Indian J. Vet. Surg. 46(1): 1-6 June 2025

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Effects of fentanyl-propofol co-induction and maintenance with constant rate infusion of dexmedetomidine-fentanyl-lignocaine-ketamine along with variable rate infusion of propofol in dexmedetomidine-midazolam-ketamine premedicated dogs

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DOI: 10.5958/0973-9726.2025.00001.8 *Received: February 2025*

The study was conducted in 10 apparently healthy adult dogs categorised as ASA class I or II without considering age and gender presented for elective surgeries. After premedication with meloxicam (0.2 mg/kg body wt.), all the animals were sedated with dexmedetomidine (2 mcg/kg body wt.), midazolam (0.2 mg/kg body wt.), and ketamine (3 mg/kg body wt.) given intravenously. Upon sedation, co-induction was done intravenously using fentanyl (5 mcg/kg body wt.) followed by propofol administered 'to effect'. After intubation and oxygen supplementation, lignocaine (2 mg/kg body wt.) was given as a loading dose. Anaesthesia was maintained using a constant rate infusion (CRI) of dexmedetomidine 2 mcg/kg/hr), fentanyl (5 mcg/kg/hr), lignocaine (50 µg/kg/min), and ketamine (40 µg/kg/min) along with a variable rate infusion of propofol, titrated as needed.

Sedation was achieved within 2.10±0.46 min, and anaesthetic maintenance lasted between 86 min and 239 min. Recovery was smooth in 90% of cases, occurring within 13.30±3.84 min after cessation of CRIs. Profound muscle relaxation, analgesia, and unconsciousness were achieved. A transient reduction in heart rate, respiratory rate, and blood pressure was observed post-induction, but mean arterial blood pressure remained adequate for tissue perfusion. In five animals with post-induction apnoea, fluctuations in the end-tidal carbon dioxide (ETCO,) and tidal volume indicated respiratory depression, necessitating assisted ventilation. To conclude, the balanced TIVA protocol demonstrated a safe, effective, and well-tolerated anaesthetic approach for canine surgical patients.

Key words: *Balanced anaesthesia, Constant Rate Infusion, Dexmedetomidine, Fentanyl, Ketamine, Lignocaine, Midazolam, Propofol*

Total intravenous anaesthesia (TIVA) provides significant advantages over inhalation anaesthesia in dogs by reducing exposure hazards and improving haemodynamic stability. This protocol follows a balanced anaesthetic approach, utilising multiple drugs to achieve key objectives such as induction, maintenance, analgesia, sedation, and muscle relaxation while minimising the adverse effects of individual agents.

Propofol produces rapid onset and short duration of anaesthesia with fast recovery, although it may cause dose-dependent respiratory depression and hypotension. Fentanyl ensures potent analgesia, reducing the overall anaesthetic requirement, while dexmedetomidine provides sedation and sympatholysis. Ketamine, as an N-methyl-D-aspartate (NMDA) antagonist, contributes to dissociative anaesthesia and profound analgesia, while midazolam enhances anxiolysis and amnesia. Additionally, lignocaine, a local anaesthetic, helps lower anaesthetic demand while offering mild cardiovascular stimulation with minimal respiratory depression.

The objective of the present study was to evaluate a balanced anaesthetic protocol by incorporating fentanyl, midazolam, dexmedetomidine, ketamine, lignocaine, and propofol for total intravenous anaesthesia in dogs.

Materials and Methods

The study was conducted in 10 apparently healthy adult dogs, irrespective of their age, gender and body weights, categorised as American Society of Anaesthesiologists (ASA) class I or II, which required general anaesthesia for various elective surgical procedures. Thirty minutes after the administration of meloxicam (0.2 mg/kg body wt.) as a pre-emptive analgesic, premedication was done using a combination of dexmedetomidine (2 mcg/kg body wt.), midazolam (0.2 mg/kg body wt.), and ketamine (3 mg/kg body wt.) combined in a single syringe and administered intravenously. Upon sedation (judged by attainment of lateral recumbency with loss of righting reflex and relaxation of abdominal muscles), co-induction was done using fentanyl (5 mcg/kg body wt.) given intravenously, which was immediately followed by propofol

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administered intravenously 'to effect', permitting endotracheal intubation. Propofol 2 mg/kg and extended at 1:1 (v:v) ratio using normal saline was loaded in 5 mL syringes and administered 0.2 mL/kg/min for induction of anaesthesia 'to-effect'. The animals were then connected to a suitable breathing circuit from the anaesthesia machine to provide 100% oxygen.

