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Anaesthetic Evaluation of Various Combinations of Xylazine, Ketamine and Tiletamine-zolazepam in Dogs

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ABSTRACT

Background: Tiletamine-zolazepam is a combination of dissociative anaesthetic with benzodiazepine agent. It is an injectable anaesthetic agent which is either used alone or in combination with other anaesthetic drugs. The objective of this study is to evaluate the anaesthetic effects of tiletamine-zolazepam alone and in combination with xylazine and xylazine-ketamine in dogs.

Methods: Eighteen dogs irrespective of age, breed, sex and body weight (requiring various surgical corrections) were randomly divided into three groups *viz*., A, B and C. Atropine sulphate (0.025mg/kg SC) was administered in all the groups followed by tiletamine-zolazepam (till effect IV) in group A, xylazine (0.5 mg/kg IM) and tiletamine-zolazepam (till effect IV) in group B and xylazine (0.5 mg/kg IM), ketamine (2.5 mg/kg IV) and tiletamine-zolazepam (till effect IV) in group C. A gap of 10 minutes was kept between administration of each drug. The efficacy of the anaesthesia was evaluated by observing clinico-physiological parameters *i.e*. induction dose, induction time, duration of anaesthesia, sternal recumbency time, complete recovery time, jaw relaxation score, pedal reflex score, palpebral reflex score (PLR), heart rate (HR), respiration rate (RR), rectal temperature, capillary refill time (CRT), systolic arterial pressure, diastolic arterial pressure, mean arterial pressure and haemoglobin oxygen saturation. These clinico-physiological parameters were evaluated at different time intervals *i.e.* 0, 10, 15, 25, 35, 45, 60, 75, 90 and 105 minutes.

Result: The induction dose of tiletamine-zolazepam observed in group A, B and C were 6.5, 5.5 and 4.0 mg/kg body weight, respectively on intravenous administration. Analgesia and muscle relaxation was observed slightly better in group C in comparison to group A and B. Heart rate increased and respiration rate decreased post induction in all three groups. Tiletamine-zolazepam with its fast and smooth induction, intermediate duration of action, excellent muscle relaxation and good compatibility with xylazine and ketamine, was found to be an effective general anaesthetic either alone or in combination. Group C with xylazine, ketamine and tiletamine-zolazepam combination required significantly lower induction dose and provided longer duration of anaesthesia in comparison to group A and B.Combining xylazine and xylazine-ketamine as pre-medicants at sub-anaesthetic doses reduced the induction dose of tiletamine-zolazepam, provided longer duration of anaesthesia, good muscle relaxation and stable physiological parameters.

Key words: Anaesthetic evaluation, Clinico-physiological parameters, Dogs, Ketamine, Tiletamine-zolazepam, Xylazine.

INTRODUCTION

General anaesthesia is defined as a state of unconsciousness which leads to the loss of protective reflexes from the administration of one or combination of anaesthetic agents. Characteristics of an ideal anaesthetics includes sedation, amnesia, analgesia and muscle relaxation (Billah *et al*., 2017). Pre-anaesthetic agents are essential for the safe anaesthetic management. Combination of specific drugs used at low doses produce more profound and desirable effects than using a single drug at a higher dose (Nam *et al*., 2013).

Xylazine is an alpha-2 adrenergic agonist with sedative, analgesic and muscle relaxant properties. It also have some alpha-1 agonist activity. The most common effect of xylazine is bradycardia with reduction in cardiac output up to 30 per cent (Landry and Maza, 2020). Ketamine hydrochloride belongs to the dissociative anaesthetic class of drug. Anaesthesia produced by dissociative anaesthetic is categorized by catalepsy, catatonia, analgesia and amnesia. Ketamine is a non-competitive antagonist at NMDA receptor (Dugassa and Fromsa, 2018).

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Tiletamine-Zolazepam is an anaesthetic combination of two drugs present in the ratio of 1:1. Tiletamine is a dissociative anaesthetic drug and is long acting. Its analgesic effect is greater than ketamine which belongs to the same class of drug. Zolazepam belongs to

benzodiazepine class of anaesthetic drugs. Zolazepam intensifies the effect of tiletamine on the central nervous system and reduces the hyperactivity of the skeletal muscle (Lee *et al*., 2018).

