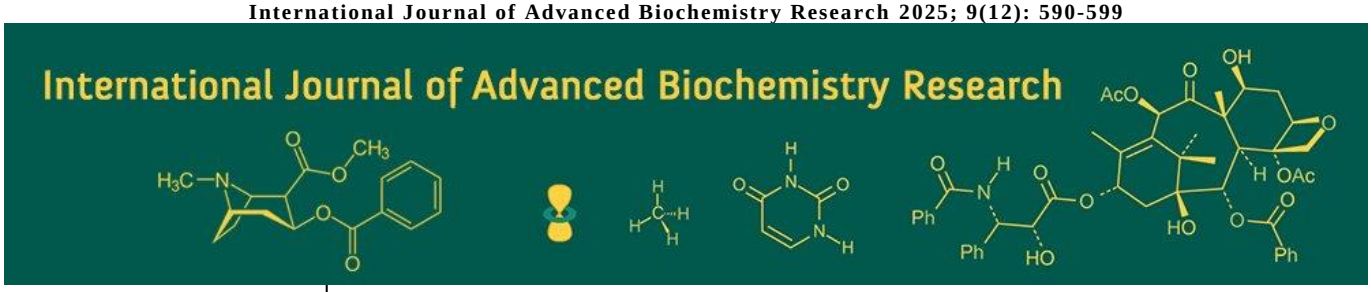

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Clinico-physiological assessment of dexmedetomidine and butorphanol as preanaesthetics to tiletamine-zolazepam anaesthesia in buffalo calves (*Bubalus bubalis*)

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Abstract
The present study was undertaken to evaluate and compare the clinico-physiological effects of dexmedetomidine and butorphanol as preanaesthetic agents prior to intravenous tiletamine-zolazepam anaesthesia in buffalo calves. Eighteen healthy non-descript buffalo calves of either sex, weighing 80-100 kg, were randomly divided into three groups (A, B, and C) of six animals each. All animals were dewormed with fenbendazole @ 5 mg/kg body weight orally prior to experimental procedures and were subjected to fasting for 24 hours and water withholding for 12 hours. Glycopyrrolate @ 0.01 mg/kg body weight I/M was administered 10 minutes before treatments in all groups. Animals in Groups B and C received dexmedetomidine @ 5 µg/kg body weight I/V and butorphanol @ 0.075 mg/kg body weight I/V, respectively, followed 10 minutes later by tiletamine-zolazepam @ 2.5 mg/kg body weight I/V in all groups. Clinical and physiological parameters were evaluated at predetermined intervals. Dexmedetomidine premedication produced superior sedation, profound muscle relaxation, and smoother anaesthetic quality compared to butorphanol. Both agents altered physiological parameters, but changes remained within clinically acceptable limits. The study concluded that dexmedetomidine is a more effective preanaesthetic to tiletamine-zolazepam for buffalo calves.

Keywords: Buffalo calves, tiletamine-zolazepam, dexmedetomidine, butorphanol, anaesthesia and clinico-physiological evaluation

Introduction
Water buffalo (*Bubalus bubalis*) is a valuable species with excellent zootechnical characteristics for both milk and meat production (Guerri *et al.*, 2021) [14]. Anaesthesia is achieved through agents that reduce neural activity at local, regional, or central levels. In surgical practice, balanced anaesthesia is crucial, as it provides the required combination of hypnosis, analgesia, and adequate muscle relaxation. General anaesthesia is regarded mandatory for any surgical intervention as it provides complete unconsciousness, better insensitivity to pain, good muscle relaxation, and freedom from reflex responses and loss of motor ability (Thurmon *et al.*, 1996) [38]. Though most surgical procedures in ruminants are carried out under local or regional analgesia, general anaesthesia may be preferred in certain complicated procedures like diaphragmatic herniorrhaphy, thoraco-pericardiotomy, repair of ruptured suspensory ligaments, orthopaedic surgery, keratoplasty and repair of ventral hernia etc. (Riazuddin *et al.*, 2004) [28]. Preanesthetic medication makes the patient easier to handle, decreases secretions and minimizes the total dose of anaesthetics to produce the desired level of anaesthesia (Arya *et al.*, 2021) [3]. Induction of anaesthesia of intractable animals safer, greatly reduces the incidence and the intensity of any adverse effects, provides pre-emptive analgesia, and smooth recovery (Kaufman *et al.*, 2005) [17]. Tiletamine-zolazepam is commonly employed for anaesthetic induction because it produces a fast onset of action along with effective muscle relaxation. Dexmedetomidine, a potent α2-adrenergic agonist, induces sedation, analgesia and muscle relaxation with minimal respiratory depression (Ragab *et al.*, 2022) [27]. Butorphanol, a mixed κ-agonist and µ-antagonist opioid, provides effective analgesia and mild sedation (Maidanskaia *et al.*, 2023) [25].

Comparative evaluation of these agents in buffalo calves as preanaesthetics to tiletamine-zolazepam is limited. Thus, the present study was designed to evaluate and compare the clinico-physiological effects produced by dexmedetomidine or butorphanol when used in combination with tiletamine-zolazepam anaesthesia.