The constant rate infusion (CRI) of dexmedetomidine, fentanyl, lignocaine, and ketamine were prepared as a single solution in an infusion bottle, while propofol was prepared as a separate solution in another infusion bottle. The rate of flow of fentanyl, dexmedetomidine, lignocaine, and ketamine CRI was taken as 3 mL/kg/hr.

The patient received dexmedetomidine 2 mcg/kg/hr, fentanyl 5 mcg/kg/hr, lignocaine 50 mcg/kg/min, and ketamine 40 mcg/kg/min.

The CRI of propofol was prepared as per the steps mentioned below:

The preparation of propofol was made based on the rule of six (Burtles, 1991). For each kg of body weight of the animal, 6 mg of propofol was taken and made up to 100 mL by adding normal saline, so that administering one mL/hr of preparation would provide the drug at one mcg/kg/min. The initial flow rate of the propofol variable rate infusion was set at a rate of 5 mL/hr, and this was administered and titrated 'to effect' as needed.

Additional fluid requirement of the animal so as to fulfil the requirement of 10 mL/kg/hr intraoperatively was met by administering an additional infusion of fluid through another intravenous catheter.

Following anaesthetic induction and intubation, a loading dose of lignocaine (2 mg/kg body wt.) was administered intravenously. Soon after, the CRI of dexmedetomidine, fentanyl, lignocaine and ketamine was administered 3 mL/kg/hr using the volumetric infusion pump to deliver dexmedetomidine 2 mcg/kg/hr, fentanyl 5 mcg/kg/hr, lignocaine 50 mcg/kg/min and ketamine 40 mcg/kg/min. Concurrently, the variable rate infusion of propofol solution was initiated @ 5 mL/hr using another volumetric infusion pump and was titrated 'to effect' as needed.

During the study, unconsciousness getting lightened intraoperatively was managed with bolus dose that exhibited nociception intraoperatively were administered microdose(s) of ketamine, dexmedetomidine, or fentanyl as the case warranted. The doses of the drugs thus administered were recorded.

The animals' eyes were protected from drying by application of lubricant eye ointment immediately after induction of anaesthesia. All the animals were monitored by the same individual from the induction of anaesthesia up to recovery. The anaesthetic and physiological parameters were recorded.

Signs like salivation, ptosis, head movements, head down, sternal recumbency, loss of righting reflex, and lateral recumbency associated with sedation recorded. Time taken for sedation was noted as the time (in min) taken from intravenous administration of dexmedetomidine, midazolam, and ketamine to attainment of lateral recumbency with loss of righting reflex. Quality of sedation and induction of anaesthesia was judged based on the smoothness of sedation and ease of induction of anaesthesia and was graded as excellent, good, moderate, or poor. Subjective analysis of depth of anaesthesia achieved was done based on the presence or absence of reflexes namely palpebral reflex, pedal reflex, skeletal muscle relaxation (loss of abdominal tone and jaw tone, resistance to open jaw and resistance to passive flexion of limbs), position of eyeball (central or ventro-medial), nystagmus and intraoperative nociception. Any unexpected observation was recorded separately. Quality of maintenance of anaesthesia was judged based on analgesia achieved, degree of muscle relaxation, absence of response to surgical stimuli, and maintenance of physiological parameters, and was graded as excellent, good, moderate, or poor. The signs like return of eye ball to centre, return of pedal reflex, rejection of endotracheal tube, head lift, sternal recumbency, and standing unassisted were noted and recorded. The time taken for recovery was noted as the time period in minutes from the stoppage of CRIs to the rejection of the endotracheal tube. The quality of recovery was judged based on the character of transition from anaesthesia to consciousness, and was graded as smooth, moderate, or rough. Duration of anaesthetic maintenance was taken as the time in minutes from initiation to weaning of CRI. Duration of anaesthesia was taken as the time in minutes from induction of anaesthesia to rejection of the endotracheal tube. The dose of propofol (mg/kg body wt.) which was administered intravenously 'to effect' for induction of anaesthesia, facilitating endotracheal intubation by the abolition of jaw muscle tone, was noted and recorded. The average CRI dose of propofol (mcg/kg/min) used in this study for each patient was calculated by adding up the total amount (mcg) of the drug administered for each patient during maintenance including both CRI and bolus amount of drug, and dividing the value by body weight of the patient and the time (min) for which the CRI was administered. The total quantity of each drug (mg or mcg) used for a patient throughout anaesthesia was noted and recorded.

