RESEARCH ARTICLE

Evaluation of the Cardiovascular Effect of Propofol using Echocardiography in Dogs

Harshal R. Patil[1]*, Gajendra S. Khandekar[1], Santoshmani D. Tripathi[1], Shalaka A. Chauhan[2], Dishant Saini[1], Rutuja L. Sawant[1]

Abstract

The propofol is commonly used anaesthetic agent in veterinary practice. Propofol has advantage of smooth and rapid induction although causes cardiovascular changes. This study was designed to evaluate cardiovascular changes after induction of anaesthesia with propofol on 12 female Mongrel dogs brought for laparoscopic ovariohysterectomy. The animals were sedated with butorphanol, induced with propofol and maintenance of anaesthesia was done with isoflurane. All dogs underwent a detailed systemic investigation including echocardiographic examination. Heart rate, pulse rate and respiratory rate decreased significantly after induction of anaesthesia, whereas echocardiographic parameters like ejection fraction and cardiac output decreased significantly by 9% and 33%, respectively. The propofol reduced the cardiac output along with decrease in arterial pressure. All these cardiovascular changes were in physiological limits and for transient period, the values of all parameters came to their normal level after recovery.

Key words: Cardiovascular changes, Echocardiography, Dog, Propofol.

Ind J Vet Sci and Biotech (2024): 10.48165/ijvsbt.20.4.13

Introduction

Propofol (2,6-di-isopropylphenol) is one of the most widely used anaesthetics due to its smooth and rapid induction (Sahinovic *et al*., 2018). To induce anaesthesia, propofol formulation may be given intravenously over a period of 30 to 90 seconds. It is recommended to administer a titrated dose of 6 to 10 mg/kg to unsedated, healthy animals and for predominated dose reduce to 1 to 4 mg/kg (Mama, 2013). Propofol should be administered slowly to minimise the risk of a relative overdose and to allow the drug's concentration in the blood and brain to equilibrate. As propofol is metabolized and redistributed in the liver and extrahepatic sites, its action is ultrashort-lived. After an anaesthesia induction dose, dogs and cats recover to ambulation within 20 min (dogs) or 30 min (cats), with a fast, smooth, and excitement-free recovery. These characteristics also make propofol a viable option for patients whose liver function is impaired (e.g., elderly patients, those with a portacaval shunt) or underdeveloped (e.g., kittens, puppies). Puppy survival is supposedly better after Caesarean section if the mother receives propofol anaesthesia induction rather than another injectable anaesthetic drug (Mama, 2013). Apnea and hypotension are the most common adverse effects, and they are dose-dependent. There have been several hypotheses about how propofol could have cardiovascular effects at clinically relevant concentrations, *viz.,* 1) direct venous vasodilation resulting in decreased left ventricular preload (Pagel *et al.,* 1998). 2) reduced systemic vascular resistance caused by arterial relaxation, possibly due to inhibition of the sympathetic nervous system (Wouters *et al.,*1995). 3) dose-dependent negative inotropic effect (Fujinaka *et al.,* 2012).

[1]Department of Veterinary Surgery and Radiology, Mumbai Veterinary College, Parel, Mumbai-400012, MAFSU, Maharashtra, India.

[2]Department of Veterinary Surgery and Radiology, Krantisinh Nana Patil College of Veterinary Science, Shirwal, Satara-412801, MAFSU, Maharashtra, India.

Corresponding Author: Harshal Patil, Department of Veterinary Surgery and Radiology, Mumbai Veterinary College, MAFSU, Parel, Mumbai-400012, India. e-mail: harshalpatil958@gmail.com.

How to cite this article: Patil, H. R., Khandekar, G. S., Tripathi, S. D., Chauhan, S. A., Saini, D., & Sawant, R. L. (2024). Evaluation of the Cardiovascular Effect of Propofol using Echocardiography in Dogs. Ind J Vet Sci and Biotech. 20(4), 60-63.

