

EVALUATION OF VECURONIUM WITH THIOPENTONE TOTAL INTRAVENOUS ANAESTHESIA (TIVA) IN CANINE ORTHOPAEDIC SURGERIES

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Present study was conducted on 12 client owned dogs presented for orthopaedic surgeries, to evaluate the vecuronium with thiopentone anaesthesia, divided into groups A and B. Atropine 0.04 mg/kg Bwt. SC followed by diazepam 0.5mg/kg Bwt. IV and pentazocine 1.5 mg/kg Bwt. IV were administered in both the groups. Induction and maintenance of anaesthesia was done by thiopentone sodium iv in both the groups but in group B, vecuronium 0.04 mg/kg was given (i/v) additionally..Neuromuscular blockade (NMB) was monitored by stimulating facial nerve using Train of four (TOF) mode of nerve stimulator. Complete jaw relaxation was recorded in group B than A. Evoked TOF responses revealed 80 to 90 % neuromuscular blockade in group B and absence of NMB in group A. Maintenance doses of thiopentone decreased in group B(0.12 ± 0.01 mg/kg/min) than A(0.20 ± 0.03 mg/kg/min with significantly lower recovery time and sternal recumbency time in group B. It is concluded from the present study that vecuronium can be used with thiopentone anaesthesia to increase muscle relaxation along with significant reduction in the dose of thiopentone without adversely affecting cardio, respiratory and haemodynamic functions in dogs.

Keywords: Dog, Neuromuscular blocker, Thiopentone, TIVA, Train of four, Vecuronium.

Balanced anaesthesia is a reversible CNS depression along with analgesia, loss of autonomic reflexes and good muscle relaxation (Lumb and Jones, 2007). Total intravenous anaesthesia (TIVA) may be a better alternative to the standard inhalational techniques when facilities are not available under field conditions.

TIVA has many potential advantages for the practicing veterinarian acting as surgeon-anesthetist as it is relatively easy to manage, non hazardous to the operation room personnel and donot require expensive apparatus for its delivery (Hasei *et al.*, 2003 and Matthews, 2007). Orthopaedic surgeries in small animal practice are painful procedures which necessitates adequate depth of anaesthesia, analgesia and good muscle relaxation during the procedure with minimal effects on vital body functions. A balanced anesthetic technique involving a combination of drugs at low doses can achieve this. (Lumb and Jones, 2007). Thiopentone sodium is a cheap and commonly used anaesthetic agent under field conditions but it is a poor analgesic and weak muscle relaxant (Vicker *et al.*, 1984). It would therefore be appropriate to use it with potent analgesic and good muscle

relaxant as a part of balanced anaesthetic protocol for orthopaedic surgeries, which require adequate analgesia and good muscle relaxation. Thiopental has an ultrashort action because it is rapidly distributed into different body tissues and localize in body fat (Brodie *et al.*, 1950).

Neuromuscular blocking agents (NMBAs) could be very useful anaesthetic adjuncts in patients undergoing orthopedic surgery to enhance muscle relaxation required to reduce fracture fragments. The use of neuromuscular blockers necessitates an efficient monitoring as there is relaxation of diaphragmatic muscles although it is least sensitive muscle. The NMBAs may be preferred over depolarizing NMBAs like succinylcholine because of its undesirable effects of increase in intracranial pressure and intraocular pressure along with electrolyte imbalance and hyperkalemia, all of which can further compromise the trauma patient. Vecuronium is nondepolarising intermediate-acting NMBA that is a structural analogue of pancuronium and is non- vagolytic. Vecuronium is not associated with heart rate (HR) or blood pressure (BP) alterations (Silver and Mirakhur, 1994). There is scarcity

of information on the use of vecuronium with thiopentone anaesthesia for orthopaedic surgery in dogs. The purpose of the present study was to evaluate the suitability of vecuronium in combination with diazepam-pentazocine thiopentone TIVA in canine orthopaedic surgeries.

