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SV Gaikwad
Department of Veterinary Surgery and Radiology, Mumbai Veterinary College, Parel, Mumbai, MAFSU, Maharashtra, India

GS Khandekar
Department of Veterinary Surgery and Radiology, Mumbai Veterinary College, Parel, Mumbai, MAFSU, Maharashtra, India

SD Tripathi
Department of Veterinary Surgery and Radiology, Mumbai Veterinary College, Parel, Mumbai, MAFSU, Maharashtra, India

Monika Rani
Department of Veterinary Surgery and Radiology, Mumbai Veterinary College, Parel, Mumbai, MAFSU, Maharashtra, India

CH Pawshe
Professor & Head, Department of ARGO, PGIVAS, Akola, MAFSU, Maharashtra, India

Corresponding Author:
Monika Rani
Department of Veterinary Surgery and Radiology, Mumbai Veterinary College, Parel, Mumbai, MAFSU, Maharashtra, India

Assessment of haematobiochemical effects of propofol combined with isofluraneversus propofol combined with sevoflurane for thoracoscopy in canines

SV Gaikwad, GS Khandekar, SD Tripathi, Monika Rani and CH Pawshe

Abstract
The present study was undertaken to evaluate the haematobiochemical effect of propofol isoflurane and propofol sevoflurane in twelve dogs with history of chronic cough, dyspnoea, laboured breathing, nasal discharge, exercise intolerance which were presented to the Department of Surgery and Radiology, Mumbai Veterinary College and Bai Sakarbai Dinshaw Petit Hospital for animals, Parel, Mumbai. These twelve dogs were randomly divided into two equal groups. In both the groups, dogs were induced with propofol (5 mg/kg) B.WT. intravenously. In both the groups dogs were premedicated with acepromazine (0.04 mg/kg) B.WT. intravenously and administration of atropine sulphate (0.04 mg/kg) B.WT and dexamethasone sodium (0.025 mg/kg) B.WT 10 minutes before induction of anaesthesia. In group I, anaesthesia was maintained using isoflurane 2.5% isoflurane and in group II, anaesthesia was maintained using sevoflurane 2.5% along with oxygen at a flow rate ranging from 500 ml/min to 1200 ml/min. History, haematobiochemical parameters were recorded at different time intervals during the study period. The present study findings suggest that induction with propofol and maintenance with isoflurane and sevoflurane proved best anaesthetic technique for thoracoscopy in dogs.

Keywords: Dog, isoflurane, sevoflurane, haematobiochemical parameters, thoracoscopy

Introduction
Selection of appropriate anaesthetic protocol is very important factor for endoscopy and thoracoscopy in veterinary medicine. Evaluation of safe and adequate anaesthetic technique for thoracoscopy has high priority in veterinary minimal invasive thoracic surgeries. Minimum invasive surgeries like Laparoscopy and thoracoscopy surgeries require specific anaesthesia. Without thorough knowledge of hemodynamic, physiological, and biochemical changes in relation to positioning of the animals during thoracoscopy procedures may cause potential complications (Richter, 2001) [30]. Hence, selection of safe anaesthetic protocol during thoracoscopic procedures is of utmost importance (Weil, 2009) [39]. Positive pressure ventilation during anaesthesia and thoracoscopy provides respiratory support to the patient by eliminating carbon dioxide and oxygenation of arterial blood after partial pneumothorax produced by thoracoscopy. Unilateral hemithorax ventilation technique is a standard procedure in human thoracoscopy which includes bronchial blockade, endobronchial intubation, and use of double lumen endotracheal tubes (Walker and Bensky, 1995) [36]. However, both bilateral lung ventilation and unilateral lung ventilation techniques have potential risks during thoracoscopy, which need critical anaesthetic monitoring of the patient. But unilateral lung ventilation has greater risk of hypoxemia due to non-functioning and collapse of entire lung leading to atelectasis in non-ventilated lung (Cohen *et al*., 1988) [5]. Even though bilateral ventilation is associated with lacunas like reduced field of view, difficulty while manipulation of intrathoracic organs and disturbance of vision due to spontaneous movements of lung, the technique has been used in veterinary as well human thoracoscopy successfully to avoid the effect of cardiopulmonary stress on the patient where unilateral lung ventilation was considered too dangerous (Hasnain and Krasna, 1994) [15]. Therefore, the objective of the study was to evaluate the hematobiochemical effects following administration of the Propofol Combined with Isoflurane Versus Propofol Combined with Sevoflurane for Thoracoscopy in dogs.

