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COMPARATIVE ANAESTHETIC EFFICACY OF PROPOFOL, THIOPENTAL SODIUM AND COMBINATION OF PROPOFOL WITH KETAMINE HYDROCHLORIDE IN DOGS

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ABSTRACT

The present study was undertaken to determine the comparative efficacy of propofol alone at two dosages, thiopental sodium and propofol in combination with ketamine hydrochloride in dogs. For this purpose, 24 healthy stray dogs were randomly divided into four equal groups viz. A, B, C and D. Groups A and B were treated with propofol at the dose rates of 6 and 10 mg/kg BW, respectively, while group C was given propofol and ketamine hydrochloride in combination @ 4 mg/kg BW each and group D was treated with thiopental sodium @ 20 mg/kg BW. Different reflexes were observed for evaluation of anaesthetic efficacy. Groups C and D showed rapid inductions, prolonged surgical stages and late recovery in most of the reflexes and group C showed smooth recovery than D. Groups A and B showed smooth induction, short surgical stages and rapid recovery. Group B also showed some disturbances in respiratory and cardiac activity of the animals. It was concluded that propofol in combination with ketamine hydrochloride is a safe anaesthetic agent for canines as an alternative of thiopental sodium for prolonged surgical procedures.

Key words: Anaesthesia, propofol, thiopental sodium, ketamine hydrochloride, dogs.

INTRODUCTION

Anaesthesia is an indispensable pre-requisite to most of the surgical interventions, both in humans and animals, so that the surgeon can perform surgical intervention with maximum precision and sagacity. Anaesthetics are available for both parenteral as well as inhalation routes in canine surgery. Due to meager facilities available for field veterinarians in Pakistan, intravenous anaesthetics are preferred because of their early and safe induction. Thiopental sodium has been the sole anaesthetic agent so far relied upon by the veterinarians for most of surgical interventions. Its unavailability or irregular availability in local market renders the veterinary surgeons incapable of performing any intervention on canine surgical patients. This situation compels the veterinary surgeons/ practitioners to look for some other suitable and safe alternative readily procurable from the market having better or an equivalent spectrum of anaesthesia.

Propofol is a unique non-barbiturate, non-steroid, short-acting general intravenous anaesthetic agent (Hofmeister *et al*., 2008). It is associated with a rapid smooth induction and a rapid recovery (VanNatta and Rex, 2006). More advantageously, it is readily available in the market. Anaesthetic stage duration of propofol could be enhanced if used in combination with ketamine hydrochloride. This hypothesis lead us to study the anaesthetic efficacy of propofol at two different dose regimens, in combination with ketamine hydrochloride and to compare it with thiopental sodium in dogs.

MATERIALS AND METHODS

Experimental animals

A total of 24 adult, apparently healthy stray dogs of either sex were selected. These animals were randomly divided into four groups (A, B, C and D), having six animals in each group. The experimental animals were kept under the same managemental and nutritional regimens during the trials. Food and water were withheld for 24 and 12 hours, respectively prior to the induction of anaesthesia to avoid regurgitation and respiratory embarrassment. These dogs were cast on lateral recumbency, with head slightly lower than the hind quarters. They were allowed to relax for some time to overcome excitement created during casting. The normal respiration rate, pulse rate and temperature of each dog were recorded.

Administration of anaesthesia

The dogs of groups A and B were treated with propofol (Propofol®, Abbot Laboratories, Pakistan) @ 6 and 10 mg/kg BW intravenously (IV), respectively. The animals of group C were given propofol @ 4 mg/kg BW IV in combination with ketamine hydrochloride (Calypsol®, Medinpex, Hungry) @ 4 mg/kg BW. Animals of group D were given intravenous injection of Pentothal sodium (Pentothal Sodium®, Abbot Laboratories, Pakistan) @ 20 mg/kg BW.

As the intravenous injection was made, the time was noted, and used as reference to describe the changes in various reflexes. A team of trained personnel was deputed to record observations for

various clinical parameters at 5 minutes interval till the complete normalization of the reflexes.

