Received: 15 February 2022, Accepted: 5 March 2022

Original Research

Journal of Advanced Veterinary Research
(2022) Volume 12, Issue 2, 135-147

Comparison of Different Anesthetic Regimens using Isoflurane and Propofol as Constant-Rate Infusion for Long-term Anesthesia in Dogs

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Abstract

The objective of the present study was to compare between three anesthetic protocols for long-term anesthesia (2 h); protocol 1: xylazine (1mg/kg)/ketamine (10mg/kg) and inhalation of isoflurane in 100% of oxygenprotocol 2: xylazine (1mg/kg)/ketamine (10mg/kg) and propofol (24mg/kg/h) by CRI, and protocol 3: propofol (5mg/kg) and propofol (12mg/kg/h) by CRI. Three clinically healthy adult mongrel dogs of both sexes were used. Food and water were withheld for 12 and 6 h before induction of anesthesia, respectively. Intravenous catheter was placed in the cephalic vein. A wash-out period of 15 days was allowed between protocols. For all protocols (1, 2, and 3), physiological parameters were recorded using a patient monitor. Depth of anesthesia and muscle relaxation were determined by recording various reflexes. Times of first limb movement, regaining swallowing reflex and extubation, sternal recumbency, and standing were recorded. Quality of recovery was also recorded. Venous blood samples were collected into EDTA-containing Vacutainer tubes immediately before anesthesia, 10min after induction with ketamine/propofol, one hour and two h of anesthesia and after complete recovery for hematological analysis by using an automated machine. Data were recorded and expressed as mean ± SD and analyzed with commercial statistical software. Results revealed slight variations among animals of the three protocols in the physiological parameters. The quality and depth of anesthesia were excellent in dogs anesthetized with isoflurane and were good in dogs during propofol infusion. The duration of deep anesthesia during propofol infusion was shorter than isoflurane, with the shortest duration in protocol 3. There were variations among animals of the three protocols in the recovery parameters. The mean scores of the recovery quality were 4.3, 4.7, and 4 for protocols 1, 2, and 3, respectively, which sited between good and excellent scores of recoveries. Slight ataxia was recorded in a dog of protocol 1. However, ataxia and urination were recorded in dogs of protocols 1 and 2. In conclusion, the effect of isoflurane and propofol on physiological parameters of dogs during long-term anesthesia was minimum and recovery was uneventful. The quality and depth of anesthesia were excellent in dogs anesthetized with isoflurane and were good in dogs during propofol infusion. The duration of deep anesthesia during propofol infusion was shorter than isoflurane, with the shortest duration in protocol 3 (12mg/kg/h). Isoflurane provides more reliable and consistent anesthetic plane plus it's not expensive as propofol. However, it requires special equipment. Propofol achieved effective anesthesia, with fast induction and less hypothermia than isoflurane administration. Apnea was recorded in two dogs after initial induction with propofol.

KEYWORDS
Long-term, Anesthesia, Dogs, Propofol, CRI

INTRODUCTION

Long surgical procedures are best managed with inhalation anesthesia. Even sick and debilitated patients recover from prolonged periods of inhalation anesthesia relatively quickly, and liver or renal impairment does not directly affect drug clearance (Bednarski, 2007). Injectable anesthesia using intramuscularly, or intravenously administered drugs has also been described (Hughes and Nolan, 1999; Ilkiw and Pascoe, 2003; and Mendes; Selmi, 2003). Xylazine is an alpha 2 adrenoceptor agonist. It has analgesic, sedative, and muscle relaxant effects (Lerche *et al.*, 2000; Hall *et al.*, 2011).

Propofol is a nonbarbiturate, nonsteroidal hypnotic agent that can be used to provide brief periods of anesthesia (5 to 10 min). The recommended dose is 4.0 to 6.0 mg/kg IV for the induction of anesthesia (Handel *et al.*, 1991; Nolan *et al.*, 1991; Taylor, 1991). Induction is smooth, as is recovery. If injected too rapidly, apnea may occur. Slow administration will prevent this complication. A 2-mg/kg IV dose has been used to induce anesthesia in camelids (Duke *et al.*, 1997). However, tracheal intubation is often difficult at this dose, and additional propofol is usually needed. A light plane of anesthesia can be maintained with a constant infusion of propofol at 0.4 mg/kg/min IV. The approximate time from discontinuation of propofol infusion to sternal recumbency is 10 to 15 min (Duke *et al.*, 1997). The use of infusion pumps enables a more precise propofol administration.

Ketamine is a dissociative anesthetic and has been used for decades in veterinary medicine. More recently, it has been rec-

ISSN: 2090-6277/2090-6269/

ognized as an N-Methyl-D-aspartate receptor antagonist and, at very low doses, can contribute substantially to analgesia by minimizing CNS sensitization (Lamont and Mathews, 2007). Ketamine has been used clinically for immobilization and anesthesia (Chen and Ensor, 1968; Thurmon *et al*., 1972). In dogs, it can increase muscle tone and can induce spontaneous movement and rough recoveries, and occasionally convulsions (Wright, 1982; Haskins *et al*., 1985). To reduce these undesirable effects, dissociative anesthetics are often used in combination with adjunctive drugs. In dogs, intravenous continuous-rate infusion of a low dose of ketamine (10 µg/kg/min) reduces the isoflurane Minimal Alveolar Concentration (MAC) by 25%, whereas the continuous-rate infusion of a combination of morphine (3.3 µg/kg/min), lidocaine (50 µg/kg/min), and ketamine (10 µg/kg/min) has reduced the isoflurane requirement as much as 45% (Muir *et al*., 2003). Xylazine is often used with ketamine for short-term anesthesia of 25 to 40 min. Isoflurane is generally considered the most widely used inhalation anesthetic in veterinary medicine, having replaced halothane in this regard. The MAC for isoflurane in healthy dogs is reported as 1.63 vol% (Eugene *et al*., 2007).

According to the available literatures, a detailed study to evaluate and compare different anesthetic protocols for long-term anesthesia techniques using isoflurane or propofol in dogs has not been reported yet. Consequently, the objective of the present study was to compare between three anesthetic protocols for long-term anesthesia (2 h): (1) Premedication by IV administration of xylazine (1mg/kg) and induction, 10 min later, by IV administration of ketamine (10mg/kg) and maintenance with isoflurane inhalation anesthesia (1.5-2.5% in 100% Oxygen). (2) Premedication by IV administration of xylazine (1mg/kg) and induction, 10 min later, by IV administration of ketamine (10mg/kg) and maintenance with propofol (24mg/kg/h) by constant-rate infusion. (3) Premedication by IV administration of xylazine (1mg/kg) and induction, 10 min later, by IV administration of propofol (5mg/kg) and maintenance with propofol (12mg/kg/h) by constant-rate infusion.

MATERIALS AND METHODS

Animals

The experiment was carried out at the Department of Surgery, Anesthesiology and Radiology, Veterinary Teaching Hospital, Faculty of Veterinary Medicine, Assiut University, Assiut, Egypt. Three clinically healthy adult mongrel dogs of both sexes (male = 2, non-pregnant, non-lactating female = 1) were housed in standard individual cages with adequate daily amounts of food and water ad libitum. Body weight range was from 12.6 to 18 kg (average = 15.6 kg). They were dewormed by administration of ivermectin at a dose of 1 ml/50 kg subcutaneously.

Methods

Food and water were withheld for 12 and 6 h before induction of anesthesia, respectively. The dog was weighed to calculate the dosage of drugs. Intravenous (IV) catheter (20-gauge) was placed in the cephalic vein. A wash-out period of 15 days was allowed between protocols.

Anesthetic protocol (1)

Dogs (n=3) were premedicated by IV administration of 1mg/kg of xylazine HCl (Xyla-ject, ADWIA Co., SAE, Egypt). Ten min later, anesthesia was induced by IV administration of 10mg/kg of ketamine (Sigma-tec Pharmaceutical Industries, SAE Egypt) and maintained by isoflurane (FORANE, Cairo Pharmaceutical and Chemical Industries, License from Abbvie, England) inhalation anesthesia (in 100% Oxygen). While the dog was in sternal recumbency, cuffed endotracheal tube was inserted. Dog was then moved onto a padded operating table (in a temperature-controlled room maintained at 21–24 °C) and positioned in right lateral recumbency. The anesthetized dog was connected with a semi-closed circle rebreathing anesthetic machine (ADOXAS2000, Prestige Equipment, Argentina). Anesthesia was maintained with isoflurane in 100% oxygen at a flow rate of 2 L/min. Anesthesia was discontinued after 2 h and dogs received supplemental oxygen (2 L/min) through endotracheal tube. All dogs were extubated at regaining swallowing reflexes. After extubation, oxygen was insufflated through nasal tube until sternal recumbency.

Anesthetic protocol (2)

Dogs (n=3) were premedicated by IV administration of 1mg/kg xylazine (1 mg/kg). Ten min later, anesthesia was induced by IV administration of ketamine (10 mg/kg) and maintained by IV propofol (Emulsion for injection, B. Braun Melsungen AG, Melsungen, Germany) at a dose of 24 mg/kg/h by constant-rate infusion using an infusion pump (JMS OT-601, Japan Medical Supply Co., LTD., Hiroshima, Japan). The dose was calculated and diluted in a net volume of 200 ml sterile normal saline and infused at a rate of 100 ml/h.