Materials and Methods

The present clinical study was undertaken on twelve clinical cases with history of chronic cough, dyspnoea, laboured breathing, nasal discharge, exercise intolerance which were referred to the Department of Surgery and Radiology, Mumbai Veterinary College and Bai Sakarbai Dinshaw Petit Hospital for animals, Parel, Mumbai. The animals were divided into two groups having six animals each. In (Group I) Laparoscopy assisted diagnostic procedure (Thoracoscopy) was carried out for the examination of thoracic cavity and diagnosis of lung parenchyma diseases by lung biopsy under isoflurane anaesthesia, while in (Group-II) laparoscopy assisted diagnostic procedure (Thoracoscopy) was carried out for the examination of thoracic cavity and diagnosis of pleural diseases with pleural fluid analysis and pleural biopsy under sevoflurane anaesthesia was carried out.

Preanaesthetics and induction anaesthetic procedures

In both the groups dogs were premedicated with acepromazine (0.04 mg/kg) B.WT intravenously and administration of atropine sulphate (0.04 mg/kg) B.WT. and dexamethasone sodium (0.025 mg/kg) b.wt. 10 minutes before induction of anaesthesia. Induction of anaesthesia was carried out with propofol (5 mg/kg) BW intravenously. After induction of anaesthesia each dog was intubated by endotracheal tube of appropriate size varying from 5.0 -7.0 F according to the size of the dog. All the patients were positioned in dorsal recumbency and atracurium was administered (0.2 mg/kg) intravenously as a bolus dose for respiratory muscle relaxation, there after the patients were shifted on volume controlled positive pressure ventilation and the dose of atracurium was repeated (0.1 mg/kg) IV, as per need.

Maintenance of anaesthesia and positive pressure ventilation

In group I, anaesthesia was maintained using isoflurane 2.5% isoflurane and in group II, anaesthesia was maintained using sevoflurane 2.5% along with oxygen at a flow rate ranging from 500 ml/min to 1200 ml/min. All the animals were maintained on volume controlled intermittent positive pressure ventilator. Intermittent positive pressure ventilation was delivered with tidal volume of 7-8 ml/kg body weight by adjusting 15-16 breaths per minute and inspiratory: expiratory (I: E) ratio of 1:2. End tidal volume of CO_2 was monitored by multi paramonitor and $EtCO_2$was achieved in between 35 to 40 mm Hg. Following completion of the surgical procedure inhalation anaesthesia was stopped by switching off the dial setting of isoflurane vaporizer and intermittent positive pressure ventilation was maintained till the initiation of self-respiration and patient was weaned off the ventilator gradually to avoid mismatch of breathing. Further, oxygen was delivered to all the dogs, till the appearance of the swallowing reflex. The endotracheal tube was then removed after deflating the cuff of the tube once the gag reflex was noted in the dogs. In the present study, all the animals were subjected to thorough systemic investigation protocol was followed for recording of parameters *viz*., history, physiological parameters, anaesthetic parameters and statistical analysis. All the dogs diagnosed with pleural effusions, pleuritis, pyothorax and lung parenchyma diseases were initially treated with standard medical protocol for two weeks however, the cases which did not responded to the treatment were further randomly divided in two groups *viz*., Group I and Group II for thoracoscopy.

History

History included age, breed, sex and body weight that was recorded at the time of presentation in all the animals of both the groups.

