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Observations on tiletamine-zolazepam-butorphanol-dexmedetomidine anaesthesia in six dogs undergoing various surgeries

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Abstract

Six client-owned dogs which underwent various surgical procedures under multimodal general anaesthesia with meloxicam premedication (0.2mg/kg IM), and induction thirty minutes later with a combination of tiletamine-zolazepam (2 mg/kg), butorphanol (0.2 mg/kg) and dexmedetomidine (5 mcg/kg) and administered intramuscularly, were studied. The signs of sedation and induction of anaesthesia, and their respective times of onset were observed and recorded. All animals received 100% oxygen through an endotracheal tube connected to a breathing circuit of anaesthesia machine. The quality of induction, quality of surgical anaesthesia and response to intraoperative surgical stimuli were noted and recorded. Prolongation of general anaesthesia, when anaesthesia becomes lighter, was done using isoflurane in oxygen with or without propofol. All observations were recorded, and the findings are reported here.

Keywords: *Multimodal general anaesthesia, tiletamine-zolazepam, butorphanol, dexmedetomidine, isoflurane*

Balanced anaesthesia involves the concept of administering small amount of several drugs targeting different components of the anaesthesia, namely unconsciousness, analgesia and muscle relaxation (Brown *et al.*, 2018). The principle of balanced anaesthesia is the current accepted method of anaesthesia which helps in maximising the desired effects and minimising the

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undesired effects of each drug, since all side effects are dose dependent (Sooryadas *et al.*, 2019). Tiletamine-zolazepam has been recently introduced as the sole veterinary anaesthetic, and studies on the drug combination are relatively unpopular. The current observations were recorded with the aim of studying the effects of a combination of tiletamine-zolazepam, butorphanol and dexmedetomidine for anaesthesia in dogs undergoing various surgeries, and the observations are reported here.

Materials and methods

Six client-owned dogs which underwent various surgical procedures under general anaesthesia following premedication with meloxicam, and later induction with a combination of dexmedetomidine, butorphanol and tiletamine-zolazepam were studied. These dogs were serially numbered from D1 to D6. All the dogs received meloxicam @ 0.2 mg/kg intramuscularly as pre-emptive analgesic. Thirty minutes later, all the dogs received an intramuscular injection with a combination of tiletamine-zolazepam @ 2 mg/kg , butorphanol @ 0.2 mg/kg and dexmedetomidine @ 5 mcg/kg administered in a single syringe for induction of anaesthesia. They were then left undisturbed in a calm and dark environment and monitored for the signs associated with sedation. The signs of sedation and their respective time of onset were observed and recorded. The time in minutes from administration of the anaesthetic combination to loss of righting reflex and abolition of jaw muscle tone was noted and recorded as the time taken for sedation. The time taken from administration of the combination to loss of laryngeal reflexes permitting endotracheal intubation was noted and recorded as the time taken for induction of anaesthesia. All the animals were observed for quality of induction, quality of surgical anaesthesia and response to intraoperative surgical stimuli. The time from induction to attainment of lighter surgical anaesthesia, or animal regained consciousness was recorded as the duration of surgical anaesthesia. Prolongation of general anaesthesia was managed using isoflurane with or without propofol. The doses were noted and recorded. All observations were recorded and interpreted.

Results and discussion

The dogs studied aged from 7 months to 9 years, weighing between 4 kg to 24.2 kg. They were of different breeds. Males and females were in equal proportion. They were classified as ASA I (n=2), ASA II (n=3) and ASA III (n=1). Three were aggressive while the rest were calm. The details about signalment, temperament and surgical procedures underwent by the dogs studied are presented in Table 1.