Anesthetic protocol (3)

Dogs (n=3) were premedicated by IV administration of xylazine (1 mg/kg). Ten min later, anesthesia was induced by IV administration of propofol (5 mg/kg) and maintained by IV propofol at a dose of 12 mg/kg/h by constant-rate infusion using an infusion pump. The dose was calculated and diluted in a net volume of 200 ml sterile normal saline and infused at a rate of 100 ml/h.

For all protocols, rectal temperature (RT), respiratory rate (RR), heart rate (HR), oxygen hemoglobin saturation (OHS), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial blood pressure (MBP) were recorded before and 10 min after administration of xylazine and then every 10 min until recovery. The six physiological parameters (HR, RR, RT, BP, OHS, and ECG) were recorded using a patient monitor (Lohmeir, Munchen, Germany). RT was measured by inserting the probe into the rectum.

The sensor of the pulse oximeter (OHS) was attached to the tongue. A five-branch cable was connected to the animal body to record lead II electrocardiogram (ECG), HR, and RR. Systolic (SBP), diastolic (DBP), and mean blood pressure (MBP) were measured indirectly with oscillometric technique, using a pediatric cuff placed around the forearm or shank or tail base. Depth of anesthesia was determined by recording palpebral, ear, and anal reflexes. Muscle relaxation was determined by recording jaw opening and tongue withdrawal reflexes. A scoring system (from 1 to 3) was developed to numerically express the values of the reflexes; where 1 means absence of the reflex, 2 means sluggish reflex, and 3 means strong reflex.

Times of first limb movement, regaining swallowing reflex and extubation, sternal recumbency, and standing were recorded. Quality of recovery was also recorded. Subjective scores for overall quality of recovery (1 = poor; 2 = marginal; 3 = fair; 4 = good; 5 = excellent) from two observers were averaged to provide an overall recovery score. A score of 1 is associated with

multiple, uncoordinated attempts to achieve sternal or standing posture resulting in a major or life-threatening injury. Score 2 is associated with excitement, paddling when recumbent, several attempts to stand, severe ataxia once standing, possible fall, and danger of self-inflicted injury. Score 3 shows some staggering and ataxia, a few unsuccessful attempts to stand, and ataxia immediately after standing up. Score 4 presents signs of slight ataxia and staggering, standing at first or second attempt, and no serious instability. A score of 5 is associated with fewer than 3 quiet, coordinated efforts to sternal or standing posture.

Venous blood samples were collected into EDTA-containing Vacutainer tubes immediately before anesthesia, 10min after induction with ketamine/propofol, one hour and two h of anesthesia, and after complete recovery. Red blood cell counts (RBC), white blood cell counts (WBC), differential leukocytic counts (DLC), hemoglobin concentration (HB), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), and platelet counts (PLT) were determined by using automated machine (Cell-Dyn 2500, Abbott Diagnostics Santa Clara, CA, USA).

Statistical Analysis

Data were recorded on a recording sheet and expressed as mean ± SD and analyzed with a commercial statistical software package (Statistical Package for Social Sciences, SPSS Inc., Chicago, IL, USA, v18.0, 2009). Repeated measures analysis of variance was used as a statistical model to evaluate differences over time and between protocols in dependent variables, including parameters of physiological and hematological functions. Tukey's HSD test was used to calculate multiple comparisons. Results were considered significant at $P < 0.05$.

RESULTS

Physiological parameters

Respiratory Rate

The respiratory rate started to significantly decrease after xylazine injection in all groups. During anesthesia, respiratory rate was significantly lower than baseline 10 min after isoflurane inhalation and propofol infusion. This decrease in respiratory rate continued to be lower than the baseline till 40 min of recovery (Fig. 1). Group 1 showed a significantly lower respiratory rate compared to groups 2 and 3 at 10, 50, and 120 min of isoflurane inhalation. Apnea was recorded in two dogs of protocol 3 after induction with propofol. These two dogs regained respiration within a minute.

Rectal Temperature

In all groups, there were non-significant decreases in rectal temperature during the long-term isoflurane inhalation anesthesia and propofol anesthesia by continuous rate infusion compared to the baseline (Fig. 2).

Group 3 showed significantly lower rectal temperature compared to group 2 at the baseline and after 10 min of xylazine injection, however, all the recorded rectal temperatures were within the normal range in dogs. Importantly, there was no significant difference between the different protocols after ketamine/propofol induction and during anesthesia by isoflurane or propofol.

Heart Rate

In group 1, heart rate was non-significantly decreased compared

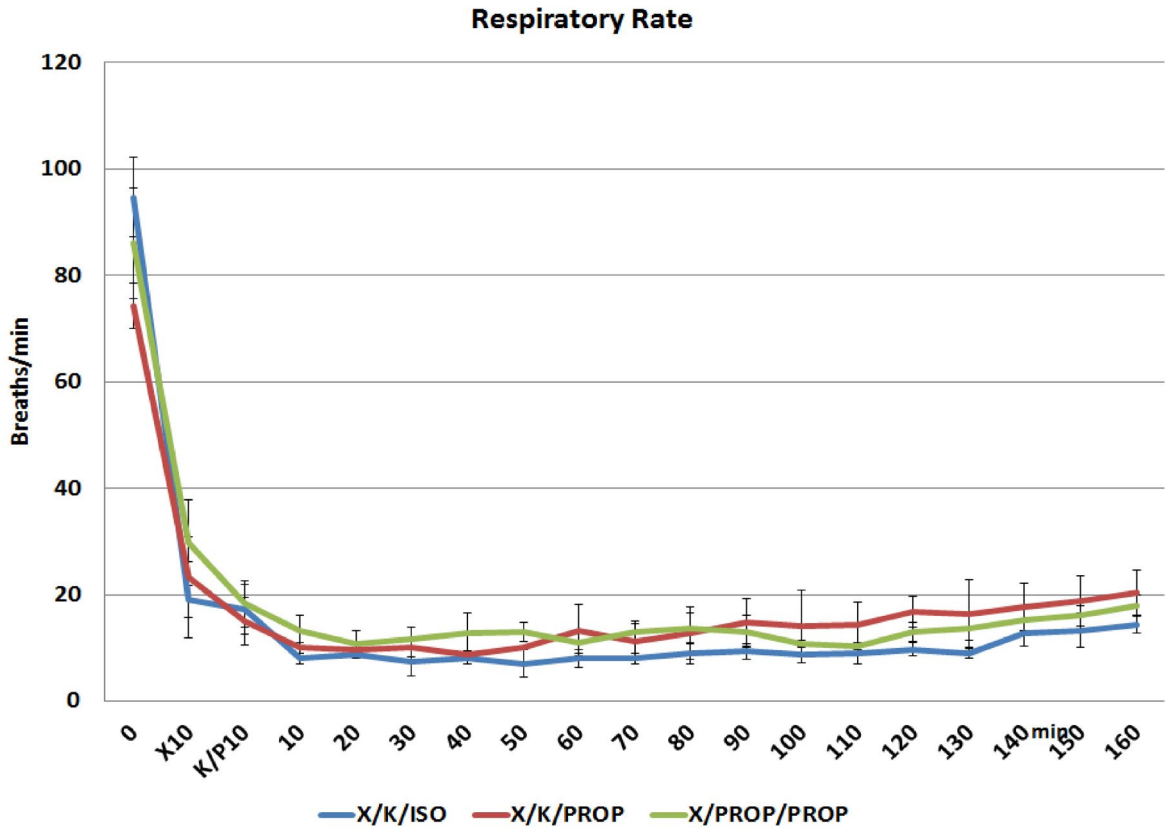

Fig. 1. Mean values (±SD) of respiratory rate of dogs during three different anesthetic protocols

to the baseline at the different time points after isoflurane inhalation. However, heart rate was significantly lower than the baseline at 10 min of isoflurane inhalation. In group 2, heart rate was non-significantly different compared to the baseline at the different time points after propofol infusion. At 70, 90, and 110 min of propofol injection, the heart rate was significantly lower than the baseline. In group 3, no significant changes were observed in the heart rate after infusion of propofol at any time point compared to the baseline (Fig. 3). After 10 min of xylazine injection, the heart rate was decreased in all groups. There was a significant