Haemato-biochemical Paramaters

4 ml of blood was collected aseptically from the cephalic vein from each dog of the two groups before surgery, during laparoscopic procedure. 3 ml blood was collected in plain vial for serum chemistry and 1 ml blood was collected in sterile vials containing EDTA. Haematobiochemical assay was performed on automatic serum analyzer and automatic cell counter. The following haematobiochemical parameters were studied.

- Hemoglobin (gm%)
- Total erythrocyte count (10^6/mm^3)
- Total Leukocyte count (10^3/mm^3)
- Differential leucocyte count (%)
- Packed cell volume (%)
- Aspartate Aminotransferase (AST), IU/L
- Alanine Aminotransferase (ALT), IU/L
- Blood Urea Nitrogen (BUN), mg/dl
- Serum creatinine (mg/dl)
- Serum Cortisol (nmol/L) (mcg/dl)

Result and Discussion

History of all dogs in both the groups are shown in Table1

Table 1: Details of the breed, approximate age, sex and weight of each dog

	Group I				Group II			
Dog No.	**Breed**	**Age (yr.)**	**Sex**	**Wt. (Kg)**	**Breed**	**Age (yr.)**	**Sex**	**Wt. (Kg)**
1	Labrador	9.5	M	15.1	Labrador	8.5	M	17
2	Mongrel	11.5	F	13.9	Labrador	9	M	18
3	Boxer	8	M	15.1	Mongrel	10	F	13
4	Mongrel	10	M	16	Pomeranian	7.5	F	12
5	Rottweiler	8.5	M	31.5	Mongrel	9	F	11.5
6	Pom cross	10.5	F	10	Mongrel	10	M	16

Haematological Parameters recorded at different time intervals in both the groups are shown in Table 2.

The Mean value of haemoglobin was non-significantly decreased during anaesthesia and thoracoscopy in both the groups. There was no significant difference in the haemoglobin value observed between the two groups. This slight decrease in haemoglobin could be due to stress of thoracoscopy and anaesthesia. Levionnois *et al*. (2006) [23] noticed significant decrease in hemoglobin concentration during propofol isoflurane anaesthesia in dogs. Kumar (2017) [20] recorded non-significant decrease in the haemoglobin in dog under propofol-isoflurane anesthesia, while significant decrease in haemoglobin was noted in isoflurane induced dogs. Sen and Kilic (2018) [31] observed decrease in haemoglobin under propofol isoflurane and propofol sevoflurane anaesthesia in dog during anaesthesia and returned up to normal baseline values after complete recovery. Costa *et al*. (2013) [6] recorded a decrease in the haemoglobin values due to administration of propofol in dogs with or without tramadol. In the present clinical study decrease in haemoglobin concentration could be due to pooling of circulatory blood cells in to spleen and lungs and also due to extravascular to intravascular shifting of fluids as to maintain the normal cardiac output of patients during anaesthesia and surgery as stated by Wagner *et al*. (1991). Similar findings were recorded by Tatelu (2009) [33], Bendale (2010) [3] and Khandekar (2011) [18] during laparoscopic surgeries in dogs. Significant decrease in PCV was observed during thoracoscopy and anaesthesia, however, there was no significant difference noted between two the groups. Decrease in the PCV value was in conjunction with the decrease in the TEC and Hb values in both the groups. Hikasa *et al*. (2002) [17] reported decrease in the packed cell volume in goats under sevoflurane and isoflurane anaesthesia. In the present study decrease in the packed cell volume could be due to shifting of fluid from the extravascular compartment to intravascular compartment for maintaining cardiac output or due to haemodilution during anaesthesia. Similar observations have been reported by Vishwanath and Ranganath (2012) [35]. Polis *et al*. (2002) [28]; Costa *et al*. (2013) [6] reported decrease in PCV during thoracoscopy in dogs under propofol sevoflurane anaesthesia. Significant decrease in the erythrocyte count was noticed during surgery and anaesthesia in both the groups. Whereas, non-significant difference was observed in between group I and II. Similarly, Sen *et al*. (2018) [31] observed significant decrease in total erythrocyte count under propofol-isoflurane and propofol-sevoflurane anaesthesia in dog. Hikasa *et al*. (2002) [17] also observed significant decrease in total erythrocyte count during isoflurane and sevoflurane anaesthesia in goats and they stated that decreased erythrocyte count during anaesthesia could be due to sequestration of RBC in spleen and decrease in blood pressure causing hemodilution. Levionnois *et al*. (2006) [23] observed slight anemia during surgery in dog operated for lung lobectomy with one lung ventilation under total intravenous anaesthesia with propofol. However, Eva *et al*. (2014) [11] observed non-significant difference in the erythrocyte count during thoracoscopic repair of diaphragmatic hernia in rabbits under propofol anaesthesia. Similarly, Frendin *et al*. (2006) [12] reported non-significant changes in erythrocyte count under propofol anesthesia in dogs. In the present study significant drop in erythrocyte count during surgery and thoracoscopy could be due to sequestration of RBC in spleen and hemodilution caused by low blood pressure as stated by Hikasa *et al*. (2002) [17] and Bayen *et al*. (2002) [2].