Post treatment monitoring

During whole of the experiment, the animals were closely monitored. The effects of anaesthetic agents on various body reflexes like corneal reflex, pupil reflex, pharyngeal reflex, mandibular tone reflex, tongue pinch reflex, anal pinch reflex and tail flaccidity were recorded. In addition to these, other parameters studied were; 1) Time taken for the induction of surgical stage of anaesthesia, 2) Duration of surgical stage of anaesthesia, 3) Recovery from anaesthetic condition to normal reflexes and 4) State of respiration, temperature and pulse rate before, during and after induction of anaesthesia.

Statistical analyses

A statistical analysis was performed using repeated measures with 2 factor Complete Randomized Design and Duncan's Multiple Range Test. All analyses were performed using the Statistical Software Package (SPSS Version 11.5). Statistical significance was assigned at $p<0.05$.

RESULTS

Ocular reflexes

Corneal reflex

The corneal reflex was absent within two minutes in dogs of all groups post medication and remained absent for almost the same time duration in all groups except group D in which it remained absent for a significantly longer time ($p<0.05$) than other groups. Then this reflex recovered in a short time in first three groups i.e. A, B and C but group D showed late recovery (Table 1).

Pupil reflex

Pupil dilated in a significantly shorter time in dogs of groups C and D than groups A and B (Table 1) after administering respective anaesthetic agents. It remained dilated for longer duration in groups B, C and D. Then it started to constrict and became normal rapidly in groups A, B and D, while group C showed late recovery ($p<0.05$).

Reflexes of head region

Pharyngeal reflex

Trend of induction of anaesthetic condition was delayed in groups A and B for pharyngeal reflex post administration of allocated anaesthesia (Table 2). For surgical stage, groups C and D showed longer duration than groups A and B but recovery was rapid in all groups, except group C which recovered later ($p<0.05$).

Mandibular tone reflex

Induction of anaesthetic condition in terms of mandibular tone reflex was rapid in groups C and D than A and B and this reflex remained absent for longer time in groups B, C and D compared to group A ($p<0.05$). The differences among the former three groups were non significant. Then recovery of the mandibular tone reflex occurred at the same intervals in all the groups and there was no difference among them (Table 2).

Tongue pinch reflex

After administration of respective anaesthetic agents, this reflex became absent at the same time in all the groups and remained absent for prolonged duration in animals of all the groups, except group A (Table 2). Then this reflex recovered quickly in groups A and B but late in other two groups ($p<0.05$).

Hind quarter reflexes

Anal sphincter reflex

In terms of anal sphincter reflex, all the groups took almost the same time for induction of anaesthetic stage after anaesthetic administration. Then it remained absent for prolonged period in groups C and D than groups A and B which showed short anaesthetic stage duration (Table 3). Similarly, recovery was delayed in both groups C and D and it was rapid in groups A and B ($p<0.05$).

Table 1: Ocular reflexes in dogs of four groups after treatment

Reflexes	Groups	Induction (minutes)	Duration (minutes)	Recovery (minutes)
Corneal reflex	Group A	1.90 ± 0.90	7.33 ± 1.00 [a]	4.33 ± 0.80 [a]
	Group B	1.67 ± 0.89	7.97 ± 1.20 [a]	3.33 ± 0.67 [a]
	Group C	1.50 ± 0.43	9.67 ± 1.00 [a]	4.67 ± 1.84 [a]
	Group D	1.59 ± 0.67	12.56 ± 0.75 [b]	9.33 ± 1.61 [b]
Pupil reflex	Group A	3.83 ± 0.65 [a]	6.83 ± 0.84 [a]	2.83 ± 0.40 [a]
	Group B	3.33 ± 0.67 [a]	10.5 ± 1.26 [b]	3.16 ± 1.12 [a]
	Group C	2.35 ± 1.10 [b]	14.17 ± 1.37 [b]	6.20 ± 1.30 [b]
	Group D	1.55 ± 0.45 [b]	12.33 ± 0.92 [b]	3.5 ± 0.50 [a]

Values with different superscripts within a column for each reflex differ significantly ($P<0.05$).

