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Dinesh
Ph.D. Scholar, Department of Veterinary Surgery and Radiology, LUVAS, Hisar, Haryana, India

RS Bisla
Director, RVDEC, Uchani, Karnal, Haryana, India

Rishi Tayal
Professor, Department of Veterinary Surgery and Radiology, LUVAS, Hisar, Haryana, India

RN Chaudhary
Assistant Professor, Department of Veterinary Surgery and Radiology, LUVAS, Hisar, Haryana, India

Ashok Kumar
Professor and Head, Department of Veterinary Surgery and Radiology, LUVAS, Hisar, Haryana, India

Correspondence
Dinesh
Ph.D. Scholar, Department of Veterinary Surgery and Radiology, LUVAS, Hisar, Haryana, India

Evaluation of efficacy and safety of atropine-midazolam-pentazocine with propofol/ ketamine for induction and isoflurane for maintenance of anaesthesia in dogs undergoing orthopedic surgical proced ures

Dinesh, RS Bisla, Rishi Tayal, RN Chaudhary and Ashok Kumar

Abstract
The objective of present study was to evaluate anaesthetic efficacy and safety of anaesthetic combinations of atropine- midazolam- pentazocine with propofol/ketamine for induction and isoflurane for maintenance in dogs undergoing orthopedic surgical procedures of longer duration. The study was carried out in 10 cases of orthopedics undergoing retrograde intramedullary pinning which, were divided into two groups. In all the cases, premedication was done with atropine-midazolam-pentazocine @0.04mg/kg, 0.5mg/kg and 1mg/kg body weight, respectively. In group A-I, 1% propofol (iv, to effect) was used for induction. Whereas, in group A-II ketamine-midazolam combination (@ 5mg/kg and 0.20 mg/kg respectively IV) was used for induction. Maintenance was done with isoflurane in 100% oxygen in both the groups. Effect on quality of anaesthesia, behavioural changes, physiological changes, haematological changes and changes in blood biochemical parameters were observed till 24 hours after recovery from anaesthesia. No significant difference was observed between two groups in different parameters at various time intervals during observation. However, induction was found to be more rapid and smooth in group A-I as compared to A-II.

Keywords: Anaesthesia, atropine, dogs, isoflurane, ketamine, midazolam, propofol

Introduction
Painful surgical procedures like orthopedic surgeries need balanced anaesthetic techniques so that adequate muscle relaxation and analgesia can be achieved. In balanced anaesthesia multiple drugs are targeted to specifically attenuate individual components of anaesthetic state; that is consciousness, analgesia, muscle relaxation and alteration of autonomic reflexes. These multiple drugs include injectable anaesthetic agents which can be used either as total intravenous anaesthesia or to induce anaesthesia prior to maintenance with an inhalant. The total intravenous anaesthesia is associated with prolonged recovery and recumbency time. These disadvantages can be overcome by administration of injectable anaesthetics for induction and maintenance with inhalant anaesthetics (Singh *et al*., 2012) [22].

Preanaesthetic medication helps both the anaesthetist and the animal. The analgesic and myorelaxant effects of premedication drugs may have prime importance for the whole anaesthesia. Atropine is an anticholinergic agent which, produces initial bradycardia followed by tachycardia, decreased secretion of salivary gland and respiratory tract. Midazolam is a water-soluble benzodiazepine having sedative, hypnotic, anticonvulscent, muscle relaxant and cardiovascular protective properties. Midazolam has been used as sedative in different doses in dogs (Butola and Singh, 2007) [3]. Preanaesthetic administration of midazolam reduces the induction dose of propofol and the concentration of isoflurane required to maintain anaesthesia during ovariohysterectomy in dogs (Stegman and bester, 2001) [23]. Pentazocine is an N-alkyl derivative of phenazocine that has agonist-antagonist action on opioid receptors. It is a useful analgesic in the dogs for both musculoskeletal and visceral pain. Ketamine is a dissociative anaesthetic agent which induces both anaesthesia and amnesia by depressing the neocortico-thalamic areas of the brain and stimulating the limbic system. It is well absorbed through oral, IM or SC route. It was found to be better than butorphanol and ketoprofen when used in buffaloes undergoing herniorrhaphy. Propofol is a non-barbiturate alkyl phenol derivative hypnotic used alone and along with other preanaesthetics (Bufalari *et al.*, 1998) [1].