The Mean value of total leucocyte counts (thousand/mm^3) was a significant decrease in total leucocyte count in both the groups during anaesthesia and returned to the baseline value 48 hours after recovery. However, non-significant difference was observed between the groups. In the present study decrease in leucocyte count could be due to cumulative effect of thoracoscopy and anaesthetic combination used in this study however, the drop in the count was within physiological limits. Hikasa *et al*. (2002) [17] observed similar kind of changes in leucocyte count in goats during isoflurane, sevoflurane and halothane anaesthesia. Immunosuppression during the anaesthesia could be due to the effect of catecholamines and glucocorticoids released during anaesthesia. Elenkov and Chrousos (2002) [10] and Wen *et al*. (2017) [38] also noticed pronounced immunosuppression during subxiphoid thoracoscopy than conventional transthoracic thoracoscopy for lung lobectomy in dogs. Similarly, Yankulov *et al*. (2013) [41] observed decrease in the leucocyte count during diagnostic thoracoscopy as well as thoracoscopic pleurodesis in human patients while treating for pleural effusions. Similar kinds of observations have been noticed under propofol-isoflurane anesthesia in dog by Tomihari *et al*. (2015) [34]. Sen *et al*. (2018) [31] also observed significant decrease in leucocyte count under propofol-sevoflurane and alphaxalone-sevoflurane anaesthesia in geriatric dogs.

