Ann. For. Res. 67(1): 272-284, 2024
ISSN: 18448135, 20652445

ANNALS OF FOREST RESEARCH
www.e-afr.org

CLINICOPHYSIOLOGICAL AND HAEMODYNAMIC EFFECTS OF DEXMEDETOMIDINE, XYLAZINE AND BUTORPHANOL AS PREANAESTHETIC AGENT IN CONJUNCTION WITH TILETAMINE-ZOLAZEPAM IN DOGS

Vikas Dehariya[1*], Neelam Tandia[2], Dharmendra Kumar[3], Priya Singh[4], Bhogindranath Meher[5],Siddharth Wadiwa[6],Himanshu Singh[7]

[1*,5,6,7] P.G. Scholar, College of Veterinary Science And A.H.,Rewa, Madhya Pradesh,India

[2,4]Assistant Professor, Department of Veterinary Surgery, College of Veterinary Science And A.H.,Rewa,
Madhya Pradesh,India

[3]Associate Professor & Head, Department of Veterinary Surgery, College of Veterinary Science And A.H.,Rewa, Madhya Pradesh,India

[1*] vikasdehariya1009@gmail.com

ABSTRACT

The study was designed in 18 dogs presented in the VCC for surgical interventions to evaluate the best suitable anaesthetic protocol and to determine the various clinicophysiological and haemodynamicaleteration before, during and after the anaesthesia. Animals were divided into three groups of six animal each and in all the groupstiletamine-zolazepam @6.5mg/kg b.wt. was administered as induction and maintainanece anaesthesia. As preanaesthetic agent atropine sulphate @0.04 mg/kg b,wt. was administered in all groups. However in group I dexmedetomidine was administered @ 0.02 mg/kg b.wt. I/V, in group II xylazine @ 1 mg/kg bwt. and in group III butorphanol @ 0.2 mg/kg bwt. was administered as premedication agents. Heart rate significantly increased after administration of tiletamine-zolazepam in all three groups, however significant decrease in respiration rate was observed in group I. the gradual decrease in the rectal temperature was observed in all three groups. A significant decrease in the spo2 value was observed in group I however in group II and III spo2 was in between 96% and 97%. MAP increased significantly in group I and II however a gradual decrease was observed in group III. All the clinico-physiological and haemodynamic parameter came near to itspreanaesthetic value at the end of the observation period.

Keywords: Heart Rate, Spo2, Map, Tiletamine-Zolazepam

INTRODUCTION:

The application of anaesthetics, as a practical method to relieve pain and muscular rigidity during surgical intervention is the most valuable research in medicine. In search of finding best suitable anaesthetic protocol for dogs that accomplish amnesia, analgesia and muscle relaxation to facilitate well-being of the surgical patient (Vedpathak*et al*., 2009).Tiletamine-zolazepam used as 1:1 mixture by weight as an injectable anaesthetic and immobilizing agent used in dogs, cats and other domestic and wild animals (Lagutchik*et al*., 1991 and Berry *et al.* 2015).Tiletamine-zolazepam has been used alone or in combination with other anesthetic agents in dogs (Kriminss*et al*., 2012a). Compared to ketamine, tiletamine-zolazepam provide longer duration of action. The addition of other anesthetic drugs is required as on top of xylazine premedication or as a mixture for reaching

complete immobilization and general anesthesia. While one of the most popular mixtures is xylazine-tiletamine/zolazepam (James *et al.,* 1999).

Xylazine and dexmedetomidine, being two α2 adrenergic receptor agonists, mediate sedative, anxiolytic and analgesic effects (Clark *et al.* 2014).Dexmedetomidine, the latest α-2 agonist, is an active optical isomer of racematemedetomidinewhich can be used as a sedative and preanaesthetic drugs in dogs. Dexmedetomidine have potent analgesic and sedative effects over medetomidine. In dogs, dexmedetomidine produces dose dependent sedation and analgesia and the intensity of these effects is similar to that produced by twice the dose of medetomidine (Kuusela*et al*., 2000). Synthetic opioids like butorphanol tartrate have both agonist and antagonist properties. Panting and respiratory depression has been reported with butorphanol (Dyson, 1990). However Ithas also reported to cause decrease in heart rate, arterial blood pressure and intestinal motility (Schnellbacher, 2010).

The purpose of the study is to compare the physiological and haemodynamic effects of dexmedetomidine, xylaxine and butorphanol when given in combination of tiletamine-zolazepam in dogs.