Materials & Methods

Selection of Animals and Experimental Design

The study was carried out in the Department of Veterinary Surgery and Radiology, College of Veterinary Science and Animal Husbandry, Anjora, Durg (C.G.). Eighteen healthy, non-descript male buffalo calves weighing 80-100 kg and aged 8 months to 1 year were randomly assigned to three groups (A, B, and C), each comprising six animals. Prior to the experiment, all calves were dewormed orally with fenbendazole (Panacur®150 VET) @ 5 mg/kg body weight. Feed was withheld for 24 hours and water for 12 hours before anaesthetic administration. Standard management and feeding practices were maintained throughout the study. A pilot trial was undertaken to determine the minimum effective drug doses for the experiment. Glycopyrrolate (Pyrolate®) @ 0.01 mg/kg intramuscularly was administered to all animals 10 min before the trial.

In Group A, anaesthesia was induced with tiletamine-zolazepam (Zoletil® 50) at 2.5 mg/kg body weight via slow intravenous injection. Group B animals received dexmedetomidine (Dextomid*) @ 2 µg/kg intravenously, followed 10 min later by tiletamine-zolazepam at the same dose. In Group C, butorphanol (Butodol®-1) @ 0.075 mg/kg body weight was administered intravenously before implementing the designated anaesthetic protocol. Ethical approval for the experimental procedures was obtained from the Institutional Animal Ethics Committee (CPCSEA).

Parameters Studied

Clinical Parameters

The assessment of anaesthesia was done on the basis of the following clinical parameters were recorded on before sedation (0), 5 mins. after sedation, on induction and 5, 15, 30, 45, 60 and 120 min interval after anaesthesia. The following clinical parameters were assessed *viz*. onset of sedation, induction of anaesthesia, record of various reflexes and behavioural responses like sedation, analgesia, jaw relaxation, palpebral reflex, pedal reflex, salivation, muscle relaxation of limb, muscle relaxation of abdomen, relaxation of anal sphincter, ataxia, regurgitation, position of eye ball, duration of anaesthesia, quality of anaesthesia, return to head rightening reflex, sternal recumbency time, standing time and complete recovery time. All the aforementioned clinical parameters, along with their corresponding numeric scoring system, are presented in Table 1, as adopted and modified by Singh *et al.*, (2013) and Guerri *et al.*, (2021) [14].

Table 1: Numeric score system used for recording of various reflexes and responses (as adopted and modified by Singh *et al.*, 2013 and Guerri *et al.*, 2021) [14].

No.	Parameters	Score			
		0	1	2	3
1.	Sedation	No sedation (standing alert, keeping the head high or normal, position of eyelids normal)	Mild (standing but appears tired, dropping of head and eyelids)	Moderate (able to sit without support, dropping of head and eyelids)	Strong (unable to sit without support, dropping of head and eyelids)
2.	Analgesia	No analgesia, strong reaction to pin pricks	Mild analgesia, weak response to pin pricks	Moderate analgesia, occasional response to pin pricks	Complete analgesia, no response to pin pricks.
3.	Jaw relaxation	Not allowing to open the jaw	Resistant to opening the jaws and closed quickly	Less resistance to opening the jaws and closed slowly	No resistance and jaws remain open
4.	Palpebral reflex	Intact and strong (quick blink)	Intact but weak (slow response)	Very weak (very slow and occasional)	Abolished
5.	Pedal reflex	Intact and strong (strong withdrawal)	Intact but weak (animal responding slowly)	Intact but very light (slow and occasional response)	Abolished completely
6.	Salivation	No salivation	Mild salivation	Moderate salivation	Excessive salivation
7.	Muscle relaxation of limb	Absent (stiff limbs)	Mild (moderate resistance to bending of limbs)	Moderate (mild resistance to bending of limbs)	Complete (no resistance to bending of limbs
8.	Muscle relaxation of abdomen	Absent (no flaccidity of abdomen)	Mild (no flaccidity of abdomen)	Moderate (no flaccidity of abdomen)	Complete (flaccid abdomen)
9.	Anal sphincter reflex	Complete anal relaxation	Mild anal relaxation	Moderate anal relaxation	Absence of anal relaxation
10.	Ataxia	Absent (no ataxia) walking without staggering	Mild (knuckling of the fetlocks) able to stand but walking with some incoordination	Moderate (crossing of the hindlimbs) able to stand but walking with extreme incoordination	Strong (attempting or assuming recumbency) unable to stand and assuming sternal recumbency
10.	Regurgitation	Absence of ruminal contents within oral cavity)	Mild (presence of small amount of ruminal contents within oral cavity)	Moderate (moderate volume of rumen contents coming out through mouth/nostrils)	Severe (large volume of rumen contents coming out through mouth/nostrils)

Physiological Parameters

The physiological parameters were observed at 0 min before anaesthesia, 10 min after premedication and post induction at 10, 20, 40, 60, 120 min post anaesthesia. Physiological parameters included rectal temperature, heart rate and respiration rate.

Statistical Analysis: Statistical analysis of the data was done using SPSS 25v statistics software program and ANOVA technique according to the method described by Snedecor and Cochran (1994) [36]. Statistically significant difference was considered at 5 per cent level.

Results

- Clinical Parameters
- Assessment of Anaesthesia

Onset of sedation

The onset of sedation (Fig 1) in group B was significantly (P<0.05) longer (4.36±0.21 min) than group A (0 min) and C (0 min).

Induction time/Induction of anaesthesia

The induction time **(Fig 1)** was non-significant among all the three groups A, B and C which was recorded as 0.38±0.04, 0.34±0.03 and 0.39±0.05 min respectively.