Signs associated with sedation were staggering gait (n=4), salivation (n=2), side to side head movements (n=5), ptosis, head down, sternal recumbency and lateral recumbency (n=6). The signs associated with

Table 1. Signalment and surgical procedure

Dog no.	Breed	Age	Sex	Body weight	ASA Class	Temperament	Surgical condition/ surgical procedure presented for
D1	Mixed breed	9 years	Male	10 kg	III	Aggressive	Aural Haematoma
D2	Non-descript	4 years	Female	17.4 kg	I	Active	Ovariohysterectomy
D3	German Shepherd	2 years	Male	24.2 kg	II	Aggressive	Hip dislocation correction
D4	Beagle	7 months	Female	10.9 kg	I	Calm	Bilateral cherry eye
D5	Lhasa apso	1 year	Male	4 kg	II	Highly aggressive	Tail amputation
D6	Spitz	1 year	Female	6.5kg	II	Calm	Femur fracture repair – Intramedullary pinning

Fig. 1. Sedation

sedation were partly in accordance with the observations made by Savas *et al.* (2001) who observed paddling of limbs, salivation, head rocking and tongue curling in a dog anaesthetised with tiletamine-zolazepam @ 10mg/kg intramuscularly. The profound sedation achieved could be attributed to the synergistic effects of dexmedetomidine (Gertler *et al.*, 2001), butorphanol (Demirkan *et al.*, 2002) and tiletamine-zolazepam (Cullen and Reynoldson, 1997). The time taken for sedation – judged by attainment of lateral recumbency with loss of righting reflex and relaxation of abdominal muscles, following administration of the drug combination ranged from 2.16 to 5.0 minutes, with a mean ± SE value of 3.89 ± 0.42 minutes. Krimins *et al.* (2012) reported 5.1 ± 0.8 minutes for attaining lateral recumbency in young-adult dogs following intramuscular injection with a combination of dexmedetomidine (7.5mcg/kg), butorphanol (0.15mg/kg) and tiletamine-zolazepam (3mg/kg). The time taken for sedation in the dogs studied was lesser than that reported by Krimins *et al.* (2012). Lesser time taken for attaining sedation could be due to the reason that the dogs studied were having clinical conditions which made them sick, contrary to healthy young adult dogs which formed the subjects of the study by Krimins *et al*. (2012) The observations on signs associated with sedation and their respective times are presented in Table 2, and animal showing signs associated with sedation is shown in Fig. 1.

Pedal reflex, palpebral reflex, jaw muscle tone and abdominal tone disappeared during the course of induction of anaesthesia, in all the dogs studied. The eyeballs rolled ventromedially in all the dogs, either towards attainment of anaesthesia or later. Intubation was easy in all the dogs upon induction of anaesthesia. Following intubation, all the dogs received oxygen through an appropriate breathing circuit connected from an anaesthesia machine. The time taken for the animals to get anaesthetised – judged by abolition of laryngeal reflexes permitting endotracheal intubation, ranged from 7.75 to 11.5 minutes

Table 2. Signs associated with sedation and time taken for sedation

Dog ID	Signs preceding sedation and their respective time from administration of the anaesthetic combination						
	Staggering gait (min)	Salivation (min)	Ptosis (min)	Head movements (min)	Head down (min)	Sternal recumbency (min)	Lateral recumbency/ Time taken for sedation (min)
D1	1.83	Not exhibited	4.5	3.75	4.67	1.9	5.0
D2	1.67	Not exhibited	3.0	Not exhibited	3.2	2.0	3.2
D3	Not exhibited	Not exhibited	4.18	4.0	4.28	3.75	4.5
D4	2.12	2.25	2.83	2.75 (along with paddling movements)	3.5	3.5	4.0
D5	1.0	Not exhibited	1.75	1.28	1.91	1.66	2.16
D6	Not exhibited	2.67	3.2	3.0	3.67	2.25	4.5
Mean ± SE							3.89 ± 0.42