Physiological parameters monitored included rectal temperature (°C), heart rate (beats per min), pulse rate (per min), respiratory rate (breaths per min) and the character of respiration, peripheral oxygen saturation (per cent), end tidal carbon dioxide ($ETCO_2$) (mmHg), invasive blood pressure (IBP), electrocardiogram (ECG) and capillary refill time were

noted and recorded before induction, after induction and every 10 min thereafter throughout the anaesthetic period until recovery. Haematological parameters analysed before induction of anaesthesia and 15 min after included total erythrocyte count (10^6/μL), total leukocyte count (10^3/μL), differential leukocyte count (per cent), haemoglobin concentration (g/dL), and volume of packed red cells (per cent). Serum biochemical parameters analysed before and after induction included alanine aminotransferase (IU/L), total protein (g/dL), and albumin (g/dL). Arterial blood gas and electrolyte analysis was performed before induction of anaesthesia, 15 min after induction and after recovery, included pH, partial pressure of oxygen (PaO_2), partial pressure of carbon dioxide ($PaCO_2$), arterial bicarbonate ion concentration (HCO^{3-}), standard base excess (BE), blood glucose (mg/dL), lactate, sodium, potassium, calcium and chloride. The data obtained during the study were analysed statistically.

Results and Discussion

Time taken for sternal recumbency and head down was 0.89±0.07 min and 1.76±0.40 min, respectively. Sedation was achieved in 2.10±0.46 min, which was shorter than 3.25±0.25 min reported by Santosh *et al.* (2013). The intravenous administration of the premedication may have contributed to the rapid attainment of sedation in the current study. This can be attributed to the lipophilic properties (Manjusha *et al*., 2023) and the rapid sedation-inducing effect of dexmedetomidine (DeGroot *et al.,* 2020).

The quality of sedation was graded as good due to the smooth and profound sedation achieved, which can be attributed to the combination of alpha-2 adrenergic agonists and ketamine, as it provides more reliable, steady, and profound sedation compared to alpha-2 agonists alone (Pan *et al*., 2021). Three animals exhibited sighing during sedation, indicating a functioning respiratory centre capable of detecting increases in PaCO2, a feature seen only in conscious or semi-conscious states (Carroll *et al*., 2008). The quality of induction of anaesthesia was also graded as good, based on smooth induction and the ease of endotracheal intubation. The co-induction protocol using fentanyl and propofol provided a smooth transition, as fentanyl citrate, a potent synthetic μ-opioid agonist, rapidly crosses the blood-brain barrier, resulting in a fast onset and short duration of action (Santosh *et al*., 2013), while propofol facilitates rapid, smooth induction with a short duration of action (Felix *et al*., 2024).

