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Comparative evaluation of efficacy and safety of two balanced anaesthetic protocols in female dogs undergoing mammary tumor resection

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Abstract
The objective of present study was to evaluate anaesthetic efficacy and safety of anaesthetic combinations of atropine-midazolam-pentazocine-propofol-isoflurane and atropine-midazolam-pentazocine-ketamine-isoflurane in female dogs undergoing mammary tumor resection. The study was carried out in 10 female dogs undergoing mammary tumor resection which, were divided in to two groups. In both the groups C-I and C-II, premedication was done with atropine-midazolam-pentazocine @0.04mg/kg, 0.5mg/kg and 1mg/kg body weight respectively. In group C-I, 1% propofol (IV, to effect) was used for induction. Whereas, in group C-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 C-I as compared to C-II.

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

1. Introduction
Mammary tumors represent approximately 25% of all canine tumors and more than 50% of all tumors in bitch (Slatter, 2003) [24]. Surgical excision remains the primary treatment of mammary neoplasia in bitch. Anaesthesia is a pre-requisite to all the surgical interventions, both in humans and animals, so that the surgeon can perform surgical intervention with maximum precision and sagacity (Suresha *et al*., 2012) [27]. Painful surgical procedures like mammary tumor resection need balanced anaesthetic techniques so that adequate muscle relaxation and analgesia can be achieved. In balanced anaesthetic protocol different drugs with different effects are used so that high dose of a single drug and their side effects can be avoided.

In veterinary practice, injectable anaesthetic techniques are preferred due to inherent peculiarities of animal patients and ease of administration of drugs (Singh *et al*., 2012) [22]

The injectable 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. Induction of anaesthesia is best accomplished by using injectable drugs because of their rapid onset of action and ease of administration (Nicholson *et al*., 2001) [17]. Induction dose vary with the general health and age of the patient. However, for longer duration surgical procedures the inhalant anaesthetics are preferred over injectable agents for maintenance of anaesthesia. The maintenance of anaesthesia with inhalant agents is also preferred because of better quality and control. 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) [25]. 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. 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) [19]. 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.

Materials and methods

Female dogs with mammary tumor presented for surgical excision 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 C-I and a combination of ketamine-midazolam (mixed in a syringe) was used in groups C-II. After induction, intubation was performed with cuffed endotracheal tube guided by laryngoscope 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 C-I and C-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 and muscle relaxation score of group C-I was found to be non-significantly higher than C-II, while analgesia score of C-II was non-significantly higher than C-I (Table-3).

Behavioural changes

Weak time and down time of both C-I and C-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 C-II was significantly higher than that of group C-I. Time of some of the recovery parameters regaining of tongue reflex, regaining of swallowing reflex, extubation and regaining of head righting reflex were non-significantly higher in group C-II than that of group C-I. Time of regain of palpebral reflex, return to sternal recumbency, standing time with ataxia and complete recovery without ataxia were significantly higher in group C-II than of group C-I (Table-4).

Physiological changes

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

Hematological changes

Decrease in the values of haemoglobin and PCV was observed till 24 hours of recovery from anaesthesia in both the groups. Mean values of hemoglobin and PCV were non-significantly higher in group C-II than C-I at different time interval during anaesthesia. At before induction and after 15 minutes of isoflurane administration mean value of hemoglobin was statistically higher in group CII (Table-6).

Blood biochemical parameters changes

Hyperglycemia was observed during the period of anaesthesia in both the groups C-I and C-II. Mean value of glucose after 24 hours of recovery returned towards base value in group C-I. Mean value of triglycerides was decreased non-significantly in both the groups during anaesthesia. Mean values of SGPT, SGOT and GGT at different time interval were found increased in both the groups during anaesthesia. The values of LDH, SGPT and SGOT were significantly higher and of GGT non-significantly higher in group C-II. Mean value of ALP was significantly higher in group C-I. Mean value of direct bilirubin was found to be non-significantly higher in group C-II (Table-7, 8, 9).