Materials and Methods

A prospective randomized blinded study was conducted on 12 client-owned, dogs of either sex (8 males and 4 females) weighing 19.25 ± 3.24 kg presented for orthopaedic surgeries (intra-medullary pinning and cross pinning). An informed consent was obtained from the owners prior to subjecting the animals to the study. The dogs were divided randomly into two equal groups, designated as group A and B. The animals were restrained properly and preanesthetic drugs were injected. Atropine was injected 0.04 mg/kg body weight (s/c). After 10 minutes of administering atropine, diazepam was injected 0.5mg/kg body weight (i/v) in both the groups. After 5 minutes of diazepam administration, pentazocine, 1.5 mg/kg body weight (i/v) was administered in both the groups. Induction was done with thiopentone (5 percent 10 mg/kg i/v till effect) after the last preanaesthetic administration and maintenance of anaesthesia was done by thiopentone 5 percent (i/v) as an intermittent bolus in both the groups. All animals were intubated after thiopentone induction and mechanical ventilation with 100% oxygen was kept ready in case it was required at any stage. Additionally in group B, at the time of incision when the surgical plane of anaesthesia (abolition of palpebral, corneal and pedal reflexes with regular patterns of breathing) was attained, vecuronium, 0.04mg/kg was given (i/v). NMBAs will block motor reflexes which are important indicators of depth of anaesthesia, which necessitated close monitoring of the autonomic reflexes like heart rate (HR), respiratory rate (RR) during the peak effect of the NMBA to ascertain the depth of anaesthesia during that period. A peripheral nerve muscle stimulator (PNMS) was used to monitor the blockade. Facial nerve was used

as a monitoring nerve in this study. The area just below the base of ear was shaved and cleaned followed by application of electrodes of the PNMS. Visual or tactile evaluation of the train of four (TOF) responses was done for evaluating neuromuscular function by observing the jaw muscles. Evoked TOF twitch intensity is a popular mode of stimulation for clinical monitoring of neuromuscular junction. Four successive stimuli are delivered at 2Hz (every 0.5 sec). The differential fading of twitches was graded from the pilot trials in 6 animals and a score was generated. Monitoring was done at every minute after injection of vecuronium. But values were recorded at every 5 min till twitches returned to baseline value. Fluid therapy (Normal saline) was used throughout the observation period.

In both the groups, various reflexes were recorded using score systems at baseline (0 min) and at 10, 20, 30, 45 and 60 min interval after the pentazocine administration. These reflexes include jaw relaxation, palpebral reflex, corneal reflex and pedal reflex. Score 1 (intact reflex), score 2 (intact but weak reflex), score 3 (very weak reflex) and score 4 (abolished reflexes). Extent of salivation was observed at different intervals as for various other reflexes and was graded from score 1(no salivation), score 2(mild salivation), score 3(moderate salivation) and score 4 (excessive salivation). The number of evoked twitches indicates the degree of receptor occupancy. Disappearance of T4, T3, T2, T1 corresponds to 0 to 75%, 80%, 90% and 100% occupancy. The evoked twitch responses was scored as; score 1 (All 4 twitches are present), score 2(observable mild decrease in amplitude of all 4 twitches), score 3 (observable moderate decrease in amplitude of 2nd, 3rd and 4th twitches), score 4 (complete absence of 3rd and 4th twitch), score 5 (complete absence of 2nd, 3rd or 4th twitch/ not palpable through hand also), score 6 (no twitch observable/palpable). The muscle twitches evoked were recorded just before injection of vecuronium in group B, then after every 5 minute interval till the complete recovery of twitches. While in group A, twitches were recorded after the induction

with thiopentone at the same intervals. Anaesthesia was maintained by bolus injections of thiopentone and the total dose of thiopentone in mg/kg/minute required for maintenance was calculated. Recovery, Sternal recumbency and Standing time was recorded and it was in minutes as the time elapsed from last injection of the drug to the appearance of pedal reflex and till the animal gets in standing position and is able to walk, respectively. Duration of anaesthesia in minutes was recorded as the time that elapsed from the time of abolition of pedal reflex to the time of reappearance of the pedal reflex. Duration of surgery was recorded as the time between the incision and last suture of the skin. The orthopaedic procedures done were intramedullary pinning and crosspinning by an expert team of surgeons. Heart rate (HR) was monitored by non-invasive blood pressure (NIBP) monitor. Respiratory rate (RR) was measured by recording the excursion of thoraco-abdomen. Rectal

temperature was recorded with the help of a digital thermometer. Haemodynamic parameters viz. mean arterial pressure (MAP-mm of Hg) and haemoglobin oxygen saturation (%) were recorded using non-invasive blood pressure monitor (NIBP) and pulse oximeter before administration of any drug (0 min) and then at 10,20,30, 45 and 60 min after anaesthesia.

