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Clinical efficacy of propofol and Ketofol anaesthesia with butorphanol by constant rate infusion using fluid bag technique in dogs

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Abstract
Twelve healthy mongrel dogs were included in the study and divided into two equal groups. All the patients were sedated with xylazine at 2 mg/kg b.wt. Group A was induced with propofol @4 mg/kg and Group B with Ketofol (1:1) @ 4 mg/kg by intravenous bolus administration. Maintenance was carried out by constant infusion of anaesthetic drugs at 6 mg/kg/hr at 5 ml/kg/hr flow rate in both the groups. Anaesthesia was maintained with fluid bag technique. Depth of anaesthesia was satisfactory in both the groups however dogs from Group A showed longer recovery time. Heart rate, rectal temperature and respiratory rate showed statistical difference ($p < 0.05$) between the groups but the values were within normal limits. On the basis of clinical and physiological observations, combination of ketamine-propofol-butorphanol was found to be satisfactory for maintenance of anaesthesia in canines.

Keywords: Ketamine, propofol, butorphanol, constant rate infusion, fluid bag technique, dog

Introduction
Surgical management of canine patients is considered to be painful and require an ideal anesthetic which produces sleep, amnesia, analgesia and muscle relaxation to facilitate well-being of the surgical patient (Slingsby and Pearson, 2000) [1]. The ideal procedural anesthetic protocol is intended to have a short onset and recovery and to result in a depressed level of consciousness and analgesia with adequate cardiovascular and respiratory function (Aoud *et al.* 2008) [2]. Constant Rate Infusion of anaesthetic drug masks the effects caused by the peaks and valleys due to intermittent bolus administrations leading to fewer sudden hemodynamic changes, lower total amount of anesthesia to be given and more rapid recovery from anesthesia. It it widely carried out by infusion pumps or automated syringe drivers. However, fluid bag technique was used in this study for maintenance with the use of microdrip infusion set. Ketamine and propofol, these two completely different anesthetics compensate each other's deficits due to their opposing physiological effects, when administered together. Butorphanol is one of the most widely used analgesics and anesthetic adjuvants in veterinary medicine. Hence, considering the strengths and weaknesses of CRI, present study was undertaken to evaluate the clinic-physiological effects of propofol and ketamine-propofol admixture with butorphanol for maintenance of anaesthesia.

Methodology
Preparation of animal and Pre-anaesthetic consideration
Twelve healthy female mongrel dogs were selected for the study. The dogs were presented to Teaching Veterinary Clinical Complex, PGIVAS, Akola for elective ovariohysterectomy. Exclusion criteria included females in oestrus, pregnant and lactating bitches. Selected dogs were divided into two equal Groups *viz*., Group A and Group B. All dogs were fasted for 8-10 hrs prior to procedure and water was withheld for 6 hrs. Clinical examination was done before procedure and confirmed fit for the procedure.

Surgical site was prepared aseptically and cephalic vein was cannulated for administration of anaesthetic drugs.

Sedation was undertaken by Inj. Xylazine @ 2mg/kg b.wt. I/M 10 min prior to induction.

Anaesthetic protocol

Ketamine-propofol admixture was prepared at 1:1 (w/w) concentration for induction and maintenance. For constant rate infusion, 30 ml admixture was prepared to add in fluid bag at the dose rate of 6mg /kg/ hr. 15 ml of propofol (150 mg) and 3 ml of ketamine (150 mg) mixed with 12 ml of normal saline to make up the volume of 15 ml was prepared in a single syringe. Before adding this admixture to normal saline bag, same volume was withdrawn.

A. Group A (n=6)

Induction- Inj. Propofol @4 mg/kg b.wt I/V bolus
Inj. Diazepam @ 0.25 mg/kg slow I/V
Maintenance- Inj. Propofol @ 6 mg/kg/hr CRI
Inj. Butorphanol @ 0.3 mg/kg/hr

B. Group B (n=6)

Induction- Inj. Ketamine-propofol admixture (1:1) I/V bolus
Inj. Diazepam @ 0.25 mg/kg slow I/V
Maintenance-Inj. Ketamine-propofol admixture @ 6 mg/kg/hr
Inj. Butorphanol @ 0.3 mg/kg/hr

In the study, for the maintenance of anaesthesia, fluid bag technique was used for CRI of anaesthetic drug. A normal saline bag of 250 ml capacity was used. Flow rate was kept 5 ml/kg/hr in both the groups. Microdrip infusion set having precision setting of ml/hr was used instead of automated pumps.