Source of support: Nil

Conflict of interest: None

Submitted 24/03/2024 **Accepted** 21/04/2024 **Published** 10/07/2024

Various parameters like clinical signs, physical examination, radiography as well as auscultation of heart and lung sounds are routinely used to diagnose cardiac affections peri-operatively. Echocardiography utilizes properties of sound wave interaction with heart tissue called reflection and scattering. Echocardiography allows direct visualization of cardiac structures, their movement as well as blood flow alteration (Gugjoo *et al*., 2013). The cardiac function is best represented by systolic ventricular function which is assessed by the left ventricular ejection phase indices, which include EF- Ejection Fraction (%), FS- Fractional Shortening (%), SV- Stroke volume (mL) and CO- Cardiac Output (mL) calculated by M-mode dimensional echocardiographic measurement (Boon, 2011). To evaluate the cardiovascular effect of propofol, echocardiography acts as outstanding diagnostic modality to understand the function of the heart at qualitative and

quantitative levels. This clinical trial was sought to determine cardiovascular changes to minimise dose-dependent adverse effect of propofol anaesthesia at the time of induction in dogs.

Materials and Methods

Twelve healthy female Mongrel dogs, aged 1.5 to 3 years, average body weight 15.76 kg, presented for ovariohysterectomy to the Department of Veterinary Surgery and Radiology, Mumbai Veterinary College, Parel, Mumbai were included in the study after informed consent from pet parents and approval of institutional animal ethical committee.

All the patients were admitted one day before examination to get acclimatize in new environment. The patients were kept nil by mouth (NBM) for 12 h. Physical, clinical examinations as well as electrocardiographic and echocardiographic examinations were carried out before subjecting the dogs to anaesthesia. The multiparameter monitor (GE B40 patient monitor) was used for monitoring cardiovascular and respiratory variables along with non-invasive BP monitoring. Dogs were positioned in right lateral recumbency for recording of ECG and appropriate cuff size was applied on left or right forelimb of dogs for BP monitoring. In the right parasternal location from 3rd to 6th intercostal area, hairs are clipped and trimmed for echocardiographic examination. A multi-frequency (1-5 MHz) cardiac probe was used and recordings were made using Aeroscan CD 10 PRO ultrasound machine. M mode echocardiographic recordings of left ventricular short axis were done at the level of midpapillary muscles (Fig. 1, 2).

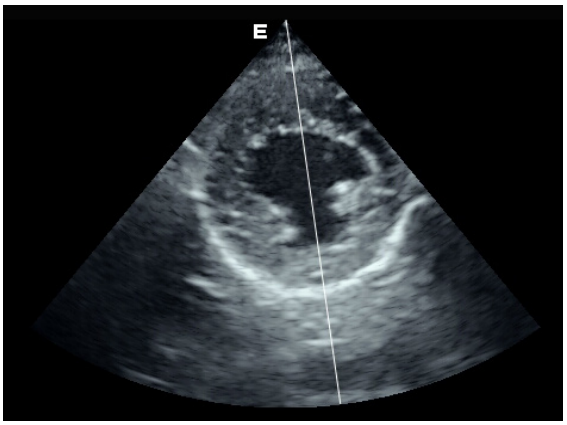

Fig 1: Echocardiogram showing right parasternal short axis view at papillary muscle level (Mushroom shape appearance).

All the dogs were premedicated with atropine sulphate (0.04 mg/kg b.wt SC), dexamethasone sodium (0.025 mg/kg b.wt SC) and butorphanol tartrate (0.5 mg/kg b.wt IV). After pre-oxygenation, anaesthesia was induced with propofol 4 mg/kg b.wt titrated till effect. Endotracheal intubation was done with cuffed ET tube. Anaesthesia was maintained with isoflurane 2.5 % during the complete surgical procedure along with oxygen at a flow rate ranging from 500 mL/min to 1200 mL/min and rebreathing bag was kept 2/3rd full of its capacity. Pop-off valve near the patient end was kept in a semi-closed position for the escape of expiratory gases.

Measurements such as HR, PR, RR, BP, M mode left ventricular echocardiography and ECG were made after induction of anaesthesia. At the end, after dogs recovered from anaesthesia all the measurements were taken once again.

The data obtained from M mode measurements were used for calculating EF, FS, SV and CO as under.

LV diastolic volume (LVVd) = $(7 \times (LVIDd)^3) / (2.4 + LVIDd)$

LV systolic volume (LVVS) = $(7 \times (LVIDs)^3) / (2.4 + LVIDs)$

Ejection Fraction EF (%) = (LVVd) - (LVVs) / (LVVd) x 100

Fractional Shortening FS (%) = (LVIDd - LVIDs / LVIDd) x 100

Stroke volume SV (mL) = (LVVd) - (LVVs)

Cardiac Output CO (mL) = SV x HR.

The data was analysed by one way analysis of variance and presented as Mean ± SEs.

