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Evaluation of haemodynamic stability during multimodal total intravenous anaesthesia with etomidate in dogs having cardiovascular diseases

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Abstract

The present study was conducted in six dogs with the objective of evaluation of the haemodynamic stability of total intravenous anaesthesia with etomidate and constant rate infusion with ketamine-lignocaine for maintaining anaesthesia in dogs having cardiovascular diseases. The dogs presented for various surgical procedures were subjected to routine clinical examination and cardiovascular evaluation. Following this, six dogs with cardiovascular diseases, presented for various soft tissue surgical procedures, were selected for the study. The cardiovascular diseases identified were mitral valvular disease, dilated cardiomyopathy, pre-clinical dilated cardiomyopathy and left ventricular hypertrophy. All the anaesthetic medications were given intravenously. The dogs were pre-anaesthetised with butorphanol and diazepam. Etomidate was given for anaesthetic induction. Ketamine at sub-anaesthetic doses and lignocaine were given for analgesia. Injection ketamine-lignocaine was administered as CRI for maintaining analgesia. Cardiovascular stability was assessed through the monitoring of vital signs, saturation of peripheral oxygen, end-tidal carbon dioxide, blood pressure and ECG. Eye ball position, pupil size and signs of nociception were also monitored. All the anaesthetic parameters were within the physiological limit with no significant difference during different periods of observation. The present protocol provided the required cardiovascular stability for the successful completion of all the six surgeries.

Keywords: *Anaesthesia, Etomidate, Cardiovascular diseases*

The administration of anaesthesia in dogs with cardiovascular disorders poses significant challenges due to pre-existing pathophysiological alterations and the haemodynamic disturbances induced by many anaesthetic agents. They impair the ability of the circulatory system to deliver adequate oxygen for survival (Congdon, 2015). Accordingly, anaesthetic management should prioritise the preservation of cardiac output, maintenance of adequate tissue perfusion, mean arterial pressure and prevention of arrhythmia.

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Anaesthetic choice in such patients depends on clinical status, haemodynamic abnormalities, pharmacological properties of the drugs, and clinician's expertise (Perkowski & Oyama, 2015). Previous studies in canine cardiac patients have primarily employed etomidate for induction and isoflurane for maintenance, although inhalant anaesthetics are known to depress cardiovascular function. Etomidate, a GABA agonist, preserves sympathetic tone and myocardial function, producing minimal alterations in heart rate and blood pressure, making it a appropriate choice for total intravenous anaesthesia (TIVA) (Forman, 2011; Rodríguez et al*.,* 2012). Multimodal anaesthesia, which combines agents targeting different stages of the nociceptive pathway and anaesthetic states, enhances anaesthetic depth while minimising individual drug doses and adverse effects (Lersch et al*.*, 2023; Ramankutty, 2024). In this context, a protocol incorporating butorphanol, diazepam, etomidate, ketamine, and lignocaine was adopted to provide a safer anaesthesia for dogs with cardiovascular disease, particularly in geriatric patients wherein haemodynamic stability is crucial. Butorphanol is an opioid having less cardiovascular depression and have better action in older patients compared to young adults. Therefore, butorphanol is considered the pre-anaesthetic agent of choice for geriatric canine patients with cardiovascular disease. Diazepam is a muscle relaxant which does not cause considerable alterations in cardiac output (Nascimento et al*.*, 2007). Ketamine has analgesic effect at sub-anaesthetic doses (Epstein, 2015). Babu (2023) reported that constant rate infusion (CRI) of lignocaine provided good analgesia in tumour resection surgeries of geriatric dogs. There is limited published evidence on the use of etomidate-based multimodal TIVA protocols in dogs with cardiovascular disease. The present study was therefore undertaken to evaluate the effects of a multimodal TIVA on haemodynamic stability in canine patients with cardiovascular disorders.