In both the groups, the values of urea and BUN were found decreased till recovery and increased at 24 hours after recovery from anaesthesia. These values were non-significantly higher in group C-II. Mean values of total proteins at different time intervals were found non-significantly decreased in both the groups C-I and C-II. The values of albumin and globulin were found decreased till recovery in both the groups. However, the value of albumin in group C-II and value of globulin in C-I were found non-significantly increased at 24 hours after recovery from anaesthesia. The values of plasma creatinine were found non-significantly decreased in group C-I and increased in group C-II till 24 hours of recovery from anaesthesia. Mean values of sodium, potassium and chloride were found non-significantly higher in group C-II than in group C-I. There was non-significant increase in values of these parameters during the period of anaesthesia and after 24 hours of recovery from anaesthesia.

Discussion

Clinical Observations (Quality of anaesthesia)

No significant difference between premedication score, maintenance score, recovery score, CNS sedation and muscle relaxation was observed between two groups. Induction score of group C-I was found to be higher than C-II, while analgesia score of C-II was higher than C-I (Table-3). For induction, propofol was found to produce more rapid and smooth induction than ketamine-midazolam combination. Morgan and Legge (1989) [16] 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 (Rampal and Sandhu, 2011) [20]. 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 score was non-significantly higher in group C-II than group C-I. The lower analgesia and sedation scores of group C-I animals might be due to the minimal analgesic and sedative-hypnotic properties of propofol (Lumb and Jones, (2007a) [13]. High maintenance and recovery score in both the groups may be due to high volatility and low blood solubility of isoflurane which provide 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 C-I and C-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 C-II was significantly higher than of group C-I (Table-4). Various reflexes were found retained with ketamine anaesthesia in all the species (Rampal and Sandhu, 2011) [20]. Due to this mean time required for loss of various reflexes was higher in group C-II. Time for disappearance of various reflexes was significantly less in group C-I because of rapid onset of action of propofol caused by its rapid uptake in to the central nervous system (Zoron *et al*., 1993) [30]. After single bolus injection, propofol induces a rapid and smooth induction followed by a short period of unconsciousness (Morgan and Legge, 1989) [16]. Regardless of time (longer time with ketamine), induction was smooth and free from excitement in both the groups C-I and C-II. Smooth and excitement free induction with ketamine-midazolam was also reported by Hellyer *et al.* 1991 [9] and Ranpariya *et al.* 2013 [18].

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 also were significantly higher in group C-II than that of group C-I. The metabolites of ketamine (e.g. norketamine) were active, which resulted in prolongation of its anaesthetic effects (Rampal and Sandhu, 2011) [20]. There is rapid recovery in propofol anaesthesia due to its rapid redistribution and metabolism. 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) [26]. 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 and ambient temprature was statistically significantly higher in group C-I than C-II at different time interval during anaesthesia (Table-5). However, the values of heart rate and rectal temperature at different interval in both the groups were statistically similar. Higher base values in group C-I might be due to high ambient temperature. The heart rate increased after atropine administration in both the groups. In group C-I, the decrease in heart rate after induction might be due to decrease in myocardial contractility by propofol (Lumb and Jones, 2007a) [13]. In group C-II heart rate was increased up to at 5 minutes of ketamine administration. Increased heart rate was observed after induction because of increased sympathetic efferent activity due to ketamine administration (Lumb and Jones, 2007b) [14]. Significant increase in heart rate has been documented after ketamine-midazolam induction (Butola and Singh, 2003 and Ranpariya *et al*., 2013) [2, 18]. Heart rate decreases during maintenance of anaesthesia because of dose dependent cardiovascular and respiratory depression caused by isoflurane.