Previously not much research has been done using different combinations of xylazine, ketamine and tiletamine-zolazepam in dogs, although literature available using such combinations in other species. Therefore, the present study was planned to evaluate and compare the anaesthetic, clinical and physiological efficacy of different anaesthetic combinations *i.e*. tiletamine-zolazepam, xylazine-tiletamine-zolazepam and xylazine-ketamine-tiletamine-zolazepam

MATERIALS AND METHODS

Animals

Approval for conducting the study on the clinical cases requiring anaesthesia for various surgical procedures was obtained vide letter no. IAEC/CVASc/VSR/474 dated 25/10/2021 from the Institutional Animal Ethics Committee of College of Veterinary and Animal Sciences, GBPUAT, Pantnagar. This study was conducted in eighteen dogs irrespective of age, breed, sex and body weight presented to Teaching veterinary clinical complex, COVAS, Pantnagar for various surgical corrections during January to July 2022. Clinical status of the animals was judged by recording rectal temperature (°F), heart rate (beats/minute) and respiratory rate (breaths/minute) and healthy animals were selected for the trial. Consent of owner was taken before allotting dog to any study group.

Study design

The animals were randomly divided into 3 groups *viz*., Groups A, B and C comprising of 6 animals in each group. Animals in each group was subjected to different anaesthetic protocol. Atropine sulphate (0.025 mg/kg SC) was administered in all the groups followed by tiletamine-zolazepam (till effect IV) in group A, xylazine (0.5 mg/kg IM) and tiletamine-zolazepam (till effect IV) in group B and xylazine (0.5 mg/kg IM), ketamine (2.5 mg/kg IV) and tiletamine-zolazepam (till effect IV) in group C. A gap of 10 minutes was provided between each drug. A single shot of tiletamine-zolazepam was given without any maintenance. In all the three groups induction was done with tiletamine-zolazepam (till effect IV). A single shot of tiletamine-zolazepam was given without maintenance dose. Induction dose is the amount of the tiletamine-zolazepam) required in respective groups for induction of anaesthesia adequate to allow placement of an endotracheal tube. It was calculated in mg/kg after completion of each trial.

All the animals were weighed first and then placed on the surgical table. An intravenous cannula was introduced into the cephalic vein for administration of anaesthetic drugs and proposed combinations of pre-anaesthetics was given. Animals were restrained after sedation. After ten minutes of premedication, tiletamine-zolazepam (zoletil-50 mg/ml) was administered intravenously till effect for induction of anaesthesia followed by endotracheal intubation with appropriate size endotracheal tube.

Clinical parameters

The clinical parameters evaluated in the study includes induction dose (mg/kg), induction time (seconds), duration of anaesthesia (minutes), sternal recumbency time (minutes), complete recovery time (minutes), jaw relaxation score, pedal reflex score and palpebral reflex score. Jaw relaxation score was evaluated by observing the resistance of opening of jaw by tying the bandage on both jaws and graded on a scale of 0 to 3 as described by (Zhang *et al*., 2021). Pedal withdrawal response to pinching of a digit or interdigital web was noted and graded on a scale of 0 to 3 as described by (Nam *et al*., 2013). Palpebral reflex was assessed by observing the blink of eyelids on touching the area around the eye and was graded on a scale of 0 to 3 (Ibrahim, 2017).

Physiological parameters

Physiological parameters evaluated are heart rate (HR) inbeats per minute, respiration rate (RR) in respiration per minute, rectal temperature (RT) in °F, capillary refill time (CRT)in seconds, Non-Invasive blood pressure (NIBP) in mmHg and Haemoglobin Oxygen Saturation (SpO_2) in %. NIBP includes Systolic arterial pressure (SAP), Diastolic arterial pressure (DAP) and Mean arterial pressure (MAP).

Monitoring of anaesthesia was done using veterinary patient monitor (model no. MMED 8000- CV Beijing Choice Electronic Technology Co. Ltd., Beijing, China. Heart rate, respiratory rate, temperature and NIBP were monitored and recorded using veterinary patient monitor. These clinico-physiological parameters were evaluated at 0, 10, 15, 25, 35, 45, 60, 75, 90 and 105 minutes. Capillary refill time was calculated by firmly pressing the animals gum surface with thumb and then releasing the thumb and the time in seconds.