Palpebral reflex was present in all the animals during anaesthesia. This may result from the effect of propofol on dopaminergic pathways in the central nervous system or interference with glycine metabolism in subcortical structures (Sear and Foex, 1991), and increased GABA-ergic inhibition might sensitize the cortex, rendering it more susceptible to seizure-like activity (Voss *et al*., 2008). This mechanism could explain the persistence of positive palpebral reflexes noted in this study. Pedal reflex was absent in all the animals during anaesthesia. The analgesic effects of dexmedetomidine are significantly enhanced when combined with agents such as midazolam, butorphanol, fentanyl, or ketamine (Ahmad *et al*., 2018). The muscle relaxation of the limbs, abdomen, and jaw was graded as good in all animals studied, indicating a sufficient plane of anaesthesia for surgical procedures attributed to the dexmedetomidine (Tiwari *et al*., 2024) and propofol (Felix *et al*., 2024) used. All animals exhibited ventromedial positioning of the eyeballs (Bustamante *et al*., 2022) throughout the anaesthesia period, indicating an adequate and profound anaesthetic depth suitable for surgery. Intraoperative nociception was observed only during highly painful events during the surgical procedure, which included removing adhesions in hernia, skin manipulations, and the use of periosteal elevator in orthopaedic procedure. This can be attributed to dexmedetomidine (Pan *et al.,* 2021) mediated through agonism at heteroreceptors in the dorsal horn of the spinal cord (Kumar *et al.,* 2020). Pre-emptive analgesia with meloxicam ketamine, lignocaine, and CRI of lignocaine and dexmedetomidine also enhanced the analgesia achieved intraoperatively. Intraoperative nociception was managed effectively with intravenous administration of ketamine at 1 mg/kg body wt.

The time taken for return of eyeball to centre was 5.80±0.94 min, return pedal reflex was 9.60±3.59 min, head lift was 25.10±5.12 min, sternal recumbency was 32.22±16.09 min, and for standing unassisted was 124.40±19.60 min. Recovery was achieved in 13.3±3.84 min. Hypothermia and longer durations of anaesthetic maintenance using CRI are associated with prolonged recovery times (Gozalo-Marcilla and Ringer, 2021). Faster recoveries in some animals were noted, which could be attributed to increased painful surgical stimuli (Sooryadas *et al*., 2019) as nociception leads to arousal. D2 exhibited a transient delirium, which could be attributed to the low concentration of propofol at the end of anaesthesia (Jones *et al*., 2024). The duration of anaesthesia maintenance was 164.80±12.63 min and the duration of anaesthesia was 181.80±13.08 min.

The dose of propofol required for the induction of anaesthesia in this study ranged from 0.4 to 1.43 mg/kg body wt., with a mean±SE value of 1.10±0.14 mg/kg body wt. This could be attributed to the use of fentanyl (Covey-Crump and Murison, 2008) and the synergistic effect of fentanyl and medetomidine (Kanda *et al*., 2024). The average CRI dose of propofol used for the maintenance of anaesthesia was 51.54±14.83 mcg/kg/min. The reduction in dose of

propofol for maintenance can be attributed to the use of other drugs in the balanced TIVA.

The rectal temperature showed a significant reduction (P<0.01) after recovery compared to their pre-induction values, which could be the result of reduced heat production due to a decreased metabolic rate during anaesthesia, the effects of anaesthetic drugs on the hypothalamus, diminished peripheral circulation, muscle relaxation (Tiwari *et al.*, 2024), α-2 receptor activation (Bisht *et al.*, 2018) and thermoregulatory centre depression by ketamine (Ahmad *et al.*, 2013).

The heart rate showed a significant reduction (P=0.033) after induction and at recovery (Fig. 1) compared to pre-induction values, which can be attributed to the use of α2-adrenoceptor agonists (Arenillas *et al.*, 2021) causing bradycardia, second-degree atrioventricular blocks, and transient increases in arterial blood pressure due to vasoconstriction. A gradual increase in heart rate observed during recovery could be attributed to ketamine, which partially counteracts alpha-2 agonist-induced peripheral vasoconstriction (Imboden *et al.*, 2023). This can also be attributed to propofol, which reduces mean arterial pressure due to a decrease in vascular resistance, cardiac contractility, and preload, and fentanyl, which causes an increase in parasympathetic tone, bradycardia, potentially impacting cardiac index and oxygen delivery negatively (Aguilera *et al.*, 2020).