The data was analyzed for statistical significance using SPSS software version 16.0. One way analysis of variance and Duncan's Multiple Range Test (DMRT) was used to compare the means at different time intervals between the groups. Paired "t" test was used to compare the mean values at different intervals with their base values in each group. The subjective data generated from the scoring of various parameters were analyzed using Kruskal Wallis test. In each analysis, the differences were considered significant at a value of $p < 0.05$.

Table 1: Mean \pm SE values of RT/SRT/ST/ Maintenance dose in groups A and B.

Groups	Recovery time(minutes)	Sternal recumbency time(minutes)	Standing time(minutes)	Maintenance dose (mg/kg/minute)
A	24.67 ^a \pm 3.84	112.33 \pm 9.65	146.83 \pm 6.88	0.20 \pm 0.03
B	10.83 ^b \pm 3.55	81.50 \pm 4.67	187.33 \pm 1.33	0.12 \pm 0.01

Values with different alphabets differ significantly ($P < 0.05$)

Table 2: Mean \pm SE values for heart rate (beats/min), respiration rate (breaths/min), mean arterial pressure (mmHg) and rectal temperature ($^{\circ}$ C) in groups A and B at different intervals

Parameters	Group	0	10	20	30	45	60
Heart rate	A	123 \pm 9	131 \pm 10	145 \pm 11	148 \pm 13	143 \pm 19	150 \pm 18
	B	115 \pm 7	136 ^{**} \pm 6	151 [*] \pm 9	142 \pm 16	145 \pm 4	162 [*] \pm 18
Respiration Rate	A	32 \pm 3	28 \pm 3	27 \pm 3	26 ^b \pm 2	26 ^{*ab} \pm 4	26 ^{*a} \pm 3
	B	28 \pm 0	22 ^{**} \pm 1	19 ^{**} \pm 0	18 ^{**a} \pm 1	19 ^{**a} \pm 2	23 ^{*a} \pm 2
Mean arterial pressure	A	86.94 \pm 4.89	87.67 \pm 5.05	88.22 \pm 4.96	77.61 ^{**} \pm 5.23 ^a	87.17 \pm 12.65	87.33 \pm 8.16
	B	82.50 \pm 5.17	85.22 \pm 1.83	82.67 \pm 1.48	85.05 ^{ab} \pm 1.00	91.67 \pm 2.78	88.72 \pm 3.44
Rectal temperature	A	39.36 \pm 0.24	38.14 ^{**a} \pm 0.18	37.90 ^{**a} \pm 0.24	37.67 ^{**a} \pm 0.27	37.44 ^{**a} \pm 0.36	37.43 ^{**a} \pm 0.30
	B	39.03 \pm 0.17	38.49 ^{*ab} \pm 0.21	38.52 ^{*ab} \pm 0.12	38.23 ^{**ab} \pm 0.21	38.23 ^{**ab} \pm 0.10	38.16 ^{**ab} \pm 0.10
SpO ₂	A	89.33 \pm 5.14	87.50 ^a \pm 2.85	90.50 \pm 2.28	88.33 ^a \pm 4.80	91.33 ^a \pm 1.61	86.17 ^{**} \pm 4.86 ^a
	B	93.00 \pm 0.82	94.17 ^b \pm 1.35	91.17 \pm 3.77	94.67 ^{*ab} \pm 0.95	93.50 ^{ab} \pm 2.45	93.50 ^{ab} \pm 2.55

*Significantly different from base value ($P < 0.05$); **significantly different from base value ($P < 0.01$); Values with different alphabets differ significantly at respective intervals ($P < 0.05$)

Results and Discussion

The pedal reflex, palpebral reflex and corneal reflex abolished after the induction of anaesthesia in both the groups. Intact palpebral reflex is a reliable indicator of a light level of anaesthesia while its absence indicates a medium or deep level of anaesthesia as also reported by Tranquilli *et al.*, (2007). Induction of anaesthesia with thiopentone resulted in complete loss of palpebral reflex and pedal reflexes (score 4) in both groups indicating that surgical plane of anaesthesia has reached after induction of anaesthesia.

