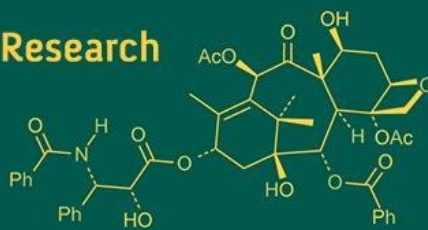
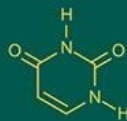
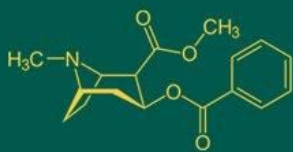


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Shreya
M.V.Sc. Student, Department
of Veterinary Surgery and
Radiology, Veterinary College,
Hassan, Karnataka, India

Dr. Nagaraju N
Assistant Professor & Head,
Department of Veterinary
Surgery and Radiology,
Veterinary College, Hassan,
Karnataka, India

Dr. Dhanalakshmi S
Assistant Professor,
Department of Veterinary
Surgery and Radiology,
Veterinary College, Gadag,
Karnataka, India

Dr. Manjunatha DR
Assistant Professor & Head,
Department of Veterinary
Clinical Complex, Veterinary
College, Hassan, Karnataka,
India

Dr. Shivakumar V
Assistant Professor,
Department of Veterinary
Medicine, Veterinary College,
Hassan, Karnataka, India

Dr. Ramesh D
Associate Professor,
Department of Veterinary
Physiology and Biochemistry,
Veterinary College, Hassan,
Karnataka, India

Dr. Girish BC
Associate Professor and head,
Department of Veterinary
Pathology, Veterinary College,
Hassan, Karnataka, India

Corresponding Author:
Shreya
M.V.Sc. Student, Department
of Veterinary Surgery and
Radiology, Veterinary College,
Hassan, Karnataka, India

Comparison of anesthetic parameters of butorphanol and buprenorphine with lignocaine, ketamine and propofol CRI in dogs

Shreya, Nagaraju N, Dhanalakshmi S, Manjunatha DR, Shivakumar V, Ramesh D and Girish BC

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Abstract

Twelve dogs presented for neutering were enrolled in a study to evaluate anesthetic parameters in elective surgery using CRI. The animals were randomly divided into two groups, with six dogs in each group and were premedicated with atropine sulphate and meloxicam, then sedated with xylazine. Upon sedation, induction was done using propofol "to effect" intravenously. Following induction, dogs of group A were administered with a loading dose of butorphanol-lignocaine-ketamine and anesthesia maintained using a continuous rate infusion (CRI) of butorphanol-lignocaine-ketamine-propofol (BLKP) and dogs of group B were administered with a loading dose of buprenorphine-lignocaine-ketamine and maintenance of anesthesia using a CRI of buprenorphine-lignocaine-ketamine-propofol (BuLKP). Quality of anesthesia was judged using parameters such as pedal reflex, palpebral reflex, jaw tone reflex and eyeball position. Drugs of both the groups provided adequate depth of anesthesia and recovery was smooth without any complications noticed, but group B CRI with buprenorphine-lignocaine-ketamine-propofol (BuLKP) provided marginally better analgesia than group A CRI of butorphanol-lignocaine-ketamine-propofol (BLKP).

Keywords: Butorphanol, buprenorphine, ketamine, lignocaine, propofol, anesthesia, dogs, maintenance, constant rate of infusion

Introduction

The concept of balanced anesthesia is use of multiple agents to produce synergistic effects to provide adequate muscle relaxation, good analgesia and unconsciousness and avoid adverse effects of the individual drugs. It reduces the dose rates of individual drugs which will reduce the untoward effects and increases the safety. Propofol and ketamine alone or in combination, are commonly used for anesthesia in small animal practice. These drugs alone or in combination may not provide adequate muscle relaxation and profound analgesia. They can be combined with Butorphanol or Buprenorphine, an opioid analgesics. But literatures regarding such a combination is very limited.

Continuous rate infusion (CRI) involves use of various intravenous anesthetic agents in combination at minimal doses to maintain low plasma concentrations of drugs and reduce use of any gaseous agents for maintenance of anesthesia. This involves use of different drugs to maintain muscle relaxation, analgesia and unconsciousness throughout the period of anesthesia.