Surgical technique

All dogs were subjected to standard ovariohysterectomy procedure by double-clamp ligation method explained by Fossum *et al.* (2007) [3].

Parameters studied

Anaesthesia was assessed based upon the reflexes exhibited during the procedure and recovery time. Physiological parameters were recorded before induction, after induction, during surgery and after recovery.

Results and Discussion

Assessment of anaesthesia

Quality of anaesthesia was judged based upon the presence or absence of various reflexes such as pedal reflex, palpebral reflex, jaw-tone, eye ball position during the procedure. In Group A induction apnoea was observed in all the patients. The reflexes were abolished after the induction and the patients were in surgical plane of anaesthesia throughout the procedure. Eye balls were placed mid-ventrally and jaw-tone was relaxed. No patient showed any reflex upon painful stimulus. In Group B, smooth induction of anesthesia without apnoea was observed as compared to Group A. Corneal and palpebral reflexes were not abolished completely in all patients (Amin and Atiyah, 2014) [4]. Eyeballs were placed mid-ventrally in all the patients.

Recovery time

Recovery time was defined as the period between the end of infusion and lifting of head. Group A patients showed longer recovery time (Thejashree *et al.* 2018) [5] than Group B however, recovery was excitement and struggle free in both the groups. Longer recovery time in Group A might be due to higher doses of propofol for short duration through infusion leading to accumulation of propofol in body tissues. Longer recovery times might also be due to the effect of diazepam which is a sedative, hypnotic (Amin and Atiyeh, 2014) [4].
Similar observations are recorded by Amin and Atiyeh (2014) [4] Njoku (2015) [6] and Thejashree *et al.* (2018) [5].

Table 1: Mean ± SE value of recovery time for both the groups expressed in min

Group	Average Recovery Time (min)
Group A	22.67 ± 1.28
Group B	15.33 ± 1.71

Clinico-physiological parameters

The pooled mean value of rectal temperature varied between the groups with 1% significance level. In Group A, the average values ranged from 101.2 ± 0.26 (before induction) to 100.8 ± 0.25 (after recovery) with the pooled mean of 101.1 ± 0.17 while in Group B it varied from 101.4 ± 0.29 to 99.8 ± 0.28 with the pooled mean of 100.7 ± 0.40. The average values showed decreasing trend till the end of infusion but it was within normal physiological range and had no clinical relevance. This decrease in rectal temperature observed in both the groups during the period of anaesthesia might be due hypothermia which is produced by sedatives and anesthetics due to depression of thermoregulatory centre, reduced basal metabolic rate and muscle activity, depression of peripheral circulation and vasodilation (Njoku, 2015) [6].
In both the groups, the mean rectal temperature value showed decreasing trend throughout the anaesthesia with pooled mean before induction 101.3 ± 0.19 to 100.3 ± 0.24 after recovery which was statistically significant (p< 0.01) but was within normal physiological limit and had no clinical significance. These observations are in accordance with Amin and Atiyah (2014) [4], Kennedy and Smith (2015) [7], Njoku (2015) [6] who observed the significant decrease in rectal temperature during propofol anaesthesia.

