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Comparative Anaesthetic Evaluation of Butorphanol, Dexmedetomidine or Acepromazine in Combination with Thiopentone Sodium for Inducing General Anaesthesia in Healthy Dogs

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ABSTRACT

Background: The present study was conducted to evaluate the anaesthetic efficacy of butorphanol, dexmedetomidine or acepromazine in combination with thiopentone sodium for inducing general anaesthesia in healthy dogs.

Methods: Eighteen adult dogs of either sex were randomly divided into three groups (ButTHIO, DexTHIO and AceTHIO) with six animals in each. Ten minutes prior to the anaesthetic administration, all the dogs were administered with glycopyrrolate @ 0.02 mg/kg I/M. The animals of group ButTHIO, DexTHIO and AceTHIO were premedicated intramuscularly with butorphanol @ 0.3 mg/kg b.wt., dexmedetomidine @ 10 µg/kg b.wt. and acepromazine @ 0.4 mg/kg b.wt. respectively. General anaesthesia was induced with thiopentone sodium @ 18 mg/kg b.wt. intravenously. Onset of sedation and anaesthesia, degree of analgesia, extent of muscle relaxation, duration of anaesthesia, complete recovery from anaesthesia and different reflexes were recorded for evaluation of anaesthetic efficacy.

Result: The onset of sedation and induction of anaesthesia was quicker in group DexTHIO followed by AceTHIO and ButTHIO. Duration of anaesthesia and complete recovery were significantly ($P<0.05$) longer in group DexTHIO as compared to group ButTHIO and AceTHIO. Analgesia was excellent in all the groups but persisted for longer duration in animals of group DexTHIO. All the reflexes abolished completely with longer duration of muscle relaxation in group DexTHIO. It could be concluded that thiopentone sodium in combination with either dexmedetomidine or butorphanol or acepromazine can be used safely for inducing surgical anaesthesia in dogs. However, dexmedetomidine-thiopentone combination produced prolonged duration of anaesthesia with better quality for long surgical procedure in dogs.

Key words: Acepromazine, Anaesthetic, Butorphanol, Dexmedetomidine, Dog, Glycopyrrolate, Thiopentone sodium.

INTRODUCTION

Anaesthesia is an integral part of veterinary surgery and a successful surgery can be performed only under safe anaesthesia. General anaesthesia is a state of reversible unconsciousness produced by a process of controlled, drug-induced intoxication of the central nervous system (CNS) in which the patient neither perceives nor recalls noxious stimuli that means general anaesthesia is characterized by unconsciousness, muscle relaxation and analgesia (Clarke *et al*., 2014). Canine suffer from large number of surgical affections that requires safe and potent anaesthesia. The main aim of anaesthesia is to prevent pain perception and provide immobility whenever needed. No single anaesthetic drug provides all of the components of general anaesthesia without depressing some vital organ function. Therefore, recent anaesthetic practices recommend varied combinations of sedatives, analgesics alongwith other general anaesthetic drugs known as balanced anaesthesia in which multiple drugs are used in low dosage with a specific purpose. The main objective is to utilize advantage of the required characteristics of selected drugs thereby reducing their ability for undesirable depression of homeostatic mechanisms (Riviere and Papic, 2009).

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Glycopyrrolate is a synthetic quaternary ammonium compound, anticholinergic with no central effects. It has a powerful and prolonged antisialagogue activity and is about five times as potent as atropine (Hall *et al.,* 2001). It blocks