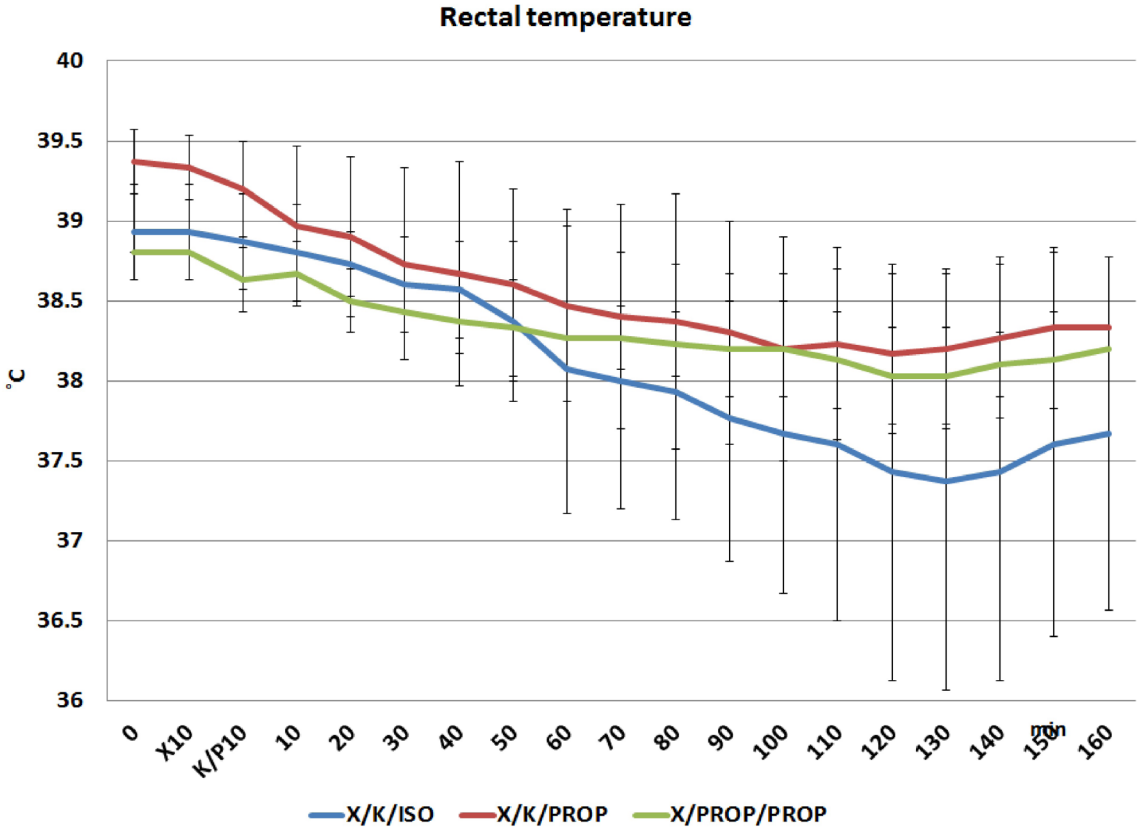

Fig. 2. Mean values (±SD) of rectal temperature of dogs during three different anesthetic protocols

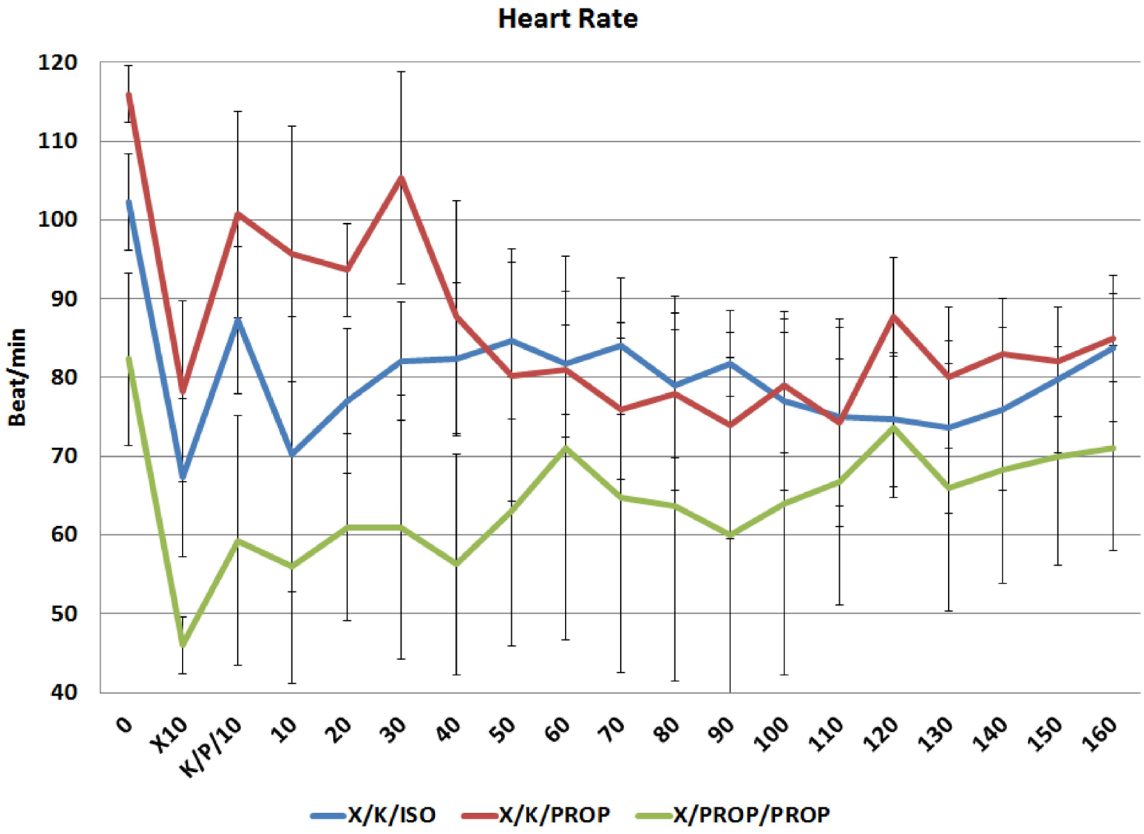

Fig. 3. Mean values (±SD) of heart rate of dogs during three different anesthetic protocols

difference between groups 2 and 3 at 10 min of xylazine injection, after ketamine/propofol injection, and 20 min of isoflurane /propofol anesthesia.

Hemoglobin Oxygen Concentration

In all groups, no significant changes were observed in the hemoglobin oxygen concentration after isoflurane inhalation and

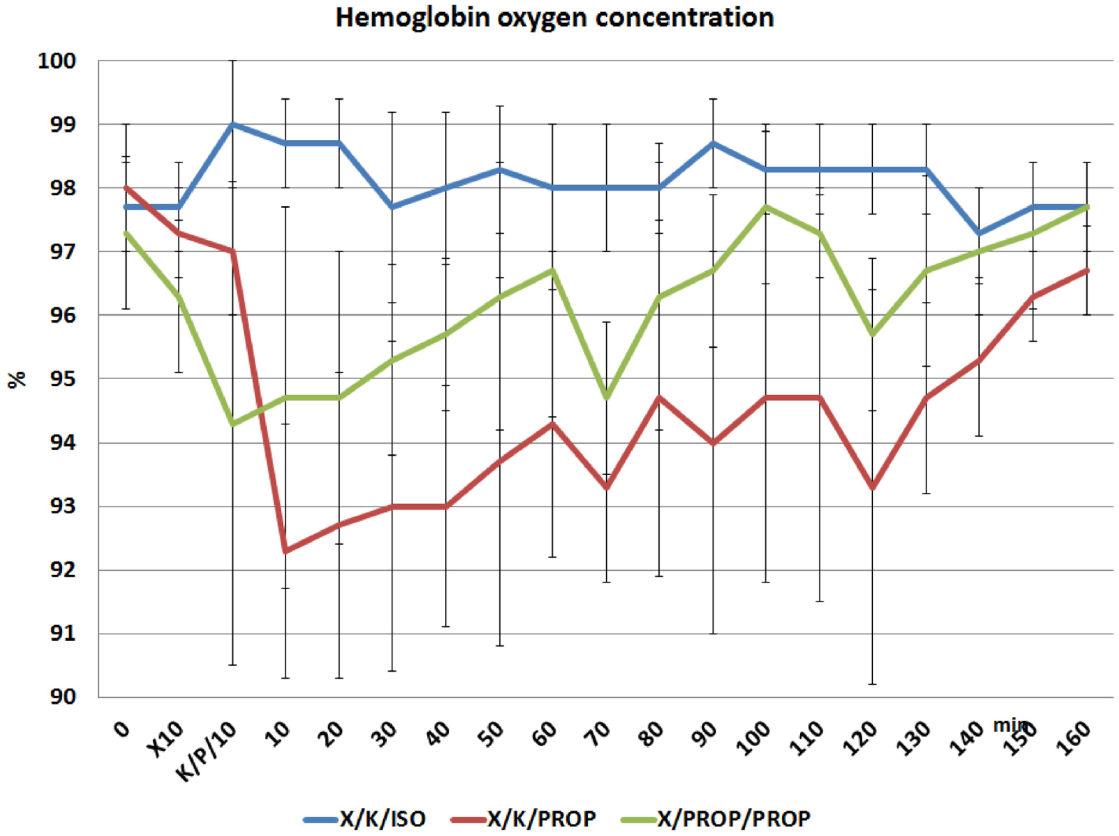

Fig. 4. Mean values (±SD) of hemoglobin oxygen concentration of dogs during three different anesthetic protocols