It has been used for induction as well as maintenance of anaesthesia in dogs. Propofol as single agent for total intravenous anaesthesia is generally unsatisfactory due to its poor analgesic property. It has antioxidant properties secondary to its phenol-based chemical structure (Riera, *et al*., 2010) [20].

Materials and methods

Orthopedic cases of dogs presented for internal fixation to the Veterinary Clinical Complex of LUVAS, Hisar, were made the subject of the study. The dogs were subjected to a detailed physical examination and were categorized according to American Society of Anaesthesiologists Classifications (Table-1). Animals were randomly divided in to two groups having five animals in each group. Solid food was withheld 12 hrs and water for at least 6 hrs prior to surgery. Atropine sulphate was injected IM @ 0.04mg/kg body weight to all the dogs irrespective of the group, 10 minutes prior to administration of midazolam. Midazolam was given @ 0.5mg/kg body weight as sedative in all the groups. Pentazocine was administered @ 1 mg/kg body weight after 10 minutes of midazolam administration. After 5 minutes of pentazocine administration, induction of anaesthesia was done with propofol/ketamine. Propofol was used in group A-I and a combination of ketamine-midazolam (mixed in a syringe) was used in groups A-II. After induction, intubation was performed with cuffed endotracheal tube and connected to Moduflex compact small animal anaesthesia machine. For maintenance of anaesthesia, isoflurane was used through agent specific vaporizer (Meditec pisces$^{R)}$ along with 100% oxygen through semi-closed rebreathing system. Concentration of inhalant anaesthetic agents was regulated to maintain adequate depth of anaesthesia after monitoring body reflexes and animal's response to surgical stimulation. Inhalation of anaesthetic agents was discontinued at the completion of surgery. All the animals were administered normal saline throughout the period of surgery. The study was divided in to five divisions: clinical observations (quality of anaesthesia), behavioural observations, physiological study, hematological study and blood biochemical study. Score for different parameters of quality of anaesthesia was assigned according to table-2. The statistical analysis of data was done with one way analysis of variance and Student *'t'* test.

Results

The mean values of different parameters of clinical observations (quality of anaesthesia), behavioural changes, physiological changes, haematological changes and blood biochemical parameters changes of both the groups A-I and A-II were compared.

Clinical Observations (Quality of anaesthesia)

No significant difference between premedication score, maintenance score, recovery score, CNS sedation and muscle relaxation was observed between the two groups. Induction score of group A-I was found to be significantly higher than A-II, while analgesia score of A-II was non-significantly higher than A-I (Table-3).

Behavioural changes

Weak time and down time of both A-I and A-II groups were statistically similar. Time for drooping of eyelids, loss of palpebral reflex, rotation of eye ball, relaxation of jaw muscles, loss of tongue reflex, loss of swallowing reflex and intubation of group A-II was significantly higher than that of group A-I. Time of all recovery parameters regaining of tongue reflex, regaining of swallowing reflex, extubation, regaining of head righting reflex, return to sternal recumbency, standing time with ataxia and complete recovery without ataxia were non-significantly higher in group A-II than that of group A-I (Table-4).

Physiological changes

The mean values of respiratory rate and heart rate were statistically higher in group A-II than A-I at different time interval during anaesthesia. However, the values of rectal temperature and ambient temperature at different interval in both the groups were statistically similar (Table-5).

Hematological changes

Hemoglobin and PCV value of both A-I and A-II group were statistically similar. At different time intervals the decrease in their values occurs in both the groups (Table-6).

Blood biochemical parameters changes

A significant hyperglycemia was observed in both the groups A-I and A-II till 24 hours after recovery in both the groups A-I and A-II. The values of SGOT, ALP and GGT were non-significantly higher in group A-II. The levels of SGPT and GGT were found decreased non-significantly in group A-I while, there was a non-significant increase in these values in group A-II at 24 hours after recovery from anaesthesia. Non-significant increase in the value of SGOT was observed in both the groups till 24 hours after recovery from anaesthesia (Table-7, 8, 9).

