B-5183
[1-7]

RESEARCH ARTICLE Indian Journal of Animal Research

Evaluation of Haemato-biochemical Effects of Tiletamine-zolazepam Alone and in Combination with Xylazine or Xylazine-ketamine in Atropinized Dogs

Sulekha[1], Manjul Kandpal[1], Shivani Singh[1]

10.18805/IJAR.B-5183

ABSTRACT

Background: Tiletamine-zolazepam is a good injectable anaesthetic widely used in veterinary patients and thus the present study was planned to evaluate the effect 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 namely A, B and C. Atropine sulphate was administered in all the groups followed by tiletamine-zolazepam in group A, xylazine and tiletamine-zolazepam in group B and xylazine, ketamine and tiletamine-zolazepam in group C. The efficacy of the anaesthesia was evaluated at different time intervals upto recovery by observing clinical, physiological and haemato-biochemical parameters.

Result: Induction dose of tiletamine-zolazepam observed in group A, B and C was 6.5, 5.5 and 4.0 mg/kg body weight, respectively. Induction time values were decreased and duration of anaesthesia was increased from group A to group C. All physiological parameters differs significantly ($p<0.05$) between the groups. Mean values of Hb, TEC, PCV, TLC, lymphocytes, monocytes, eosinophils, basophils and total proteins showed transient decrease whereas neutrophils, ALT, AST, total bilirubin, plasma glucose, BUN and serum creatinine showed transient increase in all the groups at 30 and 60 minutes. Haemato-biochemical parameters approached to baseline values upto 24 hours. Thus, it can be concluded that the various combinations of tiletamine-zolazepam with pre-medicants like xylazine and xylazine-ketamine was found to be safe with regard to their effects on haemato-biochemical parameters.

Key words: Atropinized dog, Haemato-biochemical changes, Ketamine, Tiletamine-zolazepam, Xylazine.

INTRODUCTION

General anaesthesia is a state of unconsciousness in which there is a loss of protective reflexes after administration of single or combination of anaesthetic agents. An ideal anaesthetics does have characteristics like sedation, amnesia, analgesia and muscle relaxation. A sole agent cannot provide all these characteristics, hence a combination of drugs is usually preferred. This is known as balanced anaesthesia (Billah *et al*., 2017).

Xylazine is an alpha-2 adrenergic agonist with properties like sedation, analgesia and muscle relaxation. The most common effect of xylazine is bradycardia with reduction in cardiac output up to 30 per cent (Landry and Maza, 2020). Ketamine is a non-competitive antagonist at NMDA receptor and by binding to the phencyclidine binding site, they prevent the binding of excitatory neurotransmitter, glutamate. However ketamine have poor muscle relaxation property and visceral analgesia so to compensate for this sedatives like xylazine can be co-administered (Dugassa and Fromsa, 2018).

Tiletamine-Zolazepam is an anaesthetic combination of two drugs tiletamine and zolazepam present in the ratio of 1:1. Analgesic effect tiletamine is greater than ketamine. Zolazepam belongs to benzodiazepine class. Zolazepam intensifies the effect of tiletamine on the central nervous system and reduces the hyperactivity of the skeletal muscle (Lee *et al*., 2018).

In present study three different anaesthetic combinations using anaesthetic agents tiletamine-zolazepam, xylazine-tiletamine-zolazepam and xylazine-ketamine-tiletamine-zolazepam are compared for their anaesthetic efficacy and for their effects on haemato-biochemical parameters as previously not much details are available for the same in canines. The aim of this study is to evaluate the effect of above said anaesthetic combination on haemato-biochemical parameters.

[1]Department of Veterinary Surgery and Radiology, College of Veterinary and Animal Sciences, Govind Ballabh Pant University of Agriculture and Technology, Pantnagar-263 145, Uttarakhand, India.

Corresponding Author: Sulekha, Department of Veterinary Surgery and Radiology, College of Veterinary and Animal Sciences, Govind Ballabh Pant University of Agriculture and Technology, Pantnagar-263 145, Uttarakhand, India. Email: sulkhs.vet@gmail.com

How to cite this article: Sulekha, Kandpal, M. and Singh, S. (2023). Evaluation of Haemato-biochemical Effects of Tiletamine-zolazepam Alone and in Combination with Xylazine or Xylazine-ketamine in Atropinized Dogs. Indian Journal of Animal Research. DOI: 10.18805/IJAR.B-5183.