MATERIALS AND METHODS:

The Study was conducted in 18 dogs presented for planned surgical interventions and are irrespective of sex and breed. Preanaesthetic drugs such as atropine sulphate @0.04 mg/kg bwt. I/M was given in all the groups and after 5 minutes later dexmedetomidine @0.02 mg/kg bwt. I/V in group I, xylaxine @1 mg/kg bwt I/M in group II and butorphanol @0.2 mg/kg bwt I/M in group III was administered. Induction of anaesthesia was done after 10 minutes of preanaesthetic administration with tiletamine-zolazepam @ 6.5 mg/kg bwt. I/V. maintenance was done with incremental dose of tiletamine-zolazepam as and when required. Parameters like heart rate, respiration rate, rectal temperature, Spo2, MAP were recorded before preanaesthetic administration and at 0, 5, 15, 30, 45, 60, 75 and 90 minutes interval. Means at different time intervals between groups and within group was compared using one way analysis of variance (ANOVA) and Duncan's multiple range tests (DMRT) as per the method described by (Snedecor and Cochran, 1994)

RESULT:

TABLE 1: : MEAN ± SE OF HEART RATE (BEATS/MINUTE) AT DIFFERENT TIME INTERVALS IN THREE ANAESTHETIC GROUPS

		Time intervals (minute)								
	Groups	Before	0	5	15	30	45	60	75	90
Heart rate	Group I	119.16^{d}± 0.70	112.00^{e} ±0.73	105.00^{f}±0.51	138.16^{ab}±1.40	135.66^{b}±1.22	132.16^{c}±1.13	140.00^{a} ±1.03	136.16^{b} ±1.60	130.66^{c}±1.68

	Group II	118.50^{f}±1.54	115.50^{fg}±1.64	112.16^{g}±1.79	147.66^{cd}±1.11	150.50^{bc}±1.38	157.16^{a}±0.83	151.83^{b}±0.74	145.00^{d}±0.85	137.50^{e}±1.68
	Group III	115.00^{f}±0.89	113.00^{fg}±0.93	111.00^{g}±0.51	150.33^{cd}±1.35	154.00^{b}±1.03	158.66^{a}±1.25	152.33^{bc}±1.22	147.66^{d}±0.81	141.66^{e}±1.17

- Means within group with different lower-case superscripts (a, b, c) differ significantly (p≤0.05) between time intervals from 0 minute (baseline).

- Means between groups with different upper-case superscripts (A, B,C) differ significantly (p≤0.05) from 0 minute (baseline).

TABLE 2: MEAN ± SE OF RESPIRATION RATE (BREATHS/MINUTE) AT DIFFERENT TIME INTERVALS IN THREE ANAESTHETIC GROUPS

		Time intervals (minute)								
	Groups	Before	0	5	15	30	45	60	75	90
Respiration rate	Group I	32.66^{a}±1.02	25.16^{b}±0.60	18.16^{c}±0.47	16.50^{cd}±1.08	14.83^{d}±1.04	14.16^{d}±0.70	14.66^{d}±0.80	15.66^{cd}±0.91	18.16^{c}±0.79
	Group II	36.33^{a}±0.55	34.00^{b}±0.68	32.16^{c}±0.47	27.00^{d}±0.73	25.50^{de}±0.71	24.33^{ef}±0.55	23.16^{f}±0.60	25.00^{d}±0.73	25.83^{de}±0.30
	Group III	31.16^{a}±2.13	29.00^{ab}±2.12	27.50^{abc}±2.27	26.83^{abc}±2.00	24.16^{bc}±1.60	23.00^{c}±1.36	23.66^{bc}±0.76	24.16^{bc}±0.98	26.50^{abc}±0.99

- Means within group with different lower-case superscripts (a, b, c) differ significantly (p≤0.05) between time intervals from 0 minute (baseline).

- Means between groups with different upper-case superscripts (A, B,C) differ significantly (p≤0.05) from 0 minute (baseline).

TABLE 3: Mean ± SE of Rectal Temperature (Breaths/Minute) at Different Time Intervals in Three Anaesthetic Groups

		Time Intervals (Minutes)								
	Groups	Before	0	5	15	30	45	60	75	90

Rectal temperature	Group I	101.98^{a}±0.12	101.76^{a} ±0.16	101.48^{ab}±0.23	101.20^{bc}±0.21	100.86^{cd}±0.23	100.60^{de}±0.13	100.20^{e} ±0.14	99.66^{f}± 0.10	99.25^{f} ±0.18
	Group II	101.71^{a}±0.16	101.60^{ab}±0.31	101.18^{abc}±0.33	101.00^{abc}±0.34	100.63^{bcd}±0.28	100.43^{cde}±0.30	100.18^{cde}±0.34	99.73^{de} ±0.40	99.55^{e} ±0.37
	Group III	102.05^{a}±0.18	101.96^{a} ±0.13	101.65^{ab}±0.06	101.41^{bc}±0.22	100.95^{c}±0.17	100.13^{d}±0.11	99.86^{de}± 0.09	99.56^{ef} ±0.22	99.35^{f} ±0.22

- Means within group with different lower-case superscripts (a, b, c) differ significantly (p≤0.05) between time intervals from 0 minute (baseline).