Statistical analysis

Data were expressed as Mean±Standard Error (SE). To compare the Mean values at different time intervals with their base values in each group “t” test was used (Snedecor and Cochran, 1994). Analysis of variance (ANOVA) was used to compare the mean values between different groups.

RESULTS AND DISCUSSION

Clinical parameters

Induction of anaesthesia was fast and smooth in all the groups. Induction dose in group A, B and C was 6.6, 5.5 and 4.0 mg/kg body weight, respectively. Significant difference ($p<0.05$) was observed between the groups A, B and C. Induction time of 38.00±2.0, 31.83±2.17 and 25.00±7.55 seconds was reported in group A, B and C, respectively. Highest value was reported in group A, intermediate in group B, lowest in group C and significant

difference ($p<0.05$) was observed between the groups. Values of induction dose, induction time, duration of anaesthesia, sternal recumbency time and complete recumbency time in dogs are tabulated in Table 2. Administration of xylazine in group B and xylazine-ketamine in group C significantly lowered the dose of induction and induction time. Duration of anaesthesia, sternal recumbency time and complete recovery time measured in minutes were found to be in an increasing order and being highest in group C, intermediate in group B and lowest in group A. This increase was significant ($p<0.05$) (Table 1, 2).

All the three groups showed excellent jaw relaxation score. A higher jaw relaxation score (a score of 3) was evaluated in group A and B in comparison to group C. No significant difference was present between the group ($p<0.05$). Pedal reflex score was maximum (a score of 3) in all the three groups within 5 minutes of induction. No significant difference was present between the groups and value reached zero in all the groups by 90 minutes which indicates patients recovery from anaesthesia. Palpebral reflex was present in all the groups throughout the anaesthesia. Grading criteria for jaw relaxation, pedal reflex and palpebral reflex are shown in Table 1 and their values at different time intervals are tabulated in Table 2, 3.

Physiological parameters

No report of cardiac arrythmias in any of the group was reported. The Mean±SE values of heart rate showed significant ($p<0.05$) increase post induction in all the three groups followed by a drop and again a second rise. Group C animals reported higher rise in heart rate values in comparison to other two groups. During second rise in values significant ($p<0.05$) increase in group B and C was noted at 90 and 105 minutes where 105 minutes value in group C was very significant ($p<0.01$).

The Mean ±SE respiratory values showed significant ($p<0.05$) decrease post induction in all the three groups but within the normal physiologic range. In group A and B a non-significant increase was reported from 35 to 60 minutes followed by non-significant drop upto 105 minutes in group A and increase from 90 to 105 minutes in group B. In group C, increase was reported from 45 minutes till the end of anaesthetic period.

In all the groups reduction in the rectal temperature values in descending order was observed during the observation of 105 minutes and this decrease was significant ($p<0.05$) within the group. Capillary refill time (CRT) in all the three groups showed increase after induction and this increase was significant ($p<0.05$) in group B and C. Maximum Mean ±SE value of CRT in group

Table 1: Grading of Jaw relaxation score, Pedal reflex score and Palpebral reflex score in dogs for evaluation of anaesthetic protocols in all three groups.

	Jaw relaxation score
Scale 0	Normal resistance to opening the mouth
Scale 1	The jaw can be opened, but there is still some resistance
Scale 2	Little resistance to opening the mouth and obvious muscle relaxation
Scale 3	No response
	Pedal reflex score
Scale 0	Hypersensitive or normal
Scale 1	Slightly impaired
Scale 2	Clearly weak
Scale 3	Absent
	Palpebral reflex score
Scale 0	No change in reflex
Scale 1	Moderate reflex
Scale 2	Sluggish reflex
Scale 3	Absence of reflex

These scores were evaluated at different time points.

Table 2: Induction dose, induction time, duration of anaesthesia, sternal recumbency time and complete recumbency time evaluated in dogs under three anaesthetic protocols in group A, B and C.

Groups	A	B	C
Induction dose (mg/kg)	6.5^{a}	5.5^{b}	4.0^{c}
Induction time (seconds)	38.00^{a}±2	31.83^{b}±2.17	25.00^{c}±7.55
Duration of anaesthesia (minutes)	23.76^{a}±0.72	29.60^{b}±1.37	35.50^{c}±0.87
Sternal recumbency time (minutes)	63.33^{a}±5.45	72.00^{b}±1.73	91.66^{c}±6.08
Complete recovery time (minutes)	72.00^{a}±3.60	92.33^{b}±6.08	116.66^{c}±13.23

Values with different alphabets differ significantly ($p<0.05$) between the groups.

