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ELECTROENCEPHALOGRAPHIC EVALUATION OF THIOPENTONE AND PROPOFOL ANAESTHESIA IN DOGS

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ABSTRACT

This study was aimed at comparing the delta rhythm frequencies of electroencephalographic waves after inducing either with thiopentone or propofol intravenously in basset hound dogs. Fronto-polar montage was used to obtain the electroencephalographic waves. The depth of anaesthesia was also assessed clinically by recording the clinical parameters viz., heart rate, oxygen saturation, end-tidal carbon dioxide and blood pressure as well as by checking the reflexes. The animals induced with thiopentone had a lower frequency compared to the animals induced with propofol at all time periods. The frequency obtained immediately after inducing with thiopentone was 3.50 ± 2.40 Hz whereas the frequency obtained immediately after inducing with propofol was 3.94 ± 2.25 Hz. Whereas the frequency obtained at the 60th minute time period after thiopentone induction was 2.13 ± 0.49 Hz and after propofol induction was 2.72 ± 1.56 Hz. The reflexes were absent during the observation periods.

Keywords: Electroencephalography, Delta rhythm, Dog, Anesthesia, Thiopentone, Propofol

INTRODUCTION

The functional state of the brain can be directly measured by electroencephalography (EEG) placing electrodes on different anatomical locations of brain. Cortical neuronal activity is recorded by electroencephalography. Electroencephalogram are the recordings obtained after placing electrodes on the scalp and electrocorticogram are the recordings obtained from the cortical surface (Teplan, 2002). Ascending reticular activating system of the brainstem influences the cerebral cortical neurons. Quantitative electroencephalogram analysis has been used as a sensitive method in assessing

brain function in dogs during anaesthesia to monitor unconsciousness (Moore et al., 1991; Bergamasco et al., 2003).

There are different kinds of rhythms in EEG *viz*., Delta, Theta, Alpha, Beta and Gamma rhythms. The frequencies of Delta rhythm range between 0.5-4 Hz, Theta rhythm 4-8 Hz, Alpha rhythm 8-13 Hz, Beta rhythm 13-30 Hz and Gamma rhythm above 30 Hz (Musizzaand Ribaric, 2010). Delta rhythm is observed normally during deep sleep. Alpha rhythms are commonly observed during wakefulness. Beta rhythms are seen during increased alertness and focused attention. Gamma rhythm is observed with information processing and onset of voluntary movements (Blinowskaand Durka, 2006). As the anaesthesia deepens, the frequency of the EEG waves decreases and the amplitude increases. Electroencephalogram provides a direct measurement of the functional state of the brain and according to the concentration of the anesthetic, changes in the EEG is noticed (Garcia and Sebel, 2010). Use of EEG in animals is limited because of non-cooperation of awake animals (Braueret al., 2011). A few cases have used propofol for restraining the animals to obtain the recordings in epileptic as well as healthy dogs (Accatinoet al., 1997; Bergamasco et al., 2003). Electroencephalography is a non-invasive technique to diagnose the functional state of the central nervous system and is routinely used in diagnosis of epilepsy (Flinket al, 2002; Koutroumanidisand Smith, 2005)

A quantitative analysis of EEG waves after induction of anaesthesia with thiopentone/ fentanyl showed a reduction in the alpha rhythm activity in human patients (Rundshagenet al., 2004). Thiopentone induction followed by halothane anaesthesia in geldings caused decrease in 95% spectral edge frequency after thiopentone induction (Johnson et al., 2000).

Propofol induction with 2 different doses in goats reduced the EEG frequency. Higher dose of propofol showed lower frequency (Madan et al., 2010). Electroencephalographic waves with continuous rate infusion of propofol after inducing anaesthesia with propofol in dogs had dominant delta waves (Braueret al., 2011).

In this study, the effects of thiopentone or propofol induction followed by maintaining with isoflurane anaesthesia on EEG in dogs were investigated.