Materials and methods

The study was carried out on six geriatric dogs of either gender, representing different breeds, aged between four and 17 years. These animals were presented to the Teaching Veterinary Clinical Complex, Mannuthy and the University Veterinary Hospital, Kokkalai. The selections of dogs were done through a comprehensive pre-anaesthetic evaluation, which included both general clinical examination and detailed cardiovascular assessment. Cardiovascular evaluation comprised auscultation, radiography, blood pressure monitoring, electrocardiography and echocardiography. According to the clinical findings and cardiovascular evaluation, six dogs with cardiovascular diseases categorised under ASA class III were selected for the study of proposed anaesthesia protocol. Food was withheld for approximately 12 hours and water for about 2 hours before the administration of anaesthesia. Dogs were anaesthetised as per the protocol given in Table 1. After induction endotracheal intubation was done in all the dogs and pre-oxygenated for one minute.

Anaesthetic protocol

Injection butorphanol at the dose rate 0.2mg/kg body weight and injection diazepam at the dose rate 0.25 mg/kg body weight were given intravenouly as pre-anaesthetics. Induction agents were given 5 minutes after pre-anaesthetic medication. Injection etomidate was given as induction agent intravenously 'to effect'. Injection ketamine at the dose 0.7 mg/kg body weight and lignocaine at the dose rate 2 mg/kg body weight were also given. After induction dogs were intubated and pre-oxygenated for one minute.

Anaesthesia was maintained using etomidate at the dose rate of 0.04 mg/kg body weight/min as intravenous infusion and etomidate bolus injection was given whenever the dog showed signs of recovery. Injection ketamine-lignocaine was administrated as constant rate infusion (CRI). Ketamine 10µg/kg/min and lignocaine 50µg/kg/min was given using volumetric infusion pump. Normal saline was added at a dose rate of 2.5 mL/kg to both the etomidate infusion and the ketamine–lignocaine infusion.

Quality of sedation was recorded after pre-anaesthetic medication. Sedation time was calculated as time from injection of butorphanol to the time when dog showed signs of sedation such as drooping of eyelid, ventral rotation of eyeball and recumbency. By observing the responses, quality of sedation was graded from zero (no effect) to three (good) (Dinesh et al*.,* 2019). Induction time was the time gap between administration of etomidate to time of disappearance of pedal reflex. Quality of induction of general anaesthesia was graded from one (poor) to four (excellent) (Dinesh et al*.,* 2019). According to Bodh et al*.* (2015) degree of muscle relaxation was graded from one to four (no relaxation to excellent). Quality of recovery was assessed by observing the behavioral changes after discontinuation of etomidate anaesthesia and was graded from 0 to 3 (poor to excellent) scales (Love et al*.,* 2013). The duration between discontinuation of etomidate and attaining unassisted standing position by the dog were recorded. Total duration of anaesthesia was calculated as the time interval between the disappearance of pedal reflex following the administration of etomidate and time of return of pedal reflex after stopping the administration of etomidate. The vital signs including rate of respiration (per minute), heart rate (per minute), capillary refill time (CRT), colour of visible mucous membrane and saturation of partial pressure of oxygen (SpO_2), end-tidal carbon dioxide concentration ($EtCO_2$), nocicepion, position of eyeball were all observed and recorded every five minutes. For ease of representation of data, the values at the beginning of anaesthesia, 15 minutes after commencement of anaesthesia (during anaesthesia) and at the end of anaesthesia are presented. Brown and

Henrik, (2016) recorded blood pressure, ECG and rectal temperature whereas Tilley and Smith, (2016) recorded ECG alone, before administration of pre-anaesthetic medication, 15 minutes after the beginning of anaesthesia (during anaesthesia) and after recovery. All the dogs were monitored till complete recovery. Surgeries were conducted in all dogs under aseptic conditions. For pre-emptive antibiotic coverage 12.5 mg/kg injection amoxicillin-sulbactum was given before the commencement of surgery. Post-operatively antibiotic and anti-inflammatory medicines were given orally. The data were analysed using SPSS VERSION 24.0. Repeated measures of one way ANOVA test was employed for statistical analysis.