- Means between groups with different upper-case superscripts (A, B,C) differ significantly (p≤0.05) from 0 minute (baseline).

TABLE 4: Mean ± SE of Hemoglobin Oxygen Saturation Percentages (SpO2%) at Different Time Intervals in Three Anaesthetic Groups.

		Time Intervals (Minutes)								
	Groups	Before	0	5	15	30	45	60	75	90
SpO2 %	Group I	97.50^{a}±0.22	93.50^{cd} ±0.42	88.66^{f} ±0.71	87.16^{g} ±0.70	91.33^{e} ±0.21	92.83^{d} ±0.30	93.50^{cd}± 0.22	94.33^{bc} ±0.42	95.00^{b} ±0.25
	Group II	97.83^{a}±0.16	97.83^{a}± 0.16	97.00^{b} ±0.16	96.16^{c} ±0.25	97.33^{ab}±0.30	97.50^{ab} ±0.21	97.50^{ab}± 0.34	97.66^{ab} ±0.22	97.83^{a} ±0.33
	Group III	97.66^{a}±0.21	97.66^{a}± 0.21	97.33^{a} ±0.21	97.50^{a} ±0.22	97.50^{a} ±0.22	97.33^{a} ±0.21	97.50^{a}± 0.22	97.50^{a}± 0.22	97.66^{a} ±0.21

- Means within group with different lower-case superscripts (a, b, c) differ significantly (p≤0.05) between time intervals from 0 minute (baseline).

- Means between groups with different upper-case superscripts (A, B,C) differ significantly (p≤0.05) from 0 minute (baseline).

Table 5: Mean ± SE of Mean Arterial Pressure (MAP) at Different Time Intervals in Three Anaesthetic Groups

		Time intervals (minutes)								
	Groups	Before	0	5	15	30	45	60	75	90
Mean arterial pressure (MAP)	Group I	101.66^{f}± 3.04	110.00^{e} ±1.65	146.00^{b}±1.03	152.33^{a}±1.17	156.83^{a}±1.72	146.33^{b}±1.58	133.16^{c} ±3.08	124.00^{d} ±2.25	115.16^{e}±2.32
	Group II	104.16^{e}± 3.27	109.00^{e} ±2.39	132.16^{bc}±1.60	136.83^{ab}±1.72	140.50^{a}±2.06	132.83^{bc}±2.60	126.50^{c} ±1.99	120.16^{d} ±1.62	117.83^{d}±0.83
	Group III	113.16^{a}± 3.54	111.00^{a} ±3.39	106.00^{abc}±3.65	100.83^{c}±3.10	97.16^{c} ±2.89	101.66^{bc}±2.49	106.16^{abc}±2.21	110.16^{a}^{b}±2.13	112.83^{a}±2.12

- Means within group with different lower-case superscripts (a, b, c) differ significantly (p≤0.05) between time intervals from 0 minute (baseline).
- Means between groups with different upper-case superscripts (A, B,C) differ significantly (p≤0.05) from 0 minute (baseline).

RESULT:

Heart rate was significantly decreased at 5 minute time interval when compared with 0 minute(baseline) in group I following administration of dexmedetomidine thereafter increased significantly following administration of tiletamine-zolazepam at 15 minute and 60 minutes time interval compared to baseline value. In group II and group III heart rate increased significantly after after the induction with tiletamine-zolazeoam at 15,30 and 45 minutes time interval.

Respiration rate in group I and group II decreased significantly from 5 minutes to 60 minutes time interval when compared with 0 minute baseline value. However in group III significant decrease in the respiration was observed at 45 and 60 minute time interval when compared with 0 minute basline value.

Rectal temperature in group I decreased significantly from 15 minutes to 90 minutes time interval. However in group II rectal temperature decreased from 30 minutes to 90 minutes time interval. Moreover in group III rectal temperature decreased from 15 minutes to the end of the observation period i.e. 90 minutes.

Haemoglobin oxygen saturation percentage (SpO2 %) decreased significantly in group I at 15 minutes time interval and reached to 87% when compared to to 0 minute(baseline value) thereafter it gradually start increasing at the end of the observation period and stabilized at 95% at

90 minutes. However in group II Spo2 decreased significantly at 5 and 15 minutes time interval in comparison to 0 minute(baseline value) and thereafter it remains 97% till the end of the observation period. In group III Spo2 stabilized at 97% during all the intervals in the observation period.

Mean arterial pressure (MAP) in group I and IIincreased significantly at 5, 15 and 30 minutes in comparison to 0 minute (baseline value) thereafter it gradually start decreasing till the end of the observation period (90 minutes). In group III MAP decreased significantly at 15 and 30 minutes time interval in comparison to 0 minute (baseline value).