MATERIALS AND METHODS

Two Basset Hound dogs were the subjects for electroencephalographic study. The dogs were premedicated with atropine sulphate (Tropine; Neon Laboratories,

Maharashtra, India; 0.6 mg/ml) at a dose rate of 0.045 mg/kg body weight followed by xylazine hydrochloride (Xylaxin, Indian Immunologicals Ltd. Hyderabad, India; 20 mg/ml) at a dose rate of 1 mg/kg administered intramuscularly at an interval of 10 minutes. The animal was positioned on ventral recumbency. Ear vein was cannulated using a 20G over-the-needle catheter to access the venous line. Normal saline (NS; Claris Otsuka, Ahmedabad, India; 0.9 gm; 500 ml) at a dose of 4 ml/kg/h was continuously infused using an infusion pump throughout the duration of the experiment. A 3-electrode montage was used to obtain the electroencephalogram (Fig. 1). Three 27-gauge stainless steel needle electrodes were used. The positive and negative electrodes were placed subcutaneously on the fronto-polar regions (Fp1 and Fp2) and the reference electrode on the nose mid-way between the nostril and the medial canthus of the eyes as described by Pellegrino and Sica(2004). The EEG was recorded with a digital filter with a low-pass band cut-off frequency

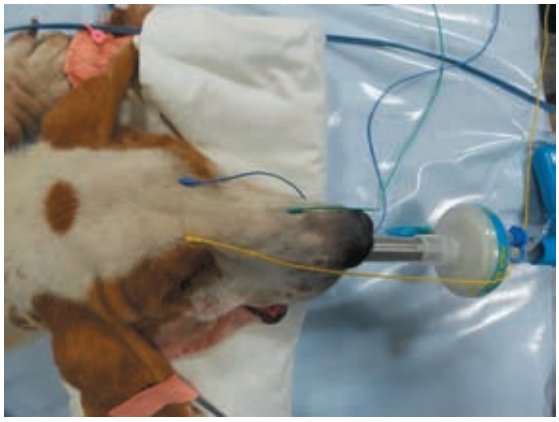

Fig. 1: Photograph showing fronto-polar montage position in dog

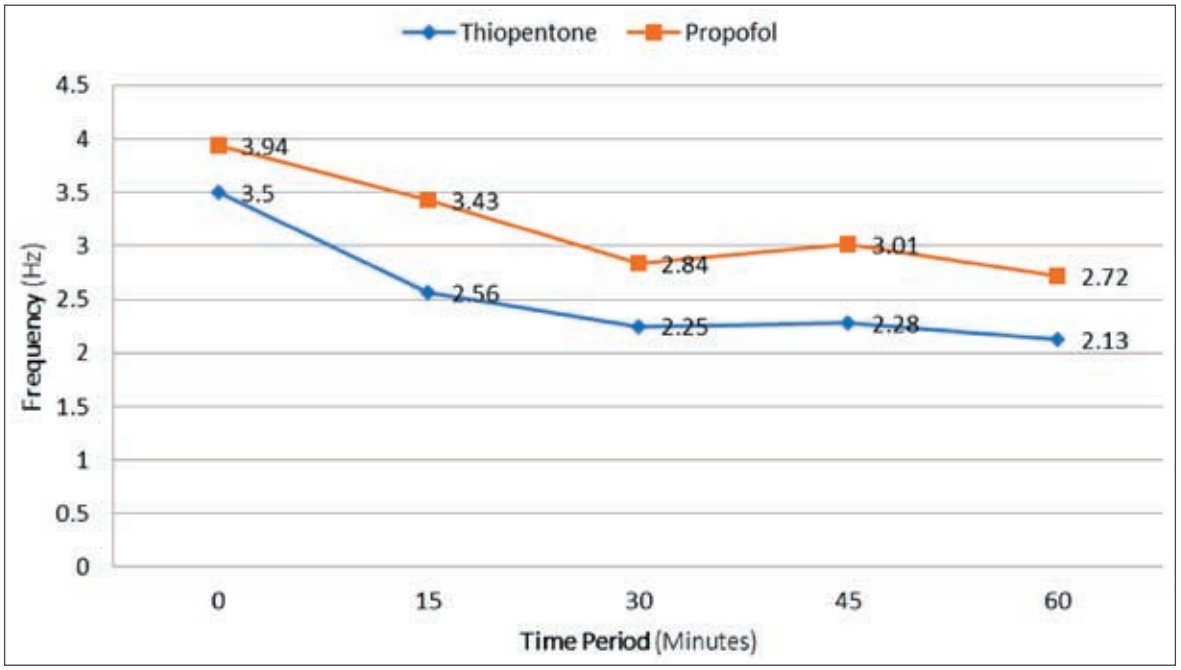

Fig. 2: Figure showing highest average frequency obtained in different groups at different time intervals