Result and discussion

Time taken for sedation to set in was 4.17 ± 0.401min. Quality of sedation was good in all dogs with mean sedation score of three (good) (Hareesh, 2016). Out of the six dogs evaluated; one four year old dog (No. VI) showed fair and moderate sedation only. Andreoni and Lynne-Hughes (2009) reported that sedative effects of opioids in young adult patients were less compared to geriatric patient. The time taken for induction of general anaesthesia was 2.27 ± 0.16 min. The mean score of induction quality was three; with moderate relaxation of jaws (Chaudhary, 2021). The extent of muscle and jaw tone relaxation was evaluated as moderate with mean score three. All dogs allowed endotracheal intubation following induction despite of mild resistance for intubation. One dog showed gagging and another dog evinced myoclonus (Dar et al*.,* 2019). These symptoms were subsided by administration of bolus injection of etomidate. Total recovery time was 97.5 ± 30.39 min. This delayed recovery could be attributed to age-related physiological changes, such as decreased hepatic and renal function, reduced cardiac output, and altered body composition, which collectively impaired drug metabolism and excretion (Grubb et al*.*, 2015). Quality of recovery was graded as good in all dogs, but recovery was poor in a 17 year old dog due to hypothermia. Hypothermia was managed with intravenous administration of warm normal saline and application of hot water bag on body (Ramankutty, 2024).

According to Dewangan and Tiwari (2015) induction dose of etomidate was 1-2 mg/kg intravenously. In the present study mean induction dose of etomidate was reduced to 0.68 ± 0.16 mg/kg body weight intravenously. The reduction in induction dose was due to the effect of pre-anaesthetic medication with butorphanol and diazepam. Anaesthesia was maintained with etomidate administered as an intravenous infusion at 0.04 mg/kg/min, supplemented with intermittent bolus doses whenever recovery signs appeared, resulting in a total etomidate requirement of 0.08 ± 0.01 mg/kg/min. All the other anaesthetics were given as per the proposed protocol.

The rate of respiration and heart rate were maintained in normal physiological limit throughout the period of anaesthesia. This observation was in accordance with Ramankutty (2024) who had done the research work in multimodal anaesthesia protocol during mammary tumour resection surgeries. Rectal temperature was maintained within the physiological level before pre-anaesthetic medication and during anaesthesia. Temperature was slightly lower than the physiological limit after recovery. The findings were similar to that of Stephan (2024) who studied on multimodal anaesthesia with lignocaine CRI in dogs.

Table 1. Signalment of the dogs

Sl. No.	Dog No	Breed	Sex	Age (years)	B. wt (kg)
1	1	Spitz	F	17.017	9.0
2	II	Labrador Retriever	F	9.0	38.5
3	III	Non descript	F	9.0	25.0
4	IV	Labrador retriever	F	8.0	37.0
5	V	Labrador retriever	F	10.0	37.0
6	IV	Siberian Husky	F	4.0	30.0
			Mean	9.5±1.73	29.42 ± 4.6

Table 2. ASA classification and echocardiography

Sl. No.	Dog No.	Surgical condition	Cardiovascular disease	ASA
1	1	Mammary tumour	Mitral valvular disease	III
2	II	Lipoma	Dilated cardiomyopathy	III
3	III	Mammary tumour	Left ventricular hypertrophy	III
4	IV	Mammary Tumour	Mitral valvular disease	III
5	V	Mammary Tumour	Mitral valvular disease	III
6	VI	Mammary Tumour	Pre-clinical dilated cardiomyopathy	III

Table 3. Mean ± SE values of rate of respiration, heart rate and temperature at different time interval

Parameter	Pre-operative	Anaesthesia	Recovery
Respiration (min)	26.33 ± 3.21[a]	17.83 ± 2.56[ab]	16.00 ± 3.26[b]
Heart rate (min)	102.33 ± 8.64	104.67 ± 8.86	102.67 ± 12.8
Temperature (°C)	38.50 ± 0.21[a]	38.16 ± 0.23[ab]	37.78 ± 0.26[b]

Means bearing different superscripts (a, b) differ significantly at 5% level of significance

Table 4. Mean ± SE values of SpO_2 and $EtCO_2$ at different time interval

Parameter	Beginning Anaesthesia	During Anaesthesia	End of Anaesthesia
SpO_2 (%)	98.00 ± 0.76	98.43 ± 0.69	98.71 ± 0.57
$EtCO_2$ (mmHg)	34.34 ± 1.43	33.14 ± 0.74	34.86 ± 0.99