peripheral muscarinic receptors, thus inhibiting cholinergic transmission. Dexmedetomidine is an alpha-2 adrenergic receptor agonist used for sedation, analgesia and also as an adjunct in anaesthesia to reduce anaesthetic requirements in procedures requiring total intravenous anaesthesia (Miller, 2009). The most common side effects of dexmedetomidine are bradycardia, decreased respiration and hypothermia. Butorphanol is a central-acting opiate analgesic with partial agonist properties and 3 to 5 times more potent analgesic than morphine. Opioid analgesic is used primarily to produce analgesia without causing loss of consciousness. These are primarily included in balanced anaesthesia protocols particularly for their analgesic effect (Kumar *et al*., 2022). Acepromazine is a phenothiazine tranquilizer that blocks dopamine receptors in the CNS and depresses the reticular activating system resulting in sedation. It is metabolized by the liver and eliminated by the kidney and as a result has longer half-life in young animals. It produces 4-8 hours effect in neonates and juveniles. It also possesses antiemetic, antihistaminic, antiarrhythmic and antishock properties because of its dopamine inhibition in the chemoreceptor trigger zone (Turi and William, 2011). Thiopentone sodium is an ultra-short acting barbiturate that has been used in various species of animals to produce a short term surgical anaeshesia. Thiopental sodium is a powerful hypnotic that produces dose-dependent depression of the central nervous system (Jadon *et al.,* 1998). Rapid intravenous injection cause fall in blood pressure. Therefore, the aim of present research was to evaluate anaesthetic efficacy of butorphanol, dexmedetomidine or acepromazine in combination with thiopentone sodium for inducing general anaesthesia in healthy dogs.

MATERIALS AND METHODS

Place of work

The present work was carried out in confinement of Department of Veterinary Surgery and Radiology and Teaching Veterinary Clinical Complex (T.V.C.C.) in College of Veterinary Science and A.H. Anjora, Durg (C.G.) during January to December 2023. The study was conducted on 18 clinically healthy dogs of either sex weighing between 10 to 20 kg body weight alongwith owner consent prior to study.

Anaesthetic design

The 18 dogs were randomly divided into three groups *viz*., ButTHIO, DexTHIO and AceTHIO, comprising of 6 animals in each. All dogs were dewormed with Praziplus (Albendazole 300 mg with Praziquental 25 mg) Tab. @ 1 Tab./10 kg body weight orally fifteen days before the start of anaesthestic study. The animals were fasted overnight and drinking water was withheld for 6 hours before the anaesthetic trial. The animals were kept under uniform feeding and managemental practices throughout the experiment. Ten minutes prior to the anaesthetic administration, all dogs were administered with glycopyrrolate @ 0.02 mg/kg b.wt. intramuscularly. The animals of group ButTHIO, DexTHIO and AceTHIO were premedicated intramuscularly with butorphanol @ 0.3 mg/kg b.wt., dexmedetomidine @ 10 µg/kg b.wt. and acepromazine @ 0.4 mg/kg b.wt. respectively. After administration of preanesthetic, the animals were kept undisturbed in a calm environment to record the onset of sedation. Thiopentone sodium @ 18 mg/kg b.wt. was administered intravenously in animals of all the groups until the pedal reflex abolished and dogs were intubated with suitable endotracheal tube of (4.5 to 8.5 OD mm) under guidance of laryngoscope and subsequently various observations were recorded upto 120 min. of study period.

Evaluation of anaesthesia

Anaesthestic evaluation was done on the basis of Onset of Sedation (Minutes), Induction of anaesthesia (Minutes), Duration of anaesthesia (Minutes) and Recovery time (Minutes). Time to extubation (Minutes), Head rightening (Minutes), Sternal recumbency time (Minutes), Standing time (Minutes) and Complete recovery time (Minutes) without ataxia and different reflexes. The quality of anaesthesia was analyzed by recording different reflexes, extent of muscle relaxation and analgesia after induction with thiopentone sodium and recorded on a scale 1 to 4 where 1 represented poor anaethesia, 2-fair anaesthesia, 3-good anaesthesia and 4-excellent anaesthesia. The degree of analgesia was assesed by pinching of the inter-digital skin of the foot and vigorous squeezing and twisting or pinching of digit or pad. Additional various reflexes and behavioral responses were also recorded using numeric score system as depicted in Table 1 at (0) base value, sedation, after induction and at 10, 20, 40, 60 and 120 minutes interval after administration of thiopentone sodium with different pre-anaesthetic combinations. Relaxation of the jaw was measured by observing the resistance to opening of the jaw while pulling apart the lower and upper jaw. The status of the palpebral reflex was recorded as a measure of depth of sedation at same time interval as for relaxation of jaw reflex. It was measured by observing a blink of the eye lids on touching the area around the medial canthus of the eyes with the index finger. The status of the pedal reflex was recorded as a measure of the depth of analgesia. It was assessed by observing the withdrawal reflex to the pinching of the inter-digital skin of the hind foot of animal. Response to intubation was recorded to assess the feasibility of intubation. If the animal allowed easy intubation, the endotracheal tube was left *in situ* and return of the laryngeal reflex was recorded as the animal started coughing. Relaxation of anal sphincter was observed depending upon the extent of outward relaxed anus. Complications like nausea, vomition, salivation, lacrimation, muscle twitching etc. were also recorded during and after anaesthesia in each group of animals, if observed.