Hematological study

Mean values of PCV of both C-I and C-II groups were statistically similar while the value of haemoglobin was significantly higher in group C-II at before induction and after 15 min of isoflurane administration (Table-6). There was non-significant decrease in haemoglobin and significant decrease in packed cell volume values during the period of anaesthesia in both the groups C-I and C-II. 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) [29, 10], shifting of fluid from extravascular compartment to intravascular compartment to maintain normal cardiac output (Wagner *et al.,* 1991) [28] during anaesthesia and due to loss of blood during surgery (Coles, 1986) [5]. Similar findings were also reported by Kelawala *et al.* (1991) [11] in goats and by Gill *et al.* (1996) [7] in dogs during anaesthesia.

Blood biochemical study

A non-significant hyperglycemia in group C-I and significant hyperglycemia in group C-II was observed during the period of anaesthesia. Mean value of glucose after 24 hours of recovery returned towards base value in group C-I. Non-significant increase was observed in the values of SGPT and SGOT at 24 hours recovery from anasethesia in both the groups C-I and C-II.

The mean values of LDH were higher than normal range (40-250 IU/L) in both the groups C-I and C-II. According to Campos (2012) [4] rapid cell proliferation and high metabolic demand led to increased level of lactate dehydrogenase (LDH) in mammary tumors in female dogs. It is the enzyme responsible for catalyzing the reversible transformation of pyruvate to lactate and essential for anaerobic cellular metabolism. This increased LDH in cancer cells ensures an efficient anaerobic/glycolytic metabolism for tumors and reduced dependence on oxygen (Giatromanolaki *et al.,* 2006) [6]. Campos *et al*. (2012) [4] reported a positive and significant

relationship with mammary tumor staging and disease evolution with LDH levels in dogs.

Mean value of direct bilirubin was found to be non-significantly higher in group C-II. In both the groups, the values of urea and BUN were found non-significantly decreased till recovery and increased at 24 hours after recovery. In young animals due to anaesthesia and stress associated with surgery release of aldosterone, vasopressin, renin and catecholamines occurred which, resulted in decreased renal blood flow, glomerular filtration rate and urine production in them (Lumb and Jones, 2007c) [15]. This led to decreased excretion of these metabolites and their increased level in blood. But in these groups geriatric patients were there undergoing mammary tumor resection. In older age the animals became less responsive to stress, catecholamines and vasopressin (Lumb and Jones, 2007c) [15]. Hemodilution caused by shifting of fluid from extravascular compartment to intravascular compartment during anaesthesia and non-responsiveness in geriatric patients might be responsible for decreased urea and BUN levels in these groups during anaesthesia.

Mean values of total proteins at different time intervals were found non-significantly decreased in both the groups C-I and C-II. The values of albumin and globulin were found decreased during anaesthesia till recovery in both the groups. However, the value of albumin in group C-II and value of globulin in C-I were found non-significantly increased at 24 hours after recovery from anaesthesia. 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) [28]. Sankar *et al*. (2011) [21] also observed hypoproteinemia, hyperglycemia, decreased PCV and hemoglobin in horses under anaesthesia either with propofol or ketamine.

Mean values of sodium, potassium and chloride were non-significantly higher in group C-II than in group C-I. In both the groups, the values of sodium and chloride were found increased non-significantly at recovery and 24 hours after recovery from anaesthesia. Increase in plasma sodium and chloride levels in the present study might be due to administration of normal saline fluid during general anaesthesia. Similar findings were also reported by Khanna *et al*. (1997) [12] and Singh *et al*. (2014) [23].