Discussion :

In group I significant Decrease in heart rate after administration of dexmedetomidine are in accordance with the findings of Congdon *et al.* (2011), Ahmed *et al*. (2013) and Micieli*et al.* (2017) who reported significant decrease in heart rate after administration of dexmedetomidine in dogs. However increase in heart rate observed after administration of tiletamine-zolazepam at later stage in group I, II and III are in agreement with the findings of Cullen and Reynoldson(1997), Hampton *et al.* (2019) and Pereira *et al*. (2019). Decrease in heart rate after dexmedetomidine administration in group I might be attributed to vagal activation by alpha 2 adrenoceptors (Bisht*et al*., 2018).

Decrease in heart rate in present study could be explained by the hypothesis of Sinclair (2003), who hypothesized that Alpha-2-agonists such as dexmedetomidine in group I and xylazine in group II reduces norepinephrine outflow within the CNS, which results into dampening of central sympathetic tone and beneficially producing sedation. This reduced sympathetic tone might be responsible for reduction in heart rate.However significant increase in the heart rate was observed due to the sympathomimetic action of tiletamine, which increases heart rate, a characteristic common to dissociative agents well documented in the literature (Almeida *et al*., 2000) and (Pireira*et al*., 2019).

However in group III initial non-significant decrease in heart rate are in agreement with Cornick and Hartsfield (1992) and Ralh and Mohindroo (2010). Similar finding was too observed by Ko*et al.* (2007), who reported increase in heart rate after tiletamine-zolazepam-butorphanol administration in dogs. The decrease in heart rate could be attributed to increased vagal tone, decrease in diastolic pressure and decrease in peripheral vascular tone caused by butorphanol administration (Cornick and Hartsfield, 1992).

Respiration rate decreases in group I in above findings are in agreement with Congdon *et al*. (2011) and Congdon *et al.* (2013) who reported a significant decrease in respiration rate after administration of dexmedetomidine in dogs however Ko*et al.* (2007) and Pereira *et al*. (2019) who observed significant decrease in respiration rate after administration of tiletamine-zolazepam in dogs. Decrease in respiration in above finding could be explained by the hypothesis of Sinclair (2003) who hypothesized that respiratory depression occurs secondary to the CNS depression produced by α2-adrenoreceptor stimulation and Sindak*et al.* (2010) who opined that respiratory

depressant effect of alpha-2 adrenergic agonists is likely to be exaggerated when used in combination with other anaesthetic and analgesic agents.

In group II decrease in respiration in above finding are in harmony with Kumar *et al.* (1979), Peshin*et al*. (1980), Kandpal*et al.* (2005) and Saikia*et al*. (2019) who reported decrease in respiration rate after administration of xylazine and Kwon *et al.* (2003), Pireira*et al.* (2019) and Anjana*et al.* (2021) who observed significant decrease in respiration rate following administration of tiletamine-zolazepam combination in dogs. Decrease in respiration rate after premedication with xylazine could be explained by the postulate of Kumar *et al.* (1979) and Sinclair (2003) who postulated that decrease in respiration rate could be due to depressive effect of xylazine on CNS and Sindak*et al.* (2010) who opined that respiratory depressant effect of alpha-2 adrenergic agonists is likely to be exaggerated when used in combination with other anaesthetic and analgesic agents.

However, in group III Initial non-significant decrease in the respiration rate are in agreement with the findings of Pachter, (1985) and Dyson (1990) who reported decrease in respiration rate after butorphanol administration in dog. Similarly, Ko*et al.* (2007), Pireira*et al.* (2019) and Anjana*et al.* (2021) observed respiratory rate depression after administration of tiletaminezolazepam combination in dogs. Decrease in respiration could be explained by the opinion of Demirkan*et al.* (2002) who opined that butorphanol, like other opioids, is a dose-related respiratory depressant.

The gradual initially non-significant thereafter significant decrease in the rectal temperature in above findings observed in group I, II and III are in the agreement with those of Hampton *et al.* (2019), Pereira *et al.* (2019), Anjana*et al*. (2021) who noticed significant drop in rectal temperature following administration of tiletamine-zolazepam in dogs. However, Koli*et al*. (2021a) observed non-significant decrease in the rectal temperature after administration of tiletamine-zolazepam in dogs. In group I partial agreement to this, Singh and Kumar (2020) observed gradual non-significant decrease in rectal temperature after administration of dexmedetomidine along with ketamine in dogs. Decrease in the rectal temperature in group I and II could be attributed to generalized sedation, decreased metabolic rate and CNS depression and loss of thermoregulatory control following administration of alpha-2 adrenoceptor agonists as stated by Lu *et al*. (2014). Tiletamine–zolazepam promotes depressant effect on temperature of dog as has been documented by Vaedo (2001). However Koli*et al.* (2021a)postulated that reduction in rectal temperature in dogs after administration of tiletamine-zolazepam as observed in all three groups in present study might be due to generalized sedation, a reduction in metabolic rate and muscle relaxation.