Submitted: 26-06-2023 **Accepted:** 11-10-2023 **Online:** 06-11-2023

MATERIALS AND METHODS

Animals

The study was conducted in 18 dogs irrespective of age, breed, sex and body weight presented to the Teaching

Veterinary Clinical Complex, Pantnagar for various surgical corrections during January to July 2022. 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. Animals were kept off feed for 12 hours and water was withheld for 6 hours prior to the surgery. These animals were randomly divided into three groups *viz*., A, B and C.

Anaesthetic protocols

Atropine sulphate (0.025 mg/kg SC) was administered in all the groups, xylazine (0.5 mg/kg IM) in group B and xylazine (0.5 mg/kg), ketamine (2.5 mg/kg IV) combining in group C. A gap of 10 minutes was kept between administration of each drug. In all the three groups induction was done by administering 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 (zoletil) 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.

Monitoring of anaesthesia

Monitoring of anaesthesia was done using veterinary patient monitor (model no. MMED 8000-CV Beijing Choice Electronic Technology Co. Ltd., Beijing, China.

Clinico-physiological parameters

Clinical parameters evaluated for the study are induction dose (in mg/kg body weight), induction time (in seconds), duration of anaesthesia (minutes), jaw relaxation score and pedal reflex score. The values of these parameters are tabulated in Table 2. Evaluation of jaw relaxation score and pedal reflex score was done as per the method described by Zhang *et al.* (2021) and Nam *et al*. (2013) respectively. Scoring parameters of jaw relaxation and pedal reflex is represented in Table 1. Physiological parameters like heart rate, respiration rate, rectal temperature and haemoglobin oxygen saturation (SpO_2) were monitored by veterinary patient monitor. Jaw relaxation score, Pedal reflex score and physiological parameters were evaluated at 0, 10, 15, 25, 35, 45, 60, 75, 90 and 105 minutes.

Haematological and biochemical parameters

Haematological parameters estimated includes haemoglobin (g/dl), total erythrocyte count (10^6/cu mm), packed cell volume (%), differential leucocyte count (%) and total leucocyte count (10^3/cu mm). Biochemical parameters includes total protein (g/dl), plasma glucose (mg/dl), blood urea nitrogen (mg/dl), serum creatinine (mg/dl), total bilirubin (mg/dl), alanine aminotransferase (IU/litre) and aspartate aminotransferase (IU/litre). These parameters were estimated at baseline 0 minute, 30 minutes, 1 hour, 6 hour and 24 hours post induction.

Statistical analysis

Data was expressed as Mean±Standard error (SE). To compare the Mean values at different time intervals with their base values in each group paired “t” test was used (Snedecor and Cochran, 1994). Analysis of variance (ANOVA) was used to compare the mean values between different groups. All data were analysed using SPSS v 15.0 statistics software program.

RESULTS AND DISCUSSION

Clinical parameters

Induction of anaesthesia was fast and smooth in all the groups. The Mean±SE values of various clinico-physiological

Table 1: Grading criteria for jaw relaxation score and pedal reflex score during evaluation of anaesthesia.

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

Table 2: Mean±SE values of induction dose (in seconds), induction time (in minutes) and duration of anaesthesia (in minutes) in groups A, B and C subjected to different anaesthetic protocols.