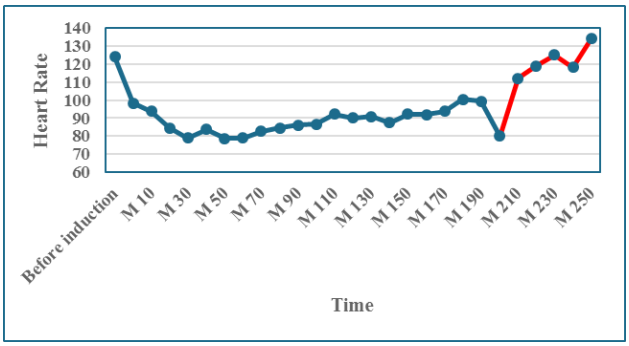

Fig. 1: Heart rate

The pulse rate showed a non-significant reduction (O=0.761) after induction and at recovery compared to pre-induction values due to the sympathetic stimulation of ketamine, which could have counteracted the bradycardia induced by the α2-adrenoceptor agonist and opioid (Ko *et al.*, 2000). The quality of the pulse was rated as good in the current study, likely due to the enhancement of haemodynamic conditions provided by ketamine infusion (Boscan *et al.*, 2005).

The respiratory rate before induction varied, with two dogs (D4 and D9) showing a range of 20-36 breaths/min., while the rest (n=8) exhibited panting. Following induction, five dogs experienced transient induction of apnoea, whereas in the others, the rate ranged from 9 to 19 breaths/min. but was shallow. End-tidal carbon dioxide (ETCO,) levels remained within the normal range (35-45 mmHg) in 8/10 animals following induction. In five animals experiencing post-induction apnoea, respiration was insufficient to maintain eucapnia. Assisted ventilation was provided to maintain eucapnia (Bustamante *et al.*, 2022), using peak inspiratory pressures of 15-20 cm H, O at rates of 4-15 breaths/min, to maintain the ETCO, at a range of 35-45 mmHg and tidal volume at a range of 6–23.75 mL/kg with an average of 14.8 mL/kg.

Peripheral oxygen saturation (SpO,) remained highly stable (Fig. 2) throughout the study, with minor fluctuations, which can be due to the vasoconstriction caused by the α-2 agonist dexmedetomidine (Kuusela *et al.*, 2000).

The mean arterial pressure (MAP) showed a significant drop (Fig. 3) immediately after induction (P=0.003) when compared to the pre-induction value, as it had negative effects on cardiac function in dogs, including decreased heart rate, mean arterial pressure, myocardial contractility, and preload mediated by vasodilation in a dose-dependent manner (Kanda *et al.*, 2024). Heamodynamic stability observed in the current study can also be attributed to ketamine (Henao-Guerrero and Ricco, 2014) and the continuous infusion of medetomidine (Carter *et al.*, 2010), which helped maintain optimum MAP (> 60 mm Hg) and tissue perfusion (Ko, 2018).

The electrocardiogram (ECG) findings indicated a significant reduction in heart rate following

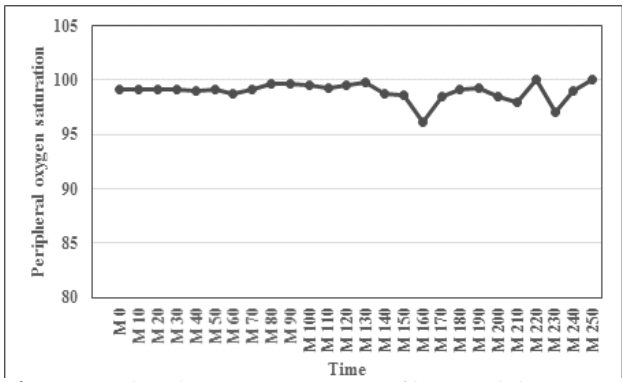

Fig. 2: Peripheral oxygen saturation of haemoglobin (SpO,)