In group I decrease in SpO2 in above findings are in agreement with Kriminsˢ*et al.* (2012b), Jena *et al.* (2014), Sethi*et al.* (2017) and Singh and kumar (2020) who reported significant decrease in SpO2 after premedication with dexmedetomidine in dogs. Decrease in SpO2% after premedication with dexmeditomodine in present study might be explained by the findings of Kriminsˢ*et al.* (2012b) and Sethi*et al.* (2017) who observed decrease in SpO2% after administration of dexmeditomidine and attributed it to respiratory depression, hypoventilation indicated by decreased arterial oxygenation and tissue perfusion.

In group II SpO2% are relatively high and remained near 97 to 98%. In present study Initial decrease in SpO2 are in agreement with Jena *et al.* (2014) who reported significant decrease in the SpO2 value after 5 minutes of administration of xylazine and hypothesized that it might be due to vasoconstriction caused by xylazine. In partial agreement to above findings, Anjana*et al*. (2021), Koli*et al*. (2021a) and Koli*et al.* (2021b) observed non-significant changes in SpO2% after administration of xylazine along with tiletamine-zolazepam combination in dogs. Decrease in respiratory rate in present study might be explained by the opinion of Thomas and Lerche (2011) and Sethi*et al.* (2017) who documented that xylazine has respiratory depressant property which could be augmented by tiletamine-zolazepam combination, since respiratory depressant property of tiletamine could be significant if used with other sedatives or anesthetics.

In group III SpO2% remained quite high and close to 97% throughout the observation period. Above findings are in agreement with the Anjana*et al*. (2021), Koli*et al*. (2021a) and Koli*et al.* (2021b) who observed high value SpO2% when tiletamine-zolazepam was administered in dogs.Thomas and Lerche (2011) documented that low dose of opioid does not cause respiratory depression.

Initial increase in MAP in group I in above finding are in agreement with Congdon *et al.* (2011), Kriminsel *et al.* (2012a) and Ahmad *et al.* (2013) who observed significant increase in MAP after administration of dexmedetomidine. Similarly increased MAP was observed in the finding of Cullen and Reynoldson (1997), Kwon *et al.* (2003) after administration of tiletamine-zolazepam combination in dogs. Lemke (2007) hypothesized that high dose of dexmedetomidine may produce hypertension due to vasoconstriction resulting from stimulation of alpha-2B adrenoceptors in the smooth muscle of blood vessels which might be responsible for increase in MAP.

In group II an initial increase in MAP are in agreement with Klide*et al*. (1975), Hsu *et al.* (1985) and Narayanan *et al.* (2011) who reported initial increase in mean arterial pressure followed by a decrease in mean arterial pressure after administration of xylazinein dogs. Similarly Cistola*et al.* (2004) observed that MAP increased significantly in the initial stage of surgical procedure following administration of xylazine-tiletamine-zolazepam combination in cats. Increases in arterial blood pressure are typically dose related, higher doses probably cause a more pronounced stimulation of peripheral adrenoreceptors and vasoconstriction (Sinclair, 2003).

However, an initial decrease in MAP in present study are in agreement with Trim (1983) and Greene *et al.* (1990). Similarly Ko*et al.* (2007) observed an initial decrease in MAP followed by an increase after butorphanol-tiletamine-zolazepam administration in dogs. Similarly Howard *et al.* (1990) observed decrease in mean arterial pressure after administration of butorphanol along with combination of tiletamine-zolazepam in dogs. However, Nisa*et al.* (2018) too observed significant decrease in MAP after butorphanol administration in dogs.

Conclusion:

All the clinicophysiological and haemodynamic parameter showed transient shift which was compensated shortly after the duration of anaesthetic procedure. However these alteration does not

have any deleterious consequences on vital organs of animal. As a result of present study suggest that dexmedetomine, xylaxine and butorphenol can be safely used as preanaesthetic drugs in combination with tiletamine-zolazepamas induction and maintenance for the surgical procedure in healthy dogs.