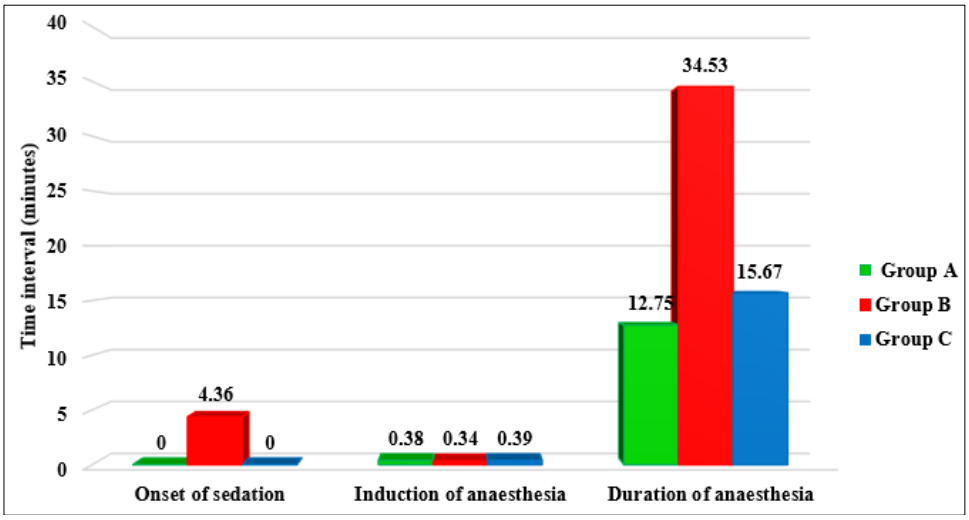

Fig 1: Onset of sedation, induction of anaesthesia and duration of anaesthesia following induction with tiletamine-zolazepam anaesthesia at various time intervals in buffalo calves

Record of various reflexes and behavioural responses

Degree of sedation score following induction with tiletamine-zolazepam was very good (score 3) in group A and C up to 15 min, while in group C up to 30 min (Fig 2). The degree of analgesia. showed complete analgesia (score 3) up to 15 min in group A and C, while up to 30 min in group B (Fig 3). Jaw relaxation was scored 3 up to 15 min in group A and C, while up to 30 min in group B (Fig 4). Palpebral reflex was very weak (score 2) in group A and C up to 15 min while abolished completely (score 3) in group B up to 30 min (Fig 5). Pedal reflex was abolished completely (score 3) in group A and C up to 15 min while in group B up to 30 min. Salivation was mild (score 1) in group A and C, whereas moderate (score 2) in group B animals. Muscle relaxation of limb and abdomen showed complete relaxation (score 3) up to 15 min in group A and C, while up to 30 min in group B animals. The ataxia scored 3 in group A and C up to 15 min, while in group B up to 30 min. Lack of anal sphincter relaxation was noted in groups A and C after sedation, while group B animals showed mild relaxation (score 1) following dexmedetomidine sedation. However, after induction with tiletamine-zolazepam, complete anal sphincter (score 3) relaxation occurred in all three groups (Fig 6). Position of eye ball was central to mildly ventro-medial in group A and C whereas, ventro-medially rotation in group B animals. No cases of regurgitation were recorded in any buffalo calf after tiletamine-zolazepam anaesthesia.

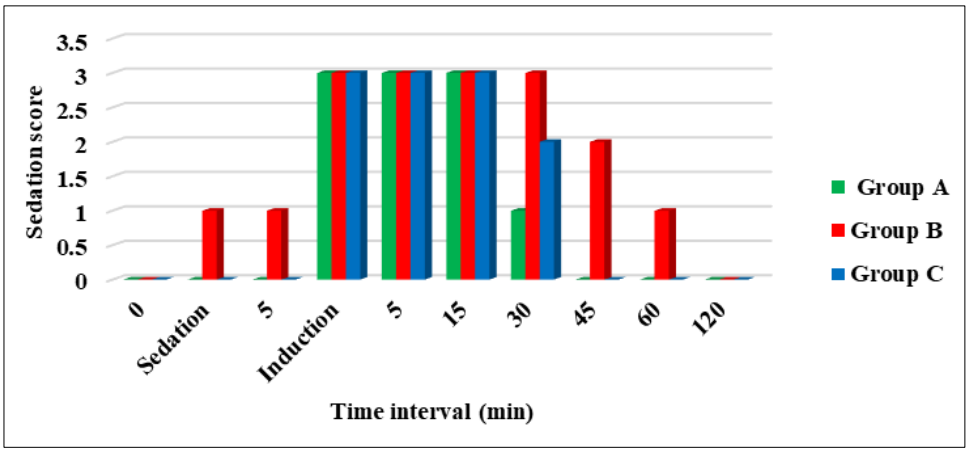

Fig 2: Effect on sedation score following induction with tiletamine-zolazepam at various time interval in different groups of buffalo calves.