Results and Discussion

The findings on evaluation of various physiological parameters observed at different time intervals are shown in Table 1. Out of 12 dogs, in 2 dogs apnoea was observed, but no other anaesthesia related complications were noticed.

There was significant decrease in HR and PR after induction of anaesthesia, but there was no significant difference between values before and after recovery. Combination of propofol and butorphanol caused significant reduction in HR and PR. There might be 2 explanation for that, first butorphanol causes depression of SA node and slows atrioventricular conduction thereby facilitating increase in the parasympathetic tone which might be the reason for decrease in the heart rate. Kellihan *et al.* (2015) and Seo *et al.* (2015) also reported a significant reduction in the heart rate after the administration of butorphanol in dogs. Second, increase in the vagal tone and reduction in sympathetic tone could be the reason for decrease in the HR after induction

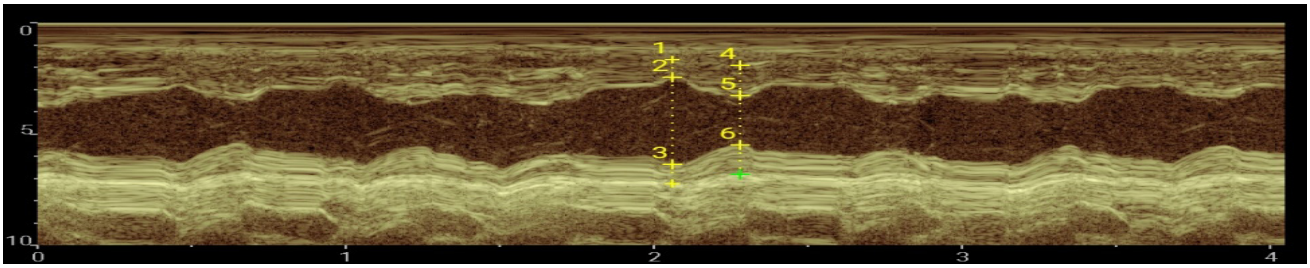

Fig 2: M mode echocardiogram dimensions (1. IVSd, 2. LVIDd, 3. LVPWd, 4. IVSs, 5. LVIDs, 6. LVPWs.)

Table 1: Physiological parameters of dogs

Physiological parameters	Before induction of anaesthesia	After induction of anaesthesia	After recovery from anaesthesia
Heart rate - HR (beats/min)	121.83 ± 4.09 [a]	96.58 ± 6.8 [b]	130.08 ±6.96 [a]
Pulse rate - PR (pulse/min)	121.66 ± 4.24 [a]	96.44 ± 6.73 [b]	130.41 ±6.79 [a]
Respiration rate - RR (breadhs/min)	30.08 ± 0.91 [b]	20.33 ± 0.77 [c]	36.16 ± 1.48 [a]
MAP (mm Hg)	99.72 ± 3.25 [a]	83.06 ± 1.83 [c]	92.97 ± 2.62 [ab]

Values in the same row with different superscripts differ significantly at p<0.05.

Table 2: Echocardiographic parameters of dogs

Parameters	Before induction of anaesthesia	After induction of anaesthesia	After recovery from anaesthesia
Ejection fraction (EF) (%)	65.88 ± 1.95 [a]	59.77 ± 2.31 [ab]	62.46 ± 1.55 [a]
Fractional shortening (FS) (%)	34.16 ± 2.21	30.91 ± 1.53	32.59 ± 1.16
Stroke volume (SV) (mL)	24.42 ± 2.34	21.71 ± 1.57	21.96 ± 3.26
Cardiac output (CO) (mL)	3148.78 ± 240.63 [a]	2103 ± 208.91 [bc]	2777.44 ± 314.5 [ab]

Values in the same row with different superscripts differ significantly at p<0.05.

of anaesthesia with propofol. Similar results have been reported by Anandmay *et al.* (2016).

A significant decrease in the respiratory rate was noticed after induction of anaesthesia which increased to normal after recovery. Anandmay *et al.* (2016) reported that propofol may cause a significant depression of respiratory function characterized by a reduction in breathing rate and it is more prominent after combination with opioids, which is in concurrence with our findings. Decrease in the respiratory rate after induction of anaesthesia could be due to the cardiopulmonary depression effect of the injectable anaesthetic propofol and butorphanol, whereas we observed apnoea in 2 patients which resolved on its own. Keates and Whittem (2012) observed apnoea after induction of anaesthesia with propofol that depended on the rate of administration.