set at 30Hz (AD Instruments). Either thiopentone (Thiosol; Neon Laboratories, Maharashtra, India; 1 gm vial) at a dose of 10mg/kg body weight or propofol (Neorof; Neon Laboratories, Maharashtra, India; 10 mg/ml) at a dose of 3mg/kg body weight was administered intravenously to induce anaesthesia and was administered as a bolus. Five experiments each were performed using thiopentone and propofol. The dogs were alternated after every experiment and repeated after a wash-out period of 10 days. Soon after induction, trachea was intubated using a cuffed endotracheal tube and was mechanically ventilated. Tidal volume and respiration rate was set at 12ml/kg bodyweight and 15 breaths/minute respectively. The inspiration:expiration ratio was 1:1.5. Anaesthesia was maintained with 1.5%

Table 1: Average highest frequency (Hz) obtained in different groups at different time intervals

Time period	**Frequency** (Hz)	
	Thiopentone	**Propofol**
0	3.50 ±2.40	3.94 ± 2.25
15	2.56 ±0.77	3.43 ± 1.33
30	2.25 ±0.64	2.84 ± 1.17
45	2.28 ±0.29	3.01 ± 1.17
60	2.13 ±0.49	2.72 ± 1.56

Table 2: Table showing different clinical parameters at different time intervals (Thio: Thiopentone group; Prop: Propofol group; SpO_2: Peripheral oxygen saturation; HR: Heart rate; $ETCO_2$: End-Tidal carbon dioxide; Systolic BP: Systolic blood pressure; Diastolic BP: Diastolic blood pressure; BPM: Beats per minute; mm of Hg: millimetre of mercury)

Interval	**HR (BPM)**		**Systolic BP (mm of Hg)**		**Diastolic BP (mm of Hg)**		**SpO_2 (%)**		**$ETCO_2$ (mm of Hg)**	
	Thio	***Prop***	***Thio***	***Prop***	***Thio***	***Prop***	***Thio***	***Prop***	***Thio***	***Prop***
Induction	119.6 ± 23.39	122.3 ± 9.6	189.6 ±65.32	194.3 ±23.54	131.4 ± 57.6	122 ± 27.07	98.75 ± 1.25	97.5 ± 2.51	35.6 ± 7.53	34.5 ± 0.7
15 mins	110 ± 15.89	111.8 ± 15.3	166 ± 58.22	129.5 ±17.37	93 ± 31.77	79.25 ± 6.13	96.6 ± 4.82	99 ± 0.81	32.2 ± 1.92	31.5 ± 1.73
30 mins	107.3 ±21.79	110.3 ± 7.36	157.5 ±49.32	142.8 ±36.51	86 ± 17.72	81 ± 19.99	98.75 ± 0.5	98.75 ± 0.5	32.25 ± 2.5	33 ± 2.16
45 mins	96 ± 23.91	109.8 ±17.88	139.6 ±44.99	128.4 ± 24.3	77.6 ± 12.12	77.8 ± 14.69	97.2 ± 5.16	99 ± 0.7	30.6 ± 1.67	31.2 ± 1.64
60 mins	90.67 ± 21.78	95.75 ± 21	158.5 ±50.81	132.3 ± 2.77	69.33 ±14.64	80 ± 22	94.33 ± 8.96	99.25 ± 0.5	32 ± 1.41	31± 1.41

Table 3: Table showing anaesthetic depth monitoring based on the Palpebral reflex, Corneal reflex, pedal reflex and eye position (Thio: Thiopentone group; Prop: Propofol group).

Interval	Palpebral Reflex		Corneal Reflex		Pedal Reflex		Eye Position	
	Thio	***Prop***	***Thio***	***Prop***	***Thio***	***Prop***	***Thio***	***Prop***
0	Absent	Absent	Absent	Absent	Absent	Absent	Ventral	Ventral
15	Absent	Absent	Absent	Absent	Absent	Absent	Central	Central
30	Absent	Absent	Absent	Absent	Absent	Absent	Central	Central
45	Absent	Absent	Absent	Absent	Absent	Absent	Central	Central
60	Absent	Absent	Absent	Absent	Absent	Absent	Central	Central

Isoflurane (Forane; Abbot Laboratories, United Kingdom; 250ml).