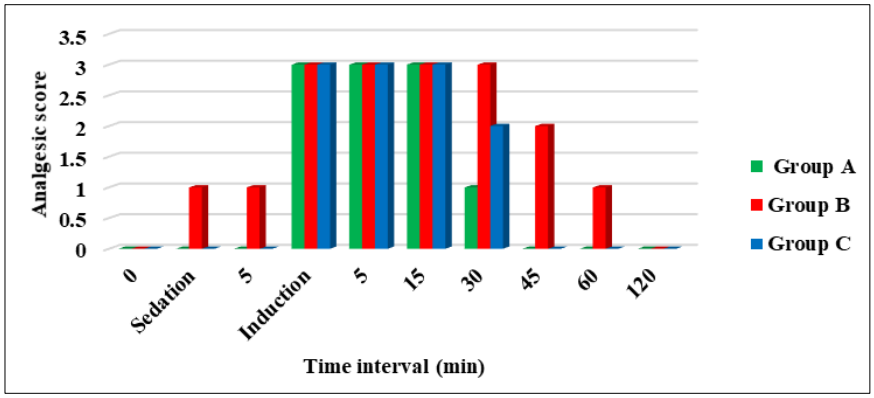

Fig 3: Effect on analgesic score following induction with tiletamine-zolazepam at various time interval in different groups in buffalo calves.

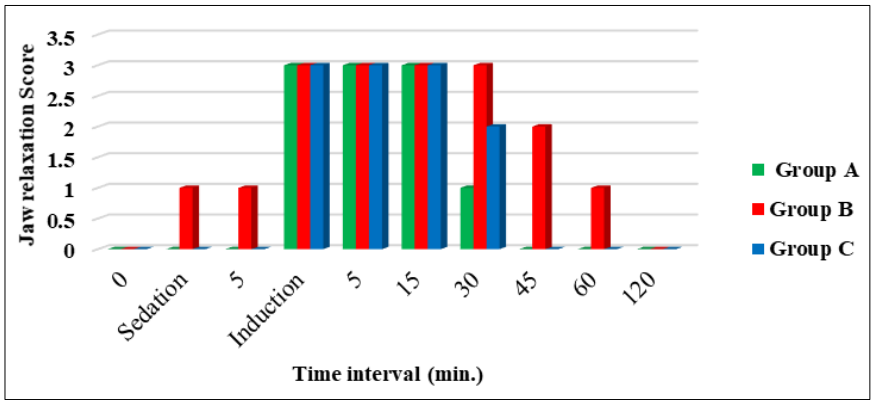

Fig 4: Effect on jaw relaxation score following induction with tiletamine-zolazepam at various time intervals in different groups in buffalo calves.

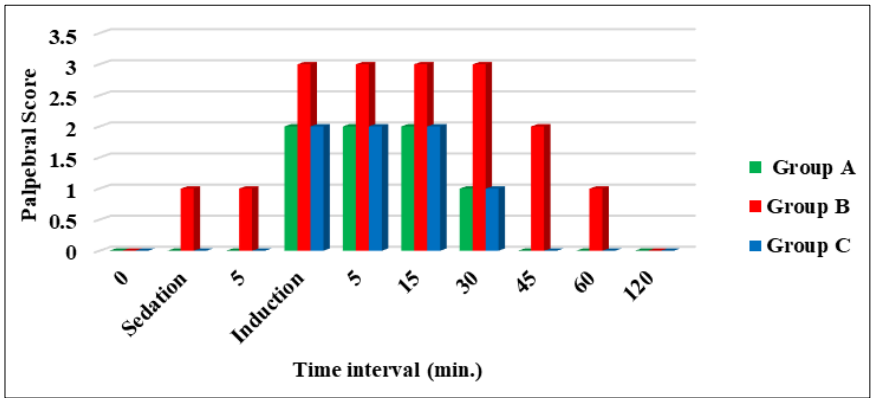

Fig 5: Effect on palpebral score following induction with tiletamine-zolazepam at various time intervals in different groups in buffalo calves.

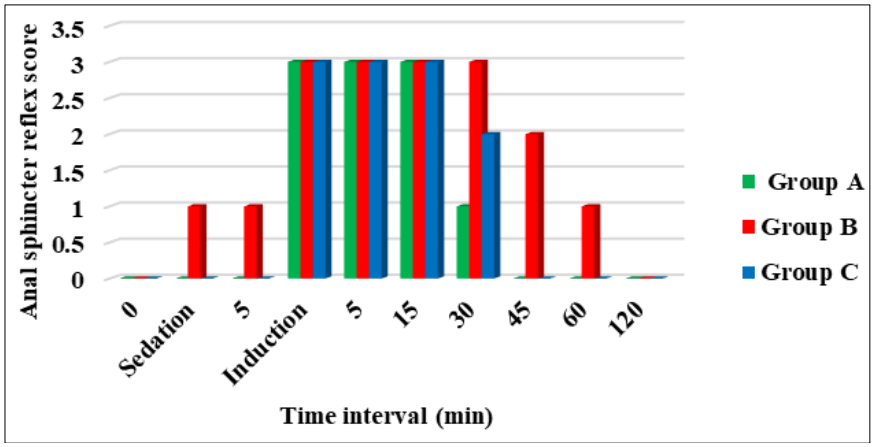

Fig 6: Effect on anal sphincter reflex score following induction with tiletamine-zolazepam at various time intervals in different groups in buffalo calves.

Duration of anaesthesia

The duration of anaesthesia (Fig 1) differed significantly among the groups, with Group B showing the longest anaesthetic period (34.53±2.86 min), followed by Group C (15.67±2.49 min) and Group A (12.75±2.84 min).