Table 1: Patient Classification

Signalment		Group C-I	Group C-II
Mean age (years)		9.10± 0.24	6.10±1.19
Gender	Male	0	0
	Female	5	5
Mean Body weight (kg)		29.10±3.12	33.9±3.15
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 C-I	Group C-II	't' value
Premedication Score	2.6±.24	2.20±0.20	1.41^{NS}
Induction Score	3.80±0.20	3.00±0.31	2.13^{NS}
Maintenance	2.80±0.83	3.20±0.44	$.94^{NS}$
Recovery	3.00±00	2.60±0.24	1.63^{NS}
CNS Sedation	2.00±00	2.00±00	0
Analgesia Score	2.20±0.20	2.60±0.24	2.88^{NS}
Muscle Relaxation	2.80±0.20	2.20±0.20	0.57^{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	Group – Mammary Tumor Resection		't' Value
	Group CI	Group CII	
Weak time°	7.60±0.40	8.80±0.58	1.69^{NS}
Down time°	14.00± 0.55	14.60±0.25	1.00^{NS}
Drooping of eyelids°°	1.40±0.25	6.00± 0.55	7.66**
Loss of palpebral reflex°°	2.60±0.25	20.40± 1.63	10.79**
Rotation of eye ball°°	1.80±0.20	6.00± 0.55	7.20**
Relaxation of jaw muscle°°	1.80±0.20	6.00± 0.55	7.20**
Loss of tongue reflex°°	1.80±0.20	6.00± 0.55	7.20**
Loss of swallowing reflex°°	1.80±0.20	6.00± 0.55	7.20**
Intubation°°	2.80±0.20	7.00± 0.55	7.20**
Regain of palpebral reflex†	5.40±0.40	11.60± 0.51	9.56**
Eyes open†	17.80±1.47	22.60± 5.89	1.48 ^{NS}
Regain of tongue reflex†	17.80±1.47	22.60± 5.89	1.40 ^{NS}
Regain of swallowing reflex†	17.80±1.47	22.60± 5.89	1.40 ^{NS}
Extubation†	18.60±2.32	23.40± 5.70	1.43 ^{NS}
Regaining of muscle tone†	17.80±1.47	24.40± 5.57	1.77 ^{NS}
Regaining of head righting reflex†	20.60± 3.03	29.20± 5.58	1.99^{NS}
Return to sternal recumbency†	21.00± 2.95	37.00± 6.21	2.91 *
Standing with ataxia†	25.40± 1.69	44.80± 5.91	3.15 *
Complete recovery†	45.60± 4.01	62.60± 1.78	3.87 **

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

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	Group C-I	Group C-II	't' Value	Group CI	Group C-II	't' Value	Group C-I	Group C-II	't' Value	Group C-I	Group C-II	't' Value
Before Drug Adm. (Base Value)	58.60± 4.35	41.20± 7.39	2.02^{NS}	108.40±10.30	111.60± 12.31	0.19^{NS}	39.10± 0.88	38.90± 0.38	0.46^{NS}	33.40± 0.60	21.80± 3.20	3.56*
At 10 min 0f Atropine	59.40± 7.03	42.60± 7.15	1.67 ^{NS}	122.40±10.28	131.60± 12.22	0.57^{NS}	39.34± 0.80	39.04± 0.52	0.69^{NS}	33.40± 0.60	21.80± 3.20	3.56*
At 15 min of Midazolam	44.40± 3.71	24.60± 4.87	4.60**	133.60± 9.60	136.40± 17.51	0.22 ^{NS}	39.10± 0.47	39.16± 0.83	0.14 ^{NS}	33.40± 0.60	21.80± 3.20	3.56*
At 5 min of Propofol/Ketamine	17.20± 4.36	17.60± 3.69	0.07 ^{NS}	116.80±19.92	141.6± 18.92	0.54 ^{NS}	39.04± 0.49	38.86± 0.71	0.46 ^{NS}	31.40± 0.87	21.80± 3.20	2.97*
At 15 min of Isoflurane	13.60± 4.02	17.80± 1.84	1.68 ^{NS}	118.40± 7.28	124.20± 12.41	0.40 ^{NS}	38.92± 0.51	38.74± 0.95	0.12 ^{NS}	31.40± 0.87	21.80± 3.20	2.97*
At 30 min of Isoflurane	11.60± 1.72	17.00± 1.41	2.42*	116.20± 6.47	116.00± 15.06	0.28 ^{NS}	38.78± 0.59	38.52± 1	0.49 ^{NS}	31.40± 0.87	21.80± 3.20	2.97*
At recovery	24.80± 6.18	28.20± 9.12	0.69 ^{NS}	129.20±11.67	119.20± 10.66	0.63 ^{NS}	38.76± 0.58	37.96± 1.37	1.96 ^{NS}	31.40± 0.87	21.80± 3.20	2.97*
At 24 hrs. of recovery	53.60± 4.71	44.80±11.96	1.23 ^{NS}	122.80± 8.69	137.60± 8.66	1.20 ^{NS}	39.00± 0.42	38.84± 0.55	0.51 ^{NS}	32.80± 0.49	21.60± 3.15	3.44*