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

parameters like heart rate, respiratory rate, rectal temperature, SpO_2, jaw relaxation score and pedal reflex score are tabulated in Table 3. Induction dose in group A, B and C was 6.6, 5.5 and 4 mg/kg BW respectively. Significant difference ($p<0.05$) was observed between the groups subjected to different pre-anaesthetic protocols. Reduction in induction dose of tiletamine-zolazepam in subsequent groups could be due to addition of premedicants like xylazine in group B and xylazine-ketamine in group C. In a similar study by Landry and Maza (2020) combination of xylazine (0.88 mg/kg), ketamine (3.52 mg/kg) and tiletamine-zolazepam (4.4 mg/kg) was used in a single syringe. Induction time of 38.0±2.0, 31.83±2.17 and 25.0±7.55 seconds was reported in group A, B and C respectively. Administration of xylazine in group B and xylazine-ketamine in group C significantly lowered the dose of induction and induction time. Dugassa and Fromsa (2018) have reported that tiletamine-zolazepam takes 45-90 seconds for induction after intravenous administration and due to higher lipid solubility along with hepatic metabolism of tiletamine-zolazepam is responsible for longer recovery time. Duration of anaesthesia in minutes was found to be in an increasing order and being highest in group C, intermediate in group B and lowest in A. This increase was significant ($p<0.05$). 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. Maximum value of jaw relaxation score in group A and B was 3 and in group C it was 2.6. Score of 2.6 indicates minute resistance to opening of jaw and score of 3 indicates no resistance to opening of jaw and excellent muscle relaxation. In all the groups very good muscle relaxation was due to inhibition of internuncial neurons at spinal cord by zolazepam (Hall *et al*., 2001). In all the three groups zero value of pedal reflex score was reported at baseline which means normal pedal reflex and maximum value reported was 3 within 5 minutes of induction. A score of 3 indicates absence of pedal reflex which showed animals were in a good analgesic state. Xylazine acts by inhibiting the interneural transmission in CNS which depresses CNS

Table 3: Mean±SE values of clinic-physiological parameters evaluated during the course of study.

Time (minutes)		RR (breaths/ minute)	HR (beats/ minute)	RT (°F)	SpO_2 (%)	Jaw relaxation score	Pedal reflex score
0	A	20.00±3.46	107.33±8.71	101.80±2.23	97.30±2	0	0
	B	24.00±3.46	118.0±4.58	101.86±0.36	98.60±1	0	0
	C	24.00±6.92	109.30±16.1	102.00±0.7	97.60±1	0	0
10	A	21.00±1.73	109.33±8.72	101.36±2.12	96.00±1.7	0	0
	B	22.00±3.46	113.33±5	101.63*±0.26	92.30*±1	0	1.00±0.0
	C	23.60±7.8	117.00±14.18	101.70*±0.5	92.00*±1.7	0.30±1.0	1.00±0.0
15	A	17.30±1.0	124.33±8.71	101.16±2.04	94.10±2.6	3.00±0.0	3.00±0.0
	B	20.66*±3.6	126.00*±9.16	101.26*±0.36	93.30*±1	3.00±0.0	3.00±0.0
	C	21.33±6	127.00±13.74	101.40*±0.5	92.60*±1	2.60±1.0	3.00±0.0
25	A	17.00*±1.73	131.30*±8.71	100.76±1.92	94.60±2	3.00±0.0	3.00±0.0
	B	19.00*±3.0	132.00*±6.24	100.90*±0.36	94.00*±1.7	3.00±0.0	3.00±0.0
	C	20.30**±6.08	136.00**±9.1	101.13*±0.4	93.36*±2	2.60±1.0	3.00±0.0
35	A	20.60±2.0	130.00*±17.32	100.30±1.83	94.90±0	2.60±1.0	2.60±0.8
	B	22.30±2.64	128.00±15.87	100.60±0.2*	94.30±1*	2.60±1.0	3.00±0.0
	C	20.00±3.46	131.10±8.2	100.80**±0.4	93.60*±2	2.00±0.0	3.00±0.0
45	A	22.60±1.0	127.00±14.79	100.00±1.75	95.10±3	1.60±1.0	2.60±0.8
	B	24.66±2.0	121.66±10	100.36*±0.2	95.00±1.7	2.00±1.0	2.60±1.0
	C	24.33±2.6	130.00±9.2	100.40**±0.30	94.60±1	1.60±1.0	2.60±1.0
60	A	23.00±3.46	122.30±16.09	99.70±1.68	95.80±1	1.30±1.7	2.30±0.8
	B	25.33±3.46	122.66±9.54	100.00*±0.2	95.00±1.7	1.60±1.0	2.30±1.0
	C	26.66±8.18	135.00±3.0	100.20**±0.45	94.90±2.6	1.00±100	2.50±1.0
75	A	22.30±2.65	126.60±8.8	99.40*±1.59	96.10±1	0.66±1.0	1.30±0.8
	B	23.66±2.64	131.30±15.72	99.70*±0.17	96.50±2.6	0.66±1.0	1.30±1.0
	C	28.30±2	136.00±3.46	99.83*±0.50	95.10±1	0.30±1.0	1.30±1.0
90	A	20.66±3.6	125.00±13.07	98.86*±1.41	96.70±2	0.33±1.0	0
	B	26.00±3.45	132.60*±13.1	99.40*±0.17	97.30±1.0	0.33±1.0	0
	C	29.20*±6.0	139.30*±2.0	99.50*±0.45	95.60±1.0	0	0
105	A	19.60±3.6	119.00±10.44	98.36*±1.41	97.20±1	0	0
	B	28.00±3.46	135.30*±9.5	99.00*±0.26	98.10±1.7	0	0
	C	30.20**±4.5	142.30**±4.35	99.20**±0.45	97.20±1.0	0	0