Group A= Propofol @ 6 mg/kg BW, IV; Group B= Propofol @ 10 mg/kg BW, IV; Group C= Propofol and Ketamine HCl @ 4 mg/kg BW each, IV; Group D= Pentothal sodium @ 20 mg/kg BW, IV.

Table 2: Reflexes of head region in dogs of four groups after treatment

Reflexes	Groups	Induction (minutes)	Duration (minutes)	Recovery (minutes)
Pharyngeal reflex	Group A	2.83 ± 0.65 [a]	6.00 ± 0.89 [a]	2.00 ± 0.22 [a]
	Group B	2.37 ± 0.42 [a]	9.33 ± 1.58 [a]	2.67 ± 1.17 [a]
	Group C	1.13 ± 0.21[b]	14.00 ± 1.37[b]	4.67 ± 0.67[b]
	Group D	1.27 ± 0.89[b]	13.00 ± 1.24[b]	2.03 ± 0.87 [a]
Mandibular tone reflex	Group A	4.66 ± 0.77 [a]	4.33 ± 0.80 [a]	3.33 ± 0.67
	Group B	3.67 ± 1.47 [a]	10.00 ± 1.26[b]	2.33 ± 1.15
	Group C	2.67 ± 0.21[b]	11.33 ± 1.11[b]	2.16 ± 0.40
	Group D	2.50 ± 1.12[b]	17.37 ± 2.14[b]	2.16 ± 0.50
Tongue pinch reflex	Group A	2.57 ± 1.30	6.67 ± 0.84[a]	1.83 ± 0.48 [a]
	Group B	2.40 ± 1.11	10.33 ± 1.50[b]	1.33 ± 0.20 [a]
	Group C	2.10 ± 0.33	14.67 ± 0.95[b]	3.50 ± 0.50[b]
	Group D	2.12 ± 0.21	14.33 ± 2.17[b]	3.17 ± 0.75[b]

Values with different superscripts within a column for each reflex differ significantly (P<0.05).
Group A= Propofol @ 6 mg/kg BW, IV; Group B= Propofol @ 10 mg/kg BW, IV; Group C= Propofol and Ketamine HCl @ 4 mg/kg BW each, IV; Group D= Pentothal sodium @ 20 mg/kg BW, IV.

Table 3: Hind quarter reflexes in dogs of four groups after treatment

Reflexes	Groups	Induction (minutes)	Duration (minutes)	Recovery (minutes)
Anal sphincter reflex	Group A	3.00 ± 0.52	3.67 ± 0.61 [a]	3.17 ± 0.49 [a]
	Group B	2.23 ± 1.10	3.53 ± 0.40 [a]	3.83 ± 1.33 [a]
	Group C	2.83 ± 0.75	8.33 ± 1.31[b]	6.33 ± 1.58[b]
	Group D	2.33 ± 0.42	9.67 ± 2.09[b]	5.83 ± 2.20[b]
Tail flaccidity	Group A	3.67 ± 1.20 [a]	5.67 ± 0.61 [a]	2.17 ± 0.60 [a]
	Group B	3.00 ± 0.54 [a]	12.00 ± 1.37[b]	3.33 ± 0.95 [a]
	Group C	1.67 ± 0.49[b]	15.57 ± 2.34[b]	5.00 ± 0.86[b]
	Group D	1.83 ± 0.48[b]	15.67 ± 2.60[b]	5.83 ± 2.20[b]

Values with different superscripts within a column for each reflex differ significantly (P<0.05).
Group A= Propofol @ 6 mg/kg BW, IV; Group B= Propofol @ 10 mg/kg BW, IV; Group C= Propofol and Ketamine HCl @ 4 mg/kg BW each, IV; Group D= Pentothal sodium @ 20 mg/kg BW, IV.