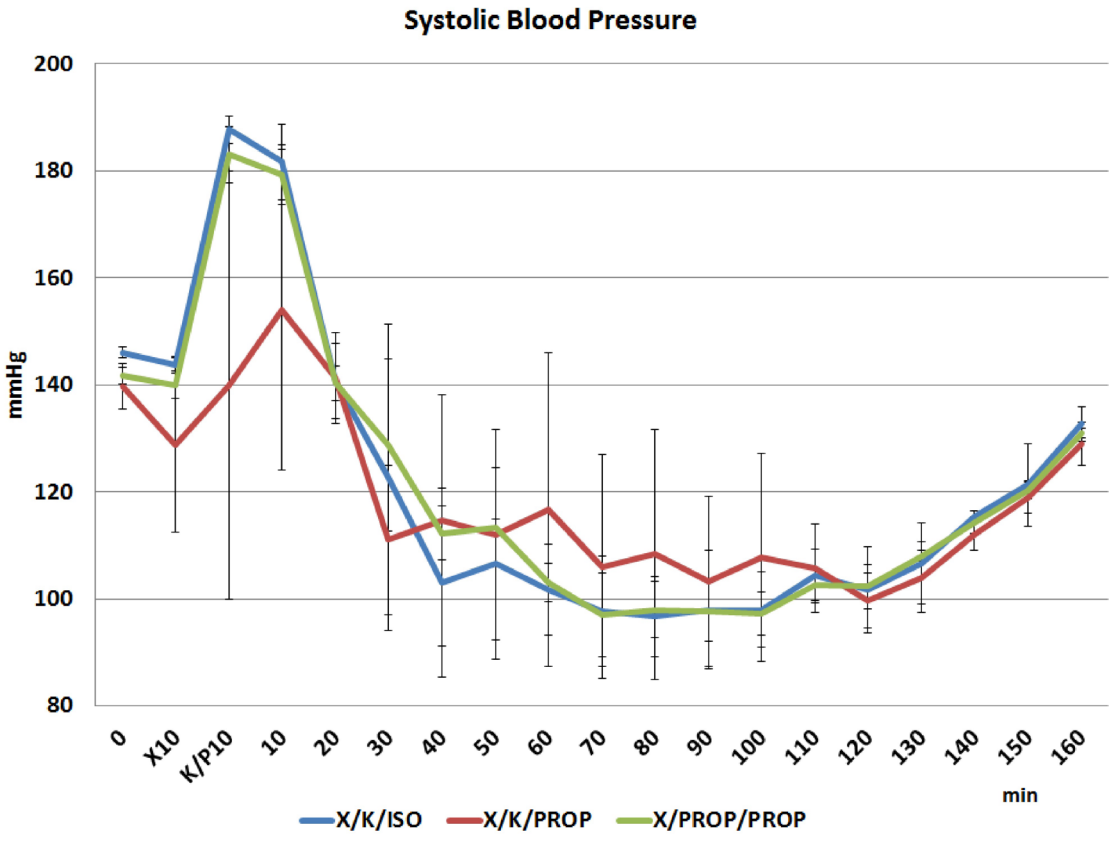

Fig. 5. Mean values (±SD) of systolic blood pressure of dogs during three different anesthetic protocols

Table 1. Mean (±SD) Scores of Reflexes and Anesthetic Quality of dogs (n=3) during different anesthetic protocols.

Time (min)		0	X10	K10	10	20	30	40	50	60	70	80	90	100	110	120	130	140	150	160
Palpebral reflex	X/K/ISOF	3 ± 0^{aC}	3 ± 0^{aC}	1.3 ± 0.5^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1±0aA	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	2 ± 0^{aB}	2.7 ± 0.6^{aC}	3 ± 0^{aC}
	X/K/PROP	3 ± 0^{aC}	3 ± 0^{aC}	2 ± 0^{aB}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aB}	2.70 ± 0.6^{bB}	3 ± 0^{aC}	3 ± 0^{aC}
	X/PROP/PROP	3 ± 0^{aC}	2.3 ± 0.6^{aBC}	1.3 ± 0.6^{aAB}	1.7 ± 0.6^{aAB}	1 ± 0^{aA}	1 ± 0^{aA}	1.3 ± 0.6^{aAB}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1.3 ± 0.6^{aAB}	1.3 ± 0.6^{aAB}	1.3 ± 0.6^{aAB}	3 ± 0^{bC}	3 ± 0^{aC}	3 ± 0^{aC}
Ear reflex	X/K/ISOF	3 ± 0^{aC}	2 ± 0^{aB}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	2.7 ± 0.6^{aC}	3 ± 0^{aC}	3 ± 0^{aC}
	X/K/PROP	3 ± 0^{aC}	2 ± 0^{aB}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	3 ± 0^{aC}	3 ± 0^{aC}	3 ± 0^{aC}
	X /PROP/PROP	3 ± 0^{aC}	2 ± 0^{aB}	1 ± 0^{aA}	1 ± 0^{aA}	1.3 ± 0.6^{aAB}	1.3 ± 0.6^{aAB}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1.3 ± 0.6^{aAB}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1.3 ± 0.6^{aAB}	1.3 ± 0.6^{aAB}	1.3 ± 0.6^{aAB}	3 ± 0^{aC}	3 ± 0^{aC}	3 ± 0^{aC}
Anal Reflex	X/K/ISOF	3 ± 0^{aB}	2 ± 0^{B}	1.3 ± 0.6^{A}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	2 ± 0^{aB}	2.7 ± 0.6^{aC}	3 ± 0^{aC}
	X/K/PROP	3 ± 0^{aB}	2 ± 0^{aB}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	2.7 ± 0.6^{bC}	3 ± 0^{aC}	3 ± 0^{aC}
	X/PRO/PROP	3 ± 0^{aB}	2 ± 0^{aB}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1.3 ± 0.6^{aAB}	1.3 ± 0.6^{aAB}	1.3 ± 0.6^{aAB}	3 ± 0^{bC}	3 ± 0^{aC}	3 ± 0^{aC}
Tongue withdraw reflex	X/K/ISOF	3 ± 0^{aB}	3 ± 0^{aB}	1.3 ± 0.6^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	3 ± 0^{aB}	3 ± 0^{aB}	3 ± 0^{aB}
	X/K/PROP	3 ± 0^{aB}	3 ± 0^{aB}	1.3 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	3 ± 0^{aB}	3 ± 0^{aB}	3 ± 0^{aB}
	X/PROP/ROP	3 ± 0^{aB}	3 ± 0^{aB}	1.3 ± 0.6^{aA}	1.3 ± 0.6^{aA}	1.3 ± 0.6^{aA}	1.3 ± 0.6^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1.3 ± 0.6^{aA}	1.3 ± 0.6^{aA}	1.3 ± 0.6^{aA}	3 ± 0^{aB}	3 ± 0^{aB}	3 ± 0^{aB}
Jaw Opening reflex	X/K/ISOF	3 ± 0^{aC}	3 ± 0^{aC}	1.3 ± 0.5^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	2 ± 0^{aB}	2.7 ± 0.6^{aC}	3 ± 0^{aC}
	X/K/PROP	3 ± 0^{aC}	3 ± 0^{aC}	1.3 ± 0^{aB}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aB}	2.70 ± 0.6^{bB}	3 ± 0^{aC}	3 ± 0^{aC}
	X/PROP/ROP	3 ± 0^{aC}	2.3 ± 0.6^{aBC}	2 ± 0.6^{aAB}	1.7 ± 0.6^{aAB}	1 ± 0^{aA}	1 ± 0^{aA}	1.3 ± 0.6^{aAB}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1.3 ± 0.6^{aAB}	1.3 ± 0.6^{aAB}	1.3 ± 0.6^{aAB}	3 ± 0^{bC}	3 ± 0^{aC}	3 ± 0^{aC}
Anesthetic quality	X/K/ISOF	3 ± 0^{aB}	3 ± 0^{aB}	1.3 ± 0.6^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	3 ± 0^{aB}	3 ± 0^{aB}	3 ± 0^{aB}
	X/K/PROP	3 ± 0^{aB}	3 ± 0^{aB}	1.3 ± 0^{aA}	1.3 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	3 ± 0^{aB}	3 ± 0^{aB}	3 ± 0^{aB}
	X/PROP/ROP	3 ± 0^{aB}	3 ± 0^{aB}	1.3 ± 0.6^{aA}	1.3 ± 0.6^{aA}	1.3 ± 0.6^{aA}	1.3 ± 0.6^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1 ± 0^{aA}	1.3 ± 0.6^{aA}	1.3 ± 0.6^{aA}	1.3 ± 0.6^{aA}	3 ± 0^{aB}	3 ± 0^{aB}	3 ± 0^{aB}

X=Xylazine, K=Ketamine, ISOF=Isoflurane, PROP=Propofol. Values of different uppercase superscript letters indicate a significant difference between the time points within the same group while values with different lowercase superscript letters indicate a significant difference between the groups at the same time point ($p<0.05$).

propofol infusion at any time point compared to the baseline (Fig. 4). Comparison between groups revealed a significantly higher hemoglobin oxygen concentration at 70 min of isoflurane inhalation compared to groups 2 and 3.

Blood Pressure

In group 1, the systolic blood pressure was significantly increased after ketamine injection to 187.7±2.5 mmHg and continued higher than the baseline (146±1 mmHg) even after 10 min of isoflurane inhalation. After 20 min of isoflurane inhalation, the systolic blood pressure returned to the normal baseline then started to significantly decrease after 40 min of isoflurane inhalation and till 10 min of recovery. Systolic blood pressure gradually increased during recovery to approach the baseline values with non-significant changes between groups. There was a significant decrease in the mean and diastolic blood pressure starting from 40 min and continued lower than the baseline till 20 min of stopping isoflurane inhalation. Starting from 30 min till 40 min of stopping isoflurane inhalation, no significant changes were observed compared to the baseline for both mean and diastolic blood pressure. In group 2, no significant changes were observed in the systolic, mean, or diastolic blood pressure after injection of propofol at any time point compared to the baseline (Fig. 5 to 7).