References :

- Ahmad, R.A., Amarpal, D., Kinjavdekar, P., Aithal, H.P., Pawde, A.M. and Kumar, D.(2013).Potentialuseofdexmedetomidinefordifferentlevelsofsedation,analgesiaand anaesthesiain dogs.*VeterinarniMedicina*, **58**(2):87-95.
- Almeida,E.M.P.D.,Nunes,N.,Fantinatti,A.P.,Santos,P.S.P.D.,Bolzan,A.A.and Rezende, M.L.D. (2000). Cardiorespiratory effects of tiletamine/zolazepamassociationindogs(*Canisfamiliaris*)pre-treatedornotbyacepromazine.*Brazilian Journal ofVeterinary ResearchandAnimalScience*,**37**: 210-215.
- Anjana,R.R.,Parikh,P.V.andKelawala,D.N.(2021).Effectsoftiletamine-zolazepamandisofluraneforinductionandmaintenanceinxylazine premedicateddogs. *IndianJournalofVeterinarySciences and Biotechnology*, **17**(4):86-88.
- Berry, S.H. (2015). Dissociative anaesthetics, In: veterinary anaesthesia and analgesia. 5thedn. John Wiley & Sons, Inc., Hoboken, USA, pp 283-287.
- Bisht, D.S., Jadon, N.S., Bodh, D. and Kandpal, M. (2018). Clinicophysiologicaland haematobiochemical evaluation of dexmedetomidine-ketamine-sevofluraneanaesthesiain dogs.*IndianJournalofVeterinarySurgery*,39(2):121-125.
- Cistola, A.M., Golder, F.J., Centonze, L.A., McKay, L.W. and Levy, J.K. (2004).Anestheticandphysiologiceffectsoftiletamine,zolazepam,ketamineandxylazine combination (TKX) in feral cats undergoing surgical sterilization. *JournalofFelineMedicineandSurgery*,**6**(5):297-303.
- Clarke KW, Trim CM, Hall LW (2014) Veterinary Anaesthesia. 11th edn. Saunders, Elsevier. 436.
- Congdon, J.M., Marquez, M., Niyom, S. and Boscan, P. (2011). Evaluation of thesedativeandcardiovascularеffectsofintramuscularadministrationofdexmedetomidinewithandwithoutconcurrentatropineadministrationindogs.*JournaloftheAmericanVeterinaryMedicalAssociation*, 239(1): 81-89.
- Congdon, J.M., Marquez, M., Niyom, S. and Boscan, P. (2013). Cardiovascular,respiratory,electrolyteandacid–basebalanceduringcontinuousdexmedetomidineinfusioninanesthetizeddogs. *VeterinaryAnaesthesiaandAnalgesia*, **40**(5):464-471.
- Cornick,J.L.andHartsfield,S.M.(1992).Cardiopulmonaryandbehavioraleffectsofcombinationsofacepromazine/butorphanolandacepromazine/oxymorphone in dogs. *Journal of the American Veterinary Medical Association*,**200**(12):1952-1956.

- Cullen,L.K.andReynoldson,J.A.(1997).Effectsoftiletamine/zolazepampremedication on propofolanaesthesia in dogs. *Veterinary Record*, 140(14): 363-366.
- Demirkan,I.,Atalan,G.,Gokce,H.I.,Ozaydin,I.andCelebi,F.(2002).Comparativestudyofbut orphanol-ketaminHClandxylazine-ketaminHClcombinations for their clinical and cardiovascular/respiratory effects in healthydogs.*TurkishJournalofVeterinaryandAnimalSciences*,**26**(5):1073-1079.
- Dyson, D. H. (1990). Update on butorphanol tartrate: use in small animals. *The Canadian Veterinary Journal*, *31*(2), 120.
- Greene, S.A., Hartsfield, S.M. and Tyner, C.L. (1990). Cardiovascular effects ofbutorphanol inhalothane-anesthetizeddogs. *AmericanJournalofVeterinaryResearch*, **51**(8):1276-1279.
- Hampton, C.E., Riebold, T.W., Le Blanc, N.L., Scollan, K.F., Mandsager, R.E. and Sisson, D.D. (2019).Effectsofintravenousadministrationoftiletamine-zolazepam,alfaxalone,ketamine-diazepam,andpropofolforinductionofanesthesia on cardiorespiratory and metabolic variables in healthy dogs beforeand during anesthesia maintained with isoflurane. *American Journal of Veterinary Research*, **80**(1):33-44.
- Howard, B.W., Lagutchik, M.S., Januszkiewicz, A.J. and Martin, D.G. (1990). Thecardiovascularresponseofsheeptotiletamine-zolazepamandbutorphanoltartrateanesthesia.*VeterinarySurgery*,**19**(6):461-467.
- Hsu, W.H., Lu, Z.X. andHembrough,F.B. (1985). Effect ofxylazineon heartrate and arterial blood pressure in conscious dogs, as influenced by atropine, 4-aminopyridine, doxapram and yohimbine. *Journal of the American VeterinaryMedicalAssociation*,**186**(2):153-156.
- James, S.B., Cook, R.A., Raphael, B.L., Stetter MD, Kalk P., MacLaughlin K., and Calle P.P. (1999). Immobilization of babirusa (Babyrousababyrussa) with xylazine and tiletamine/zolazepam and reversal with yohimbine and flumazenil. J Zoo Wildl Med. 30(4): 521-525.
- Jena, B., Das, J., Nath, I., Sardar, K.K., Sahoo, A., Beura, S.S. and Painuli, A.(2014).Clinicalevaluationoftotalintravenousanaesthesia usingxylazineordexmedetomidinewith propofolin surgical management of caninepatients.*VeterinaryWorld*,**7**(9):671-680.
- Kandpal, M., Jadon, N.S., Kumar, A. andKumar, S. (2005). Studies on reversalof clinico-physiological effects of xylazine with yohimbine in dogs. *Indian JournalofVeterinarySurgery*,**26**(1):39-40.
- Klide, A.M., Calderwood, H.W. and Soma, L.R. (1975). Cardiopulmonary effectsofxylazineindogs.*AmericanJournalofVeterinaryResearch*,**36**(7):931-935.
- Ko, J.C.H., Payton, M., Weil, A.B., Kitao, T. and Haydon, T. (2007). Comparisonof anesthetic and cardiorespiratory effects of tiletamine–zolazepam–butorphanolandtiletamine–zolazepam–butorphanol–medetomidineindog.*Veterinary Therapeutics*, **8**(2):113-126.
- Koli, P.H., Parikh, P.V., Mahla, J.K. and Barot, H.M. (2021a). Clinical attributesoftiletamine-zolazepaminducedanesthesiawithandwithoutxylazinepremedicationindogs. *TheIndianJournalofVeterinarySciencesandBiotechnology*, **17**(4):61-65.