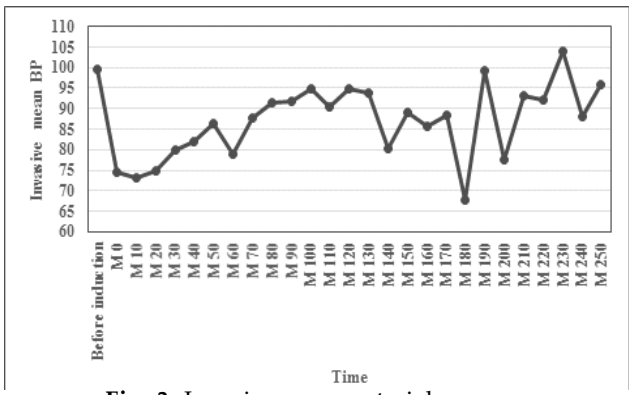

Fig. 3: Invasive mean arterial pressur

induction in all the animals studied. Capillary refill time (CRT) remained less than 2 seconds (Girard *et al.*, 2010) throughout the duration of anaesthesia in all the animals.

There was a significant decrease (P<0.05) in Alanine Aminotransferase (ALT) values after recovery when compared to baseline values before induction. The decrease in ALT values might be attributed to increased MAP and adequate organ perfusion resulting from the anaesthetic drugs used. No significant change was noted in total protein (P>0.05), albumin (P>0.05) and globulin (pP>0.05) during the different stages of anaesthesia.

Blood pH showed a significant decrease, from pre-induction values after induction and after recovery (P<0.001), which could be due to fentanyl and propofol, which induce dose-dependent respiratory depression (Vasileiou *et al.,* 2009) and sympathomimetic effects of ketamine. The respiratory acidosis observed in the present study after recovery may also be attributed to impaired clearance of carbon dioxide from the alveoli, which occurred following extubation and rejection of the endotracheal tube.

PaO, increased significantly after induction, which could be attributed to 100 per cent inspired oxygen supplied. Low FiO, (low oxygen intake), lower barometric pressure (e.g. high altitude), hypoventilation (increased PaCO) and metabolic changes affecting respiratory quotient can lead to a change in PaO, PaCO, increased significantly after induction of anaesthesia, due to the induction apnoea and the shallow respiration causing decreased carbon dioxide clearance from the body.

Bicarbonate showed a significant reduction after recovery (P=0.004) and base excess decreased significantly from pre-induction after recovery (P<0.001). Blood glucose levels showed no significant change during different stages of anaesthesia. Lactate showed no significant changes (P=0.169), with values remaining stable pre-induction, post-induction, and after recovery (Nagashima *et al*., 2022).This indicates that blood pressure management, fluid replacement, and oxygenation strategies were adequate to maintain optimum tissue perfusion during anaesthesia.

No significant variations (P=0.59) in sodium were observed during different stages of anaesthesia. Potassium levels showed no significant fluctuations throughout the study, with values of 3.80±0.15 mmol/L pre-induction, 3.82±0.09 mmol/L post-induction, and 4.10±0.09 mmol/L post-recovery (P=0.590). Similarly, calcium levels remained relatively stable, with non-significant changes (P=0.077) during different stages of anaesthesia. In contrast, chloride levels showed a significant increase after recovery (P=0.002). This increase in chloride levels might be attributed to fluid therapy and CRI with normal saline, which is known to cause hyperchloremic acidosis (Uilenreef *et al.,* 2008).

To conclude, the balanced TIVA protocol demonstrated a safe, effective, and well-tolerated anaesthetic approach for canine surgical patients. It provided stable cardiovascular function, smooth induction and recovery, and good intraoperative conditions. While respiratory depression was observed in animals with post-induction apnoea, it was manageable with assisted ventilation. The protocol ensured adequate analgesia for both soft tissue and orthopaedic procedures, with additional ketamine supplementation required for highly painful interventions. These findings highlight the potential of this balanced TIVA approach as a reliable anaesthetic technique in veterinary practice.

Acknowledgements

The authors acknowledge the support and facilities provided by the Dean, College of Veterinary and Animal Sciences, Pookode, Wayanad, Kerala for the current study.

References

Aguilera, R., Sinclair, M., Valverde, A., Bateman, S. and Hanna, B. 2020. Dose and cardiopulmonary effects of propofol alone or with midazolam for induction of anaesthesia in critically ill dogs. Vet. Anaesth. Analg. **47**: 472-480.