In group 3, a significant decrease in the systolic blood pressure starting from 70 min and continued lower than the baseline till 110 min of propofol infusion. During recovery, no significant changes were recorded when compared to the baseline value. The mean blood pressure was significantly decreased 40 min after propofol injection and continued to be lower than the baseline till 30 min of stopping propofol infusion. At 40 min of recovery from propofol, the systolic blood pressure increased to a non-significant level compared to the baseline. The diastolic blood pressure was reduced to 82.3±11 mmHg 40 min of propofol injection compared to 112±3 mmHg (baseline value). The DBP continued to be lower than the baseline till 20 min of recovery. During recovery, BP gradually increased towards the baseline values without significant changes between groups (Fig. 5 to 7).

Electrocardiograph (ECG)

Electrocardiograph showed a normal sinus rhythm before premedication in all dogs. Bradyarrhythmia with increased PR and ST interval were recorded after xylazine administration; however, a relative tachyarrhythmia was observed after ketamine administration. Moreover, an inverted T wave was noticed during anesthesia in all dogs. A decrease in QRS and T wave amplitudes with an increase in PR interval were recorded during isoflurane anesthesia and during the early recovery period. ECG showed dysrhythmia with irregular ST intervals and asystole during early periods of propofol anesthesia. The ECG was quite regular towards the end stages of propofol anesthesia.

Quality and Depth of Anesthesia

The quality and depth of anesthesia were excellent in dogs anesthetized with isoflurane (protocol 1). The mean set value of the isoflurane vaporizer was 1.54% (range =1-4.5%). However, anesthesia was good in dogs during propofol infusion in the two protocols (2 and 3). The duration of deep anesthesia during propofol infusion was shorter than isoflurane, with the shortest duration in protocol 3 (Table 1).

Palpebral reflex

In protocols 1 and 2, the palpebral reflex was absent after ketamine injection. The reflex continued to be lost 10 min after turning off the vaporizer of isoflurane. After 40 min of turning off the

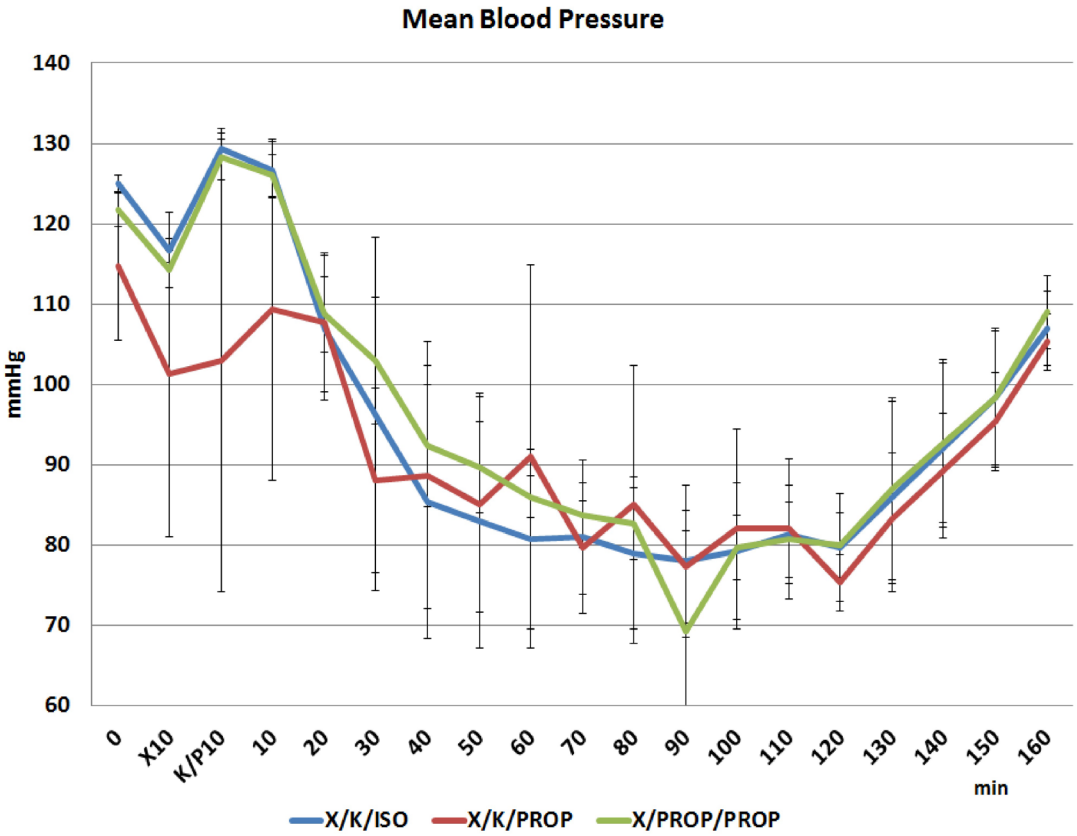

Fig. 6. Mean values (±SD) of mean blood pressure of dogs during three different anesthetic protocols

vaporizer, the palpebral reflex returned to normal in all dogs with a score of 3 ± 0. In protocol 2, the reflex continued to be lost until 20 min and returned to normal reflex with a score of 3 ± 0 after 30 min of stopping propofol infusion. In protocol 3, the palpebral reflex was absent after propofol injection and continued to be lost until 10 min of stopping propofol infusion. The reflex returned to normal with a score of 3 ± 0 after 20 min of stopping propofol infusion (Table 1).

Ear Reflex

Ear reflex disappeared 10 after ketamine injection and stayed absent during anesthesia of the three protocols. It returned to normal after 30 min of turning off the isoflurane vaporizer and after 20 min of stopping propofol infusion in protocols 2 and 3 (Table 1).

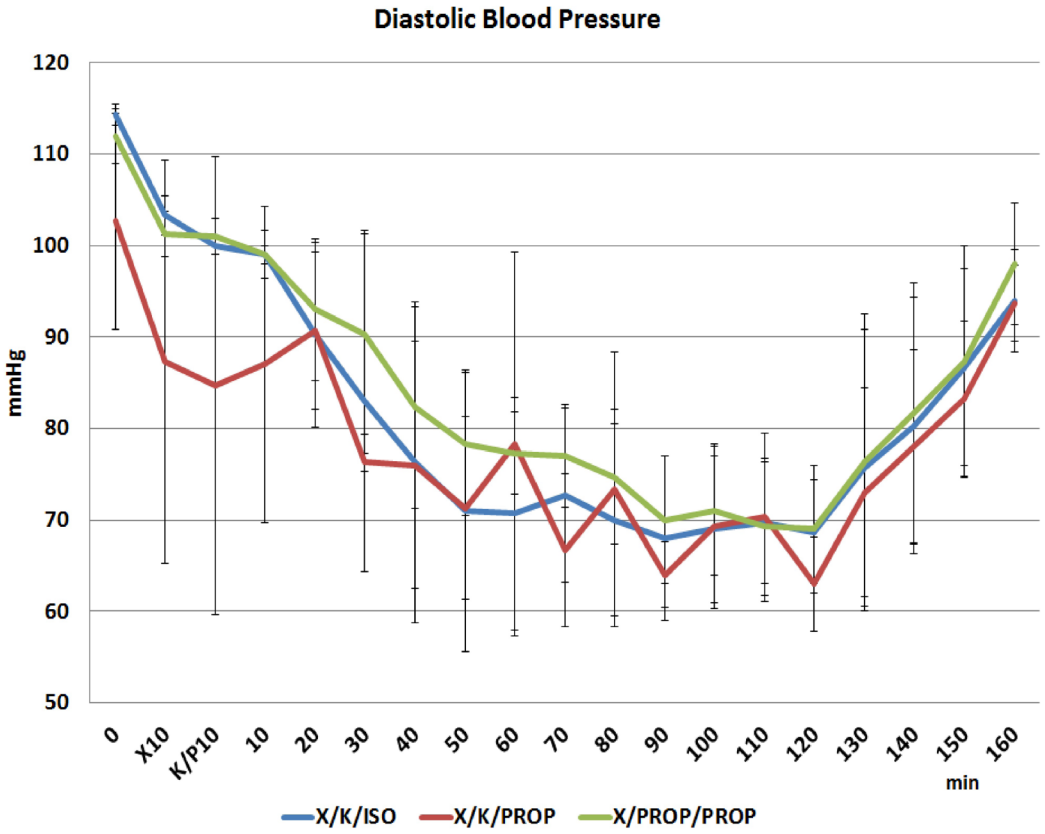

Fig. 7. Mean values (±SD) of diastolic blood pressure of dogs during three different anesthetic protocols

Table 2. Mean (±SD) hematological parameters (RBCs, HB, HCT, MCV, MCHC) in dogs (n=3) during different anesthetic protocols.