The Mean values of neutrophil count, eosinophil count, monocyte count and Lymphocyte count was changed non-significantly in both within the groups and between the groups during anaesthesia and thoracoscopy. Neutrophilia during diagnostic thoracoscopy and thoracoscopic pleurodesis was also noticed by Froudarakis *et al*. (2006) [13] However, severe neutrophilia was seen during thoracoscopic pleurodesis than diagnostic thoracoscopy in human patient treated for pleural effusions. Similarly, Wen *et al*. (2017) [38] also found significant increase in neutrophil count during and following subxiphoid thoracoscopic pulmonary lobectomy in dogs. However, Cocelli *et al*. (2012) [4] stated that propofol inhibits phagocytosis and respiratory burst and causes neutrophilia during propofol isoflurane anaesthesia in dogs. However, Rizzo *et al*. (2011) [29] observed decrease in the neutrophil count due to isoflurane anaesthesia in human patients; similar observations were also reported by Heine *et al*. (2000) [16]. Eva *et al*. (2014) [11] observed non-significant changes in the eosinophil count during thoracoscopic repair of diaphragmatic hernia in rabbit model. Froudarakis *et al*. (2006) [13] observed decreased peripheral blood eosinophil count during thoracoscopic talc poudrage for treatment of pleural effusions in dog, Costa *et al*. (2013) [6] also noticed non-significant changes in eosinophil count under propofol anesthesia in dogs. Mayhew *et al*. (2012) [26] observed eosinophilia on histopathological examination of lung tissue obtained by thoracoscopic lung biopsy with vessel sealing device in dogs. The corticosteroid administered during preanaesthetic medication could result in non-significant changes in eosinophil count. Similar observations have been reported by Froudarakis *et al*. (2006) [13] and Parrillo and Fauci (1979) [27] stating that it could be due to after administration of corticosteroid migration of eosinophil in other tissues after administration of corticosteroid leading to reduction in peripheral blood count of eosinophil. Liu *et al*. (2013) [22] observed significant decrease in the lymphocyte count during trans-oral and trans-thoracic thoracoscopic surgeries in dogs under ketamine-xylazine and isoflurane anaesthesia while, Lugo *et al*. (2002) [25] noticed non-significant decrease in the lymphocyte count during thoracoscopically guided pulmonary biopsy in horses up to the 48 hours after surgery and the count returned to the baseline values on the 14th day of surgery. Similarly, Wen *et al*. (2017) [38] observed decreased lymphocyte count in the subxiphoid thoracoscopy than trans-thoracic thoracoscopy during lung lobectomy in dogs and noticed that lymphocyte recovery rate was slower in subxiphoid thoracoscopy group. Froudarakis *et al*. (2006) [13] noticed, thoracoscopic talc poudrage induced lymphopenia in dogs during treatment of pleural effusions and stated that neutrophilia caused by inflammation releases endogenous steroids in circulation, elevated levels of glucocorticoids in circulation resulted in temporary leucopenia which could be due to redistribution of peripheral blood lymphocytes in to other lymphoid organs, whereas, Parrillo and Fauci (1979) [27] stated that lymphopenia resulted due to neutrophilia however, the inflammation resolves within 24 hours of surgery. Tomihari *et al*. (2015) [34] also noticed decrease in the peripheral blood lymphocyte count during propofol and isoflurane anaesthesia in dogs, they noticed drop in the lymphocyte count till 2 hours post anaesthesia. Kumar (2017) [20] also noticed non-significant changes in the lymphocyte count in dogs under propofol and isoflurane anaesthesia. Similarly, Lugo *et al*. (2002) [25], Costa *et al*. (2013) [6] and Lu *et al*. (2015) [24] also noticed non-significant changes in the monocyte count during thoracoscopic guided lung biopsy in horses. Similar kind of non-significant changes in the monocyte count was also recorded by Wen *et al*. (2017) [38] during subxiphoid and transthoracic thoracoscopic lung lobectomy in canine model.

Table 2: Different haematological parameters recorded at different time intervals in both the groups (Mean±SE).

Haematological Parameters	Group	Before	During	48 hrs. after
Hb (g/dl)	I	11.87± 0.29	11.58±0.20	11.73±0.17
	II	11.32±0.25	11.03±0.15	11.18±0.20
PCV (%)	I	36.23±1.13	34.52±1.08	33.38±1.17
	II	35.16±1.38	33.03±1.12	32.59±0.97
TEC (x10^6/µL)	I	6.52±0.19	6.16±0.21	6.36±0.19
	II	6.12±0.22	5.63±0.15	5.94±0.23
TLC (/µL)	I	23316.67±1442.71	22116.67±1661.66	22270.00±1232.41
	II	24366.67±1879.27	22283.33±1502.00	23083.33±2082.10
Neutrophils (%)	I	77.33±1.91	78.33±1.78	77.67±2.23
	II	74.83±0.83	75.17±1.08	74.50±1.78
Lymphocytes (%)	I	17.33±2.03	16.67±1.80	17.17±2.24
	II	20.67± 0.92	20.17±0.83	20.83± 1.40
Monocytes (%)	I	1.33±0.21	1.33±0.21	1.33±0.21
	II	1.33±0.21	1.50±0.22	1.50±0.22
Eosinophils (%)	I	4.00±0.68	3.67±0.49	3.83±0.48
	II	3.17±0.31	3.17±0.40	3.17±0.60