Values are expressed as Mean±Standard Error (SE).

B was 4.0 and in group C it was 3.3. These values were higher than the normal physiologic range.

In group A, B and C, biphasic increase in the value of Systolic arterial pressure (SAP) was reported over the study time. Significant ($p<0.05$) increase was seen in group A at 25 and 105 minutes and in group B at 5 and 105 minutes whereas very significant increase ($p<0.01$) in group B was noted at 25 minutes. Overall significantly high SAP values were seen in group C as compared to other two groups. Diastolic arterial pressure (DAP) values reported an increase in first 15 minutes post induction followed by non-significant reduction and second rise was observed at 75 minutes following an increasing trend till 105 minutes. Significantly higher values of Diastolic arterial pressure was noted in third group in comparison to first two groups. Similar trend was observed in values of Mean arterial pressure (MAP) where biphasic increase was reported in three groups. In Group A, this increase was significant at 25 and 105 minutes ($p<0.05$) and in group B, mean arterial pressure was significantly increased at 20 and 105 minutes ($p<0.05$) and very significantly at 10 minutes ($p<0.01$).

In all the three groups a drop in oxygen saturation value was observed at 25 minutes followed by an increase in the values throughout the anaesthetic period. In group B and C, significant ($p<0.05$) lower values were reported as compared to the baseline value at 10, 15, 25, 35 minutes post induction. Group A showed non-significant ($p>0.05$) changes. Values were within the normal physiologic range throughout the anaesthetic period and no significant difference was present between the groups.

The Mean ±SE values of haemoglobin oxygen saturation in all the three groups reported dropped post induction and thereafter an increase was noticed till the end of anaesthetic period. These changes were within normal physiologic range.

Table 3: Jaw relaxation score, pedal reflex score and palpebral reflex scores as evaluated in dogs at predefined time points under general anaesthesia with three anaesthetic protocols in group A, B and C.

Minutes		Jaw relaxation score	Pedal reflex score	Palpebral reflex score
0	A	0	0	0
	B	0	0	0
	C	0	0	0
10	A	0	0	0
	B	0	1.0±0.0	0
	C	0.30±1.0	1.00±0.0	0.30±1.0
15	A	3.00±0.0	3.00±0.0	0.33±1.0
	B	3.00±0.0	3.00±0.0	0.60±1.0
	C	2.60±1.0	3.00±0.0	1.00±0.0
25	A	3.00±0.0	3.00±0.0	1.00±0.0
	B	3.00±0.0	3.00±0.0	1.00±0.0
	C	2.60±1.0	3.00±0.0	1.00±0.0
35	A	2.60±1.0	2.60±0.8	0.60±1.0
	B	2.60±1.0	3.00±0.0	0.30±1.0
	C	2.00±0.0	3.00±0.0	0.30±1.0
45	A	1.60±1.0	2.60±0.8	0.30±1.0
	B	2.00±1.0	2.60±1.0	0.30±1.0
	C	1.60±1.0	2.60±1.0	0.30±1.0
60	A	1.30±1.7	2.30±0.8	0
	B	1.60±1.0	2.30±1.0	0
	C	1.00±100	2.50±1.0	0
75	A	0.66±1.0	1.30±0.8	0
	B	0.66±1.0	1.30±1.0	0
	C	0.30±1.0	2.00±0.0	0
90	A	0.33±1.0	0	0
	B	0.33±1.0	0	0
	C	0	0	0
105	A	0	0	0
	B	0	0	0
	C	0	0	0
F value		5.18^{NS}	1.69^{NS}	0.85^{NS}

Scoring for these clinical parameters was done on a scale 0 to 3. Data is expressed as Mean±SE.

Mean ±SE values for respiration rate, heart rate, rectal temperature, SAP, DAP, MAP and SpO_2 are present in Table 4.

No adverse reaction like arrythmias or post induction apnoea was reported in any of the eighteen patient. Induction was smooth and quick in all the three groups. The duration of anaesthesia was longest in group C, along with least required dose of induction and shortest induction time in comparison with group A and B.