with a mean ± SE of 9.81 ± 0.61 minutes. Anaesthetic induction following intramuscular administration of the drug combination was judged as smooth in all six dogs studied, based on uneventful and smooth transition from consciousness to unconsciousness, with easy and smooth intubation. Good quality of sedation and induction of anaesthesia was also observed by Manasa *et al.* (2021). Krimins *et al.* (2012) in their study on dexmedetomidine-butorphanol-tiletamine-zolazepam combination in dogs reported that endotracheal intubation could be completed in all dogs in less than or equal to 7 minutes following intramuscular injection. Verma *et al.* (2019) reported that the time taken for induction of anaesthesia in dogs was 7.33 ± 3.72 minutes following intramuscular injection of dexmedetomidine-butorphanol-midazolam-ketamine combination. The authors also reported that induction was smooth following injection of the combination. The smoothness of induction of anaesthesia in the dogs studied correlated well with the findings reported above. The time taken for abolition of pedal reflex, palpebral reflex, jaw muscle tone and abdominal tone, ventromedial rotation of eyeballs and the time taken for induction of anaesthesia are presented in Table 3. Animal after induction and endotracheal intubation is shown in Fig. 2.

Fig. 2. Upon induction and endotracheal intubation

Heart rate and pulse rate were found reduced in all dogs following induction of anaesthesia, which later increased during surgical stimulation. Strength of the pulse was judged as good at all time periods, suggesting that all dogs had good pulse pressure and thereby adequate tissue perfusion. The observations on heart rate and rate and character of pulse following induction can be attributed to the increase in systemic vascular resistance following peripheral vasoconstriction and thereby increase in blood pressure and reflex reduction in heart rate associated with administration of dexmedetomidine (Murrell and Hellebrekers, 2005). Increase in heart rate and pulse rate observed later could be due to increase in sympathetic tone caused by surgical stimulation (Latson and O'Flaherty, 1993). The rate of respiration was within normal limits in all the dogs, and this observation was similar to that of Shravya *et al.* (2018). However, the character of respiration observed was shallow in three dogs (D2, D4 and D6) following induction of anaesthesia to till recovery. Since the shallow respiration did not maintain ideal end tidal carbon dioxide tensions in three dogs, assisted respiration was done by squeezing the reservoir

Table 3. Time taken for induction of anaesthesia and abolition of reflexes

Dog ID	Pedal reflex abolished (min)	Palpebral reflex abolished (min)	Jaw muscle tone abolished (min)	Abdominal tone abolished (min)	Ventromedial deviation of eyeballs (min)	Time taken for induction/ endotracheal intubation (min)	Quality of induction
D1	7.0	15.0	8.0	7.0	9.0	11.0	Smooth
D2	4.0	4.1	7.0	6.0	4.18	7.75	Smooth
D3	8.0	12.5	9.0	8.0	9.5	10.5	Smooth
D4	6.91	9.6	9.33	4.83	5.0	11.5	Smooth
D5	5.67	10.83	8.0	5.83	11.25	9.0	Smooth
D6	7.83	14.67	7.5	5.34	14.25	9.83	Smooth
Mean ± SE						9.81 ± 0.61	

bag to peak inspiratory pressures of 15 to 20 cm H_2O at a rate of 4 to 15 times per minute, to maintain eucapnea. The reduction in respiration noticed in the three dogs could be attributed to the suppression of respiratory centre by the anaesthetic drugs. Krimins *et al.* (2012) also observed the development of hypoventilation and respiratory acidosis in dogs anaesthetised with dexmedetomidine-butorphanol-tiletamine-zolazapam combination. According to Ko (2013), hypoventilation occured as a result of CNS depression at the respiratory centre caused by the anaesthetic drugs, and can be easily managed by assisting ventilation. Values of peripheral oxygen saturation of haemoglobin were within normal limits in 5 out of the 6 dogs studied. It was found low in one dog (D2) following induction and later till recovery. The lower values could be due to errors in the pulse oximetry readings due to peripheral vasoconstriction caused by dexmedetomidine (DeMeulenaere, 2007). Capillary refill time was observed to be less than 2 seconds in all the dogs following induction and later till recovery.