resulting in muscle relaxation and analgesia (Williams *et al*., 2002). Dissociative anaesthetics bind to opioid receptors and also binds to monoaminergic receptors contribute to anti-nociception (Dugassa and Fromsa, 2018).

Physiological parameters

Heart rate values showed significant ($p<0.05$) increase in first 25 minutes in all three groups followed by a non-significant drop. Again, a second rise in heart rate (A: 126.60±8.80, B: 131.30±15.70 and C: 136.00±3.46) was reported in all the groups at 75 minutes. Both tiletamine and ketamine increases the sympathetic tone and decreases vagal tone which leads to increased heart rate (Landry and Maza, 2020). Kim *et al.* (2007) have stated that positive inotropic effect of tiletamine counter balances the bradycardic effect of xylazine. Respiration rate (A:17.00±1.73, B:19.00±3.0 and C:20.30±6.08) was significantly ($p<0.05$) lowered in three groups post induction at 25 minutes. However, this drop was transient and values again increased. Similar results were obtained by Lee *et al.* (2018) in dogs using tiletamine- zolazepam where respiratory frequency decreased after 5 minutes of administration. Findings similar to group B were reported by Salve *et al.* (2020) and Flores *et al.* (2009) which could be due to depression of respiratory centre located in medulla oblongata by anaesthetic agents. According to Gomez-Villamandos (2013) tiletamine-zolazepam leads to mild to moderate respiratory depression. Rectal temperature was reported to be highest at 0 minute and it kept on decreasing throughout th2e anaesthetic period and in all the groups lowest values were reported at 105 minutes. Findings similar to group A and B have been reported by Flores *et al.* (2009). Significant reduction in rectal temperature 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). Haemoglobin oxygen saturation values reported drop at 25 minutes in all three groups followed by an increasing trend in the values throughout the anaesthetic period. Group A showed non-significant changes. Similar results have been reported by Flores *et al.* (2009) where immediate non-significant drop in oxygen saturation values post induction was observed followed by an increase throughout the anaesthetic period. This could be due to depression of respiratory centre by anaesthetic agents.

Haemato-biochemical parameters

Haematological parameters in all the three groups followed similar trend. The Mean±SE values of various haematological parameters are present in Table 4. The Mean±SE values of Haemoglobin (A:13.33±2.64, B:10.86± 0.88, C:11.90±0.81), total erythrocyte count (A:5.90±1.20, B:5.90±0.20, C:4.74±1.32), packed cell volume (A:38.66±7.0, B:40.80± 10.40, C:40.90±10.01), total leucocyte count (A:12.50±6.30, B:11.56±5.20,C:10.74±0.96), lymphocytes (A:30.00±3.46, B:26.30±8.00,C:22.00±0.50), monocytes (A:1.66±1.00, B:1.00±1.73,C:1.60±1.00), eosinophils (A:0.33±1.00,

Table 4: Mean±SE values of haematological parameters.