This study investigated the anaesthetic effects of tiletamine-zolazepam alone and in combination with xylazine and xylazine-ketamine in dogs. administration of tiletamine-zolazepam in combination resulted in reduced dose of induction. Ksenija *et al.* (2012) have used an induction dose of 7 mg/Kg body weight for tiletamine-zolazepam in dogs using atropine sulphate as pre-medicant similar to group A. Hafez *et al.* (2017) have administered xylazine at 1 mg/kg along with tiletamine-zolazepam at 6 mg/kg body weight in dogs. Landry and Maza (2020) have used combination of xylazine (0.88 mg/kg), ketamine (3.52 mg/kg) and tiletamine-zolazepam at 4.4 mg/kg body weight in a single syringe in dogs and it was reported that this combination provided balanced anaesthesia by targeting different drug receptors in CNS and thus reducing the volume of individual anaesthetic agent. Induction time was also significantly reduced with addition of xylazine and xylazine-ketamine. An induction time of 33.10±2.59 seconds under xylazine-tiletamine-zolazepam anaesthesia in dogs was observed which could be due to analgesic effect of xylazine (Koli *et al*., 2021). As per Landry and Maza (2020) an average duration of anaesthesia reported in dogs under xylazine, ketamine and tiletamine-zolazepam anaesthesia was 48.4 minutes. Koli *et al.* (2021) have stated that combination of xylazine and tiletamine- zolazepam produces longer duration of anaesthesia in dogs as compared to tiletamine- zolazepam given alone. In this study Sternal recumbency time increased with addition of xylazine and xylazine-ketamine to tiletamine-zolazepam. Longer duration of resumption to sternal recumbency in B and C group could be due to sedative effect of xylazine and dissociative effects of ketamine in addition to tiletamine. Significant ($p<0.05$) difference was observed between the groups which could be due to sedation associated with xylazine and dissociative effect of ketamine in addition to tiletamine-zolazepam. Dissociative anaesthetics are lipid soluble and undergo hepatic metabolism which could be responsible for longer recovery time (Dugassa and Fromsa, 2018).

In all the groups very good muscle relaxation was due to inhibition of internuncial neurons at spinal cord by zolazepam (Hall *et al*., 2001). Excellent jaw relaxation score in group A and B. This higher value in A and B group could be due to zolazepam and addition of alpha-2 adrenergic agent in group B. Group C had ketamine which leads to muscle stiffness and catalepsy reducing the muscle relaxation score a bit. Xylazine being an alpha-2 adrenergic agonist inhibits dopamine and catecholamines blocking the nerve impulse to CNS and leads to relaxation of striated muscles (Munif *et al*., 2021). Pedal reflex was absent in all the groups post induction denoting a good state of analgesia. Although group B and C have better analgesia as compared to group A which could be due to addition of xylazine. Xylazine acts by inhibiting the interneural transmission in CNS which depresses CNS resulting in muscle relaxation and analgesia (Williams *et al*., 2002). Palpebral reflex was intact in all three groups. In a similar study by Hampton *et al.* (2019) and Salve *et al.* (2022) patients showed persistent palpebral reflex under tiletamine-zolazepam anaesthesia in dogs. Presence of palpebral reflex and open eyes are characteristic of dissociative anaesthetics (Dugassa and Fromsa, 2018).

In this study significantly higher heart rate in all three groups with slightly higher values in group C. Gomez-Villamandos *et al.* (2013) have stated that the positive chronotropic effects of the dissociative anaesthetics counteracts the bradycardic effect of the alpha- 2 agonists. Dissociative anaesthetics increases outflow in sympathetic nervous system which inhibits reuptake of norepinephrine resulting in high concentration of circulating catecholamines and sinus node stimulation (Hampton *et al*., 2019). Decreased values of respiration rate in all the groups were noticed and similar findings were reported by Salve *et al.* (2022) and Flores *et al.* (2009) which could be due to depression of respiratory centre located in medulla oblongata by anaesthetic agents. Tiletamine-zolazepam leads to mild to moderate respiratory depression (Gomez-Villamandos 2013). Decreasing rectal temperature in all three groups throughout the study period could be due muscle relaxation, reduction in metabolic rate and depression of thermoregulatory centre by anaesthetic agents (Munif *et al*., 2021 and Lu *et al*., 2014). Higher values of capillary refill time reported post induction and significant difference present between the groups could be due to presence of alpha-2 agonists. Xylazine causes intense vasoconstriction which declines the blood flow to many organs (Cistola *et al*., 2004). Similar result was reported by Landry and Maza (2020) under xylazine, ketamine and tiletamine- zolazepam anaesthesia in dogs where thirty percent of patients were having CRT more than 3 seconds.