Anaesthesia became light at, 37 minutes in D1 (undergoing surgery for haematoma auris), 42 minutes in D4 (undergoing surgery for bilateral cherry eye) and 43 minutes in D6 (undergoing surgery for femur fracture repair) following induction of anaesthesia. Isoflurane was administered (1-1.5%) in oxygen, upon anaesthesia getting light, to deepen the plane of anaesthesia and prolong its duration till the end of the surgical procedure. In the dog undergoing tail amputation (D5), anaesthesia became light during disarticulation of coccygeal vertebrae (15th minute), which required intravenous administration of propofol to deepen anaesthesia prior to maintenance with isoflurane (1%) in oxygen. Propofol required calculated to 1 mg/kg. The dog that underwent correction of hip dislocation (D3) exhibited signs of nociception during reduction of the dislocation (13th minute). Signs of nociception disappeared after reduction of the dislocated hip. The dog that underwent ovariohysterectomy (D2) did not show any signs of nociception during surgery. Latest concepts related to anaesthesia state that nociceptive pathways have strong connections with arousal pathways (Brown *et al.*, 2018; Sooryadas *et al.*, 2019) The observations on anaesthesia getting light at various time periods in dogs D1, D4, D5 and D6 could be attributed to the severity of painful stimuli associated with their respective surgical procedures. Animal upon recovery is shown in Fig. 3.

Fig. 3. Recovery

Recovery from anaesthesia was smooth in 3 dogs (D2, D3 and D6), rough in one dog (D1), while two dogs (D4 and D5) showed transient delirium. Dogs D2 and D3 which did not receive propofol or isoflurane for prolongation and/or maintenance of anaesthesia, recovered at 53 minutes and 40 minutes respectively following induction of anaesthesia with the injectable combination. Recovery was smooth in both these animals. Dogs D1, D4, D5 and D6 which received isoflurane for prolonging and maintenance of anaesthesia recovered at 7, 10, 8 and 20 minutes following weaning from isoflurane. Recovery was smooth in one of these dogs (D6). Dogs D4 and D5 showed vocalisation and paddling upon recovery, which was transient and was rough in dog D1. Emergence delirium and stormy recoveries were reported with tiletamine-zolazepam and isoflurane (Cullen and Reynoldson, 1997; Donaldson *et al.*, 2000; Savvas *et al.*, 2005).

Conclusion

The observations on sedation, induction and duration of surgical anaesthesia following intramuscular administration of tiletamine-zolazepam-butorphanol-dexmedetomidine combination in dogs undergoing various surgical procedures are reported here. The combination provided smooth induction of anaesthesia and provided surgical anaesthesia for varying periods ranging from 15 to 53 minutes. Respiratory depression was noticed in three dogs which could be easily managed by squeezing the reservoir bag to assist ventilation. Prolongation of general anaesthesia, when anaesthesia becomes lighter, was done using isoflurane in oxygen with or without propofol. Recovery was smooth in three dogs. Short period of vocalisation and paddling were observed in the rest. From the findings in this study, it could be concluded that, the anaesthetic drug combination provides adequate multimodal surgical anaesthesia for varying durations for various soft tissue and orthopaedic procedures. The duration of surgical anaesthesia vary depending on the level of surgical pain involved in the procedure. Respiratory depression may happen in some dogs with this combination, and it is recommended to manage this by assisting ventilation using an ambu bag or reservoir bag of the anaesthesia machine. For procedures lasting long durations or for procedures involving severe pain, analgesic and muscle relaxant effects achieved need to be sustained. This could be done by maintaining plasma levels of the respective drugs through continuous rate infusions, and more studies would be required in this regard.

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Conflict of interest

The authors declare that there is no conflict of interest in this work.

References

Brown, E.N., Pavone, K.J. and Naranjo, M. 2018. Multimodal general anesthesia: theory and practice, *Anaesth. Analg.* **127**: 1246-1258.