Mean values of urea, BUN and plasma creatinine were found increased during anaesthesia in both the groups A-I and A-II till 24 hours after recovery from anaesthesia. These values were non-significantly higher in group A-I. Mean value of albumin was found decreased till recovery in both the groups A-I and A-II. However non-significant increase in albumin value at 24 hours after recovery was observed in group A-I. Mean values of total proteins and globulin were found decreased in both the groups A-I and A-II during anaesthesia till 24 hours after recovery. No significant changes in the values of triglycerides, total cholesterol, LDH, total bilirubin, sodium, potassium and chloride were observed during the whole period of observation.

Discussion

Clinical Observations (Quality of anaesthesia)

No significant difference between premedication score, maintenance score, recovery score, CNS sedation and muscle relaxation was observed between the two groups. Induction score of group A-I was found to be higher than A-II (Table-3). For induction, propofol was found to produce more smooth and rapid induction than with ketamine. Morgan and Legge (1989) [17] also observed a rapid and smooth induction followed by a short period of unconsciousness after single bolus injection of propofol. Low induction score with ketamine-midazolam combination might be due to retention of various reflexes with ketamine anaesthesia in all the species (Hall *et al*., 2014) [8]. Due to this mean time required for loss of various reflexes was higher in this group, which resulted in longer intubation time, prolonged induction and low induction score. The analgesia and sedation scores of A-II animals were non-significantly higher than A-I. The lower analgesia and sedation scores of group A-I animals might be

due to the minimal analgesic and sedative-hypnotic properties of propofol (Lumb and Jones, 2007a) [14]. High maintenance and recovery score in both the groups might be due to high volatility and low blood solubility of isoflurane which provided relatively rapid induction and recovery and easy control of the depth of anaesthesia. Also, low solubility of isoflurane in fatty tissues avoids accumulation in obese subjects (Hall *et al*., 2014) [8].

Behavioural changes

Weak time and down time of both A-I and A-II groups was statistically similar. Time for drooping of eyelids, loss of palpebral reflex, rotation of eye ball, relaxation of jaw muscles, loss of tongue reflex, loss of swallowing reflex and intubation of group A-II was significantly higher than of group A-I (Table-4). Various reflexes were found retained with ketamine anaesthesia in all the species (Hall *et al*., 2014) [8]. Due to this mean time required for loss of various reflexes was higher in group A-II. Time for disappearance of various reflexes in group A-I was significantly less because of rapid onset of action caused by rapid uptake of propofol by the central nervous system (Zoron *et al*., 1993) [28]. Propofol induces depression by enhancing the effect of the inhibitory neurotransmitter GABA and decreasing the brain metabolic activity (Concas *et al.,* 1991) [5]. Induction was smooth and free from excitement in group A-II also. Midazolam is commonly given to enhance muscle relaxation and facilitate intubation in dogs and cats co-administered ketamine (Hellyer *et al*., 1991 and Ilkiw *et al*., 1998) [9, 12]. Smooth and excitement free induction with ketamine-midazolam in dogs was also reported by Hellyer *et al.* 1991 [9] and Ranpariya *et al*. 2013 [19].

Time of all recovery parameters regaining of tongue reflex, regaining of swallowing reflex, extubation, regaining of head righting reflex, return to sternal recumbency, standing time with ataxia and complete recovery without ataxia in group A-II were significantly higher than of group A-I. The metabolites of ketamine (e.g. norketamine) were active, which resulted in prolongation of its anaesthetic effects (Hall *et al*., 2014) [8]. Due to this, time of all recovery parameters was higher in this group. There is rapid recovery in propofol anaesthesia due to its rapid redistribution and metabolism (Hall *et al*., 2014) [8]. The time of all recovery parameters was also affected by maintenance on inhalant anaesthesia by isoflurane. In inhalation anaesthesia factors influencing recovery are alveolar ventilation, cardiac output, anaesthetic agent solubility and duration of anaesthesia (Stoelting *et al.,* 1969) [24]. The low blood solubility of isoflurane provides relatively rapid induction and recovery and easy control of the depth of anaesthesia. Also, low solubility of isoflurane in fatty tissues avoids accumulation in obese subjects (Hall *et al*., 2014) [8].