Recovery time

Return of head rightening reflex: The return of the head-righting reflex (Fig 7), varied significantly among groups, with mean HRR times of 18.67±3.73 min in Group A, 42.85±4.28 min in Group B, and 21.37±2.41 min in Group C.

Sternal recumbency time

Sternal recumbency time (Fig 7) varied significantly among the treatment groups, with mean values of 25.48±3.38 min in Group A, 61.58±4.36 min in Group B, and 31.29±3.45 min in Group C.

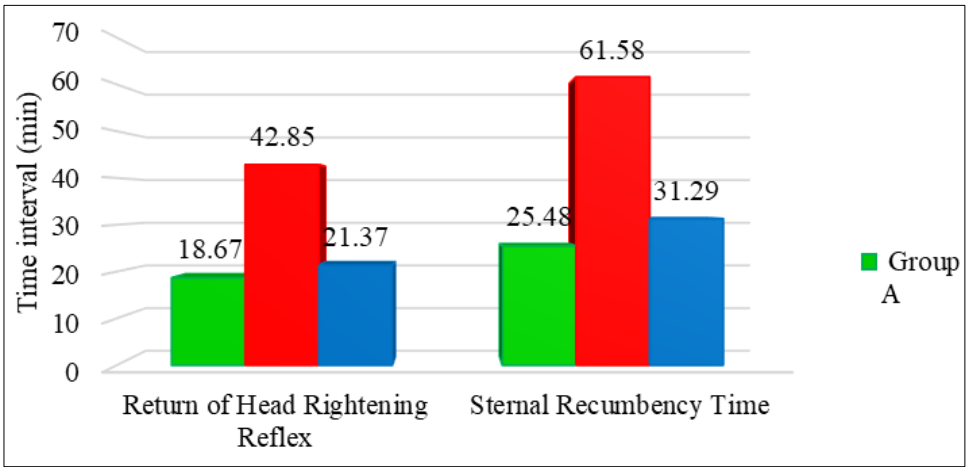

Fig 7: Return of head rightening reflex (min) and sternal recumbency time (min) following induction with tiletamine-zolazepam anaesthesia at various time intervals in different groups of buffalo calves.

Standing time

Standing time (Fig 8) differed significantly among groups, with mean values of 34.58±2.85 min in Group A, 83.62±4.35 min in Group B and 36.87±3.48 min in Group C.

Complete Recovery time

Complete recovery (**Fig 8**), varied markedly among treatment groups, with mean times of 40.48±2.35 min (Group A), 106.71±4.87 min (Group B) and 49.68±4.72 min (Group C).

Quality of anaesthesia

Quality of anaesthesia (Fig 9) was excellent (scored 4) after administration with tiletamine-zolazepam in all the three groups and characterized by rapid induction, excellent muscle relaxation and analgesia (as adopted and modified by Bodh *et al.*, 2013) [5].

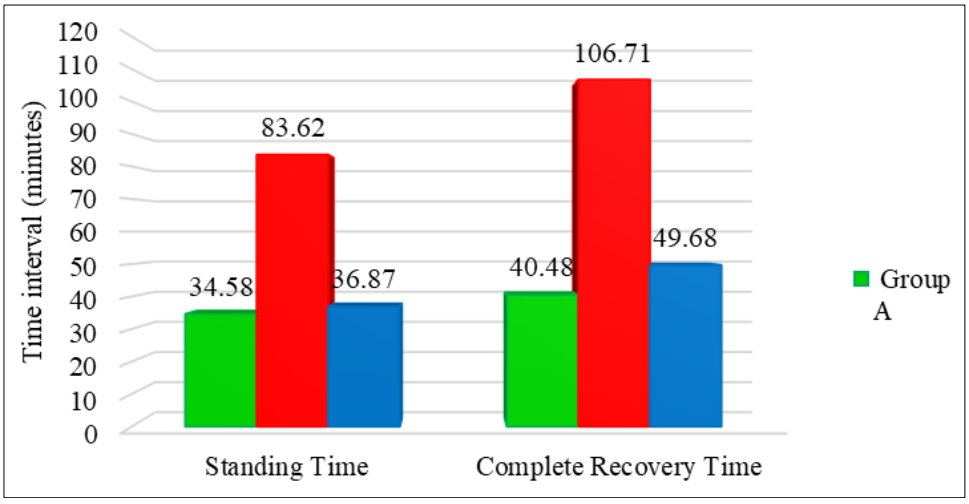

Fig 8: Standing (min) time and complete recovery time (min) following induction with Tiletamine-Zolazepam at various time intervals in different groups of buffalo calves.

Physiological Parameters: Rectal temperature (˚F)

A significant (P<0.05) decrease in the rectal temperature in animals of group A, up to 20 min Animals of group B, showed a non-significant decrease in the rectal temperature after sedation which further decreased significantly (P<0.05) up to 40 min following induction, while animals of group C, showed a non-significant decrease in rectal temperature after sedation which further decreased significantly (P<0.05) up to 20 min after induction. This trend is evident from the Table 2 and illustrated in Fig 10.