Statistical analysis

The data collected was statistically analysed using analysis of variance (ANOVA) and Duncan's multiple range

tests (DMRT). Comparison within and between groups was done using SPSS v25 statistics software program and data presented as Mean±S.E. The subjective data generated from the scoring of various parameters were analysed using the Kruskal Wallis Test. Statistically the differences were considered at 5 per cent level of significance.

RESULTS AND DISCUSSION

Onset of sedation

In group DexTHIO, there was marked sedation with lowering of the head after glycopyrrolate-dexmedetomidine administration and the animal went to lateral recumbency comparatively early as compared to group ButTHIO and AceTHIO where mild sedation was observed as shown in Table 2. All the animals remained conscious but were unable to stand when disturbed. No cases of salivation and vomiting were observed in all the three groups. There was excellent sedation in group DexTHIO as compared to group ButTHIO and AceTHIO while both groups showed mild sedation. Comparison between groups revealed rapid onset and profound sedation after administration of dexmedetomidine in group DexTHIO. The faster onset of sedation was recorded with dexmedetomidine with thiopentone sodium in the present study as also confirmed by various workers (Verma *et al.,* 2023; Dewangan *et al*., 2024). The rapid onset of sedation could be attributed to the sedative and analgesic effect of dexmedetomidine when combined with thiopentone sodium. Similar findings have been documented by Flacke *et al.* (1993) and Lemke (2004) and Bhat *et al*. (2017). The use of preanaesthetic agents before induction in the present study for reducing anxiety in order to smoothen anaesthetic induction, maintenance and recovery phase.

Onset of anaesthesia (minutes)

Onset of anaesthesia was rapid, smooth and free from any untoward reactions like struggling and paddling in all the three groups. The findings are concurrent with Kassem *et al*. (2019) after xylazine-thiopentone sodium in dogs. The shorter onset of anaesthesia was noted in group DexTHIO (0.52±0.05 min.) as compared to group ButTHIO (0.59±0.10 min.) and AceTHIO (0.57±0.03 min.). Onset of anaesthesia was quicker in animals premedicated with dexmedetomidine as compared to those butorphanol or acepromazine. This might be due to the effect of dexmedetomidine which produces sufficient degree of sedation prior to induction with thiopentone sodium. All the reflexes abolished completely after induction of thiopentone sodium anaesthesia in all three groups suggesting that the surgical stage of anaesthesia had reached which are in agreement with earlier researchers under thiopentone anaesthesia in dogs (Jadon *et al*., 1998).

Duration of ananesthesia (minutes)

The mean duration of anaesthesia in group DexTHIO was significantly (P<0.05) longer (59.83±2.57 min.) than group

Table 1: System of recording of various reflexes and responses (adapted and modified after Amarpal *et al.*, 1996).