		Hb (gm/dl)	PCV (%)	TEC (10^6cu mm)	TLC (10^3 cu mm)	Neutrophils (%)	Leucocytes (%)	Monocytes (%)	Eosinophils (%)	Basophils (%)
Baseline	A	14.26±2.71	41.33±3.60	6.63±0.11	13.5±5.01	66.60±2.64	32.00±3.0	2.33±1	0.33±1	0.21±0.01
	B	14.96±1.31	46.80±9.63	6.60±0.75	14.85±4.01	70.00±3.46	27.30±3.6	1.33±1	1.00±0	0.25±0.01
	C	16.13±1.21	51.97±4.16	7.13±0.60	15.38±1.91	68.30±2.64	27.60±3.6	2.33±1	1.00±0	0.19±0.01
30 mins	A	13.86±2.60	41.26±7.35	6.33±0.95	13.00±4.2	67.00±1.73	31.60±2.6	2.33±1	0.33±1	0.15±0.01
	B	13.40*±0.45	43.96±9.82	5.90±0.2	13.37±4.64	70.66±3.6	27.00±5.56	1.33±1	0.66±1	0.20±0.02
	C	13.90*±0.65	45.43±11.75	5.97±0.76	13.53±1.21	71.00±3.0	26.33±3	1.66±1	1.00±0	0.17±0.01
60 mins	A	13.33±2.64	38.66±7.0	5.90±1.20	12.50±6.30	68.66±2	30.00±3.46	1.66±1	0.33±1	0.10±0.02
	B	10.86*±0.88	40.80**±10.4	5.90*±0.20	11.56*±5.2	71.33±7	26.30±8	1.00±1.73	0.33±1	0.15*±0.01
	C	11.90*±0.81	40.90*±10.01	4.74*±1.32	10.74*±0.96	76.00*±1.73	22.00*±0.5	1.60±1	0.33±1	0.10±0.02
6 hours	A	13.53±2.60	38.86±7.79	6.03±1.01	13.10±3.3	68.66±2	30.00±3.46	2.30±1	0.33±1	0.18±0.02
	B	12.33±0.60	41.70±11.22	5.56*±0.20	12.85*±4.44	71.00±6	26.60±7.5	1.00±1.7	0.33±1	0.19±0.01
	C	12.14±0.24	41.58*±9.90	5.12*±1.23	10.80*±0.19	75.00*±0.5	24.33*±4	1.30±1	0.33±1	0.13±0.02
24 hours	A	13.76±2.60	40.13±9.69	6.16±0.98	13.72±3.89	68.00±1.73	30.60±2.6	2.30±1	0.33±1	0.20±0.01
	B	13.53±0.95	43.60±12.81	5.86±0.10	13.60±4.24	70.33±4	27.10±5	1.30±1	1.30±1	0.24±0.02
	C	12.73±0.51	43.81±8.75	5.43±1.0	9.14±0.85	72.00±3.46	25.66±2	2.30±2	1.00±0	0.19±0.02

Table 5: Mean±SE values of biochemical parameters.

		Total protein (g/dl)	Plasma glucose (mg/dl)	BUN (mg/dl)	Creatinine (mg/dl)	Total bilirubin (mg/dl)	ALT (IU/L)	AST (IU/L)
Baseline	A	5.80±0.52	78.06±15.33	19.80±7.33	0.57±0.05	0.09±0.01	37.00±30.13	24.10±9.16
	B	6.81±0.77	78.40±3.20	14.69±3.46	0.67±0.09	0.07±0.008	55.59±25.02	37.60±13.70
	C	7.17±0.61	75.70±6.45	17.60±9.32	0.70±0.21	0.08±0.02	39.16±19.07	14.42±3.16
30 mins	A	5.67±0.50	78.56±17.21	20.86±5.57	6.0±0.02	0.10±0.07	40.63±28.82	26.56±10.24
	B	6.40±0.94	80.10±6.1	15.98±4.20	0.69±0.07	0.08±0.04	62.12±8.5	42.60±4.60
	C	6.43*±0.26	78.03*±6.97	23.39±4.33	0.81±0.47	0.09±0.03	52.70±25.40	21.94±2.86
60 mins	A	5.51±0.31	82.66±14.93	23.56±3.73	0.62±0.02	0.11±0.08	44.73±24.59	30.70±8.92
	B	6.11*±1.08	82.50*±4.33	17.30±3.20	0.72*±0.07	0.09±0.03	70.00**±10.46	50.20*±5.60
	C	5.91*±0.1	82.30*±7.50	28.87±4.90	0.93±0.72	0.10±0.05	72.23*±24.79	30.80*±4.52
06 hours	A	5.55±0.38	80.53±13.70	22.40±3.41	0.61±0.04	0.11±0.04	42.23±26.34	27.53±8.43
	B	6.35±0.93	80.76*±2.71	15.93±2.69	0.69±0.11	0.08±0.08	61.20±10.41	45.50±9.20
	C	6.57±0.37	77.33±5.29	24.21±6.18	0.78±0.35	0.09±0.008	59.43*±16.50	25.04*±6.11
24 hours	A	5.67±0.38	77.70±14.85	21.23±4.97	0.59±0.05	0.09±0.03	37.30±30.31	22.36±2.69
	B	6.67±0.87	79.23±1.73	15.08±3.47	0.67±0.09	0.08±0.02	55.50±26.36	37.20±14.35
	C	6.94±0.33	75.63±5.20	18.57±9.29	0.71±0.21	0.08±0.08	42.74±16.86	18.13±6.34