Physiological study

The mean values of respiratory rate, heart rate, rectal temprature and ambient temprature were statistically similar in both the groups at different time intervals during anaesthesia. Respiratory rate and rectal temprature were significantly decreased in both the groups A-I and A-II during anaesthesia (Table-5). The heart rate significantly increased after atropine administration in both the groups. In group A-I, significant decrease in heart rate after induction might be due to decrease in myocardial contractility by propofol (Lumb and Jones, 2007a) [14]. In group A-II increased heart rate was observed after induction because of increased sympathetic efferent activity due to ketamine administration (Lumb and Jones, 2007b) [15]. Significant increase in heart rate has been documented after ketamine-midazolam induction (Butola and Singh, 2003 and Ranpariya *et al*., 2013) [2, 19]. Heart rate decreases during maintenance of anaesthesia because isoflurane causes dose dependent cardiovascular and respiratory depression.

Hematological study

Hemoglobin and PCV values of both A-I and A-II group were statistically similar (Table-6). At different time intervals during anaesthesia their values were found decreased in both the groups. Decrease in these values might be due to the splenic dilation resulting in splenic sequestration of R.B.C.s (Welberg *et al*., 2006 and Hewson *et al*., 2006) [26, 10], shifting of fluid from extravascular compartment to intravascular compartment to maintain normal cardiac output (Wagner *et al.,* 1991) [25] during anaesthesia and due to loss of blood during surgery (Coles, 1986) [4]. Similar findings were also reported by Kelawala *et al.* (1991) [13] in goats and by Gill *et al*. (1996) [6] in dogs during anaesthesia. Significant decrease in PCV, RBC and WBC was observed in goats during isoflurane anaesthesia (Hikasa *et al*., 2002) [11].

Blood biochemical study

A significant hyperglycemia was observed during the period of anaesthesia and 24 hours after recovery in both the groups A-I and A-II. Mean values of glucose, triglycerides, total cholesterol and LDH at different time interval in both groups were found to be statistically similar. However base values of glucose and triglycerides were non-significantly higher in group A-II. In group A-II one of the dog was diabetic having blood glucose level above 265mg/dl, which resulted in higher base value in group A-II. The values of SGOT, ALP and GGT were found to be non-significantly higher in group A-II. The higher level of ALP and lower level of SGPT in group A-II might be due to more number of young animals in this group. Due to higher osteoblastic activity in young age the level of ALP is higher in them as compared to adults. Similar findings with ALP and SGPT levels in dogs have also been reported by various workers (Mundim *et al*., 2007 and Wolford *et al.,* 1988) [18, 27].

Mean values of urea, BUN and plasma creatinine were found increased non-significantly till 24 hours after recovery from anaesthesia in both the groups. These values were non-significantly higher in group A-I. Due to anaesthesia and stress associated with surgery release of aldosterone, vasopressin, renin and catecholamines occurred (Lumb and Jones, 2007c) [16]. Renal blood flow, glomerular filtration rate and urine production are generally decreased with surgery in any patient. This led to decreased excretion of these metabolites and their increased level in blood.

Mean value of albumin was found decreased till recovery in both the groups A-I and A-II. However non-significant increase in albumin value at 24 hours after recovery was observed in group A-I. Mean values of total proteins and globulin were found decreased in both the groups A-I and A-II during anaesthesia till 24 hours after recovery. This decrease might be due to hemodilution caused by shifts in body fluids from extravascular compartment to intravascular compartment to maintain normal cardiac output during anaesthesia (Wagner *et al.,* 1991) [25]. Sankar *et al*. (2011) [21] also observed hypoproteinemia, hyperglycemia, decreased

PCV and hemoglobin in horses under anaesthesia either with propofol or ketamine. However mean values of these parameters were non-significantly higher in group A-I. No significant changes in the values of triglycerides, total cholesterol, LDH, total bilirubin, sodium, potassium and chloride were observed during the whole period of observation.

