFERENCES

Adetunji A, Ajadi RA, Adewoye CO, Oyemakinde BO (2002). Total intravenous anaesthesia with propofol: repeat bolus versus continuous infusion technique in xylazine-premedicated dogs. Israel Journal of Veterinary Medicine 57:139-144.

Alam N, Hobbelink E, Van Tienhoven A, Van de Ven P, Jansma E, Nanayakkara P (2014). The impact of the use of the Early Warning Score (EWS) on patient outcomes: a systematic review. Resuscitation 85(5):587-94.

Alipour M, Tabari M, Alipour M (2014).Paracetamol, ondansetron, granisetron, magnesium sulfate and lidocaine and reduced propofol injection pain. Iranian Red Crescent Medical Journal 16:16086.

Aoki M, Wakuno A, Kushiro A, Mae N., Kakizaki M, Nagata S, Ohta, M (2017). Evaluation of total intravenous anesthesia with propofol-guaifenesin-medetomidine and alfaxalone-guaifenesin-medetomidine in Thoroughbred horses undergoing castration. *The* Journal of Veterinary Medical Science 79(12):2011-2018.

Bergmann I, Gohner A, Crozier TA, Hesjedal B, Wiese CH, Popov AF, Bauer M, Hinz JM (2013). Surgical pleth index-guided remifentanil administration reduces remifentanil and propofol consumption and shortens recovery times in outpatient anaesthesia. British Journal of Anaesthesia 110(4):622-628.

Chang PY, Wu CW, Chen HY, Chen HC, Cheng KI, Lu IC (2014).Influence of intravenous anesthetics on neuromonitoring of the recurrent laryngeal nerve during thyroid surgery. The Kaohsiung Journal of Medical Sciences 30(10):499-503.

Hedenqvist P, Edner A, Fahlman Å, Jensen-Waern, M (2013). Continuous intravenous anaesthesia with sufentanil and midazolam in medetomidinepremedicated New Zealand White rabbits. BMC Veterinary Research 9(1)-21.

Izer JM, Whitcomb TL, Wilson P (2014). Atipamezole reverses ketamine-dexmedetomidineanesthesia without altering the antinociceptive effects of butorphanol and buprenorphine in female C57BL/6J mice. Journal of the American Association for Laboratory Animal Science 53(6):675-683.

Khan SA, Epstein JH, Oliva KJ, Hassan MM, Hossain MB, Rahman MA, Elahi MF, Mamun MA, Haider N, Yasin G, Desmond J (2011).Hematology and serum chemistry reference values of stray dogs in Bangladesh. Open Veterinary Journal 1(1):13-20.

Krausz AA, Krausz MM, Picetti E (2015). Maxillofacial and neck trauma: a damage control approach. World Journal of Emergency Surgery 10(1):31.

Kumar G, Stendall C, Mistry R, Gurusamy K, Walker D (2014). A comparison of total intravenous anaesthesia using propofol with sevoflurane or desflurane in ambulatory surgery: systematic review and meta-analysis. Anaesthesia 69(10):1138-1150.

Poller, C, Hopster K, Rohn K, Kästner SB (2013).Nociceptive thermal threshold testing in horses – effect of neuroleptic sedation and neuroleptanalgesia at different stimulation sites. BMC Veterinary Research 9(1):135.

Quandt J (2013). Analgesia, Anesthesia, and Chemical Restraint in the Emergent Small Animal Patient. Veterinary Clinics Small Animal 43(4):941-53.

Sasai T, Tokioka H, Fukushima T, Mikane T, Oku S, Iwasaki E, Ishii M, Mieda H, Ishikawa T, Minami E (2014). Reliability of central venous pressure to assess left ventricular preload for fluid resuscitation in patients with septic shock. Journal of Intensive Care 2(1):58.

Sriganesh K, Balachandar R, Bagepally B, Saini J, UmamaheswaraRao GS (2017). Effect of propofolanesthesia on resting state brain functional connectivity in indian population with chronic back pain. Neurology India 65(2):286.