The present study aimed at comparing the anesthetic parameters with butorphanol-lignocaine-ketamine-propofol and buprenorphine-lignocaine-ketamine-propofol as continuous rate infusions (CRI) in dogs.

Materials and Methods

The present study was conducted in twelve healthy dogs presented for neutering at the Department of Veterinary Surgery and Radiology, Veterinary College Hassan. The animals were randomly divided into two groups (group A and group B), with each group comprising six dogs. All dogs of both the group were pre-medicated with atropine sulphate @ 0.04 mg/kg and meloxicam @ 0.2 mg/kg administered subcutaneously. Ten minutes later, administration

of inj. xylazine @ 1 mg/kg IM was done for sedation. This followed by induction using propofol at 2 mg/kg IV, administered to effect in both the groups. After induction, group A received a loading dose comprising 2% lignocaine at 2 mg/kg, butorphanol at 0.2 mg/kg and ketamine at 2 mg/kg intravenously. Anesthesia maintained using a constant rate infusion (CRI) of butorphanol (0.2 mg/kg/hr), lignocaine (50 µg/kg/min), ketamine (40 µg/kg/min), and propofol (6 mg/kg/hr) in normal saline. For group B after induction, administration of loading dose of 2% lignocaine at 2 mg/kg,

buprenorphine at 0.02 mg/kg, and ketamine at 2 mg/kg intravenously. Maintenance of anesthesia in this group achieved using a CRI of buprenorphine (2.5 µg/kg/hr), lignocaine (50 µg/kg/min), ketamine (40 µg/kg/min) and propofol (6 mg/kg/hr). For both the groups each drug drawn into separate sterile disposable syringes and then mixed with normal saline to achieve a final volume of 60 ml, suitable for the syringe pump used. The amount of each drug was calculated using the formula provided below. The flow rate of the continuous rate infusion (CRI) was set @ 60 ml/hr.

$$\text{Volume of drug added (ml)} = \frac{\text{dose of the drug (}\mu\text{g/kg/min)} \times \text{final volume of solution (ml)}}{\text{rate of flow of CRI (ml/kg/min)} \times \text{concentration of drug (}\mu\text{g/ml)}}$$

Anesthetic parameters *viz.*, degree of palpebral reflex, degree of analgesia assessment using pedal reflex, degree of muscle relaxation using assessment of jaw tone reflex and eyeball position were recorded at before induction, immediately after induction, start of CRI at 0th min, 15th, 30th, 45th and 60th min interval of anesthesia. Duration of anesthesia, time taken for recovery and quality of recovery were evaluated. Pedal reflex was recorded as a measure of depth of analgesia in the scale of 0-3. Degree of palpebral reflex was observed by blink in

response to light tap on the medial or lateral canthus of eye in the scale of 0-3. Degree of muscle relaxation was observed by relaxation of jaw tone in the scale of 0-3. Reflexes graded from 0 to 3 using the score system as per Ahmad *et al.* (2011) [1] is shown in table 1.

The mean and standard errors for various parameters studied in both the groups were calculated using descriptive statistics. Recorded data was analysed by student 't' test to compare between two groups.

Table 1: System of recording of various reflexes and responses (Ahmad *et al.*, 2011) [1]

Parameters	Score			
	0	1	2	3
Palpebral reflex	Intact and strong (quick blink)	Intact but weak (slow response)	Very weak (very slow and occasional response)	Abolished (no response)
Pedal reflex	Intact and strong (strong withdrawal)	Intact but very light (slow and occasional response)	Intact but very light (slow and occasional response)	Abolished completely (no response)
Jaw tone reflex	Not allowing to open the jaws	Resistant to opening the jaws and closed quickly	Less resistance to opening the jaws and closed slowly	No resistance and jaws remain open

Results

Reflexes at various interval were recorded before and after the start of CRI (Table 2). In the dogs of group A and group B, complete presence of palpebral reflex (score = 0) was noted prior to induction. After induction, in group A and group B the reflex varied between score 1 to 2. From the time continuous rate infusion (CRI) was initiated (0 minutes) until the end of surgery, the palpebral reflex was completely absent (score = 3) in both the groups. During the surgical plane of anesthesia, a complete loss of the palpebral reflex was observed in both groups.