Table 1: Patient Classification

Signalment		Group A-I	Group A-II
Mean age (months)		13.00±4.32	10.00±3.67
Gender	Male	5	5
	Female	0	0
Mean Body weight (kg)		24.28±2.79	19.16±2.36
Bone fractured	Femur	3	2
	Tibia	2	2
	Humerus	0	1
Procedure- Intramedullary pinning		5	5
Physical Status- ASA 2		5	5

Table 2: Scoring scales for different parameters of quality of anaesthesia

Parameters	Score				
	0 (No effect)	1 (Poor)	2 (Fair)	3 (Good)	4 (Excellent)
Premedication quality		Animal standing alert, head high, all body reflexes present	Decreased alertness with no reduction in palpebral and pin prick reflexes	Animal calm, mild ataxia, minimal restrain needed	Animal completely calm, good ataxia, no restrain needed, spontaneous sternal or lateral recumbency
Induction quality		Obvious excitement, makes attempt to stand, tightly closed jaws, inability to intubate trachea	Mild excitement, slightly prolonged induction, moderate resistance to opening of jaws, longer intubation time	No excitement, mild resistance to opening of jaws, mild reflex response to intubation	No resistance to opening of jaws, Easy and quick intubation without any reflex response to intubation
Maintenance quality		Variable body reflexes, variable respiration, variable vaporizer settings, strong response to surgical stimulation with arousal and struggling	Variable respiration, variable vaporizer settings, moderate response to surgical stimulation	Good sedation, smooth respiration, slight variation in vaporizer settings, mild response to surgical stimulation	Good sedation, smooth respiration, constant vaporizer setting, no response to surgical stimulation
Recovery quality		Prolonged struggling, premature attempts to stand	Transient excitement with some struggling	Smooth, easy transition to alertness, resumption of sternal recumbency	Smooth, excitement free, animal standing on its own
Sedation	No sedation, alert, open eyes	Mild sedation, mild palpebral reflex, moderate corneal reflex	Moderate sedation, drooping of eyelids, no palpebral reflex, mild corneal reflex	Deep sedation, drooping of eyelids, ventral rotation of eye ball, no palpebral and corneal reflex	
Analgesia	No analgesia, strong response to surgical stimulation	Mild analgesia, weak response to surgical stimulation	Moderate analgesia, occasional response to surgical stimulation	Deep analgesia, no response to surgical stimulation	
Muscle relaxation	No relaxation, stiff limbs	Mild relaxation, moderate resistance bending of limbs	Moderate relaxation, mild resistance to bending of limbs	Deep relaxation, no resistance to bending of limbs	

Table 3: Comparison of mean scores depicting quality of anaesthesia

Parameters	Group A-I	Group A-II	't' value
Premedication Score	2.20± 0.37	2.00±00	0.53^{NS}
Induction Score	3.80±0.20	2.8±0.20	3.53**
Maintenance	3±00	3.20±0.20	1^{NS}
Recovery	3±00	3±00	0
CNS Sedation	2.00±00	2.20±0.20	1^{NS}
Analgesia Score	2.20±0.20	2.60±0.24	1.26^{NS}
Muscle Relaxation	3.00±00	2.80±0.20	1^{NS}

*Significant ($P<0.05$), **Highly Significant ($P<0.01$), ^{NS}Non Significant

Table 4: Comparison of scores (Mean±standard error) in time format of minutes depicting behavioural changes