Corneal reflex, is the blinking induced by gently touching the cornea, is variable, but is usually lost shortly after the palpebral reflex is abolished. After administration of thiopentone corneal reflex abolished in both the groups completely indicating that surgical plane of anaesthesia has reached after induction of anaesthesia. There were occasional and very weak reflexes shown at some intervals, indicating the need to intermittent bolus administration of drugs. Pedal reflex is an indicator of the depth of analgesia and anaesthesia after anaesthetic administration. It is intact when the anaesthesia is light and is abolished when the anaesthesia is complete or deep. The loss of pedal reflex in thiopentone anaesthesia is due to general CNS depression and analgesia. The absence of salivation is needed to prevent involuntary aspiration into the respiratory tract in anaesthetized animals where swallowing reflex is lost. The atropine is used which causes the cessation of salivary secretions, which is common antisialagogue in dogs, as also recorded by Brock (2001).

Jaw tone after the administration of preanesthetic was not affected much whereas jaw tone attained a score of 3 after the induction of anaesthesia with thiopentone in both the groups. Thiopentone is a weak muscle relaxant and it doesn't cause motor blockade but muscle relaxation is produced through general CNS depression. Complete jaw relaxation (score 4) was recorded in group B from 20 min to 45 min which decreased to score of 3 at the end of observation. The abolition of jaw tone in

groups B at 20 min was observed which might due to vecuronium effect at the time when animal was in surgical plane of anaesthesia. A complete ventromedial rotation of the eye ball was recorded after induction of anaesthesia with thiopentone in group A and eyeball came to central position after vecuronium injection in group B.

In group A, evoked TOF twitch intensity remained at its base value score of 1 throughout the anaesthesia. This is due to absence of neuromuscular blockade. Group B animals at 5, 10, 15, 20, 25, 30 and 35 min had significant neuromuscular blockade compared to animals of group A. (Fig. 1). The use of vecuronium, which is a neuromuscular blocker, caused sufficient muscle relaxation in group B. The dose of NMBA vecuronium used in the present study, never lead to score of 5. There will be respiratory paralysis when more than 2 twitches (score 5) in TOF are absent, which necessitates mechanical ventilation. As the diaphragm is less sensitive compared to the muscles of limbs. Thus a low dose may be enough for facilitation of fracture reduction. Maintenance dose of thiopentone was decreased in groups B than A. This follows the definition of balanced anaesthesia, a single drug may be used to achieve low level of sedation and analgesia while combined use of various drugs may be preferred as it results in minimal suppression of vital organ function, reduction of dose of individual drugs, minimize the potential side effects of any single drug and provide speedy recovery as also recorded by Heavner, (1996). Thiopentone dose for maintenance was less might be due to problems in accurately assessing the redosing time during the peak effect of vecuronium when all reflexes were blocked. Repeated doses of thiopental have a cumulative effect. Prolonged periods of anaesthesia may result from this effect if numerous doses are administered. Recovery from thiopentone anaesthesia is mainly as a result of redistribution, with metabolism and elimination playing a minor role as also narrated by Thurmon *et al.* (1994). The decrease in thiopentone maintenance dosing in group B was responsible for the early

recovery and early sternal recumbency than group A. The higher standing time in group B than group A might be because of residual effect of neuromuscular blocking agent

vecuronium because no reversal of neuromuscular blockade was done in the present study.