Time (Min)		Before	After induction	After 1h	After 2h	Recovery
RBCs (x10^6/µl)	X/K/ISOF	7.45±0.92^{bA}	6.14±0.8^{aA}	5.53±0.9^{aA}	5.73±0.54^{aA}	6.58±0.48^{bA}
	X/K/PROP	6.47±0.45^{abA}	6.1±0.46^{aA}	4.93±0.66^{aA}	4.8±0.69^{aA}	5.06±0.58^{aA}
	X/PROP/PROP	5.61±0.17^{aA}	5.2±0.3^{aA}	4.73±0.45^{aA}	4.67±0.69^{aA}	5.24±0.55^{abA}
HB (g/dl)	X/K/ISOF	18.27±1.30^{bA}	15.77±1.46^{aA}	14.23±2.85^{aA}	13.93±1.027^{aA}	15.8±1.6^{aA}
	X/K/PROP	16.67±0.90^{bC}	15.26±1.079^{aBC}	12.33±1.34^{aAB}	11.97±1.46^{aA}	12.5±1.05^{aAB}
	X/PROP/PRO	13.73±0.95^{aA}	12.66±1.15^{aA}	11.6±1.4^{aA}	11.76±2.5^{aA}	13.1±2.29^{aA}
HCT (%)	X/K/ISOF	52.17±2.55^{bA}	39.36±12.46 ^{aA}	39.07±8.85^{aA}	40±1.45^{aA}	44.47±3.25^{aA}
	X/K/PROP	51±2.72^{bB}	45.73±4.28^{aAB}	38±4.03^{aA}	36.9±4.39^{aA}	35.17±6.35^{aA}
	X/PROP/PROP	41.1±4^{aA}	29±4.5^{aA}	35±5^{aA}	36.1±9.24^{aA}	39.17±6.78^{aA}
MCV (fl)	X/K/ISOF	70.6±6.06^{aA}	70.66±4.38^{aA}	70.28±4.22^{aA}	70.09±4.58^{aA}	67.46±0.05^{aA}
	X/K/PRO	79±4.03^{aA}	78.1±4.27^{aA}	77.3±4.43^{aA}	77.16±4.31^{aA}	76.4±5.15^{aA}
	X/PROP/PROP	72.9±4.9^{aA}	72.9±4.4^{aA}	72.93±3.95^{aA}	76.46±8.17^{aA}	74.43±6.81^{aA}
MCHC (g/dl)	X/K/ISOF	34.96±0.76^{bA}	34.55±1.37^{aA}	36.68±1.08^{bA}	34.78±1.41^{aA}	35.45±1.05^{bA}
	X/K/PROP	32.66±0.05^{aC}	32.63±0.05^{aBC}	32.43±0.11^{aAB}	32.4±0.1^{aA}	32.46±0.05^{aABC}
	X/PROP/PROP	33.56±0.95^{aBA}	33.36±0.85^{aA}	33.2±0.7^{aA}	32.86±1.65^{aA}	33.43±1.05^{aBA}

X=Xylazine, K=Ketamine, ISOF=Isoflurane, PROP=Propofol. Values of different uppercase superscript letters indicate a significant difference between the time points within the same group while values with different lowercase superscript letters indicate a significant difference between the groups at the same time point ($p<0.05$).

Anal Reflex

There was a significant reduction in the anal reflex (i.e. anal dilatation) score after injection of ketamine in protocols 1 and 2 or after propofol injection in protocol 3 (Table 1). The anal reflex score continued to be absent during anesthesia in the three protocols. The reflex returned to normal after 40 min of turning off the isoflurane vaporizer. It returned to normal reflex after 30 and 20 min of stopping propofol infusion in protocols 2 and 3, respectively. Comparison between groups, showed comparable scores of anal reflexes at the different time points except at 140 min of anesthesia whereas group 1 showed a a significantly lower value compared to groups 2 and 3.

Tongue Withdrawal Reflex

Tongue withdrawal reflex was absent 10 min of ketamine injection in protocols 1 and 2. While it was absent after 40 min of propofol infusion in protocol 3. The reflex returned to normal 20 min of stopping isoflurane inhalation and propofol infusion (Table 1).

Jaw Opening Reflex

Jaw opening reflex was absent 10 min of ketamine injection in protocols 1 and 2. While it was absent after 20 min of propofol infusion in protocol 3. The reflex returned to normal 40, 30, and 20 min in protocols 1, 2, and 3, respectively (Table 1). Comparison between groups, showed non-significant differences between the scores of jaws opening reflexes at the different time points except at 20 min of recovery whereas group 1 showed a significantly lower value compared to groups 2 and 3.

Quality of Recovery

There were variations among animals of the three protocols in the recovery parameters. The mean scores of the recovery quality were 4.3, 4.7, and 4 for protocols 1, 2, and 3, respectively, which sited between good and excellent scores of recoveries. Slight ataxia was recorded in a dog of protocol 1. However, ataxia and urination were recorded in dogs of protocols 1 and 2.
The mean periods for dogs to regain swallowing reflex were 8 (range=5-14), 9.7 (range=6-17), and 6.7 (range=1-13) min for protocol 1, 2, and 3, respectively. The mean times for the dogs to firstly move the limbs were 11.3 (range=9-15), 12 (range=7-19), and 7.3 (range=1-14) min for protocol 1, 2, and 3, respectively. The mean periods for dogs to take the sternal recovery were 21 (range=14-33), 24.7 (range=12-33), and 11.7 (range=2-18) min for protocol 1, 2, and 3, respectively. The mean periods for dogs to stand were 24.7 (range=19-35), 33 (range=23-42), and 14.7 (range=3-24) min for protocols 1, 2, and 3, respectively.

Hematological Analysis

In all groups, no significant changes in the RBCs count, HB concentration, HCT, MCV, WBCs count, and differential leucocytic count were observed at the different time points after induction, during isoflurane inhalation, or propofol infusion, and during recovery compared to the baseline values (Tables 2 and 3).
During recovery, the RBCs count was significantly lower in group 2 compared to group 1. In group 2, there was a significant decrease in HB concentration, HCT, and MCHC after 1 hour of propofol infusion. The hemoglobin concentrations were also lower than the baseline after 2 h and during recovery from propofol infusion. Group 2 showed a significant lower MCHC compared to group

Table 3. Mean (±SD) hematological parameters (WBCs, Neutrophils, Lymphocytes, Eosinophils, Monocytes, Basophils, PLT) in dogs (n=3) during different anesthetic protocols.

Time		Before	After Ketamine	After 1 h	After 2 h	Recovery
WBCs ($x10^3$/µl)	X/K/ISO	$10.86±3.9^{aA}$	$11.11±1.87^{aA}$	$12.53±2.93^{aA}$	$11.13±0.76^{aA}$	$11.43±3.60^{aA}$
	X/K/PROP	$16±0.69^{aA}$	$16.33±2.09^{aA}$	$15.66±5.57^{aA}$	$14.93±5^{aA}$	$16.76±4.70^{aA}$
	X/PROP/PROP	$13.1±4.59^{aA}$	$14.46±5.44^{aA}$	$15.86±7.94^{aA}$	$12.13±4.27^{aA}$	$15.03±7.19^{aA}$
Neutrophils ($x10^3$/µl)	X/K/ISO	$5.87±2.72^{aA}$	$6.36±2.42^{aA}$	$6.66±1.07^{aA}$	$6.57±3.29^{aA}$	$6.77±4.44^{aA}$
	X/K/PROP	$5.58±0.72^{aA}$	$5.55±0.61^{aA}$	$4.64±2.13^{aA}$	$3.55±2.02^{aA}$	$4.09±2.02^{aA}$
	X/PROP/PROP	$2.673±0.71^{aA}$	$3.61±0.85^{aA}$	$3.04±1.38^{aA}$	$2.46±0.67^{aA}$	$3.62±0.78^{aA}$
Lymphocytes ($x10^3$/µl)	X/K/ISO	$2.63±1.40^{aA}$	$2.92±1.99^{aA}$	$3.34±1.48^{aA}$	$2.85±1.74^{aA}$	$2.9±0.79^{aA}$
	X/K/PROP	$6.37±1.37^{aBA}$	$6.84±1.56^{aA}$	$6.51±1.25^{aA}$	$7.61±0.59^{bA}$	$8.1±0.96^{aA}$
	X/PROP/PROP	$7.94±2.73^{bA}$	$8.66±3.22^{aA}$	$10.08±4.42^{aA}$	$7.24±2.16^{bA}$	$8.24±5.18^{aA}$
Eosinophils ($x10^3$/µl)	X/K/ISO	$0.21±0.08^{abA}$	$0.26±0.25^{aA}$	$0.36±0.09^{aA}$	$0.17±0.15^{aA}$	$0.14±0.08^{aA}$
	X/K/PROP	$0.32±0.01^{bA}$	$0.33±0.03^{aA}$	$0.31±0.11^{aA}$	$0.26±0.14^{aA}$	$0.29±0.15^{aA}$
	X/PROP/PROP	$0.13±0.04^{aA}$	$0.18±0.10^{aA}$	$0.22±0.21^{aA}$	$0.12±0.03^{aA}$	$0.35±0.29^{aA}$
Monocytes ($x10^3$/µl)	X/K/ISO	2.14±3Aa	$1.52±2.11^{aA}$	$1.96±2.53^{aA}$	$1.51±2.05^{aA}$	$1.6±1.67^{aA}$
	X/K/PROP	$3.71±0.41^{aA}$	$3.62±1.40^{aA}$	$4.19±2.11^{aA}$	$3.5±2.53^{aA}$	$4.27±2.04^{aA}$
	X/PROP/PROP	$2.32±1.54^{aA}$	$2.02±1.56^{aA}$	$2.53±2.04^{aA}$	$2.18±1.78^{aA}$	$2.78±2.36^{aA}$
Basophils ($x10^3$/µl)	X/K/ISO	$0±0^{aA}$	$0±0^{aA}$	$0±0^{aA}$	$0±0^{aA}$	$0±0^{aA}$
	X/K/PROP	$0±0^{aA}$	$0±0^{aA}$	$0±0^{aA}$	$0±0^{aA}$	$0±0^{aA}$
	X/PROP/PROP	$0±0^{aA}$	0±0aA	$0±0^{aA}$	$0±0^{aA}$	$0±0^{aA}$
PLT ($x10^3$/µl)	X/K/ISO	$488.33±32.50^{aAB}$	$403±43^{aAB}$	$408.33±95.50^{aAB}$	$362±63^{aA}$	$656.33±180.50^{bB}$
	X/K/PROP	$281.66±74.74^{aA}$	$400.33±170.76^{aA}$	$362.33±118.16^{aA}$	$336.33±111.35^{aA}$	$319.66±124.60^{aBA}$
	X/PROP/PROP	$274.33±136.50^{aA}$	$222±44.93^{aA}$	$200.66±89.66^{aA}$	$200±79^{aA}$	$204.33±98.78^{aA}$