Parameters	0	1	2	3	4
Analgesia	Strong reaction to pinching of the inter- digital skin of the foot	Weak responses to pinching of the inter-digital skin of foot	Occasional response to pinching of the inter-digital skin of the foot	No response to pinching of the inter-digital skin of the foot	-
Relaxation of jaw	Not allowing to open the jaws	Resistant to opening of the jaws and would close quickly	Less resistance to opening of the jaws and would close slowly	No resistance and jaws would remain open	-
Palpebral reflex	Quick blink	Slow blink	Very slow and occasional blink	No blink	-
Pedal reflex	Strong withdrawal	Slow withdrawal	Occasional withdrawal	No withdrawal	-
Response toIntubation	Do not permit entry of tube into the mouth	Allow entry but will chew	Allow deeper entry but will cough	Difficult incubation with coughing	Easy intubation without coughing
Anal sphincter relaxation	Complete anal relaxation	Moderate anal relaxation	Mild anal relaxation	Absence of anal relaxation	-

ButTHIO (22.16±0.74 min.) and AceTHIO (20.17±0.94 min.). Dogs that received dexmedetomidine with thiopentone sodium had a significantly (P<0.05) greater duration of anaesthesia as compared to those which received butorphanol and acepromazine with thiopentone. Similarly, Kassem *et al*. (2019) also reported longer duration of anaesthesia following xylazine and thiopentone sodium in dogs. Longer duration of anaesthesia in group DexTHIO might be due to additive effect of dexmedetomidine with thiopentone sodium (Jadon *et al*., 1998). However, administration of butorphanol in group ButTHIO and acepromazine in group AceTHIO resulted in comparatively shorter increase in duration of anaesthesia. Similar observation of longer duration of anaesthesia with alpha-2 agonist in combination with thiopentone sodium have also been reported by Kassem *et al*. (2019) and Saini *et al*. (2019).

Record of various reflexes and responses

After induction with thiopentone sodium, all the reflexes disappeared indicating that animals were in perfect stage of surgical anaesthesia. Similar findings about reflexes were also reported by Muhammad *et al*. (2009); Bhat *et al*. (2018) after administration of thiopentone sodium in dogs. The degree of analgesia was better and remained for longer period of time in animals of group DexTHIO as compared to other two groups post-anaesthesia which might be due to accumulative effect of dexmedetomidine along with thiopentone sodium (Fig 1). Analgesic action of dexmedetomidine is mainly through spinally mediated and interruption of nociceptive pathways to the ventral root of the dorsal horn which reduces spinal reflexes (Talukder and Hikasa, 2009; Dewangan *et al*., 2024). The degree of relaxation of jaw was excellent and persisted for longer duration in animals of group DexTHIO as compared to group ButTHIO and group AceTHIO (Fig 2). This could be attributed to synergistic interaction between the dexmedetomidine and thiopentone sodium. The degree of palpebral reflex after induction with thiopentone showed complete loss of reflex in all the groups indicated by absence of eyelids blink which extended for longer duration

Table 2: Time taken for occurrence of various signs associated with sedation after various pre-anaesthetic administration in different groups.

Group (n=6)	Salivation (min.)	Ptosis (min.)	Nodding (min.)	Head down (min.)	Sternal recumbency (min.)	Lateral recumbency (min.)
ButTHIO	Absent	2.33±0.28^{B}	4.17±0.36^{B}	6.69±0.27^{B}	7.67±0.43^{B}	9.34±0.22^{B}
DexTHIO	Absent	1.66±0.21^{A}	2.66±0.22^{A}	4.50±0.18^{A}	5.83±0.34^{A}	7.47±0.25^{A}
AceTHIO	Absent	2.50±0.23^{B}	4.19±0.32^{B}	6.82±0.43^{B}	7.89±0.28^{B}	9.69±0.19^{B}

AB- Value bearing different superscript vary significantly (P<0.05) between group.