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

Parameters	Hemoglobin (g/dl)			PCV (%)		
Intervals	Group C-I	Group C-II	't' Value	Group C-I	Group C-II	't' Value
Before Drug Adm. (Base Value)	10.52± 1.21	13.18± 1.56	1.34 ^{NS}	40.18± 1.63	39.70± 3.09	0.42 ^{NS}
Before Induction	10.52± 1.63	11.78± 1.77	0.52*	41.40 ± 2.11	34.24± 4.44	1.45 ^{NS}
At 5 min after induction	8.82± 1.64	11.18± 1.32	1.51 ^{NS}	34.10± 2.81	35.00± 2.94	0.22^{NS}
After 15 min of Isoflurane adm	8.48± 1.29	11.94± 1.57	1.70 *	32.66± 2.49	35.62± 3.67	0.66 ^{NS}
At recovery	8.94± 1.66	11.30± 1.43	1.07 ^{NS}	32.42± 3.03	34.98± 3.44	0.55 ^{NS}
At 24 hrs. of recovery	9.66± 1.31	12.58± 2.52	1.02 ^{NS}	37.98± 2.86	35.98± 5.49	0

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	C-I	C-II	't' Value	Group C-I	Group C-II	't' Value	Group C-I	Group C-II	't' Value	Group C-I	Group C-II	't' Value
Before Drug Adm. (Base Value)	96.88± 8.76	76.72± 2.71	2.19^{NS}	39.46± 6.94	61.02± 1.96	1.85^{NS}	18.44±3.24	28.51± 0.92	1.22^{NS}	1.89± 0.23	1.45± 0.32	1.81^{NS}
Before Induction	93.28± 15.70	103.12± 10.91	0.51 ^{NS}	42.96± 10.83	68.48± 10.22	1.71 ^{NS}	20.07± 5.06	32.00± 4.78	1.78^{NS}	1.64± 0.10	1.42± 0.08	1.69^{NS}
At 5 min after induction	111.16± 22.95	107.66± 20.05	0.11 ^{NS}	39.96± 10.37	57.60± 2.95	1.63 ^{NS}	18.67± 8.85	26.91± 1.38	1.42^{NS}	1.66± 0.14	1.38± 0.07	1.80^{NS}
After 15 min of Isoflurane adm	120.42± 22.27	117.22± 18.40	0.11 ^{NS}	39.42± 13.60	52.90± 7.33	0.87 ^{NS}	18.42± 6.36	24.72± 3.42	0.54^{NS}	1.61± 0.14	1.30± 0.07	2.18^{NS}
At recovery	128.62± 19.38	128.12± 20.43	0.01 ^{NS}	33.92± 10.27	58.36± 1.96	2.33 ^{NS}	15.84± 4.80	27.27± 0.92	1.33^{NS}	1.60± 016	1.71± 0.32	0.31^{NS}
At 24 hrs. of recovery	96.42± 9.04	120.56± 12.57	2.20 ^{NS}	51.52± 14.29	68.06± 13.56	0.83 ^{NS}	24.07± 6.68	31.80± 6.34	0.87^{NS}	1.74± 0.22	1.85± 0.25	0.32^{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	**C-I**	**C-II**	**'t' Value**	**C-I**	**C-II**	**'t' Value**	**C-I**	**C-II**	**'t' Value**	**C-I**	**-II**	**'t' Value**
Before Drug Adm. (Base Value)	333.20± 75.77	553.00± 44.76	2.49*	13.72± 2.80	26.24± 5.98	1.89 ^{NS}	14.92± 3.71	34.80± 2.92	4.21*	79.60± 8.50	42.40± 8.50	3.93**
Before Induction	383.80± 142.39	464.20± 132.66	0.41^{NS}	13.20± 3.56	25.26± 4.12	2.21*	21.74± 6.46	39.54± 7.17	1.84^{NS}	79.00± 9.04	36.00± 7.12	3.73**
At 5 min after induction	300.80± 101.65	443.20± 54.69	0.10^{NS}	11.06± 2.27	27.28± 5.56	2.70*	15.34± 6.41	35.10± 3.17	2.76*	77.60± 9.01	42.60± 5.89	3.25*
After 15 min of Isoflurane adm	297.00± 116.88	496.40± 108.17	0.62^{NS}	14.14± 2.57	26.32± 7.76	1.48 ^{NS}	18.14± 8.92	38.00± 2.02	2.17^{NS}	69.20± 12.28	38.20± 6.12	2.25^{NS}
At recovery	284.20± 93.85	567.80± 49.94	12.66^{NS}	18.00± 5.92	25.90± 5.73	0.95 ^{NS}	18.86± 6.98	38.24± 5.57	2.17^{NS}	69.60± 12.67	39.20± 7.66	2.05^{NS}
At 24 hrs. of recovery	337.60± 103.15	485.40± 42.68	1.32^{NS}	20.36± 7.31	26.54± 4.80	0.70 ^{NS}	22.36± 11.14	48.96± 9.93	1.78^{NS}	70.80± 13.67	48.40± 7.76	1.42^{NS}