- Koli,P.H., Parikh, P.V.andMahla,J.K.(2021b).Clinical studiesongeneralanaesthesia using tiletamine-zolazepamcombinationasanaesthetic induction fordiagnosticMRIindogs.*InternationalJournalofCurrentMedicalandPharmaceuticalResearch,***7**(9):5986-5991.
- Krimins, R. A., Ko, J. C., Weil, A. B., Payton, M. E., & Constable, P. D. (2012a). Hemodynamic effects in dogs after intramuscular administration of a combination of dexmedetomidine-butorphanol-tiletamine-zolazepam or dexmedetomidine-butorphanol-ketamine. *American journal of veterinary research*, *73*(9), 1363-1370.
- Krimins,R.A.,Ko,J.C.,Weil,A.B.andPayton,M.E.(2012b).Evaluationofanesthetic, analgesic, and cardiorespiratory effects in dogs after intramuscularadministrationofdexmedetomidine–butorphanol–tiletamine-zolazepamordexmedetomidine-tramadol-ketaminedrugcombinations. *AmericanJournalofVeterinaryResearch*,**73**(11):1707-1714.
- Kumar,A.,Pandiya,S.C.andSingh,H.(1979).Canineanaesthesiawithacombination of Ketamine and Xylazine in experimental and clinical cases. *IndianJournalof Animal Health*,**18**(1):39-43.
- Kuusela, Raekallio, Anttila, Falck, Mölsä, &Vainio. (2000). Clinical effects and pharmacokinetics of medetomidine and its enantiomers in dogs. *Journal of veterinary pharmacology and therapeutics*, *23*(1), 15-20.
- Kwon,Y.S.,Jeong,J.H.andJang,K.H.(2003).Comparisonoftiletamine/zolanzepam,xylazine-tiletamine/zolazepamandmedetomidine-tiletamine/zolazepam anesthesia in dogs. *Journal of Veterinary Clinics*, **20**(1): 33-41.
- Lagutchik, M. S., Januszkiewicz, A. J., Dodd, K. T. and Martin, D. G. (1991). Cardiopulmonary effects of a tiletamine-zolazepam combination in sheep. *American journal of veterinary research*, *52*(9), 1441-1447.
- Lemke, K.A. (2007). Anticholinergics and sedatives. *In*: Tranquilli, W.J., ThurmonJ.C,Grimm,K.A(eds.).LumbandJonesveterinaryanesthesiaandanalgesia, 4th Edn.,BlackwellPublishing,Oxford, England,pp203-240.
- Lu, D.Z., Jiang, S., Yu, S.M. and Fan, H.G. (2014). A comparison of anestheticandcardiorespiratoryeffectsoftiletamine-zolazepam/xylazineandtiletamine-zolazepam/xylazine/tramadolindogs.*PakistanVeterinaryJournal*,**34**(1):63-67.
- Micieli, F., Santangelo, B., Reynaud, F., Mirra, A., Napoleone, G., Della Valle, G.andVesce,G.(2017).Sedativeandcardiovascularеffectsofintranasalorintramusculardexmedetomidineinhealthydogs. *VeterinaryAnaesthesiaandAnalgesia*, 44(4):703-709.
- Narayanan, M.K., Rajankutty, K., Amma, T.S., Syam, K.V. and Devanand, C.B.(2011). Midazolam with glycopyrrolatexylazine combination for premedication inketamine anaesthesia in dogs. *Journal of Veterinary and Animal Sci*ence, **42**: 48-52.
- Nisa,K.,Lim,S.Y.,Osuga,T.,Yokoyama,N.,Tamura,M.,Nagata,N.andTakiguchi, M. (2018). The effect of sedation with a combination of butorphanoland midazolam on quantitative