Tail flaccidity

In groups A and B, the flaccidity of tail was achieved later than groups C and D post medication. Then it remained flaccid for longer duration in groups B, C and D, while it was short in group A (Table 3). But recovery was rapid in group B as that of A and it was delayed in groups C and D (p<0.05).

Pulse rate

There was an increase in pulse rate in all groups after administration of respective anaesthetic agents. A sharp increase in pulse rate was noted within 5 minutes in groups B and D, and this trend was observed for 15 minutes and then it decreased continuously in group B, while group D showed fluctuations but decreasing trend towards normal (Fig. 1A). Groups A showed increase in pulse rate up to 10 minutes and then it started to decrease and came to baseline within 30 minutes, while group C did not show any observable difference in pulse rate up to 40 minutes post medication.

Respiration rate

A fall in respiration rate was observed in dogs of all the groups after administration of respective anaesthesia. Groups A and B showed rapid increasing trends after 5 minutes and became normal within 20 and 30 minutes, respectively (Fig. 1B). Group C showed decreasing trend up to 15 minutes and then it started increasing and became normal after 30 minutes. Respiration rate decreased up to 15 minutes in group D and then increased but remained lower than the baseline up to 40 minutes.

Body temperature

Body temperature decreased in dogs of all the groups within 5 minutes of administration of anaesthetic agents. But this decrease was marked in groups A and C, other two groups showed continuous decrease in body temperature up to 20 minutes (Fig. 1C). Then these both groups (B and D) showed increasing trend and body temperature became normal within 40 minutes.

DISCUSSION

Selection of anaesthetic agents depends upon species or breed of the animal, nature of surgical operation, susceptibility of the patient to the action of

anaesthetic drug and health status of the animal to be anaesthetized. Thiopental sodium had been the sole anaesthetic agent upon which veterinarians have relied in canine surgery but sometimes it is not readily available in the market. So, to resolve this problem, propofol, a new anaesthetic agent, was evaluated in our study at two different dose regimens (6 and 10 mg/kg), in combination with ketamine hydrochloride.