Parameters	A-I (Minutes)	A-II (Minutes)	't' value
Weak time°	9.00± 0.55	8.20± 0.37	1.20^{NS}
Down time°	14.60±0.25	14.20± 0.37	0.89^{NS}
Drooping of eyelids°°	1.30±0.20	3.80± 0.37	5.89**
Loss of palpebral reflex°°	3.20± 0.49	25.80± 2.13	10.33**
Rotation of eye ball°°	3.00± 0.55	9.80± 2.15	3.05*
Relaxation of jaw muscle°°	2.00± 00	4.00± 0.32	6.32**
Loss of tongue reflex°°	2.00± 00	4.20± 0.37	5.87**
Loss of swallowing reflex°°	2.00± 00	4.20± 0.37	5.87**
Intubation°°	3.60± 0.60	5.40± 0.25	2.77*
Regain of palpebral reflex†	6.40± 1.03	8.80± 1.02	1.65^{NS}
Eyes open†	14.60± 1.25	15.20± 1.43	0.31 ^{NS}
Regain of tongue reflex†	14.60±1.25	15.20± 1.43	0.31 ^{NS}
Regain of swallowing reflex†	14.60±1.25	15.20± 1.43	0.31 ^{NS}
Extubation†	15.60±1.25	16.00± 1.41	0.21 ^{NS}
Regaining of muscle tone†	15.00±1.41	15.80± 1.24	0.42 ^{NS}
Regaining of head righting reflex†	20.00± 0.84	25.80± 5.23	1.09 ^{NS}
Return to sternal recumbency†	21.20± 1.24	30.20± 6.58	1.34 ^{NS}
Standing with ataxia†	24.80± 1.16	40.80± 7.58	2.08 ^{NS}
Complete recovery†	50.80± 4.14	64.40± 5.99	1.86 ^{NS}

*Significant (P<0.05), **Highly Significant (P<0.01), ^{NS}Non Significant
°after administration of Midazolam °°after administration of Ketamine/Propofol
†after discontinuation of Isoflurane

Table 5: Comparison of scores (Mean±standard error) in format of rate/minute and (°C) depicting physiological changes

Parameters	Respiratory rate (breaths/min)			Heart Rate (beats /min)			Rectal temperature(°C)			Ambient temperature(°C)		
Intervals	A-I	A-II	't' Value	A-I	A-II	't' Value	A-I	A-II	't' Value	A-I	A-II	't' Value
Before Drug Adm. (Base Value)	39.00±7.62	39.00±6.30	0	123.20±4.17	111.60±10.18	1.05^{NS}	39.16±0.65	38.50±0.61	1.65^{NS}	21.40±3.20	21.60±2.34	0.16^{NS}
At 10 min 0f Atropine	36.80±18.99	38.40±10.99	0.16^{NS}	136.40± 4.66	133.20± 8.70	0.32^{NS}	39.10±0.57	38.54±0.64	1.44^{NS}	21.40±3.20	21.60±2.34	0.16^{NS}
At 15 min of Midazolam	24.40± 4.73	30.40±2.92	1.07^{NS}	122.20± 3.16	130.40±10.96	0.71^{NS}	38.96±0.61	38.32±0.57	1.69^{NS}	21.40±3.20	21.60±2.34	0.16^{NS}
At 5 min of Propofol/ ketamine	16.00± 2.45	21.00±4.24	1.61^{NS}	108.80±20.71	134.4± 6.43	1.49^{NS}	38.80±0.69	38.16±0.62	1.52^{NS}	21.40±3.20	21.60±2.34	0.16^{NS}
At 15 min of Isoflurane	13.20± 1.74	14.60±1.33	0.63^{NS}	97.20± 9.58	128.20± 9.17	2.33 *	38.60±0.79	37.88±0.75	1.46^{NS}	21.40±3.20	21.60±2.34	0.16 ^{NS}
At 30 min of fIsolurane	11.00± 2.15	12.80±2.76	0.53^{NS}	99.80±7.00	104.20± 7.21	0.43^{NS}	38.50±0.90	37.72±.85	1.40^{NS}	21.40±3.20	21.60±2.34	0.16^{NS}
At recovery	23.40± 2.35	21.60±1.60	0.63^{NS}	102.80± 8.38	102.00±11.73	0.05^{NS}	38.14± 0.48	37.58±0.35	0.93^{NS}	21.40±3.20	21.60±2.34	0.16^{NS}
At 24 hrs. of recovery	48.60±8.17	36.20±2.65	1.44^{NS}	127.60± 7.60	120.00± 9.14	0.63^{NS}	38.84±0.27	38.58±0.17	0.79^{NS}	21.60±2.44	21.80±2.24	0.06^{NS}

*Significant (P<0.05), **Highly Significant (P<0.01), ^{NS}Non Significant

Table 6: Comparison of scores (Mean±standard error) in format of g/dl and (%) depicting hematological changes