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

B: 0.33±1.00, C: 0.33±1.00) and basophils (A:0.10±0.02, B: 0.15±0.01, C:0.10±0.02) showed transient decrease in their values at 60 minutes. Their values started increasing thereafter reaching almost the baseline value by 12 hours. All these variations present were within the normal physiologic values. According to Hampton *et al.* (2019) reduction in haemoglobin was seen in dogs while inducing with tiletamine-zolazepam and it was attributed to haemodilution with no fluid loss via conduction or evaporation. Hafez *et al.* (2017) have observed a drop in the values of haemoglobin, PCV, TEC and TLC values with tiletamine-zolazepam anaesthesia. The spleen enlarges during general anaesthesia which results in sequestration of red blood cells and leads to reduced haematocrit and haemoglobin values (Hawkey, 1985). Abdul *et al.* (2015) have attributed significant reduction in granulocytes due to stress involved in the procedure. In a study by Yohannes *et al*. (2018) reduced value of eosinophils have been reported due to pooling of circulating blood cells in the spleen and other reservoirs post ketamine-xylazine anaesthesia. Neutrophils showed an increase at 60 minutes followed by reduction at 6 hours and reached baseline value by 24 hours. Neutrophilia could be attributed to the stress caused by anaesthetic drugs, surgical trauma and activation of the adrenal cortex (Rubio *et al*., 2022). All these changes in the haematological parameters were within the normal physiologic range.

Biochemical parameters were within normal physiologic range throughout the study period in all the three groups and reached near to baseline value by 24 hours. The Mean±SE values of various biochemical parameters are tabulated in Table 5. The Mean±SE value of total protein showed a decrease at 60 minutes whereas plasma glucose, Blood urea nitrogen (BUN), serum creatinine, total bilirubin, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) showed an increase till 60 minutes followed by a reverse trend thereafter approaching the baseline value by 24 hours. Hampton *et al*. (2019) presented similar report where drop in total protein values were observed post induction with tiletamine- zolazepam. The decrease in total proteins could be due to hemodilution or secondary elevation of globulins (Dewangan *et al*., 2016). Surgical and anaesthetic stress leads to the altered endocrine secretion of the insulin antagonisms like growth hormone (Rubio *et al*., 2022). Increase in BUN levels might be due to temporary inhibitory effect of drugs on renal blood flow resulting in consequent reduction in glomerular blood flow (Dewangan *et al*., 2016). After induction with tiletamine-zolazepam anaesthesia with decreasing creatinine value in dogs (Koli *et al*., 2021). Kamal *et al.* (2019) observed increased bilirubin concentration at 20 and 40 minutes post induction under xylazine-ketamine anaesthesia in dogs.

Hafez *et al.* (2017) in a study have reported similar changes in ALT and AST and contrary results have been reported by Koli *et al.* (2021) with regards to BUN and serum creatinine. General anaesthetics reduces the blood flow to the liver which can cause harm and alter the permeability of hepatocytes resulting in leakage of liver enzymes and their elevated levels (Vikers *et al*., 1984; Pandey and Sharma, 1994; Tiwari *et al*., 1999).