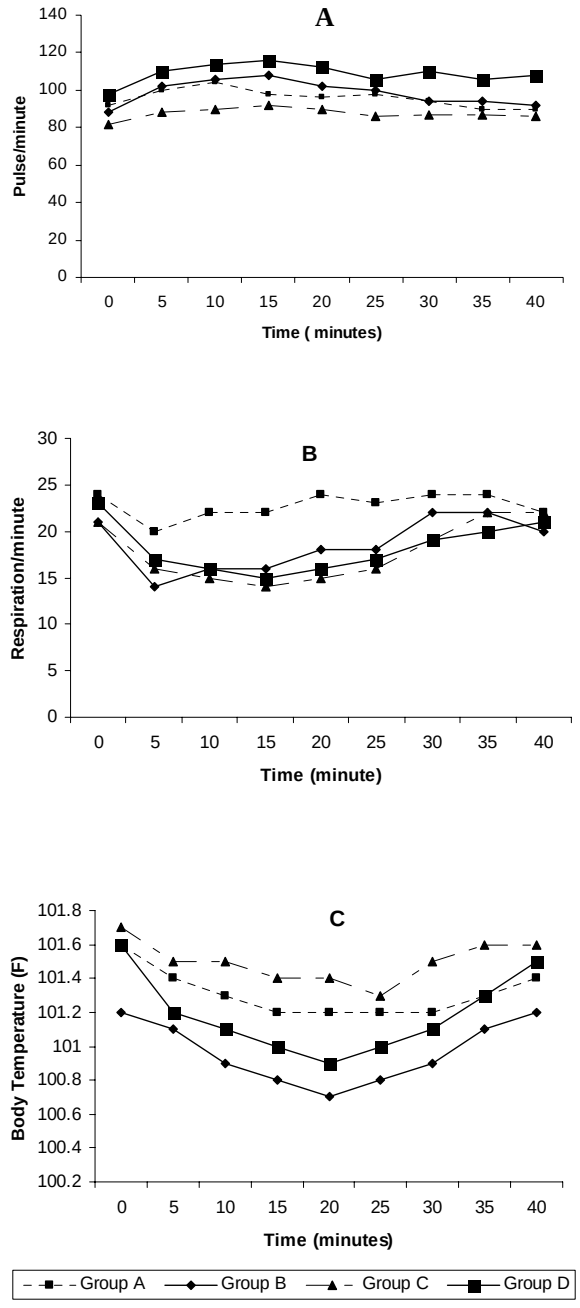

Fig 1: Pulse rate (A), respiration rate (B) and body temperature (C) in dogs of four groups at different time intervals after treatment.

In our study, animals of groups A and B given propofol alone at the dose rate of 6 and 10 mg/kg BW, respectively, showed rapid and smooth induction. All body reflexes disappeared and animals were in perfect surgical stage for a short duration. One of the disadvantages of propofol is that it may cause apnoea (Hofmeister *et al*., 2008) which was also observed in our study in two animals of group B. These animals showed apnoea of 50-120 seconds. The difference in our observation from previous studies was that apnoea occurred only in animals which were administered with a higher dose of propofol. Incidence and apnoea was not observed in groups A and C. These results showed that administration of ketamine with propofol avoids respiratory depression, which was seen when propofol was used alone (Kazuto *et al*., 2001). Recovery was smooth and rapid in propofol administered animals (VanNatta and Rex, 2006; Hofmeister *et al*., 2008) and it was also observed in our study. These results showed that in canine surgery propofol can be safely used for smooth induction of anaesthesia and significantly quicker recovery and earlier return of psychomotor function compared with thiopental but for shorter duration. No nausea and vomiting were seen during propofol anaesthesia, which is similar to the findings of Ronald and Miller (1981).

The presence of reflexes of head region in thiopentone administered animals is previously reported by many workers (Muir and Hubbel, 1991; Kumar *et al.*, 1995) which was also observed in our study. Body temperature decreased in all groups but it was more severe in animals administered with thiopentone (Kumar *et al.*, 1995), while propofol administered group did not show any significant decrease which was not according to the finding of Kelawala and Persania (1992). Heart rate increased in animals of all the groups during anaesthesia. These findings are in accordance with those of Muir and Hubbel (1991), Kelawala and Persania (1992) and Portella *et al.* (1996).

In group D, where thiopental sodium was used as anaesthetic agent, induction was rapid and smooth but struggling type of movement during induction observed in one animal showed that animal felt pain. Temperature decreased during surgical stage of anaesthesia which is also reported by Short (1987). The heart rate increased during anaesthesia, which is in agreement with the findings of Likiw *et al.* (1991) and Kumar *et al.* (1995). The heart rate after recovery from anaesthesia returned to normal. Respiration rate decreased during anaesthesia, which is in accordance with the findings of Likiw *et al.* (1991). The recovery from anaesthesia was not smooth, which do not agree with findings of Kumar *et al.* (1995).

While comparing the results of four groups, thiopental sodium showed longest duration of surgical anaesthetic stage but recovery was not smooth. On the other hand, propofol showed rapid coordinated

induction and recovery. Heart rate increased up to greater extent by thiopentone than by propofol at lower doses i.e. group A and C, while propofol at higher doses caused respiratory depression and also caused tachycardia for a shorter duration.

Ketamine is a dissociative anaesthesia, when used in combination with propofol, reduced the dose of propofol required for the induction of anaesthesia and also prolonged the anaesthetic stage. Moreover, it avoided respiratory depression, which was seen when propofol was used alone at higher dose.

Conclusion

It was concluded from the study that propofol is a safe anaesthetic agent for canines @ 6 mg/kg BW for short term surgical interventions and it could be used as an alternative of thiopental sodium in combination with ketamine hydrochloride for prolonged surgical procedures.

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