Table 2: Mean ± SE values of rectal temperature of both groups expressed in degrees of Fahrenheit

Interval Group	Before induction	After induction	During surgery	After recovery	Pooled mean
Group A	101.2 ± 0.26	101.6 ±0.32	100.9 ± 0.13	100.8 ± 0.25	101.1± 0.17 ^{B}
Group B	101.4 ± 0.29	101.4± 0.28	100.4 ± 0.35	99.8 ± 0.28	100.7 ± 0.40 ^{A}
Pooled mean	101.3 ± 0.19 ^{II}	101.5± 0.20 ^{II}	100.6 ± 0.19 ^{I}	100.3 ± 0.24 ^{I}	

Means bearing different superscripts differ significantly

Respiration rate was recorded as breaths/min. In the present study, average respiration rate in Group A before induction, after induction, during surgery and after recovery was observed to be 16.67 ± 3.49, 15.67 ± 3.80, 18.33 ± 2.80 and 25.5 ± 5.49 respectively with the pooled mean of 19.04 ± 2.22. In Group B it was 40.67 ± 3.22, 74.67 ± 13.62, 85.67 ± 20.86 and 79 ± 15.47 with the pooled mean of 16.63 ± 1.94. The respiratory rate varied significantly (p< 0.05) between intervals. The pooled mean value for both the groups before induction was 14.83 ± 2.27 which increased to 23.67 ± 2.96 after recovery. The values depict that respiratory rate in Group A was stable and within limits under propofol anesthesia. Constant rate infusion of propofol for a short period of time did not cause respiratory depression and hence avoiding the peaks and troughs in respiration during anesthesia. These observations are corroborated with Ilkiw *et al.* (2003) [8], Kennedy and Smith (2015) [7], Njoku (2015) [6].

Table 3: Mean ± SE values of respiratory rate of both groups expressed in breaths per minute

Interval Group	Before induction	After induction	During surgery	After recovery	Pooled mean
Group A	16.67 ± 3.49	15.67 ± 3.80	18.33 ± 2.80	25.5± 5.49	19.04 ± 2.22
Group B	40.67 ± 3.22	74.67 ± 13.62	85.67 ± 20.86	79 ± 15.47	16.63 ± 1.94
Pooled mean	14.83 ± 2.27 ^{I}	15.08 ± 1.99 ^{I}	17.75 ± 1.66 ^{I}	23.67± 2.96 ^{II}	

Means bearing different superscripts differ significantly

Heart rate was recorded manually as beats/min. The average value of heart rate in Group A ranged from 49.67 ± 6.84 to 53.33 ± 5.55 with the pooled mean value of 54.38 ±2.97 while in Group B it varied from 40.67 ± 3.22 to 79 ± 15.47 with pooled mean of 70 ±10.04. There was significant difference (p< 0.05) in heart rate between Group A and Group B, but the values were within normal physiological range. Comparatively lower heart rate in Group A was observed than Group B which shows that this decrease in heart rate might be due to sympatholytic effect of propofol or increased vagal tone or the combination of effect of preanesthetics i.e. xylazine and diazepam along with propofol anesthesia. The heart rate in Group B was stable and above the values after induction due to cardio-stimulant effect of ketamine. It is observed that, in both the groups pooled mean value of heart rate before induction was 45.17 ±3.85 which showed increasing trend throughout the anaesthesia up to 66.17 ± 8.74 till recovery. Heart rate was stable in both the groups and varied non-significantly within intervals. These observations are in agreement with Kennedy and Smith (2015) [7], Njoku (2015) [6], Shinde *et al.* (2018) [9] and Thejashree *et al.* (2018) [5].

Table 4: Mean ± SE values of heart rate of both groups expressed in beats per minute

Interval Group	Before induction	After induction	During surgery	After recovery	Pooled mean
Group A	49.67 ± 6.84	63 ± 7.21	51.5 ± 4.87	53.33 ± 5.55	54.38^{A} ±2.97
Group B	40.67 ± 3.22	74.67 ± 13.62	85.67 ± 20.86	79.00 ± 15.47	70.00^{B} ±10.04
Pooled mean	45.17 ± 3.85	68.83 ± 7.56	68.58 ± 11.44	66.17 ± 8.74	

Conclusion

In the present study, it was observed that ketamine-propofol admixture (1:1) had reduced the total amount of propofol needed for both induction and maintenance rendering it to be cost-effective. Also the recovery was smooth and early with minimal physiological alterations. Hence it can be concluded that, ketamine-propofol-butorphanol constant rate infusion using fluid bag technique is suitable for maintenance of anaesthesia in canines for Ovario-hystrectomy.

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