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 required dose for induction. Transient changes were seen in haematological and biochemical parameters which were within the normal physiologic range. So based on the above

study it can be concluded that the various combinations of tiletamine-zolazepam with pre-medicants like xylazine and xylazine-ketamine was found to be safe with regard to their effect on haemato-biochemical parameters.

ACKNOWLEDGEMENT

The author would like to thank the Department of Veterinary Surgery and Radiology, Pantnagar for their support and assistance during the research period. This research did not receive any specific grant from any funding agencies.

Conflict of interest

Authors declare no conflict of interest.

REFERENCES

Abdul, A.A., Gabriel, D., Sadiq, Y.A., Mobolaji, L.F. and Onoruoyiza, M.M. (2015). Lumbosacral epidural analgesia with ketamine alone or in combination with xylazine in dogs. International Journal of Veterinary Science. 4(3): 111-117.

Billah, A.K.M.M., Sultana, S., Hossain, M.A., Hashim, M.A., Begum, T., Rahman, B. and Rashid, M. (2017). Evaluation of different premedicants in canine anaesthesia. Research in Agriculture Livestock and Fisheries. 4(3): 209-214.

Dewangan, R., Tiwari, S.K., Sharda, R. and Kalim, M.O. (2016). Haemato-biochemical response to xylazine-propofol anaesthesia in dogs. International Journal of Environmental Science and Technology. 5(4): 2331-2336.

Dugassa, J. and Fromsa, A. (2018). Review on dissociative anaesthetics and compatible drug combinations in veterinary clinical practice. Veterinary Medicine Open Journal. 3(1): 21-30. doi: 10.17140/VMOJ-3-129.

Flores, S.A., Zerpa, H.A., Ascanio, E.R., Rojas, J.A., Brinceno, E.C., Arrieta, D. and Maniglia, G.C. (2009). Evaluation of Tiletamine/Zolazepam anesthesia induction in dogs submitted to different premedication protocols. Revista Cientifica De La Facultad De Ciencias Veterinarias. 50(1): 11-18.

Gomez-Villamandos, R.J., Martinez, C., Navarrete, R., Morgaz, J., Dominguez, J.M., Lopez, I., Munoz, P., Fernandez, A. and Granados, M.M. (2013). Romifidine and low doses of tiletamine-zolazepam in dogs. Veterinary Anaesthesia and Analgesia. 40: 40-47. doi: 10.1111/vaa.12054.

Hafez, S.G., Nouh, S.R. and Elkammar, M.H. (2017). Evaluation of total intravenous anesthesia using ketamine HCL or telazol in mongrel dogs. Alexandria Journal of Veterinary Sciences. 53(2): 99-106.

Hall, L.W., Clarke, K.W. and Trim, C.M. (2001). General Pharmacology of Injectable Agents used in Anaesthesia. In: Veterinary Anaesthesia. 10th Edn., W.B. Saunder's Co, London, pp113-131.

Hampton, C.E., Riebold, T.W., LeBlanc, N.L., Scollan. K.F., Mandsager, R.E. and Sisson, D.D. (2019). Effects of intravenous administration of tiletamine-zolazepam, alfaxalone, ketamine-diazepam and propofol for induction of anesthesia on cardiorespiratory and metabolic variables in healthy dogs before and during anesthesia maintained with isoflurane. American Journal of Veterinary Research. 80: 33-44.

Hawkey, C.M. (1985).Changes in blood count during sedation and anaesthesia. British Veterinary Zoological Society Newsletter. 19: 27-31.

Kamal, M.M., Mishra, P., Akter, M.A., Hasan, M., Hashim, M.A. and Alam, M.M. (2019). Effects of two anaesthetic combinations (Xylazine-ketamine and xylazine-propofol) on clinical and haematological profile in dogs. Bangladesh Veterinary Journal. 53(1-4): 9-17.

Kim, J.M., Park, C.S., Jun, M.H. and Kim, M.C. (2007). Antagonistic effects of yohimbine in pigs anaesthetised with tiletamine-zolazepam and xylazine. Veterinary Record. 161: 620-624.