According to Gomez-Villamandos *et al.* (2013) sympathetic stimulation by dissociative anaesthetic agents counter balance the bradycardia induced by alpha-2 adrenoceptor thus further increasing the arterial blood pressure. This could be the reason for biphasic increase in the Systolic arterial pressure (SAP). Lee *et al.* (2018) in dogs under tiletamine-zolazepam anaesthesia where significant increase in SAP values were reported. Transient drop in the SAP could be due to activation of alpha-2 receptors in vascular smooth muscles in response to increasing arterial pressure which would lead to vasoconstriction (Jee *et al*., 2010). Jang *et al.* (2008) have reported biphasic increase in DAP values in dogs with atropine and tiletamine-zolazepam anesthesia similar to group A findings. In a report by Lu *et al.* (2014) dogs under

Table 4: Respiration rate, heart rate, rectal temperature, SAP, DAP, MAP and SpO_2 were evaluated using veterinary patient monitor at predefined time intervals.

Time (minutes)		RR(breaths/ minute)	HR (beats/ minute)	RT (°F)	CRT (seconds)	SAP (mm Hg)	DAP (mm Hg)	MAP (mm Hg)	SpO_2 (%)
0	A	20.00±3.46	107.33±8.71	101.80±2.23	1.00±0	119.30±8.7	88.00±1.73	98.40±3.99	97.30±2
	B	24.00±3.46	1180.0±4.58	101.86±0.36	1.00±0	124.00±6.0	93.00±4.5	103.30±4.6	98.60±1
	C	24.00±6.92	109.30±16.1	102.00±0.7	1.00±0	120.00±3.46	104.30±2.6	97.30±1.16	97.60±1
10	A	21.00±1.73	109.33±8.72	101.36±2.12	1.00±0	123.00±9.16	89.00±1.73	100.30±4.2	96.00±1.7
	B	22.00±3.46	113.33±5	101.63*±0.26	3.30*±1.0	127.60±6.55	96.30±6.08	106.70±6.1	92.30*±1
	C	23.60±7.8	117.00±14.18	101.70*±0.5	3.30*±1.5	126.30±5.56	106.30±5.56	103.80±8.29	92.00*±1.7
15	A	17.30±1.0	124.33±8.71	101.16±2.04	3.00±0	129.00±9.16	92.60±8	104.70±8.3	94.10±2.6
	B	20.66*±3.6	126.00*±9.16	101.26*±0.36	3.30*±1.0	134.33*±6	102.60*±5.2	113.17*±5.49	93.30*±1
	C	21.33±6	127.00±13.74	101.40*±0.5	3.30*±1.5	137.00±3.0	111.00±17.5	114.10*±3.92	92.60*±1
25	A	17.00*±1.73	131.30*±8.71	100.76±1.92	3.00±0	136.00*±6.24	95.33±10	108.80*±8.6	94.60±2
	B	19.00*±3.0	132.00*±6.24	100.90*±0.36	4.00*±0	139.00**±1.73	106.60**±5.2	117.40**±3.99	94.00*±1.7
	C	20.30**±6.08	136.00**±9.1	101.13*±0.4	3.30*±1.5	142.60*±4.3	115.00*±9.6	120.88*±3.38	93.36*±2
35	A	20.60±2.0	130.00*±17.32	100.30±1.83	3.00±0	132.30±12.16	91.60±7	105.22±8.5	94.90±0
	B	22.30±2.64	128.00±15.87	100.60±0.2*	3.30±1.0*	131.66±12.64	101.00±1.73	111.60±0.9	94.30±1*
	C	20.00±3.46	131.10±8.2	100.80**±0.4	3.00**±0	151.00**±6.2	112.30±8.18	130.70**±7.8	93.60*±2
45	A	22.60±1.0	127.00±14.79	100.00±1.75	3.00±0	125.00±7.5	89.60±3.6	101.40±4.9	95.10±3
	B	24.66±2.0	121.66±10	100.36*±0.2	3.30*±1.0	127.33±2.64	96.00±10	106.40±0.88	95.00±1.7
	C	24.33±2.6	130.00±9.2	100.40**±0.30	2.30±1.5	141.60*±6	107.30±5.56	123.77*±9.6	94.60±1
60	A	23.00±3.46	122.30±16.09	99.70±1.68	2.30±1	121.60±6.5	85.30±8.18	97.43±6.9	95.80±1
	B	25.33±3.46	122.66±9.54	100.00*±0.2	3.00±0	124.30±2	93.30±3.6	103.60±3.06	95.00±1.7
	C	26.66±8.18	135.00±3.0	100.20**±0.45	2.30±1.5	135.00±7.5	100.30±11.2	114.66±8.5	94.90±2.6
75	A	22.30±2.65	126.60±8.8	99.40*±1.59	2.00±1.0	128.00±7.5	88.00±13.07	101.30±10.9	96.10±1
	B	23.66±2.64	131.30±15.72	99.70*±0.17	2.30±1.0	129.30±2.0	99.66±4	109.50±3.33	96.50±2.6
	C	28.30±2	136.00±3.46	99.83*±0.50	2.30±1.5	130.60±3.6	108.30±9.53	107.70±7.21	95.10±1
90	A	20.66±3.6	125.00±13.07	98.86*±1.41	1.30±2.0	131.00±4.5	92.30±6.08	105.00±5.3	96.70±2
	B	26.00±3.45	132.60*±13.1	99.40*±0.17	2.00±0	133.30±2.64	102.00*±1.73	112.44±2.0	97.30±1.0
	C	29.20*±6.0	139.30*±2.0	99.50*±0.45	1.60±1.5	136.30±5.5	112.30±5.5	114.50±4.09	95.60±1.0
105	A	19.60±3.6	119.00±10.44	98.36*±1.41	1.00±0	133.60*±5.5	94.00±6.24	107.10±5.2	97.20±1
	B	28.00±3.46	135.30*±9.5	99.00*±0.26	1.60±1.0	136.00*±1.73	104.00*±1.7	114.60*±1.0	98.10±1.7
	C	30.20**±4.5	142.30**±4.35	99.20**±0.45	1.06±1.5	139.30*±5.29	113.60*±5.29	117.50*±5.45	97.20±1.0
F value		13.51*	1.28^{NS}	0.70*	19.95**	7.85*	19.57*	15.16*	0.83^{NS}