Ahmad, R.A. and Amarpal, Gugjoo, M.B. 2018. Dexmedetomidine: Systemic effects and clinical application in animals. Pharm. Innov. J. **7:** 272-278.

Ahmad, R.A., Amarpal, Kinjavdekar, P., Aithal, H.P., Pawde, A.M. and Kumar, D. 2013. Potential use of dexmedetomidine for different levels of sedation, analgesia and anaesthesia in dogs. Vet. Med. **58:** 87-95.

Arenillas, M., Canfrœn, S., Aguado, D. and de Segura, I.A.G. 2021. Sedative and analgesic effects of two subanaesthetic doses of ketamine in combination with methadone and a low dose of dexmedetomidine in healthy dogs. Vet. Anaesth. Analg. **48**: 545-553.

Bisht, D.S., Jadon, N.S., Bodh, D. and Kandpal, M. 2018a. Clinicophysiological and haematobiochemical effects of dexmedetomidine-propofol-sevoflurane anaesthesia in dogs. Indian J. Anim. Sci. **88**: 887-891.

Boscan, P., Pypendop, B.H., Solano, A.M. and Ilkiw, J.E.2005. Cardiovascular and respiratory effects of ketamine infusions in isoflurane-anesthetized dogs before and during noxious stimulation. Am. J. Vet. Res. **66**: 2122-2129.

Bustamante, R., Canfrœn, S., de Segura, I.A.G. and Aguado, D. 2022. Intraoperative effect of low doses of ketamine or dexmedetomidine continuous rate infusions in healthy dogs receiving propofol total intravenous anaesthesia and epidural anaesthesia: A prospective, randomised clinical study. Res. Vet. Sci. **143**: 4-12.

Carroll, L.G. 2008. Small Animal Anaesthesia and Analgesia, 1st edn. Wiley-Blackwell. p 283.

Carter, J.E., Campbell, N.B., Posner, L.P., Swanson, C. 2010. The hemodynamic effects of medetomidine continuous rate infusions in the dog. Vet. Anaesth. Analg. **37**: 197-206.

Covey-Crump, G.L. and Murison, P.J. 2008. Fentanyl or midazolam for co-induction of anaesthesia with propofol in dogs. Vet. Anaesth. Analg. **35**: 463-472.

DeGroot, W.D., Tobias, K.M., Browning, D.C. and Zhu, X. 2020. Examination of laryngeal function of healthy dogs by using sedation protocols with dexmedetomidine. Vet. Surg. **49**: 124-130.

Felix, A., Ndossi, D. and Mpanduji, D. 2024. Effects of total intravenous anesthesia using ketamine and propofol combinations on physiological and anesthetic parameters in xylazine-premedicated mixed-breed dogs. Appl. Vet. Res. **3**: 2024006-2024006.

Girard, N.M., Leece, E.A., Cardwell, J.M., Adams, V.J. and Brearley, J.C. 2010. The sedative effects of low dose medetomidine and butorphanol alone and in combination intravenously in dogs. Vet. Anaesth. Analg. **37**: 1-6.

Gozalo-Marcilla, M. and Ringer, S.K. 2021. Recovery after general anaesthesia in adult horses: a structured summary of the literature. Animals **11**: 1777.

Henao-Guerrero, N. and Riccó, C.H. 2014. Comparison of the cardiorespiratory effects of a combination of ketamine and propofol, propofol alone, or a combination of ketamine and diazepam before and after induction of anaesthesia in dogs sedated with acepromazine and oxymorphone. Am. J. Vet. Res. **75:** 231-239.

Imboden, T.J., Pownall, W.R., Rubin, S., Spadavecchia, C., Schöllhorn, B. and Rohrbach, H. 2023. Determination of a safe sedative combination of dexmedetomidine, ketamine and butorphanol for minor procedures in dogs by use of a stepwise optimization method. Acta. Vet. Scand. **65**: 41.