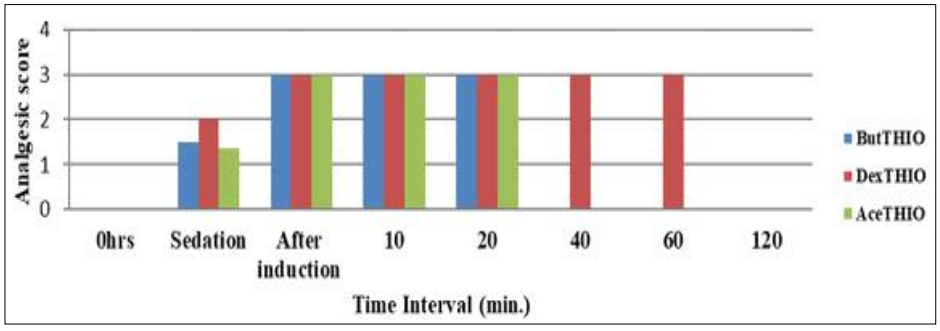

Fig 1: Analgesia score at various time intervals in different groups.

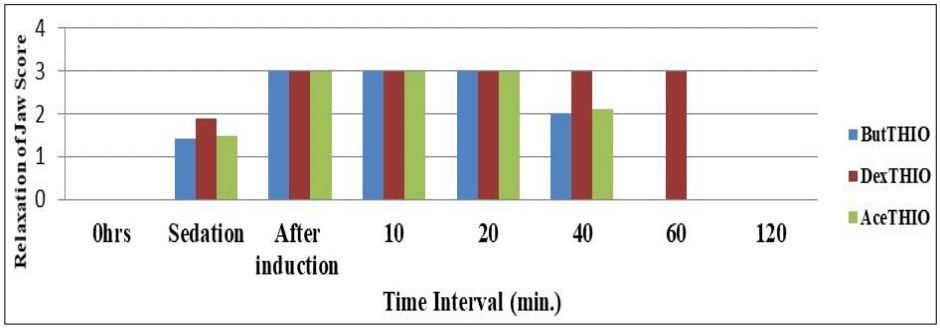

Fig 2: Relaxation of jaw score at various time intervals in different groups.

in animals of group DexTHIO as compared to group ButTHIO and AceTHIO during the complete period of observation (Fig 3) The pedal reflex abolished for longer period of time in animals of group DexTHIO post anesthesia as dexmedetomidine caused deep sedation for longer duration (Fig 4). The loss of pedal reflex in thiopentone anaesthesia was due to general CNS depression and analgesia. The endotracheal tube was retained for longer period of time in animals of group DexTHIO as compared to other two groups *i.e*. ButTHIO and AceTHIO (Fig 5). This might be due to synergistic interaction of alpha-2 agonist drug (Dexmedetomidine) with thiopentone sodium causing abolition of laryngeal reflexes for longer duration. Mild anal sphincter muscle relaxation was observed in group ButTHIO and AceTHIO after sedation with butorphanol and acepromazine respectively whereas, dexmedetomidine resulted in moderate anal sphincter muscle relaxation in animals of group DexTHIO (Fig 6). After induction with thiopentone sodium complete anal sphincter muscle relaxation was recorded this could be attributed to synergistic interaction of preanaesthetics like butorphanol, dexmedetomidine and acepromazine with thiopentone sodium. In group DexTHIO animals, after dexmedetomidine-thiopentone administration, there was excellent muscle relaxation for longer duration which is expected due to prior administration of dexmedetomidine activating alpha-2 adrenoceptors present in the spinal cord (Branson *et al.,* 1993). The present findings are in agreement to Muhammad *et al.* (2009) after thiopentone anaesthesia in dogs.