Capillary refill time was less than two seconds in all the dogs throughout the anaesthesia. This was an indication of normal tissue perfusion (Trenholme and Pang, 2024). Saturation of peripheral oxygen remained within the normal range without any significant difference throughout the period of anaesthesia. This was in accordance with Hareesh (2016) whose research was on maintenance of anaesthesia with etomidate in geriatric dogs. This indicated normal peripheral oxygen saturation (Pedersen et al*.,* 2003). $EtCO_2$ concentration was slightly below the normal physiological level during the period of observation. In the present study, $EtCO_2$ values ranged between 30mm Hg and 40 mm Hg. The value was lowest during the surgery. Childress et al*.* (2018) reported that $EtCO_2$ represented the body's perfusion so that the reduction was proportional to hypoperfusion. Ramankutty (2024) also noticed decreased $EtCO_2$ level when dogs were anaesthetised with isoflurane anaesthesia and the author stated that this could be due to fresh oxygen flow in the breathing circuit which diluted the $EtCO_2$ values which could be correlated with the present study. Nociception during surgery was expressed as increase in respiratory rate and heart rate (Hellyer et al*.,* 2007). In the present study, the initial nociceptive stimuli were abruptly replaced by recovery signs. These signs were observed in five dogs at the time of the initial skin incision made using surgical diathermy (White and Kehlet, 2010). Signs of arousal diminished upon giving incremental bolus dose of etomidate. In all the six cases position of the eyeball was ventromedial which indicated surgical plane of anaesthesia.

There was statistically significant difference in the blood pressure at various periods of observation of anaesthesia, but the mean values of blood pressure were within the normal physiological limit. Ketamine, in contrast, typically increased sympathetic tone; however, in multimodal anaesthesia protocol its hypertensive effect might be blunted, leading to a net reduction in blood pressure (Djuric et al*.,* 2020).

All ECG parameters remained within the normal range, with no statistically significant variations. Three dogs with MVD showed transient sinus arrhythmia during anaesthesia. According to Ware (2011), severe cases of MVD exhibited ECG findings of sinus arrhythmia. DCM affected dog showed reduced R amplitude and sinus arrhythmia during anaesthesia. Reduced R amplitude might be due to 'Brody effect' which stated that amplitude of the QRS complex was reduced by under-filled ventricles (Cote, 2010). The reduced R amplitude was also within

Table 5. Mean ± SE values of blood pressure variables at different time interval

Blood pressure	Pre-operative	Anaesthesia	After Recovery
Systolic BP	138.33 ± 6.53*	131.67 ± 5.88*	142.67 ± 6.18*
Diastolic BP	83.17 ± 5.22*	74.83 ± 4.13*	78.83 ± 4.21*
MAP	104.83 ± 5.64*	93.83 ± 4.47*	100.17 ± 4.74*

The means bearing * differ significantly at 5 % level of significance.

Table 6. Mean ± SE values of ECG parameters at different time interval

Parameter	Pre-operative	Anaesthesia	Recovery
HR(beats/min)	105.5 ± 9.07	105 ± 20.1	108 ± 17.73
PD(sec)	0.04 ± 0.004	0.04 ± 0.004	0.04 ± 0.004
P amplitude(mV)	0.167 ± 0.033	0.133 ± 0.017	0.133 ± 0.017
QRS (sec)	0.038 ± 0.002	0.038 ± 0.002	0.038 ± 0.002
R amplitude (mV)	0.817 ± 0.135	0.842 ± 0.13	0.791 ± 0.132
QT (sec)	0.190 ± 0.007	0.200 ± 0.017	0.197 ± 0.017

the normal reference range. R amplitude came back to pre-anaesthetic state after recovery. Stephan (2024) also reported that sinus arrhythmia observed during anaesthesia was transient and no interventions were required (Table 6).

Conclusion

As all the dogs selected for the study were having pre-existing cardiovascular diseases, maintaining haemodynamic stability and preserving normal cardiac function were considered as the primary objectives in adopting the present protocol. The adopted protocol ensured haemodynamic stability which was evident through the normal vital signs and the other monitoring parameters, enabled successful completion of all the six surgical procedures. This multimodal anaesthesia protocol was found to be safe in dogs having cardiovascular diseases.

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Conflict of interest

The authors declare that they have no conflict of interest.

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