All left ventricular ejection phase indices obtained from M mode dimensional measurements at different intervals are represented in Table 2.

There was a significant decrease in EF of around 9% after induction of anaesthesia, which returned to pre-induction value after recovery. The cardiac output significantly decreased around 33% after induction of anaesthesia. No significant changes were observed in FS and SV. But all changes remained within physiological limits. This could be due to any mechanism that acts on CO and vascular resistance or cardiac contractibility.

The propofol has negative inotropic effect that means the cardiac contractibles will be affected. The cardiac output indirectly depends on SV and HR. SV is primarily affected by preload, afterload and myocardial contractility. If negative inotropic effect of propofol decreases contraction, end result will be decreased in SV and so that of CO (Pagal and Warltier, 1993). But, Ismail *et al.* (1992) and Fujinaka *et al.* (2012) observed that negative inotropic effect of propofol was relatively less harmful when used in clinical concentration.

The vasodilatory effect of propofol causes all cardiovascular charges. This may be due to both a reduction in sympathetic tone as well as a direct effect on smooth muscles (Cattai *et al.,* 2018). The generalised vasodilatation and decrease in systemic vascular resistance (Wouters *et al.,* 1995) causes decrease in preload. Ejection faction indices like FS, EF, SV all decreases by decrease in preload. This might be the reason for decrease in EF and CO in our study. A dose-dependent ventilatory depression as well as decreased systemic blood pressure, cardiac output, and SVR are also caused due to propofol (Muzi *et al*., 1992). Mulier *et al.* (1991) reported reduced CO at low as well as at high dose, along with decrease in SV and the slope of E following propofol anaesthesia. Similar decrease in CO and other ejection phase indices due to anaesthetic agent mainly propofol with premedication with butorphanol were reported by Lopes *et al*. (2009).

The mean arterial pressure (MAP) decreased significantly after induction of anaesthesia as compared to pre-induction value as a result of premedication and propofol, which increased after recovery, but still lower than pre-induction value (Table 1). Decrease in MAP could be due to vasodilatory effect as explained above or due to attenuation of arterial baroreflex by decrease in sympathetic tone by propofol (Ebert *et al.,* 1992; Sato *et al.,* 2005). Although propofol does not directly affect baroreflex sensitivity, it may increase vagal tone and decrease sympathetic tone through a central mechanism (Cattai *et al.,* 2018). The vasodilatory effect of propofol causes decrease in vascular resistance which ultimately leads to a decrease in the blood pressure (Shintaku *et al*., 2014). Robinson *et al*. (1997) suggested that inhibition of sympathetic tones may explain the lower blood pressure with propofol anaesthesia. Propofol causes a drop in arterial pressure in healthy dogs, and the magnitude of this drop may be strictly dependent on propofol plasma concentrations (Cattai *et al.,* 2018).

Conclusion

The propofol reduces the cardiac output along with decrease in arterial pressure as well as causes respiratory depression when used in combination with butorphanol. All these cardiovascular changes are in physiological limits and for transient period, all the values comes to their normal level after recovery.

Acknowledgement

The authors acknowledge the research facilities provided by Department of Veterinary Surgery and Radiology, Mumbai Veterinary College, Parel, Mumbai, for conducting this study.

References

Anandmay, A.K., Dass, L.L., Sharma, A.K., Gupta, M.K., Singh, K.K., & Roy, B.K. (2016). Clinico-anaesthetic changes following administration of propofol alone and in combination of meperidine and pentazocine lactate in dogs. *Veterinary World, 9*(11), 1178.

Boon, J.A. (2011) *Veterinary Echocardiography*. John Wiley & Sons, Chichester, UK.

Cattai, A., Rabozzi, R., Ferasin, H., Isola, M., & Franci, P. (2018). Haemodynamic changes during propofol induction in dogs: new findings and approach of monitoring. *BMC Veterinary Research, 14,* 1-8.

Ebert, T.J., Muzi, M., Berens, R., Goff, D., & Kampine, J.P. (1992). Sympathetic responses to induction of anaesthesia in humans with propofol or etomidate. *Anesthesiology*, *76*(5), 725-733.

Fujinaka, W., Shimizif, J., Iribe, G., Imaoka, T., Oshima, Y., Kiyooka, T., Morita, K., & Mohri S. (2012). Effects of propofol on left ventricular mechanoenergetics in the excised cross-circulated canine heart. *Acta Med Okayama, 66*, 435-442.