Biochemical Parameters recorded at different time intervals in both the groups are shown in Table 3

Mean value of aspartate aminotransferase was significant increase in AST was observed during anaesthesia and thoracoscopy within both the groups, whereas, no significant change was noticed in between two groups. Dabir *et al*. (2015) Dabir have also reported significant increase in the aspartate aminotransferase enzyme in dogs during open thoracostomy under propofol and isoflurane anaesthesia, whereas, Dhumeaux and Haudiquet (2009) [8] reported no abnormalities in aspartate aminotransferase values during thoracoscopic assisted lung resection in dog. Similar findings have been reported by Bakhtiari *et al*. (2006) [1], Vishwanath and Ranganath (2012) [35].

The mean value of alanine aminotransferase was non-significant decrease in the ALT was observed during anaesthesia and thoracoscopy in both the groups, whereas, there was no significant change noted in between the two groups. Dabir *et al*. (2015) [7] also reported non-significant changes in alanine aminotransferase enzyme during and post open thoracotomy in dogs under propofol and isoflurane anaesthesia, whereas, Dhumeaux and Haudiquet (2009) [8] reported no abnormalities in alanine aminotransferase value during thoracoscopic assisted lung resection in dog.

Mean value of blood urea nitrogen was non-significant decrease in the BUN was observed during anaesthesia and thoracoscopy in both the groups, whereas, there was significant change noticed in between the two groups during anesthesia and thoracoscopy. Similarly, Dhumeaux and Haudiquet (2009) [8] also reported non- significant changes in BUN during thoracoscopic assisted lung resection in dog, while, Wormser *et al*. (2014) [11] reported increase in the blood urea nitrogen value post-surgery in one cat during thoracoscopic lung surgery. Mean value of serum creatinine was changed non significantly during anaesthesia and thoracoscopy within and between the groups. The Mean value of serum cortisol was significantly increased in the serum cortisol level was noticed during anaesthesia and thoracoscopy in both the groups, whereas cortisol returned to baseline value after complete recovery of the patients. There was no significant change noted in between the two groups. Inada *et al*. (2004) [19] reported that immunosuppressive effect of propofol was less as compared to isoflurane anaesthesia and Isoflurane anaesthesia showed more serum cortisol than propofol during anaesthesia in human patients. Walsh *et al*. (1999) [37] reported increase in the cortisol levels during thoracoscopy as well as open thoracotomy in dogs during Pericardiotomy; however more physiological stress and serum cortisol was noticed in thoracostomy procedure in dog than thoracoscopy. Similar observations were also reported by Gloudemans (2013) [14], Dupre (2001) [9] and Landreneau *et al*. (1993) [21]. However, Hikasa *et al*. (2002) [17] reported no change in the cortisol level during sevoflurane anaesthesia in goats.

Table 3: Biochemical parameters recorded at different time intervals in both the groups (Mean±SE)

Sero-Biochemical	Groups	Before	During	48 hrs. after
ALT(IU/L)	I	70.50±3.84	68.00±4.30	83.67±2.58
	II	88.67±7.93	85.00±7.14	89.67±7.11
AST(IU/L)	I	68.83±4.85	72.00±4.88	80.17±4.32
	II	79.00±10.85	93.33±12.08	84.00±11.70
BUN (mg/dL)	I	15.45±0.98	13.87±0.69	14.95±0.82
	II	18.93±1.16	16.93±1.09	18.05±1.12
Serum Creatinine (mg/dL)	I	1.25±0.10	1.10±0.04	1.18±0.07
	II	1.20±0.14	1.23±0.10	1.37±0.07
Serum cortisol (µ/dl)	I	5.2±0.36	6.2±0.28	5.3±0.33
	II	4.6±0.30	5.7±0.23	5.4±0.18

Conclusions
It is concluded that minor changes observed in haematobiochemical parameters.

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Conflict of interest
No potential conflict of interest relevant to this article was reported.

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