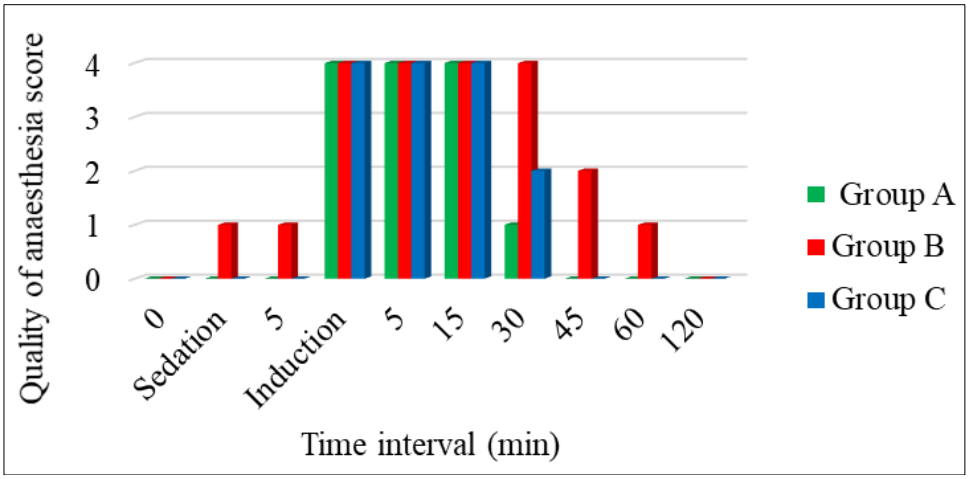

Fig 9: Effect on quality of anaesthesia score following induction with tiletamine-zolazepam at various time intervals in different groups of buffalo calves.

Table 2: Effect on physiological parameters following induction with tiletamine-zolazepam anaesthesia at various time intervals in different groups (Mean±S.E.) of buffalo calves.

Parameter	Group (n=6)	0 (min)	10 min after sedation (min)	10 (min)	20 (min)	40 (min)	60 (min)	120 (min)
Rectal temperature (°F)	A	101.24±0.46^{Ac}	100.37±0.55^{Abc}	98.84±0.37^{Aa}	99.72±0.47^{Bab}	100.02±0.25^{Babc}	100.38±0.19^{Bbc}	101.08±0.33^{Ac}
	B	101.62±0.47^{Ae}	100.88±0.35^{Ade}	100.13±0.38^{Bbc}	102.88±0.40^{Ab}	97.75±0.36^{Aa}	99.18±0.14^{Abc}	101.43±0.11^{Ae}
	C	101.15±0.68^{Ac}	101.13±0.09^{Abc}	100.63±0.40^{Aa}	99.78±0.27^{Bb}	100.08±0.27^{Bbc}	100.42±0.30^{Bbc}	101.03±0.36^{Ac}
Heart rate (beats per min)	A	60.67±0.49^{Aa}	62.83±0.48^{Cb}	64.33±0.49^{Bb}	66.33±0.49^{Bc}	62.83±0.60^{Bb}	61.17±0.70^{Ba}	60.50±0.56^{ABa}
	B	61.17±0.60^{Ae}	50.33±0.84^{Ac}	56.83±0.79^{Ab}	64.17±0.60^{Aa}	69.33 ±0.88^{Ac}	62.00±0.97^{Aa}	59.17±0.60^{Be}
	C	60.00±0.58^{Ab}	66.50±0.76^{Ba}	67.67±0.80^{Cde}	68.17±0.60^{Ce}	63.12±0.60^{Cd}	61.60±0.95^{Cc}	60.48±0.65^{Ab}
Respiration rate (breaths per min)	A	21.83±0.31^{Ac}	21.50±0.62^{ABbc}	18.17±0.31^{Ba}	17.33±0.42^{Ba}	18.33±0.42^{Ba}	20.50±0.22^{Bb}	21.67±0.49^{Bbc}
	B	22.17±0.60^{Af}	18.17±0.48^{Ae}	15.00±0.37^{Ac}	13.00±0.37^{Ab}	11.50±0.22^{Aa}	16.83±0.48^{Ad}	20.33±0.49^{Ae}
	C	22.50±0.43^{Ad}	23.47±0.56^{Bd}	19.67±0.33^{Cbc}	17.17±0.48^{Ba}	18.50±0.34^{Bb}	19.83±0.31^{Bc}	21.50±0.34^{Bd}

abcde- Value bearing different superscript vary significantly (P<0.05) within group
ABC- Value bearing different superscript vary significantly (P<0.05) among group

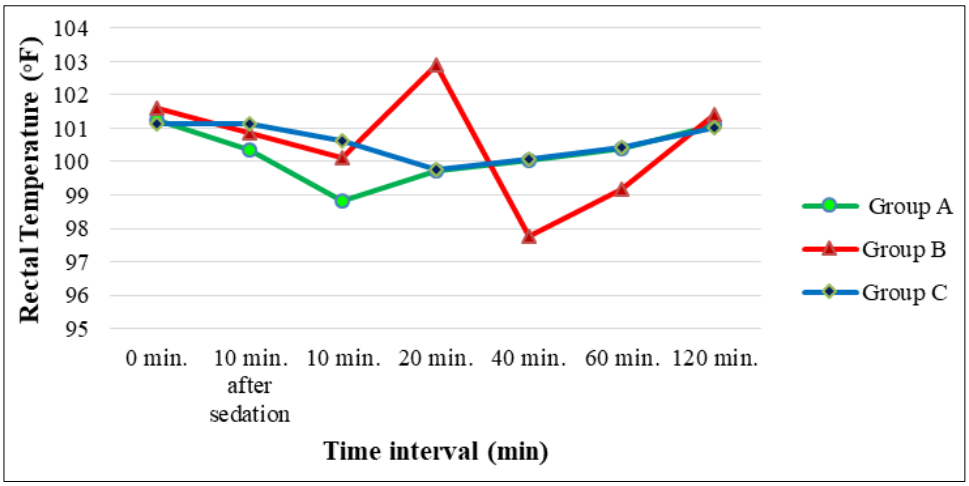

Fig 10: Effect on rectal temperature (°F) following induction with tiletamine-zolazepam at various time interval in different groups in buffalo calves.