Electroencephalographic recordings were obtained for 60 minutes. The electroencephalographic waves were processed later to obtain the frequency values. The EEG waves were processed at 4 different intervals viz., immediately after the induction with either thiopentone or propofol after endotracheal intubation, after 15 minutes of induction, after 30 minutes of induction and after 60 minutes of induction, using LabChart 8 reader. The gaseous anaesthetic was discontinued after the study period of 60 minutes. The animals started recovering from anaesthesia within 4-5 minutes after disconnecting the gaseous anaesthetic. The waves were analysed at a FFT size of 64k to determine the frequency. The clinical parameters viz., heart rate, peripheral oxygen saturation of haemoglobin (SpO_2) and end-tidal carbon dioxide ($ETCO_2$) were recorded at every 15 minutes interval during the observation period. Blood pressure was measured non-invasively using a cuff (CM1202; Bladder size: 9.8 x 18 cm) wrapped around the metacarpal region. The depth of anaesthesia was also measured clinically by monitoring the reflexes viz., palpebral, corneal and pedal reflexes. The statistical analysis of the data were done using T-test.

RESULTS AND DISCUSSION

The three-electrode fronto-polar montage was effective in obtaining the EEG waves. The EEG waves were analysed using LabChart8 reader to determine the frequencies at specific time intervals (Table 1 and Fig. 2). The highest average frequency obtained immediately after inducing with thiopentone was 3.50 ± 2.40Hz whereas for propofol the frequency was 3.94 ± 2.25Hz. The highest average frequency obtained at 15 minutes, 30 minutes, 45 minutes and 60 minutes after thiopentone induction were 2.56 ± 0.77 Hz, 2.25 ± 0.64 Hz, 2.28 ± 0.29 Hz and 2.13 ± 0.49 Hz respectively.

The highest average frequency obtained at 15 minutes, 30 minutes, 45 minutes and 60 minutes after propofol induction were 3.43 ± 1.33 Hz, 2.84 ± 1.17Hz, 3.01 ± 1.17 Hz and 2.72 ± 1.56 Hz respectively. No significant differences were observed between the groups at any time intervals.

The average values of heart rate immediately after induction with thiopentone was 119.6 ± 23.39 beats per minute whereas for propofol was 122.3 ± 9.6 beats per minute. The heart rate observed at 60 minutes for thiopentone and propofol groups were 90.67 ± 21.78 beats per minute and 95.75 ± 21 beats per minute. The heart rate pattern remained stable throughout the procedure. The average values of systolic and diastolic blood pressure immediately after thiopentone induction were 189.6 ± 65.32 mm of Hg and 131.4 ± 57.6 mm of Hg respectively. The systolic and diastolic blood pressure at 60 minutes for thiopentone group were 158.5 ± 50.81 mm of Hg and 69.33 ± 14.64 mm of Hg respectively. The average values of systolic and diastolic blood pressure immediately after propofol induction were 194.3 ± 23.54 mm of Hg and 122 ± 27.07 mm of Hg respectively. At 60 minutes, the values were 132.3 ± 2.77 mm of Hg and 80 ± 22 mm of Hg for thiopentone and propofol groups respectively. The average values of peripheral oxygen saturation of haemoglobin (SpO_2) immediately after induction with thiopentone was 98.75 ± 1.25 % whereas for propofol was 97.5 ± 2.51 %. At 60 minutes, the values were 94.33 ± 8.96 % and 99.25 ± 0.5 % for thiopentone and propofol groups respectively. The average values of end-tidal carbon dioxide ($ETCO_2$) immediately after induction with thiopentone was 35.6 ± 7.53 mm of Hg whereas for propofol it was 34.5 ± 0.7 mm of Hg. The values for thiopentone and propofol group at 60 minutes were 32 ± 1.41 mm of Hg and 30 ± 0.81 mm of Hg respectively. There were no significant differences between the two groups in SpO_2, heart rate, $ETCO_2$, systolic blood pressure and diastolic blood pressure at any observation period (Table 2). The reflexes viz., pedal reflex, corneal reflex and palpebral reflex, were absent at all the time intervals of observations. The eyeball position immediately after induction with thiopentone or propofol was ventral in position in all the cases, which later took a central position from 15 minutes time period onwards (Table 3).