Recovery time

Extubation of endotracheal tube was performed following return of swallowing reflex or pharyngeal reflex (Fig 7). Time to extubation was significantly ($P<0.05$) longer for group DexTHIO (61.26±2.57 min.) followed by group ButTHIO

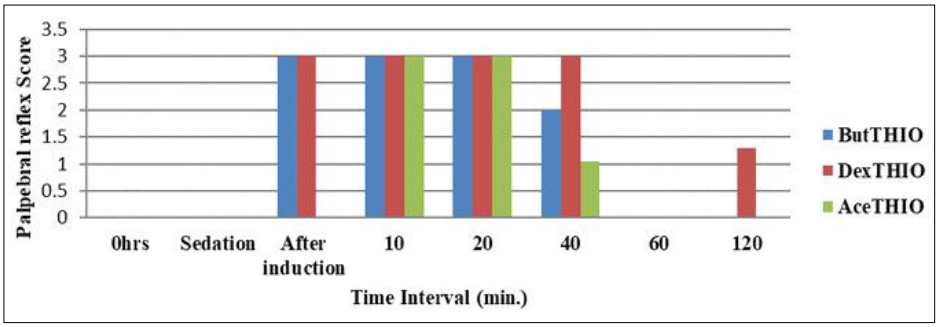

Fig 3: Palpebral reflex score at various time interval in different groups.

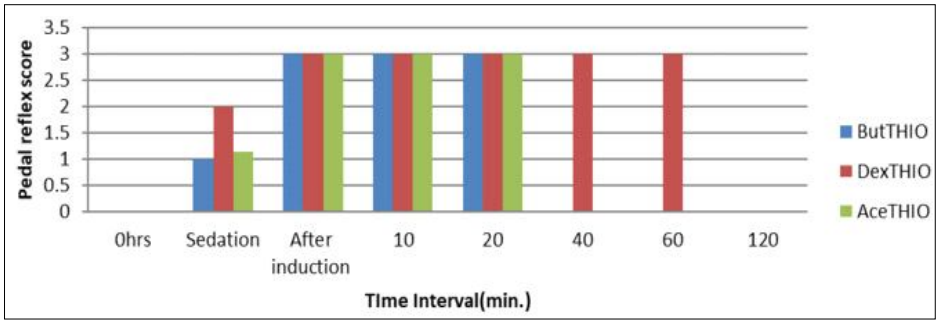

Fig 4: Pedal reflex score at various time interval in different groups.

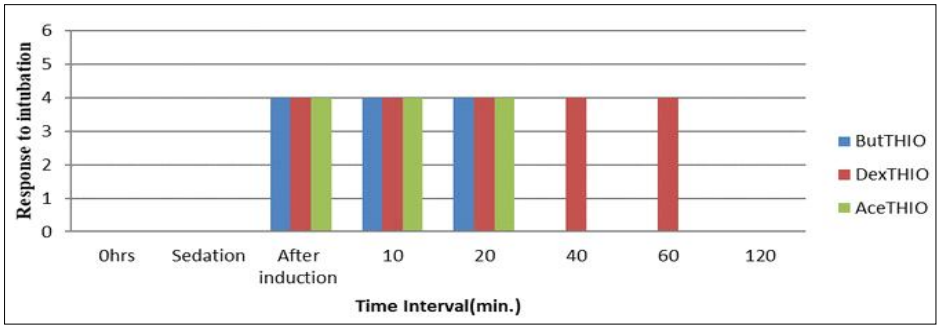

Fig 5: Response to intubation at various time interval in different groups.