Heart rate

A significant (P<0.05) increase in heart rate up to 20 min in group A. In group B, a significant (P<0.05) decrease in heart rate was noted after sedation with dexmedetomidine which later on increased significantly (P<0.05) up to 40 min after induction. Animals of group C, also showed a significant (P<0.05) increase in heart rate after administration of butorphanol which further increased significantly up to 20 min. This trend is evident from the Table 2 and illustrated in Fig 11.

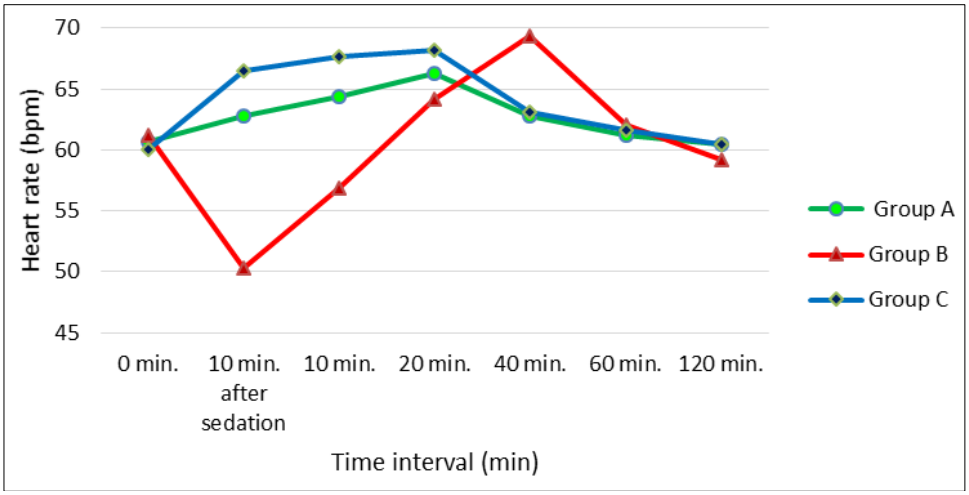

Fig 11: Effect on heart rate (bpm) following induction with tiletamine-zolazepam at various time interval in different groups in buffalo calves.

Respiration rate: The respiration rate was noted a significant (P<0.05) decreased up to 20 min in group A. In group B, there was a significant (P<0.05) decrease in the respiration rate after premedication with dexmedetomidine which further decreased significantly (P<0.05) up to 40 min after induction. The animals of group C, showed a non-significant decrease in respiration rate after premedication with butorphanol which further significantly (P<0.05) decrease up to 20 min after induction. This trend is evident from the Table 2 and illustrated in Fig 12.

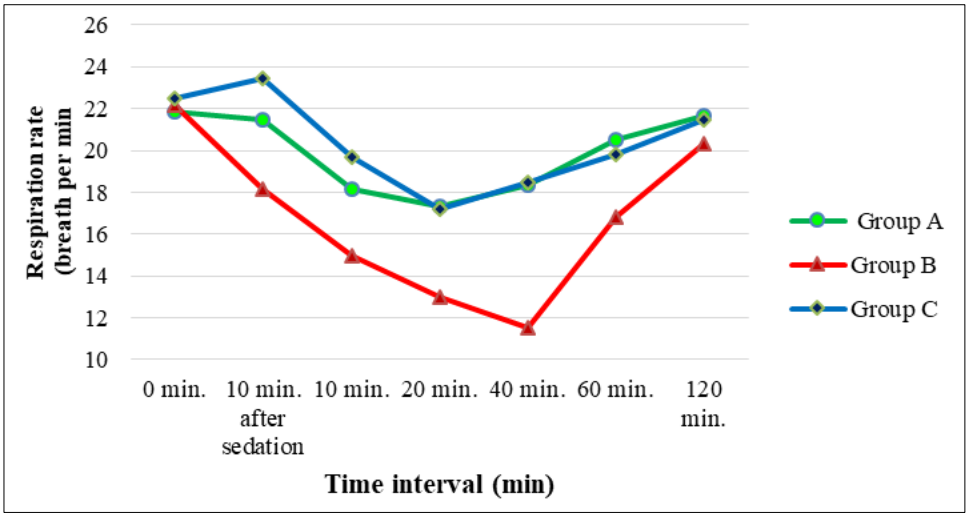

Fig 12: Effect on respiration rate (breath per min) following induction with tiletamine-zolazepam at various time interval in different groups in buffalo calves.

Complication

All animals in Groups A and B exhibited smooth, uncomplicated recoveries following tiletamine-zolazepam anaesthesia, with no post-anaesthetic complications observed, whereas animals in Group C displayed varying degrees of excitement during recovery.