Cullen, L.K. and Reynoldson, J.A. 1997. Effects of tiletamine/zolazepam premedication on propofol anaesthesia in dogs. *Vet. Rec.* **140** (14): 363-366.

DeMeulenaere, S. 2007. Pulse oximetry: uses and limitations. *J. Nurse Pract.* **3** (5): 312-317.

Demirkan, İ., Atalan, G., Gökce, H. İ., Özaydin, İ. and Çelebi, F. 2002. Comparative study of butorphanol-ketamine HCl and xylazine-ketamine HCl combinations for their clinical and cardiovascular/respiratory effects in healthy dogs. *Turk. J. Vet. Anim. Sci*. **26** (5): 1073-1079.

Donaldson, L.L., Dunlop, G.S., Holland, M.S. and Burton, B.A. 2000. The recovery of horses from inhalant anesthesia: a comparison of halothane and isoflurane. *Vet. Surg.* **29** (1): 92-101.

Gertler, R., Brown, H.C., Mitchell, D.H. and Silvius, E. N. 2001. Dexmedetomidine: a novel sedative-analgesic agent. *Proc. Bayl. Univ. Med. Cent.* **14** (1): 13-21.

Ko, J. C. 2013. *Small Animal Anaesthesia and Pain Management*. (2nd Ed.) Manson Publishing, London, UK, 336p.

Krimins, R.A., Ko, J.C., Weil, A.B. and Payton, M.E. 2012. Evaluation of anesthetic, analgesic, and cardiorespiratory effects in dogs after intramuscular administration of dexmedetomidine–butorphanol–tiletamine-zolazepam or dexmedetomidine-tramadol-ketamine drug combinations. *Am. J. Vet. Res.* **73** (11): 1707-1714.

Latson, T.W. and O’flaherty, D. 1993. Effects of surgical stimulation on autonomic reflex function: assessment by changes in heart rate variability. *Brit. J. Anaesth.* **70** (3): 301-305.

Manasa, M.R., Dileepkumar, K.M., Anoop, S., Ramankutty, S., Beena, V. and John Martin, K.D. 2021. Evaluation of haematological and serum biochemical profile of propofol induced isoflurane anaesthesia in geriatric dogs premedicated with diazepam and butorphanol. *J. Vet. Anim. Sci.* **52** (1): 81-84.

Murrell, J.C. and Hellebrekers, L.J. 2005. Medetomidine and Dexmedetomidine: a review of cardiovascular effects and antinociceptive properties in the dog. *Vet. Anaesth. Analg.* **32**: 117-127.

Savvas, I., Plevraki, K. and Raptopoulos, D. 2001. Aerophaia and gastric dilation following tiletamine/zolazepam anaesthesia in a dog. *Vet. Rec.* **149** (1): 20-21.

Savvas, I., Plevraki, K., Raptopoulos, D. and Koutinas, A.F. 2005. Blood gas and acid–base status during tiletamine/zolazepam anaesthesia in dogs. *Vet. Anaesth. Analg.* **32**: 94–100.

Shravya, G.S., Amritha, A., Jayakumar, C., Kurien, M.O., Martin, J. and Mercey, K.A. 2018. Effect of Anaesthetic Protocols on Dam in Canine Emergency C-section. *J. Vet. Anim. Sci.* **49**(2): 54-58.

Sooryadas. S., Verma, A., Souljai J.S., Varghese, R., and Jineshkumar, N.S. 2019. Theory of multimodal balanced anaesthesia and its practice. *J. Indian. Vet. Assoc.* **17**(3): 7-11.

Verma, A., Sooryadas, S., Dinesh, P.T. and George, C. 2019. Evaluation of dexmedetomidine-butorphanol-midazolam-ketamine (DBMK) balanced anaesthesia in dogs. *J. Indian Vet. Assoc.* **17**: 56-58. ■