X=Xylazine, K=Ketamine, ISOF=Isoflurane, PROP=Propofol. Values of uppercase superscript letters indicate a significant difference between the time points within the same group while values with different lowercase superscript letters indicate a significant difference between the groups at the same time point ($p<0.05$).

1 during recovery. In group 1, there was a significant decrease in the platelets count after 2 h of isoflurane inhalation (362 ± 63 platelet) compared to the baseline value (488.33 ± 32.50 platelet). At recovery, no significant change was recorded compared to the baseline value. Group 3 demonstrated a significant lower platelets count compared to group 1 during recovery.

DISCUSSION

There were slight variations in the effect of anesthesia on the physiological parameters among animals of the three protocols. Apnea was recorded in two dogs of protocol 3 after induction with propofol. The quality and depth of anesthesia were excellent in dogs anesthetized with isoflurane and were good in dogs during propofol infusion. The duration of deep anesthesia during propofol infusion was shorter than isoflurane, with the shortest duration in protocol 3. There were variations among animals of the three protocols in the recovery parameters. The mean scores of the recovery quality were 4.3, 4.7, and 4 for protocols 1, 2, and 3, respectively, which sited between good and excellent scores of recoveries. Slight ataxia was recorded in a dog of protocol 1. However, ataxia and urination were recorded in dogs of protocols 1 and 2. Results of this study revealed that the use of isoflurane in xylazine-ketamine pre-medicated dogs gave satisfactory results with low side effects relative to other two different protocols.

During isoflurane anesthesia, there was a significant decrease of respiratory rate compared to propofol in the present study. Isoflurane has been cited to be a profound respiratory depressant. Therefore, respiration must be monitored closely in dogs as well as horses and supported when necessary (Klid, 1976; Steffey and Howland, 1977). The decrease in respiratory rate has been attributed to a central effect or as a result of accumulation of carbon dioxide (hypercapnia) and then respiratory acidosis (Kuusela *et al*., 2003 and Abdelhakiem *et al*., 2019). Apnea was currently recorded in two dogs (protocol 3) after induction with propofol. A similar result has been recorded in dogs after initial boluses of propofol (Robertson *et al*. 1992). Maintenance of adequate respiration has been cited to be a prime requirement for safe anesthesia and inadequate tissue oxygenation may lead to an acute cessation of vital organ function (McDonell and Kerr, 2007). Increasing depth of anesthesia with isoflurane has been reported to increase respiratory depression (Stanski, 2000). However, the respiratory rate did not differ between treatments during propofol infusion and propofol/isoflurane anesthesia in dogs of another study (Kuusela *et al*., 2003). Dogs of the present study did not need ventilation support during propofol infusion. In another study, ventilatory support during continuous propofol infusion has been recommended because respiratory depression and apnea should be expected as potential adverse effects after intravenous administration of propofol to dogs, particularly when administered at rapid rates of infusion (Keegan and Greene, 1993).

A non-significant decrease in the rectal temperature was currently observed during isoflurane inhalation and propofol infusion. There were no differences between groups in temperature in similar long-term propofol or isoflurane anesthesia in dogs (Thompson *et al*., 2002). On the other hand, there was a significant reduction of body temperature after isoflurane over time in the dogs (Lozano *et al*., 2009; Browning, *et al*., 2019). However, rectal temperature has been decreased during propofol anesthesia (Robertson *et al*. 1992), total intravenous anesthesia of propofol with fentanyl (Yamashita *et al*., 2004), total intravenous anesthesia of propofol plus ketamine (Seliskar, 2007), and constant rate infusion of propofol (Njoku, 2015). Rectal temperatures have been taken during surgery to avoid hypothermia. Hypothermia is a common complication of general anesthesia and surgery. Amongst other deleterious effects, it is associated with slower recovery from anesthesia, likely due to a number of different mechanisms (Pottie *et al*., 2007). The decrease in body temperature may be attributed to the reduction of the muscle activity of anesthetized animals. as Additionally, the recumbent position of unconscious animals during anesthesia and the environmental temperature around anesthetized animals may reduce the body temperature. Hypothermia impairs drug metabolism and potentially prolongs recovery from anesthesia (Insler and Sessler, 2006; Bornkamp *et al*., 2015). Moreover, ketamine administration minimizes the incidence of hypothermia as a result of the peripheral vasoconstriction that results from an increase of norepinephrine concentration. Peripheral vasoconstriction limits blood flow to the extremities thus minimizing the amount of heat loss to the environment and decreasing the extent of redistribution hypothermia (Ikeda *et al*., 2001). In contrast, propofol administration has been associated with peripheral arterial and venous vasodilation, resulting in an increase in blood flow to the extremities and loss of heat to the environment via radiation and convection as demonstrated by before (Bornkamp *et al*., 2015). To prevent heat loss, the use of warm-air blankets or resistive warming systems has been cited to be necessary for maintaining normal body temperature (Bornkamp *et al*., 2015).

The present work showed no significant variation in heart rate except at 10 min of isoflurane inhalation where heart rate was lower than the baseline. A significant decrease in HR after Xylazine administration then a slight increase after Ketamine administration has been observed in dogs (Green *et al*., 1981). After 10 min of isoflurane administration, there was a significant decrease in HR, this decrease of HR was followed by a non-significant change until the end of 2 h, which was in accordance with the results reported elsewhere (Mutoh *et al*., 1995). Moreover, Polis *et al*. (2001) have found non-significant changes in heart rate over time during isoflurane anesthesia in mongrel dogs. However, dogs anesthetized with isoflurane have had higher values for heart rate than with propofol (Keegan and Greene, 1993; Kuusela *et al*., 2003). Claeys *et al*. (1988) have shown that heart rate did not change significantly at any time during anesthesia-induced and was maintained with propofol. In a comparative study of propofol or propofol and ketamine for induction of anesthesia in dogs (Lerche *et al*., 2000; Seliskar, 2007), it has been found that heart rate was consistently higher in propofol and ketamine group during anesthesia. Heart rate increased during anesthesia in all cases during continuous infusion of propofol in dogs premedicated with methotrimeprazine has been studied (Aguiar *et al*., 2001). In contrast, heart rate decreased significantly during propofol, propofol-lidocaine, and propofol-lidocaine-ketamine anesthesia in dogs (Mannarino *et al*., 2012).

Results of the present study revealed no significant changes in the hemoglobin oxygen concentration during anesthesia. This indicated good ventilation during the long-term anesthesia in all protocols. The higher % at 70 min of isoflurane inhalation than propofol might be attributed to inhalation of pure oxygen with isoflurane rather than air during propofol infusion.

Blood pressure was monitored indirectly in the current study using an oscillometric monitor. It has been concluded that non-invasive blood pressure measurements with a new oscillometric monitor provided an excellent means of detecting arterial hypotension in anesthetized dogs. The metatarsal site for cuff placement was slightly better than the metacarpal or anterior tibial site (Sawyer *et al*., 2004). Blood pressure increased after ketamine induction in the present study. Haskins *et al*. (1985) have reported that ketamine increased systemic blood pressure in dogs. There was a significant decrease in the mean and diastolic blood pressure starting from 40 min and continued lower than the baseline. The obtained results were in agreement with previously published studies, which reported a consistent and significant decrease of mean arterial pressure after isoflurane inhalation in dogs (Steffey and Howland., 1977; Mutoh *et al*., 1995). Moreover, it has been reported that progressive increases in depth of isoflurane anesthesia produce corresponding decreases in blood pressure (Steffey and Mama, 2007).

Propofol, however, has been cited to decrease mean arterial blood pressure (Henao-Guerrero and Riccó, 2014) with effects on blood pressure that happen without any effect on heart rate (Mohamadnia *et al*., 2008).