In both group A and group B dogs, a complete presence of the pedal reflex (score = 0) was observed before induction. Following induction, the pedal reflex varied between pedal score 1 to 3 in group A and group B. At the start of the CRI (0th min) group A pedal reflex was noted between the score 2 to 3 and group B it was score 3 for all the dogs. From the 15th minute continuous rate infusion (CRI) until the end of surgery, the pedal reflex remained entirely absent (score = 3) in both the groups.

In both Group A and Group B dogs, a complete presence of the jaw tone (score = 0) was observed before induction. Following induction, the jaw tone score varied between the score 2 and 3 in group A and B. From the initiation of the continuous rate infusion (CRI) at 0th minute up to the surgery, the jaw tone remained entirely absent (score = 3) in both the groups. Throughout the surgical plane of anesthesia, a total loss of the jaw tone was noted in both groups.

All the 12 animals of group A and group B had their eyeballs in ventromedial position throughout the period of anesthesia. Signs associated with recovery were time taken immediately after weaning of CRI (Table 2). Signs observed were for recovery time (rejection of endotracheal tube), return of pedal reflex, return of eyeballs to central position, head lift, sternal recumbency and standing unassisted. The time taken for recovery (rejection of endotracheal tube) from the time of weaning of CRI had a Mean ± SE value of group A-13.16±1.64 minutes and group B-13.33±0.88 minutes. The time taken for return of pedal reflex from the time of weaning of CRI had a Mean ± SE value of group A-17.50±1.92 minutes and group B-21.67±0.95 minutes. The time taken for eyeballs to return to central position from the time of weaning of CRI had a Mean ± SE value of group A-24.33±2.64 minutes and group B-26.67±1.33 minutes. The time taken for head lift from the time of weaning CRI had a Mean ± SE value of group A-32.16±4.04 minutes and group B-37.50±1.02 minutes. The time for attaining sternal recumbency from the time of weaning CRI had a Mean ± SE value of group A-47.16±4.62 minutes and group B-50.00±3.66 minutes. The time taken for standing unassisted after weaning of CRI had a Mean ± SE value of group A-70.67±1.99 minutes and group B-75.83±3.72 minutes. Quality of recovery observed in all cases of group A and B was smooth. Statistically no significant difference in recovery parameters ($p \geq 0.05$) was observed between the groups except the return of pedal reflex which resulted statistically significant difference ($p \leq 0.05$).

Table 2: Mean $\pm$ SE of anesthetic parameters taken

Parameters	Groups	Time interval						
		Before induction	After induction	0 th min of CRI	15 th min	30 th min	45 th min	60 th min
Degree of palpebral reflex	A	0 $\pm$ 0	1.67 $\pm$ 0.21	3 $\pm$ 0	3 $\pm$ 0	3 $\pm$ 0	3 $\pm$ 0	3 $\pm$ 0
	B	0 $\pm$ 0	1.83 $\pm$ 0.17	3 $\pm$ 0	3 $\pm$ 0	3 $\pm$ 0	3 $\pm$ 0	0 $\pm$ 0
Degree of analgesia (Pedal reflex)	A	0 $\pm$ 0	2.17 $\pm$ 0.31	2.5 $\pm$ 0.22	3 $\pm$ 0	3 $\pm$ 0	3 $\pm$ 0	3 $\pm$ 0
	B	0 $\pm$ 0	2.33 $\pm$ 0.20	3 $\pm$ 0	3 $\pm$ 0	3 $\pm$ 0	3 $\pm$ 0	0 $\pm$ 0
Degree of muscle relaxation (jaw tone)	A	0 $\pm$ 0	2.33 $\pm$ 0.21	3 $\pm$ 0	3 $\pm$ 0	3 $\pm$ 0	3 $\pm$ 0	3 $\pm$ 0
	B	0 $\pm$ 0	2.67 $\pm$ 0.21	3 $\pm$ 0	3 $\pm$ 0	3 $\pm$ 0	3 $\pm$ 0	0 $\pm$ 0