Gugjoo, M.B., Hoque, M., Saxena, A.C., &Zama, M.M.S. (2013). Radiographic, electrocardiographic and echocardiographic features of dilatation cardiomyopathy in dogs. *Indian Journal of Veterinary Surgery, 90*(12), 54-56.

Ismail, E.F., Kim, S.J., Salem, M.R., & Crystal, G.J. (1992). Direct effects of propofol on myocardial contractility in in situ canine hearts. *Anesthesiology, 77*(5), 964-972.

Keates, H., & Whittem, T. (2012). Effect of intravenous dose escalation with alfaxalone and propofol on occurrence of apnoea in the dog. *Research in Veterinary Science, 93*(2), 904-906.

Kellihan, H.B., Stepien, R.L., Hassen, K.M., &Smith, L.J. (2015). Sedative and echocardiographic effects of dexmedetomidine combined with butorphanol in healthy dogs. *Journal of Veterinary Cardiology, 17*(4), 282-292.

Lopes, P.C.F., Nunes, N., Sousa, M.G., Paula, D.P., Carareto, R., Nishimori, C., & Camacho, A. A. (2009). Effects of several FiO_2 on the echocardiographic parameters in dogs undergoing continuous infusion of propofol. *Arquivo Brasileiro de Medicina Veterinária e Zootecnia, 61,* 345-352.

Mama, Khursheed (2013). *Clinician's Brief,* Administration of propofol, an IV anaesthetic, can result in dose-dependent effects, ranging from sedation to general anaesthesia. 17-20. (https://assets.ctfassets.net/4dmg3l1sxd6g/2lFkMJq9E0qDYtVKOsKeA3/85c73bdbd8d1eaf5c8e29c0e78b72bcd/propofol-8491-article.pdf).

Mulier, J.P., Wouters, P.F., Van Aken, H., Vermaut, G., & Vandermeersch, E. (1991). Cardiodynamic effects of propofol in comparison with thiopental: Assessment with a transesophageal echocardiographic approach. *Anesthesia and Analgesia, 72*(1), 28-35.

Muzi, M., Berens, R. A., Kampine, J. P., & Ebert, T. J. (1992). Venodilation contributes to propofol-mediated hypotension in humans. *Anesthesia & Analgesia*, *74*(6), 877-883.

Pagel, P.S., & Warltier, D.C. (1993). Negative inotropic effects of propofol as evaluated by the regional preload recruitable stroke work relationship in chronically instrumented dogs. *Anesthesiology*, *78*(1), 100-108.

Pagel, P.S., Hettrick, D.A., Kersten, J.R., Lowe, D., & Warltier, D.C. (1998). Cardiovascular effects of propofol in dogs with dilated cardiomyopathy. *The Journal of the American Society of Anesthesiologists, 88*(1), 180-189.

Robinson, B.J., Ebert, T.J., O'brien, T.J., Colinco, M.D., & Muzi, M. (1997). Mechanisms whereby propofol mediates peripheral vasolidation in humans: Sympathoinhibition or direct vascular relaxation? *The Journal of the American Society of Anesthesiologists, 86*(1), 64-72.

Sahinovic, M. M., Struys, M. M. R. F., & Absalom, A. R. (2018). Clinical pharmacokinetics and pharmacodynamics of propofol. *Clinical Pharmacokinetics*, *57*(12), 1539-1558.

Sato, M., Tanaka, M., Umehara, S., & Nishikawa, T. (2005). Baroreflex control of heart rate during and after propofol infusion in humans. *British Journal of Anaesthesia, 94*(5), 577-581.

Seo, J.I., Han, S.H., Choi, R., Han, J., Lee, L., & Hyun, C. (2015). Cardiopulmonary and anesthetic effects of the combination of butorphanol, midazolam and alfaxalone in Beagle dogs. *Veterinary Anaesthesia and Analgesia, 42*(3), 304-308.

Shintaku, T., Ohba, T., Niwa, H., Kushikata, T., Hirota, K., Ono, K., ... & Murakami, M. (2014). Effects of propofol on electrocardiogram measures in mice. *Journal of Pharmacological Sciences*, *126*(4), 351-358.

Wouters, P.F., Van de Velde, M.A., Marcus, M.A., Deruyter, H.A., & Van Aken, H. (1995). Haemodynamic changes during induction of anaesthesia with eltanolone and propofol in dogs. *Anaesthesia and Analgesia, 81*(1), 125-131.