Parameters	Hemoglobin (g/dl)			PCV (%)		
Intervals	Group AI	Group AII	'T' Value	Group AI	Group AII	'T' Value
Before Drug Adm. (Base Value)	10.70± 1.13	9.14± 0.94	1.06 ^{NS}	30.30± 2.25	29.72± 3.45	0.14 ^{NS}
Before Induction	9.50± 1.12	8.86± 1.39	0.35^{NS}	27.46 ± 3.68	28.28± 4.54	0.14 ^{NS}
At 5 min after induction	9.06± 0.81	8.56± 1.17	0.35 ^{NS}	25.90± 4.19	27.60± 3.72	0.30 ^{NS}
After 15 min of Isoflurane adm	8.72± 0.78	9.02± 1.63	0.16 ^{NS}	25.96± 3.47	28.92± 5.19	0.47 ^{NS}
At recovery	8.16± 1.06	7.98± 1.11	0.11 ^{NS}	24.76± 3.91	25.84± 3.63	0.20 ^{NS}
At 24 hrs. of recovery	9.82± 0.92	8.70± 1.27	0.71 ^{NS}	29.86± 1.88	28.80± 3.89	0.24 ^{NS}

*Significant (P<0.05), **Highly Significant (P<0.01), ^{NS}Non Significant

Table 7: Showing effects of different anaesthetic combinations on blood biochemical parameters (Glucose, Urea, BUN and Plasma Creastinine) at different time intervals during anaesthesia

Parameters	Glucose (mg/dL)			Urea (mg/dL)			BUN (mg/dL)			Plasma Creatinine (mg/dL)		
Intervals	A-I	A-II	't' Value	A-I	A-II	't' Value	A-I	A-II	't' Value	A-I	A-II	't' Value
Before Drug Adm. (Base Value)	97.76± 6.83	137.50±36.91	1.05 ^{NS}	29.26± 4.49	24.00±3.17	0.95^{NS}	13.67±2.10	11.21±2.10	0.95^{NS}	0.89±0.22	0.63±0.22	1.08^{NS}
Before Induction	121.36±20.28	139.18±32.62	0.46 ^{NS}	24.42± 3.12	40.60±14.58	1.08 ^{NS}	11.41±1.46	18.97±6.81	1.08^{NS}	0.83±0.19	0.75± 0.12	0.34^{NS}
At 5 min after induction	128.14±18.89	151.62±30.11	0.66 ^{NS}	27.38± 4.05	41.08±14.88	0.88 ^{NS}	12.79±1.89	19.19±6.96	0.88^{NS}	0.80±0.18	0.72± 0.13	0.37^{NS}
After 15 min of Isoflurane adm	160.44±32.71	168.92±32.49	0.18^{NS}	49.38±20.99	39.96±14.64	0.36 ^{NS}	23.07±9.81	18.67±6.84	0.36^{NS}	1.16±0.46	0.76± 0.15	0.83^{NS}
At recovery	179.26±33.62	169.52±29.17	0.21^{NS}	49.72±21.65	39.02±13.95	0.41 ^{NS}	23.23±10.12	18.23±6.52	0.41^{NS}	1.25±0.40	0.74± 0.14	1.19^{NS}
At 24 hrs. of recovery	159.60±28.84	159.64±33.08	0.01^{NS}	51.10±20.55	42.82±13.45	0.33 ^{NS}	23.87± 9.60	20.01±6.28	0.33^{NS}	1.18±0.34	0.70± 0.14	1.29^{NS}

Table 8: Showing effects of different anaesthetic combinations on blood biochemical parameters (LDH, ALT, AST and ALP) at different time intervals during anaesthesia