Table 3: Mean $\pm$ SE of various recovery parameters observed

Group No.	Signs associated with recovery and their respective times (min) following weaning from CRI						Quality of recovery
	Time taken for recovery (rejection of ET tube) (min)	Return of pedal reflex (min)	Return of eyeballs to centre (min)	Head lift (min)	Sternal recumbency (min)	Standing unassisted (min)	
Group A	13.16 $\pm$ 1.64	17.50 $\pm$ 1.92	24.33 $\pm$ 2.64	32.16 $\pm$ 4.04	47.16 $\pm$ 4.62	70.67 $\pm$ 1.99	Smooth
Group B	13.33 $\pm$ 0.88	21.67 $\pm$ 0.95	26.67 $\pm$ 1.33	37.50 $\pm$ 1.02	50.00 $\pm$ 3.66	75.83 $\pm$ 3.72	Smooth

Discussion

In both the groups from the start of CRI till the end of surgery a complete loss of the palpebral reflex was observed. These results were comparable to those reported by Bayan *et al.* (2021) [3], observing complete loss of palpebral reflex during the maintenance phase of anesthesia, with gradual return during recovery. This was consistent with the findings of Vijay *et al.* (2024) [10], Chandramohan *et al.* (2024) [5] and Kenjale *et al.* (2022) [8] where similar reflex suppression and recovery patterns were noted in dogs undergoing CRI of different drug combinations. The absence of the palpebral reflex in all animals undergoing surgery is likely resulting from the synergistic action of the drugs administered as a continuous rate infusion for anesthesia maintenance.

In group A from the 15th min of CRI till the end of surgery a complete loss of the pedal reflex was observed whereas in group B from the start of the CRI pedal reflex was abolished. Kenjale *et al.* (2022) [8] reported that the lack of the pedal reflex in all animals during the surgical procedure suggested a robust analgesic effect and a consistent surgical plane of anesthesia. Similarly, Vijay *et al.* (2024) [10] reported the same findings with the CRI of midazolam, ketamine, and lignocaine. Chandramohan *et al.* (2024) [5] also noted complete loss of pedal reflex from peak sedation until the end of anesthesia in dogs administered dexmedetomidine, lignocaine, ketamine, and propofol via CRI.

The muscle relaxation was adequate in both groups for surgical procedures throughout the study period. The profound muscle relaxation observed in the current study could be due to the synergistic effects of the drugs (butorphanol/buprenorphine, propofol, ketamine, and lignocaine) used. This was in accordance with the findings of Kenjale *et al.* (2022) [8] and Vijay *et al.* (2024) [10].

Eyeball was ventromedial in all the animals throughout the period of anesthesia. This was similar with the findings of Kenjale *et al.* (2022) [8] suggesting a surgical plane of anesthesia attributing to the analgesia produced by the synergistic effect of the drugs, given as continuous rate infusion, for maintenance of anesthesia. Grimm *et al.* (2015) [6] reported that eyeball position during general anesthesia maintenance is a reliable indicator of anesthetic depth. Therefore, the ventromedial rotation of the eyeballs observed in the present study is suggestive of adequate depth of anesthesia.

In the present study, recovery time was quicker in group A compared to group B, the difference was not statistically

significant, but longer recovery time in group B can be attributed to longer half-life of buprenorphine, this was similar to the findings of Burbaitè *et al.* (2024) [4], reporting that buprenorphine is an overall superior anesthetic agent compared to butorphanol for dogs undergoing OHE. Time taken for return of pedal reflex in group A and group B showed statistical significant difference which can be attributed to superior analgesic effects compared to butorphanol providing an adequate period of effective postoperative analgesia reported by Warne *et al.* (2014) [11], Barbarossa *et al.* (2017) [2]. The other recovery parameters in the current study for group A and group B did not differ much, which is in accordance with the report of Raušer *et al.* (2002) [8], reporting the time taken for return of eyeballs, head lift and standing unassisted are more strongly influenced by other drugs used in anesthesia than by the specific opioid used. The smooth recovery observed in the current study could also be due to the elevated serum concentration of propofol at the end of anesthesia which was put forth by Jones *et al.* (2024) [7], noting that continuous infusion or bolus administration of propofol towards the end of anesthesia reduced the incidence of emergence delirium during recovery.

Conclusion

In conclusion, the anesthetic CRI combinations provided deep and satisfactory anesthesia with adequate analgesia and muscle relaxation for elective surgical procedure. The anesthetic maintenance was satisfactory with adequate depth of anesthesia for elective surgical procedure, adequate relaxation of muscle, loss of pedal and palpebral reflexes, safe and smooth recovery from anesthesia. However, buprenorphine CRI provided marginally better analgesia comparatively to butorphanol CRI.

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