In the present study, the positioning of the fronto-polar electrodes (Fp1 and Fp2) montage was as described by Pellegrino and Sica (2004). The recording technique followed in this study was efficient in obtaining the EEG waves. The fronto-polar electrodes allow the recording of electrical

activity from the orbitofrontal area. There were no significant differences between the frequencies of both the groups at any time period. The frequency band obtained after induction with either thiopentone or propofol and at different time intervals were having a dominant delta type of rhythms, which is a dominant feature in deep sleep as well as in deep anaesthesia.

In the current study, xylazine at a dose rate of 1 mg/kg intramuscularly was used to sedate the animal. Artifacts in the EEG are common in veterinary practice. To reduce these artifacts, Tepper and Shores(2014) used medetomidine (2 microgm/kg IV) or dexmedetomedine (1 microgm/ kg IV) followed by atipamezole (10 microgm/kg IM) was used. Pellegrino and Sica (2004) used xylazine to restrain the animal and found that xylazine at a dose rate of 1 mg/kg subcutaneously provided good relaxation and produced a clean recording, free of artifacts and noises along a period of at least 30 minutes. Janget al (2004) studied the effect of tiletamine/ zolazepam combination with xylazine or medetomidine on electroencephalograms in dogs. They observed that tiletamine/ zolazepam injection produced slow and high amplitude waves with low amplitude spikes. In xylazine-tiletamine-zolazepam and medetomidine-tiletamine-zolazepam groups, slow and high waves were seen. And while awakening, the waves changed to fast waves with low amplitude. In our study, administration of xylazine produced sedation and muscle relaxation.

In the current study, the group where propofol was used for induction produced dominant delta rhythms. Bergamasco et al. (2003) used propofol to anaesthetize beagle dogs to quantitatively analyse the electroencephalographic findings and reported that there was an increase in the slow frequency band (delta rhythm), whereas the alpha and beta frequency bands were constantly throughout the recording. The use of propofol at a dose rate of 6 mg/kg as a bolus followed by continuous intravenous infusion at a dose of 0.5-0.9 mg/kg/min produced a dominant delta and theta rhythms in the EEG wave pattern. It was also observed that the delta and theta frequency band was initially more prominent in anterior areas which later became generalized. In our study, propofol (3 mg/kg) was administered as a bolus. The group where thiopentone, at a dose of 10 mg/kg intravenously as a single bolus, was used for induction also produced dominant delta rhythms and the frequency was lower compared to the frequency obtained in animals where propofol was used. Martoftet al. (2001) used thiopentone at a dose rate of 0.6ml/ kg of 2.5% thiopentone solution intravenously, half dose was administered

as a bolus and the second half at a rate of 1ml/s, for induction in pigs and found that there was a significant decrease in the EEG frequencies. In the present study, the differences in the frequencies obtained in two groups at different time intervals were not significant, but a lower frequency waves were obtained in the thiopentone induced animals compared to the propofol induced animals.

In the present study, there was a reduction in heart rate, systolic blood pressure and diastolic blood pressure from the initial values in both the groups. In the current study, the reflexes, viz., palpebral reflex, corneal reflex and pedal reflex, to measure the depth of anaesthesia remained absent at all time periods. In studies conducted in dogs anaesthetised with sodium pentobarbital, halothane or isoflurane, butorphanol alone significantly decreased arterial pressures, heart rates and systemic vascular resistance and increased cardiac index (Schurig et al., 1978; Greene et al., 1990; Bulafariet al., 1997). Ribeiro et al (2009) compared the clinical signs of depth of anaesthesia and cerebral state index responses in dogs during induction of anaesthesia with propofol. They concluded that the cerebral state index decreased from the baseline to plane E but no significant correlation was observed between cerebral state index and these anaesthetic planes.

In the present study, the use of either thiopentone or propofol for induction followed by maintenance with isoflurane anaesthesia produced a dominant delta rhythm throughout the observation period. The EEG waves in thiopentone induced animals had a lower frequency compared to propofol induced animals but no significant differences were observed between the groups at any time period. There were no significant differences in the clinical parameters between the groups at particular time intervals. The reflexes were also absent in both the groups at all the time periods observed.

SUMMARY

Thiopentone induced group had a deeper anaesthesia compared to propofol, which was evident from the EEG frequencies, while haemodynamic and ventilatory parameters were preserved.

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