(23.68±0.66 min.) and AceTHIO (21.15±1.05 min.). Head rightening was significantly (P<0.05) longer in group DexTHIO (66.04±2.62 min.) followed by group ButTHIO (26.23±0.71) and AceTHIO (25.67±1.68 min.). Sternal recumbency time was significantly (P<0.05) longer in animals of group DexTHIO (78.14±1.97) followed by group ButTHIO (30.33±1.01) and AceTHIO (28.50±2.08 min.). Standing time was significantly (P<0.05) longer for group DexTHIO (84.21±2.34min.) followed by group ButTHIO (35.43±0.87 min.) and AceTHIO (33.87±2.13 min.). Complete recovery time was significantly (P<0.05) longer for group DexTHIO (92.83±2.98min.) followed by group ButTHIO (38.66±1.11min.) and group AceTHIO (37.87±2.13 min.) respectively. Longer time to extubation in animals of group DexTHIO might be due to action of dexmedetomidine which causes greater depression of laryngeal reflex with thiopentone sodium as compared in animals of group ButTHIO and AceTHIO which showed shorter time. The difference in the head rightening, sternal recumbency time, standing time and complete recovery time from anaesthesia in between groups was statistically significant (P<0.05) in group DexTHIO and non-significant in group ButTHIO and AceTHIO. All the animals recovered very smoothly, excitement free with no shivering and struggling after thiopentone sodium anaesthesia. Smooth recovery from thiopental sodium was observed in this study confirms the finding of Bhat *et al*. (2018) and Saini *et al*. (2017). The longer head rightening, sternal recumbency time, standing time and complete recovery time from anaesthesia in group DexTHIO as compared to group ButTHIO and AceTHIO might have resulted from additive effect of thiopentone sodium with dexmedetomidine (α_2 agonist). Similar findings have also been reported by Jadon *et al*. (1998) and Saini *et al*. (2017) in dogs. Contrarily to our study, Redondo *et al*. (2000) documented vocalization or uncoordinated movements during recovery from romifidine-thiopentone sodium anaesthesia however, recovery was smooth without any apparent clinical consequences. Similarly, Muhammad *et al*. (2009) also reported recovery from thiopentone sodium anaesthesia was not smooth in dogs.

Quality of anaesthesia

The sedation was poor to fair after administration of glycopyrrolate+butorphanol and glycopyrrolate+ acepromazine whereas it was good after with glycopyrrolate+ dexmedetomidine anaesthesia (Fig 8). All the reflexes were abolished after induction of anaesthesia with thiopentone sodium suggesting stage of surgical anaesthesia which might be due to synergistic interaction of preanaesthetics like butorphanol, dexmedetomidine, acepromazine with thiopentone sodium. It means quality of anaesthesia was excellent with good muscle relaxation, narcosis and analgesia after administration of thiopentone in all the three groups. Similar observations were also reported by Grimm *et al*. (1998). In the present study, all the reflexes *viz*. palpebral, pedal, jaw were completely abolished but longer duration of muscle relaxation along with analgesia was recorded in group DexTHIO up to 60 min. as compared to

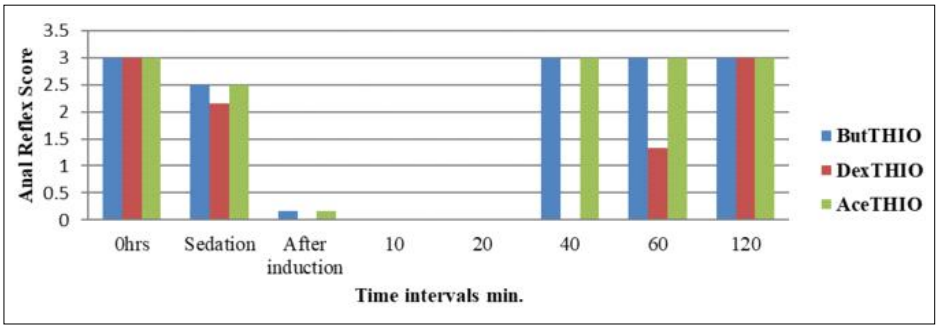

Fig 6: Anal reflex score at various time interval in different groups.

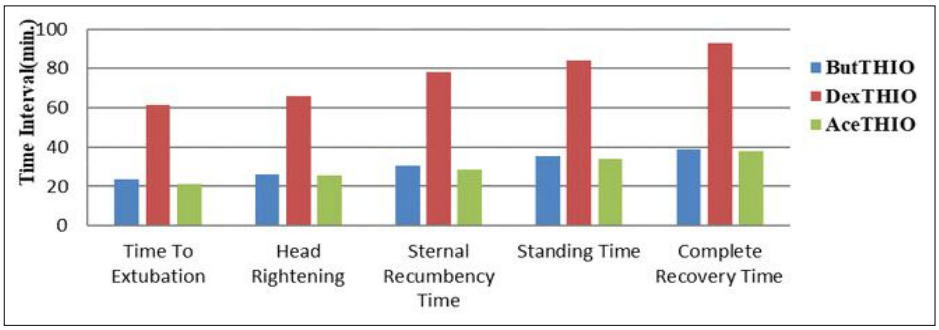

Fig 7: Recovery from anaesthesia in different groups.