Koli, P.H., Parikh, P.V., Mahla, J.K. and Barot, H.M. (2021). Clinical attributes of tiletamine-zolazepam induced anesthesia with and without xylazine premedication in dogs. Indian Journal of Veterinary Science and Biotechnology. 17(4): 61-65.

Landry, J. and Maza, P. (2020). Effectiveness of the anaesthetic combination of tiletamine, zolazepam, ketamine and xylazine for the sterilisation of street dogs in field clinics. Veterinary Record Case Report. 8: e000953. doi:10.1136/vetreccr- 2019-000953.

Lee, J.Y., Son, S.J., Jang, S., Choi, S. and Cho, D.W. (2018). Antagonistic effect of flumazenil on tiletamine- zolazepam-induced anaesthesia in Beagle dogs. Veterinary Medicine. 63(12): 555-560.

Lu, D.Z., Jiang, S., Yu, S.M. and Fan, H.G. (2014). A comparison of anesthetic and cardiorespiratory effects of tiletamine-zolazepam/xylazine and tiletamine-zolazepam/xylazine/tramadol in dogs. Pakistan Veterinary Journal. 34(1): 63-67.

Munif, M.R., Alam, M.M. and Alam, M.A. (2021). Hemato-biochemical changes during xylazine-ketamine and xylazine-thiopentone anesthesia in dogs. Bangladesh Journal of Veterinary Medicine. 19(2): ISSN: 1729-7893. DOI: 10.33109/bjvmjd2021sam2.

Nam, S.W., Shin, B.J. and Jeong, S.M. (2013). A comparison of anaesthetic and cardiorespiratory effects of tiletamine-zolazepam/xylazine and tiletamine- zolazepam/xylazine/tramadol in dogs. Journal of Veterinary Clinics. 30(6): 421-427.

Pandey, S.K. and Sharma, I.J. (1994).Effect of diazepam-ketamine anaesthesia on liver and kidney function in canine and surgical patient. Indian Journal of Animal Sciences. 64: 48-50.

Rubio, M., Satue, K., Carrillo, J.M., Hernandez, G.A., Cuervo, B., Chicharro, D., Damia, E., Del-Romero, A. and Sopena, J. (2022). Changes in hematological and biochemical profiles in ovariohysterectomized bitches using an alfaxalone-midazolam-morphine-sevoflurane protocol. Animals (Basel). 12(7): 914. doi: 10.3390/ani12070914.

Snedecor, G.W. and Cochran, W.G. (1994). Statistical Methods, 8th Edition, Iowa State University Press, Ames.

Salve, S.P., Thorat, M.G., Raulkar, R.V. *et al*. (2020). Clinical Efficacy of tiletamine-zolazepam and ketamine-diazepam combination on quality of anesthesia for ovariohysterectomy in dog. Acta Scientific Veterinary Science. 4(2): 2582- 3183.

Tiwari, S.K., Kumar, A., Jadon, N.S. and Parikh, P.V. (1999). Haematological and Biochemical response to epidural xylazine or detomidine without local anaesthetics in buffaloes. Indian Journal of Animal Sciences. 69: 85-87.

Vikers, M.D., Schnieden, H. and Smith, F.G. (1984). Drugs in Anaesthetic Practice-6th ADN Publication. Butterworths. 63-95.

Williams, L.S., Levy, J.K., Robertson, S.A., Cistola, A.M. and Centonze, L.A. (2002). Use of the anesthetic combination of tiletamine, zolazepam, ketamine and xylazine for neutering feral cats. Journal of American Veterinary Medicine Association. 220(10): 1491-5. doi: 10.2460/javma.2002.220.1491.

Yohannes, G. (2018). Hematological and physiological effects of ketamine with and without xylazine in dogs. International Journal of Cell Science and Molecular Biology. 5(1): IJCSMB.MS.ID.555654.

Zhang, Z., Du, X., Bai, H., Shen, M., Ma, X., Li, R., Jin, X. and Gao, L. (2021). Cardiopulmonary (No Ventilation) and anesthetic effects of dexmedetomidine-tiletamine in dogs. Frontiers in Veterinary Science. 8: 674862. doi: 10.3389/fvets.2021.674862.