In protocol 2, no significant changes were observed in the systolic, mean, or diastolic blood pressure after injection of propofol at any time point compared to the baseline. Similar results were reported in another study on dogs with induction of anesthesia by propofol at 24 mg/kg/h. There was no association with any unacceptable degree of arterial hypotension (Hall and Chambersa, 1987). In addition, arterial blood pressure was well maintained in Greyhounds and non-Greyhounds under the effect of intravenous infusion of propofol (Robertson *et al*. 1992). In contrast, blood pressure in dogs decreased significantly under the effect of propofol, propofol-lidocaine, and propofol-lidocaine-ketamine (Mannarino *et al*., 2012; Okushima *et al*., 2014). The dogs' heart rate and mean arterial blood pressure were higher with total intravenous anesthesia with propofol or propofol/ketamine in spontaneously breathing dogs premedicated with medetomidine (Seliskar, 2007).

In protocol 3, MBP, and DBP decreased after 40 min and SBP decreased after 70 min of propofol injection and all continued lower than the baseline till the recovery. This result was in agreement with another study, which demonstrated the occurrence of hypotension after induction of fast propofol intravenous injection, and significant reductions in systolic and diastolic arterial pressure during anesthesia (Chaudhri *et al*., 1992; Amengual *et al*., 2013).

MAP was higher in propofol compared to isoflurane in the present study, a result that agreed with Keegan and Greene (1993) who have shown that mean values for MAP in the propofol group was significantly higher than in the isoflurane group, and heart rate was significantly higher in dogs anesthetized with isoflurane compared to propofol (Keegan and Greene, 1993; Kuusela *et al*., 2003).

ECG findings of dogs of the present study revealed bradyarrhythmia after xylazine and inverted and decreased intensity of T-waves after ketamine administration, during anesthesia, and during recovery. It has been reported that alpha2-agonists cause heart block and bradyarrhythmia (Muir and Manson, 1996). The most encountered arrhythmogenic effects of xylazine include sinoatrial block, atrioventricular block, bradycardia, first- and second-degree heart block AV dissociation, and sinus arrhythmia (Dunkle *et al*., 1986; Greene and Thurmon 1988). However, electrocardiographic changes have been cited to be transient during clinical evaluation of xylazine-propofol anesthesia in dogs (Soordaya, 2001). Electrocardiography has revealed first-degree atrioventricular block, sinoatrial block, sinus arrhythmia, and wandering pacemaker in the sinoatrial node (Peshin *et al*., 1980). Moreover, the configuration and magnitude of the T-wave have varied considerably between species (Muir and Manson, 1996). Isoflurane has been reported to affect the passive electrophysiological properties of the heart by changing membrane fluidity and depressing gap functions, resulting in cardiac arrhythmias and mechanical contraction abnormalities. Isoflurane has also been cited as sensitizing myocardium to catecholamines and producing pronounced effects upon HR and rhythm because of general membrane depressant effects (Muir and Manson, 1996).

The quality of anesthesia was excellent with isoflurane and good with propofol infusion in dogs of the present study. It has been cited that the depth of anesthesia is often more of a factor (Lumb, 2002) and care should be taken to ensure that dogs are at an appropriate anesthetic depth to prevent consciousness (Hofmeister *et al*., 2008). However, increasing the depth of anesthesia with isoflurane may increase hypotension and respiratory depression (Stanski, 2000). Short and Bufalari (1999) have studied propofol anesthesia in dogs and found that in non-premedicated dogs, the quality of induction, anesthesia, and recovery following propofol is desirable. Muscle relaxation and the degree of analgesia observed with propofol alone are suitable for minor diagnostic procedures. Propofol has been used for cesarean section surgery with generally good results (Dailland *et al*., 1989). The presence of a pedal withdrawal reflex and marked cardiovascular responses to this noxious stimulus suggests that propofol anesthesia may not be of sufficient depth for surgery to be carried out (Aguiar *et al*., 2001).

In a comparison of the anesthetic efficacy and cardiopulmonary effects of continuous rate infusions of alfaxalone-2-hydroxypropyl-β-cyclodextrin and propofol in dogs (Ambros *et al*., 2008), alfaxalone-HPCD produced clinically acceptable anesthetic quality and hemodynamic values ideal for use as a CRI.

The ocular reflex was lost after ketamine injection and continued until the end of the anesthesia. In addition, there was a significant reduction in the anal reflex. Isoflurane showed adequate muscle relaxation for operations at normal levels of anesthesia. These results were in accordance with the results of previous studies (Klid, 1976; Steffey and Howland, 1977). There was a significant reduction in the reflexes of the present dogs with good muscle relaxation during isoflurane inhalation and propofol anesthesia. Moreover, isoflurane anesthesia resulted in increased likelihood of absent reflexes. These findings suggest that isoflurane provides a more stable and consistent anesthetic plane (Browning, *et al*., 2019).

A brisk palpebral reflex was present for the first 30-40 min of the propofol infusion and spontaneous blinking was noted (Nolan *et al*., 1993). The pedal reflexes were reduced over time during the maintenance of propofol-ketamine anesthesia with repeat bolus and constant rate infusion of propofol in dogs (Njoku, 2015). The presence of a pedal withdrawal reflex and marked cardiovascular responses to the noxious stimulus suggest that anesthesia with continuous infusion of propofol in dogs premedicated with methotrimeprazine may not be of sufficient depth for surgery to be carried out (Aguiar *et al*., 2001). Some side effects such as involuntary movements, muscle tremors, and twitching have been observed following induction of anesthesia with propofol (Amengual *et al*., 2013). In a clinical evaluation of xylazine - propofol anesthetic in dogs (Soordaya, 2001), palpebral reflex has been found to be sluggish in both groups during induction and throughout the period of maintenance.

The quality of recovery was good (protocol 3) to excellent (protocols 1 and 2) in dogs of the present study. The recovery was generally quiet and fast, although some side effects such as ataxia and urination were reported in dogs of the present study. It has been reported that animals may show dizziness, arrhythmia, ataxia, or shivering for a few minutes during recovery as side effects of anesthesia (Klid 1976; Steffey and Howland, 1977). Recovery period after isoflurane anesthesia was markedly delayed compared to the propofol infusion group, and this was in agreement with (Kuusela *et al*., 2003). However, Lozano *et al*. (2009) have reported that isoflurane was suitable for outpatient anesthesia in dogs with neurological conditions and provides a good and smooth recovery where dogs recovered to sternal recumbency rapidly. In a comparison of isoflurane with sevoflurane for anesthesia induction and recovery in adult dogs (Johnson *et al*., 1998), recovery time and quality are comparable. No difference in recovery quality during total intravenous anesthesia with propofol versus a propofol-ketamine combination in healthy Beagle dogs (Kennedy and Smith, 2015).

Generally, in this study, there were no significant changes in hematological parameters (RBCs count, HB concentration, WBCs counts, HCT, and MCV) during anesthesia and recovery compared to baseline values. Significant differences were recorded during in RBCs count between groups 1 and 2. However, it has been reported that there was a slight decrease in RBCs and WBCs counts after 2h of isoflurane anesthesia in dogs, which was attributed to the vasodilation and immuno-suppression effects of isoflurane, respectively (Tomihari *et al*., 2015).

In protocol 2, significant decreases in HB, HCT, and MCHC were recorded one hour of propofol infusion and in HB concentration two h of propofol infusion. These decreases may be due to sequestration of red blood cells in the non-splenic site. This result was also explained in previous studies in which the authors have demonstrated that propofol does not cause measurable splenic enlargement (O'Brien *et al*., 2004; Wilson *et al*., 2004). In contrast to the present findings, it has been reported that an increase in HB concentration was recorded after induction of anesthesia with

propofol in dogs (Soordaya, 2001). In the present study, there were no changes in WBCs, the values of total leucocyte counts, platelets, differential leukocyte counts during different intervals. These findings were in agreement with the results of the previous studies (Anandmay, 2016; Chandrashekharappa and Ananda, 2009). These non-significant changes may be resulted from the enhancement in antioxidant efficacies and erythrocytes protection of propofol against oxidative damage (Tsuchiya, 2002 and Volti, 2006). Moreover, it was reported that propofol antagonizes the effects of forced peroxidation of red cells at anesthetic and sub-anesthetic concentrations (Ansley, 1998). In contrast, a comparison of the immunological effects of propofol and isoflurane for maintenance of anesthesia has been reported in healthy dogs (Tomihari *et al*., 2015). The number of lymphocytes in peripheral blood decreased after 2 hr of anesthesia. These results suggest that, compared to propofol, isoflurane had more strongly immuno-suppression caused by anesthesia, and propofol itself might have some immuno-protective effects. Thus, total intravenous anesthesia with propofol might benefit immunological support in the perioperative period of dogs (Tomihari *et al*., 2015).

CONCLUSION

In conclusion, the effect of isoflurane and propofol on physiological parameters of dogs during long-term anesthesia is minimum and recovery is uneventful. The quality and depth of anesthesia are excellent in dogs anesthetized with isoflurane and are good in dogs during propofol infusion. The duration of deep anesthesia during propofol infusion is shorter than isoflurane, with the shortest duration in protocol 3 (12mg/kg/h). Isoflurane provides more reliable and consistent anesthetic plane plus it's not expensive as propofol. However, it requires special equipment. Propofol achieves effective anesthesia, with fast induction and less hypothermia than isoflurane administration. However, apnea is recorded in two dogs after initial induction with propofol.

CONFLICT OF INTEREST

Authors declared that they have no conflict of interests.

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