Parameters	LDH (IU/L)			ALT/SGPT (IU/L)			AST/SGOT (IU/L)			ALP (IU/L)		
Intervals	A-I	A-II	't' Value	A-I	A-II	't' Value	A-I	A-II	't' Value	A-I	A-II	't' Value
Before Drug Adm. (Base Value)	173.40±14.88	204.00±58.54	1.23^{NS}	53.88±13.66	39.76±12.88	0.75^{NS}	21.16±4.65	31.38±6.88	1.47^{NS}	100.00±20.76	187.60±48.76	1.65^{NS}
Before Induction	154.00±31.06	164.20±61.11	0.73^{NS}	46.06±8.31	37.24± 9.09	0.71^{NS}	26.30±4.34	35.12±9.97	0.81^{NS}	86.00±22.92	185.60±40.50	2.57^{NS}
At 5 min after induction	147.80±20.23	191.00±46.69	0.84^{NS}	49.82±10.60	37.62±11.13	0.79^{NS}	27.72±6.08	33.54±9.00	0.53^{NS}	93.80± 21.94	156.20±35.50	1.49^{NS}
After 15 min of Isoflurane adm	143.20±35.62	220.80±61.56	1.09^{NS}	42.22± 9.16	39.51±13.53	1.65^{NS}	29.60±5.71	32.12±6.29	0.29^{NS}	82.80± 19.13	177.80±43.03	2.01^{NS}
At recovery	143.00±26.25	233.40±43.18	0.04^{NS}	40.20±12.05	39.54±12.55	0.03^{NS}	29.40±4.54	31.72±8.25	0.24^{NS}	76.80± 17.72	165.60±35.28	2.24^{NS}
At 24 hrs. of recovery	219± 43.42	182.40±50.26	0.55^{NS}	39.58± 9.38	44.35±12.53	0.30^{NS}	26.10±4.41	53.50±17.42	1.52^{NS}	90.40± 18.56	170.80±35.22	2.52^{NS}

Table 9: Showing effects of different anaesthetic combinations on blood biochemical parameters (GGT, Total Proteins, Albumin, Globulin) at different time intervals during anaesthesia

Parameters	GGT (IU/L)			Total proteins (g/dL)			Albumin (g/dL)			Globulin (g/dL)		
Intervals	A-I	A-II	't' Value	A-I	A-II	't' Value	A-I	A-II	't' Value	A-I	A-II	't' Value
Before Drug Adm. (Base Value)	3.30±1.04	5.42±1.44	1.19^{NS}	9.29±0.29	8.11±0.45	2.21^{NS}	2.97±0.27	2.27±0.21	2.21^{NS}	6.32±0.53	5.84±0.48	0.67^{NS}
Before Induction	3.66±1.05	3.82±1.54	0.08^{NS}	9.18±0.30	7.61±0.35	2.43 *	2.72±0.29	2.37±0.36	0.77^{NS}	6.45±0.52	5.23±0.57	1.58^{NS}
At 5 min after induction	1.94±0.52	4.00±1.30	1.47^{NS}	8.73±0.33	7.69±0.54	1.65^{NS}	3.25±0.24	2.43±0.48	1.52^{NS}	5.48±0.54	5.25±0.34	0.35^{NS}
After 15 min of Isoflurane adm	2.58±0.37	3.80±0.46	2.01^{NS}	8.66±0.23	7.43±0.36	1.74^{NS}	2.82±0.34	2.19±0.24	1.51^{NS}	5.84±0.49	5.23±0.49	0.87^{NS}
At recovery	2.74±0.77	6.52±0.86	3.24^{NS}	8.45±0.19	7.01±0.57	1.78^{NS}	2.74±0.47	1.96±0.24	1.47^{NS}	5.71±0.64	5.09±0.42	0.81^{NS}
At 24 hrs. of recovery	2.92±0.87	6.22±1.25	2.16^{NS}	9.25±0.72	7.45±0.13	2.03^{NS}	3.78±0.44	2.09±0.24	3.34^{NS}	5.47±0.48	5.36±0.51	0.16^{NS}

*Significant (P<0.05), **Highly Significant (P<0.01), ^{NS}Non Significant

Conclusions

Based on the present study, propofol was found to be better induction agent than midazolam-ketamine in terms of early loss of various reflexes, higher score of induction quality and early recovery. The anaesthetic combinations of A-I (atropine-midazolam-pentazocine-propofol) and A-II (atropine-midazolam-pentazocine-ketamine) followed by maintenance with isoflurane were found to be safe and effective in dogs undergoing orthopedic surgery.

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