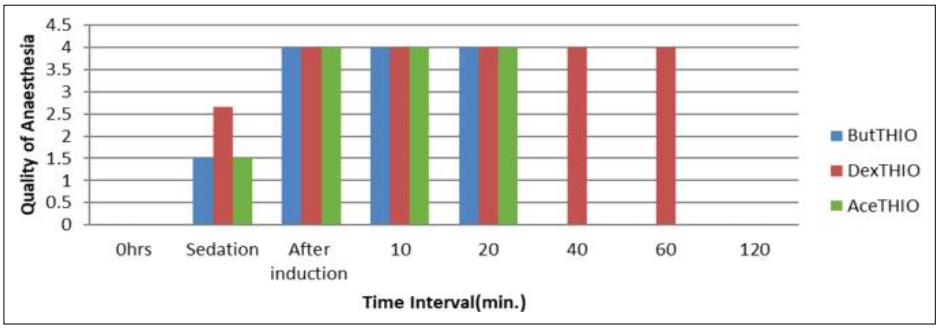

Fig 8: Quality of anesthesia score at various time interval in different groups.

groups ButTHIO and AceTHIO which was 20 min. post anaesthesia. Loss of laryngeal reflexes alongwith endotracheal tube intubation persisted up to 60 min. in group DexTHIO while for lesser time up to 20 min. in groups ButTHIO and AceTHIO respectively. The above findings are in concurrent with Muhammad *et al.* (2009) and Bhat *et al*. (2018) after administration of thiopentone sodium in dogs.

Complications (If any)

Salivation, defecation, nausea, vomition and lacrimation were absent in animals of all the three groups. In present study, salivation was not observed in any of the group which could be attributed to glycopyrrolate antimuscarinic effect. Contrarily, Bhat *et al*. (2017) and Bhat *et al*. (2018) observed mild salivation at 10 min after thiopentone sodium administration. Voluntary urination was recorded in 5 animals out of 6 in group DexTHIO after reappearance of pedal reflex with inhibition of release of antidiuretic hormone in dogs or osmotic diuretic effect of increased blood agonist. Straightening of legs was recorded in 2 animals out of 6 in group AceTHIO at the time of recovery which might be due to hyper sensitivity in response to noise. The above findings are in agreement with Redondo *et al.* (2000) who reported paddling, hperextension of the forelimbs and opisthotonus after thiopentone sodium in dogs. Yawning was also recorded in 3 animals out of 6 in group AceTHIO after sedation with acepromazine which could be attributed due to light state of anaesthesia where dog opens the jaw, curls the tongue and simulate a yawn (Lumb and Jones, 1996).

CONCLUSION

Based on the present study, it could be concluded that thiopentone sodium in combination with butorphanol, dexmedetomidine and acepromazine proved to be safe general anaesthetic in dogs. Howeve, dexmedetomine alongwith thiopentone sodium combination produced quicker onset and excellent analgesia with muscle relaxation of longer duration suitable for major surgical procedures in canines.

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Disclaimers

The views and conclusions expressed in this article are solely those of the authors and do not necessarily represent the views of their affiliated institutions. The authors are responsible for the accuracy and completeness of the information provided, but do not accept any liability for any direct or indirect losses resulting from the use of this content.

Informed consent

All animal procedures and handling techniques for experiments were approved by the Institutional Animal Ethical Committee (IAEC).

Conflict of interest

The authors declare that there are no conflicts of interest regarding the publication of this article. No funding or sponsorship influenced the design of the study, data collection, analysis, decision to publish or preparation of the manuscript.

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