Jones, H., Robson, K., Maddox, T. and Alderson, B., 2024. Incidence and risk factors for poor recovery quality in dogs recovering from general anaesthesia—a prospective case control study. Vet. Anaesth. Analg. **51**: 227-234.

Kanda, T., Akashi, N., Kawamura, N., Neki, Y., Osumi, M., Sugino, R., Iwasaki, H., Kadowaki, Y. and Itoi, T. 2024. Effect of fentanyl constant-rate infusions with or without medetomidine on the minimum infusion rate of propofol required to prevent motor movement in dogs. J. Vet. Med. Sci. **86**: 266-271.

Ko, J.C., 2018. Anesthesia monitoring and management. *In*: Small Animal Anesthesia and Pain Management. 2nd edn. Veterinary Colour Handbook Series, CRC Press. pp 107-140.

Ko, J.C., Fox, S.M. and Mandsager, R.E. 2000. Sedative and cardiorespiratory effects of medetomidine, medetomidine-butorphanol, and medetomidine-ketamine in dogs. J. Am. Vet. Med. Assoc. **216**: 1578-1583.

Kumar, R., Aakanksha, A.K., Verma, N.K., Saxena, A.C. and Hoque, M. 2020. Systemic effects and clinical application of dexmedetomidine. Pharm. Innov. J. **9**: 241-246.

Kuusela, E., Raekallio, M., Anttila, M., Falck, I., Mölsä, S. and Vainio, O. 2000. Clinical effects and pharmacokinetics of medetomidine and its enantiomers in dogs. J. Vet. Pharmacol. Therap. **23**:15-20.

Manjusha, K.M., Kinjavdekar P., Amarpal, Rohit, K., Sharun K., Islam, Saxena, A.C. and Pawde, A.M. 2023. Evaluation of tiletamine-zolazepam as an induction agent for ovariohysterectomy under isoflurane anaesthesia in dogs. Indian J. Vet. Surg. **44**: 37-40.

Nagashima, J.K., Gonçalves, L.A., Pereira, M.A., Talib, M.S., de Olveira, C.M., Ambrósio, A.M. and Fantoni, D.T. 2022. Microcirculation assessment of dexmedetomidine constant rate infusion during anesthesia of dogs with sepsis from pyometra: a randomized clinical study. Vet. Anaesth. Analg. **49**: 536-545.

Pan, S.Y., Liu, G., Lin, J.H. and Jin, Y.P. 2021. Efficacy and safety of dexmedetomidine premedication in balanced anesthesia: a systematic review and meta-analysis in dogs. Animals **11**: 3254. https://doi.org/10.3390/ani11113254.

Santosh, K.M., Ahmad, R.A., Kinjavdekar, P., Aithal, H.P., Pawde, A.M. and Kumar, D. 2013. Evaluation of midazolam-ketamine with dexmedetomidine and fentanyl for injectable anaesthesia in dogs. Vet. Arh. **83**: 509-524.

Sear, J.W. and Foex, P. 1991. Is propofol the ideal anesthetic agent of the 90's? Rev. Esp. Anestesiol. Reanim. **38**: 139-140.

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

Tiwari, K., Jadon, N.S., Pandey, P. and Kandpal, M. 2024. Clinico-physiological studies of atropine-tiletamine-zolazepam-sevofluraneanaesthesia with or without dexmedetomidine premedication in dogs. Indian. J. Anim. Sci. **94** :506-512.

Uilenreef, J.J., Murrell, J.C., McKusick, B.C. and Hellebrekers, L.J. 2008. Dexmedetomidine continuous rate infusion during isoflurane anaesthesia in canine surgical patients. Vet. Anaesth. Analg. **35**: 1-12.

Vasileiou, I., Xanthos, T., Koudouna, E., Perrea, D., Klonaris, C., Katsargyris, A. and Papadimitriou, L. 2009. Propofol: a review of its non-anaesthetic effects. Eur. J. Pharmacol. **605**: 1-8.

Voss, L.J., Sleigh, J.W., Barnard, J.P. and Kirsch, H.E. 2008. The howling cortex: seizures and general anesthetic drugs. Anesth. Analg. **107**: 1689-1703.