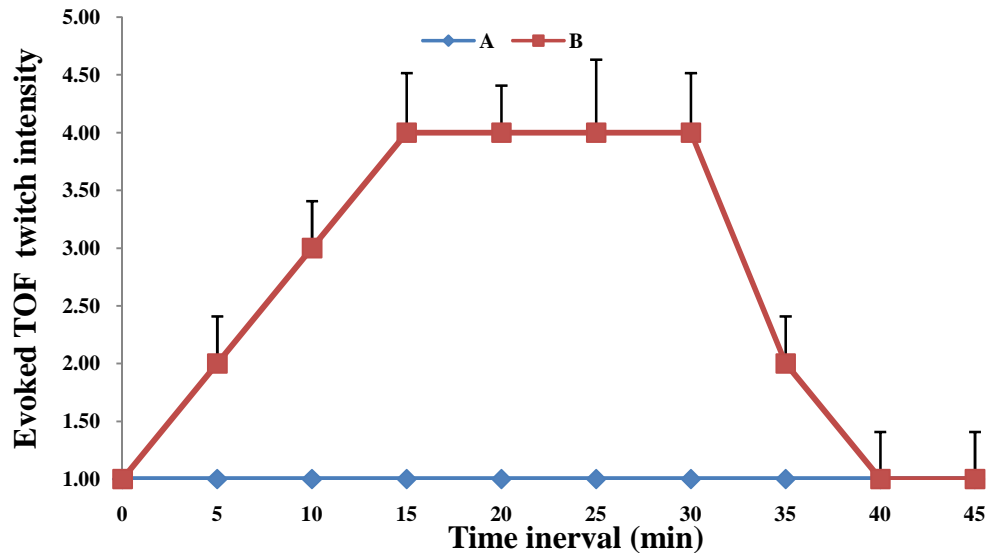


Fig. 1 : Median \pm SD values for evoked train of four (TOF) twitch intensity score in groups A and B at different intervals

Apart from the quality of anaesthesia, the haemodynamic effects of an anaesthetic agent have an important role in determining the outcome during and after anaesthesia as also reported by Adetunji *et al.* (2002). In this study HR increased in both the groups from the baseline values after the induction of anaesthesia but HR remained within the normal physiological range. This finding could be explained by ability of thiopentone to reduce vagal tone and increase in sympathetic tone as also reported by Haberer *et al.* (1993). Use of atropine as preanaesthetic agent might have also caused the heart rate to increase as found by Brock (2001). Similar findings were also reported after the administration of thiopentone in dogs by Muhammad *et al.* (2009). Vecuronium shows a low propensity to liberate histamine and possesses a negligible ganglionic blocking action; hence cardiovascular side effects are unlikely to be seen during clinical use. Decrease in RR after thiopentone administration may be due to depression of respiratory center of the brain. Relaxation of respiratory muscles by

vecuronium might have caused the respiration rate to decrease further than group A.

Rectal temperature decreased significantly in both the groups. During anaesthesia, the factors known to contribute to the development of hypothermia include the anaesthetic agents in use, patient physical status, surface area of the surgical preparation, operative site, anaesthetic depth, length of surgery, infusion of cold fluids and environmental temperature.

In the present study non-significant increase in blood pressure occurred, which is in agreement to Rawlings and Kolata (1983), who have found that, by 5 min after administration of thiopental, heart rate, aortic pressure, peripheral vascular resistance, and left ventricular systolic and end-diastolic pressures increase. Sympathetic tone and catecholamines are increased during induction of anaesthesia with thiopentone, which results in an increased HR and blood pressure. The study revealed a non-significant difference in MAP values between groups at all time intervals might be due to minimal effect of vecuronium on haemodynamic

parameters as also narrated by Hall *et al.* (2001).

Low pulse oximeter readings are indicative of reduced arterial oxygenation and diminished tissue perfusion. However, vasoconstriction may also lead to low pulse oximeter readings as also reported by Leppanen *et al.* (2006). No significant changes were seen in the haemoglobin saturation of both the groups. The RR decreased significantly in vecuronium group (group B) but supplemental 100% oxygen was given in these cases, which maintained their SpO₂ values close to the baseline values.

Conclusions

It was concluded that Vecuronium can be used with thiopentone anaesthesia to increase muscle relaxation without further affecting cardiac, respiratory and haemodynamic parameters in dogs. Vecuronium might have a dose sparing effect on the maintenance dose of thiopental in canine orthopaedic surgeries. In conclusion, thiopentone-vecuronium combination needs further investigations and studies to consider it safe for use in dogs.

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