**Significant at 1% level of significance, (P<0.01). *Significant at 5% level of significance, (P<0.05).

Data is expressed as Mean±SE.

xylazine and tiletamine-zolazepam anaesthesia similar to second group showed biphasic increase in DAP values. Cullen and Reynoldson (1997) and Lee *et al.* (2018) have observed significant increase in MAP values in dogs under tiletamine-zolazepam anaesthesia. Drop in the MAP values could be due to xylazine as blood pressure is known to show peak after xylazine administration for 5-10 minutes then falling below baseline values in dogs (Lu *et al*., 2014). Salve *et al.* (2022) have reported significant decrease in oxygen saturation values under xylazine and tiletamine-zolazepam anaesthesia in dogs which could be due to reduced respiratory depth by alpha-adrenergic agonist action of xylazine. Hypoxemia also decreases oxygen saturation value and tiletamine-zolazepam is potentially respiratory depressant and hypoxemic in nature (Cistola *et al*., 2004 and Lee *et al*., 2018).

CONCLUSION

Tiletamine-zolazepam resulted in fast and smooth induction, however premedication with xylazine in group B and xylazine-ketamine in group C significantly reduced its dose for induction. In group C tiletamine-zolazepam induced anaesthesia in xylazine-ketamine premedicated dogs required minimum induction dose and provided longer duration of anaesthesia, better analgesia and sedation as compared to group A and group B. Based on the finding of the present study, anaesthetic regimen of group C can be effectively used for surgery of short to intermediate duration in dogs.

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Conflict of interest statement

Authors declare no conflict of interest.

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