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

Parameters	GGT (IU/L)			Total proteins (g/dL)			Albumin (g/dL)			Globulin (g/dL)		
Intervals	C-I	C-II	't' Value	C-I	C-II	't' Value	C-I	C-II	't' Value	C-I	C-II	't' Value
Before Drug Adm. (Base Value)	3.16± 0.49	3.46± 1.13	0.29^{NS}	9.29± 0.19	9.46± 0.82	0.22 ^{NS}	3.07± 0.45	2.55± 0.22	1.06 ^{NS}	6.22± 0.52	6.91± 0.66	0.79^{NS}
Before Induction	3.24± 1.47	4.32± 1.33	0.54^{NS}	8.22± 0.66	8.96± 0.49	0.90^{NS}	2.33± 0.20	2.41± 0.19	0.31 ^{NS}	5.89± 0.78	6.55± 0.46	0.72^{NS}
At 5 min after induction	3.82± 1.19	5.84± 0.91	1.35^{NS}	8.17± 0.42	9.25± 0.57	1.52 ^{NS}	2.67± 0.26	2.47± 0.13	0.68 ^{NS}	5.49± 0.54	6.77± 0.56	1.65^{NS}
After 15 min of Isoflurane adm	3.58± 0.94	5.12± 0.99	1.13^{NS}	8.25± 0.49	8.38± 0.66	0.15^{NS}	2.49± 0.39	2.24± 0.22	0.56 ^{NS}	5.76±0.22	6.13± 0.54	0.64^{NS}
At recovery	3.78± 0.86	5.66± 1.13	1.32^{NS}	8.21± 0.57	8.15± 0.82	0.05^{NS}	2.49± 0.44	2.11± 0.21	0.75 ^{NS}	5.72± 0.79	6.03± 0.66	0.30^{NS}
At 24 hrs. of recovery	3.25± 0.98	4.60± 1.63	0.76^{NS}	8.52± 1.3	8.61± 0.61	0.06 ^{NS}	1.86± 0.13	2.58± 0.32	2.07 ^{NS}	6.66± 1.22	6.03± 0.59	0.46^{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 C-I (atropine-midazolam-pentazocine-propofol) and C-II (atropine-midazolam-pentazocine-ketamine) followed by maintenance with isoflurane were found to be safe and effective in female dogs undergoing mammary tumor resection.

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