contrast-enhanced ultrasonography of duodenuminhealthydogs.*Journal ofVeterinaryMedical Science*, **80**(3):453-459.

- Pachter,I.J.andEvens,R.P.(1985).Butorphanol. *DrugandAlcoholDependence*, **14**(3-4):325-338.
- Pereira, S.A., Henrique, F.V., Medeiros, L.K., Silva, J.K., Goes, A.B., Vaz, A.F.and Nobrega, P.I. (2019). Anesthetic quality and cardiovascular and respiratoryeffectsofcontinuousintravenousinfusionof tiletamine-zolazepaminbitches.*Brazilian VeterinaryResearch*,39(3):214-220.
- Peshin,P.K.,Kumar,A.andSingh,H.(1980).Cardiovascular,respiratory,haematologicalands edativeeffectsofxylazineindogs. *IndianJournalofVeterinarySurg*ery,**1**:12-17.
- Ralh,P.andMohindroo,J.(2010).Evaluationofbutorphanol-acepromazine-glycopyrrolate and butorphanol-midazolam-glycopyrrolate as preanaesthetic tothiopentoneanaesthesiaindogs. *Indian Journal of Veterinary Surgery*, **31**(2):123-126.
- Saikia, B., Das, H., Bayan, H., Paul, R., Debbarma, A. and Sarma, N. (2019).Effects of propofol, ketamine and their combination (ketofol) as total intravenousanaesthesia(TIVA)oncardiopulmonaryparametersinatropineandxylazinepremedicated dogs.*InternationalJournalofChemicalStudies*,**7**(1):2193-2195.
- Schnellbacher, R. (2010). Butorphanol. *Journal of Exotic Pet Medicine*, *2*(19), 192-195.
- Sethi,S.,Singh,J.,Nath,I.,Das,R.K.,Nayak,S.andSahu,R.K.(2017).Haemato-biochemical comparision of xylazine/dexmedetomidine in combinationwithbutorphanol/pentazocineaspreanestheticketamineanaesthesiaincaninepyometra patients.*ThePharmaInnovation*,**6**(9): 393-399.
- Sinclair, M.D. (2003). A review of the physiological effects of α2-agonists relatedtotheclinicaluseofmedetomidineinsmallanimalpractice. *TheCanadianVeterinaryJournal*,**44**(11):885-897.
- Sindak, N., Camkerten, I. and Ceylan, C. (2010). Clinical evaluation of ketamine-xylazineanesthesiainbozovagreyhounds. *Journal of Animal and VeterinaryAdvances*, **9**(15): 2025-2029.
- Singh, R. and Kumar, P. (2020). Cardiopulmonary effects of dexmedetomidine,midazolamandbutorphanolaspreanaestheticstoketaminehydrochlorideanaesthesiain dogs.*JournalofChemicalResearchAdvances*,**1**(1):10-17.
- Singh, R. and Kumar, P. (2020). Cardiopulmonary effects of dexmedetomidine,midazolamandbutorphanolaspreanaestheticstoketaminehydrochlorideanaesthesiain dogs.*JournalofChemicalResearchAdvances*,**1**(1):10-17.
- Snedecor,G.W.andCocharan,W.G.(1994).Statisticalmethods,6thEdn.,OxfordandIBHpublishingCo.,New Delhi,pp350.
- Thomas, J.A. and Lerche, P. (2011). Anesthesia and Analgesia, 4thEdn., MosbyElsevier,Missouri,USA,pp81-82.
- Trim,C.M.(1983). Cardiopulmonary effects of butorphanol tartrate indogs.*AmericanJournal ofVeterinaryResearch*,**44**(2):329-331.

- Vaedo, J.C. (2001). Tiletamine-Zolazepam association in dissociative anesthesiaofdogs,originalprotocolofuse.*BrazilianJournalofAnimalHealthandProduction*, **1**(1):19-26.
- Vedpathak, H. S., Tank, P. H., Karle, A. S., Mahida, H. K., Joshi, D. O. and Dhami, M. A. (2009). Pain Management in Veterinary Patients. *Veterinary World*, *2*(9).