Discussion

Sedation began earlier in group B than in the other groups, likely due to the rapid onset of dexmedetomidine associated with its lipophilicity (Dewangan *et al.*, 2025) [10]. Gurukar (2016) [15] similarly recorded a sedation onset of 3.17±0.36 min following intravenous dexmedetomidine at 2.5 µg/kg body wight in cattle. Cagnardi *et al.* (2017) [6] also noted that dexmedetomidine produced dependable and prolonged sedation in calves. Animals premedicated with dexmedetomidine exhibited a shorter induction time compared with the other groups, probably due to its synergistic effects, which provided adequate sedation before tiletamine-zolazepam administration. This enhanced response may be attributed to dexmedetomidine's α2-receptor agonism in the locus coeruleus, which promotes sedation, hypnosis, and analgesia (Sinclair, 2003) [31]. In the present study, rapid induction (<60 seconds) was observed across all three groups with no significant intergroup variation, consistent with the findings of Ukkali (2022) [40], who reported an induction time of 35.84±0.57 seconds in cattle receiving tiletamine-zolazepam.

Tiletamine-zolazepam produced a rapid onset of sedation in all groups, which aligns with its known pharmacokinetic profile in large ruminants, where tiletamine's NMDA-receptor antagonism and zolazepam's benzodiazepine-like action contribute to rapid central nervous system depression (Akaraphutiporn *et al.*, 2024) [2]. Analgesia following induction was excellent across treatments, likely due to tiletamine's potent interaction with the PCP site of the NMDA receptor and its non-competitive antagonistic effect, which can interrupt sensory transmission and sustain

analgesia beyond the period of anaesthetic action (Lin *et al.*, 1993) [24]. Previous studies also support the superior analgesic efficacy of tiletamine-zolazepam compared with other anaesthetic combinations: Singh (2021) reported better analgesia and a longer duration of effect than ketamine or propofol with midazolam premedication in calves, while Ukkali (2022) [40] found it superior to ketamine-midazolam in cattle. Sindak (2003) [32] recorded excellent analgesia with xylazine-tiletamine-zolazepam relative to xylazine-ketamine in calves. Additional evidence from buffaloes and small ruminants indicates similarly strong analgesic and muscle-relaxant properties (Bodh *et al.*, 2015; Sahu, 2024). Lin and Walz (2014) [4, 29, 21] reported that combination of tiletamine and zolazepam produce better muscle relaxation, analgesia and duration of action than ketamine alone**.** Similarly, Carroll *et al.* (1997) [6] documented that tiletamine-zolazepam @ 5.5 mg alone induced sufficient analgesia for ovariectomy operation in goats. In group B, jaw relaxation and overall muscle relaxation persisted for up to 30 minutes after TZ administration, a longer duration than in groups A and C, likely due to the additional α2-agonist, which enhances muscle relaxation through inhibition of α2-adrenoceptors at the spinal interneuron level (Sinclair, 2003) [31]. Following induction with TZ, all groups demonstrated marked muscle and anal sphincter relaxation, attributable to the combined relaxant effects of zolazepam and the α2-agonist dexmedetomidine, whereas tiletamine itself does not significantly affect muscle tone or cranial and spinal reflexes (Dewangan *et al.*, 2025) [10]. Similar findings were reported by Sulekha *et al.* (2024) [37], who attributed strong muscle relaxation to zolazepam's inhibition of internuncial neurons in the spinal cord (Hall *et al.*, 2001). Saini *et al.* (2017) [16, 30] noted that dexmedetomidine provided profound analgesia and muscle relaxation, and when combined with TZ, prolonged jaw relaxation, supporting its suitability as a premedicant. Palpebral reflex was very weak in group A and C while abolished completely in group B. This effect is likely due to the combined action of zolazepam, a benzodiazepine, and tiletamine, a dissociative anaesthetic, which together exert complementary modulation at the interneuronal junction by influencing both benzodiazepine and NMDA receptors (Ukkali, 2022) [40] Similarly, Singh *et al.* (2013) observed complete abolition of palpebral reflex after administration of α2-agonist in buffaloes. Following induction with TZ anaesthesia, pedal reflex was completely absent in all three groups, indicating achievement of a surgical plane of anaesthesia. This surgical depth was maintained for a longer period in group B, persisting for up to 30 min. These findings were in concurrence with Pawde *et al.* (2000) [26] in buffalo calves and Ragab *et al.* (2022) [27] in goats after ketamine, propofol or ketamine and ketamine-propofol anaesthesia respectively up to 60 min.

The extended duration of anaesthesia observed in group B appears to result from the additive effects of dexmedetomidine combined with tiletamine-zolazepam (Sahu, 2024) [29]. Similar findings have been documented in goats, where tiletamine-zolazepam-xylazine produced a longer anaesthetic period (100.83±43.37 min) than ketamine-xylazine (95.17±12.32 min) (Gicana *et al.*, 2021) [13]. In the present study, animals in group B also demonstrated significantly ($P<0.05$) longer times for return of head-righting reflex, sternal recumbency, standing, and complete recovery compared with groups C and A. The deeper sedation and prolonged analgesia produced by dexmedetomidine when used with TZ likely contributed to slower metabolic activity and delayed redistribution and metabolism of the drugs. Conversely, the shorter recovery periods in groups A and C suggest more rapid metabolic clearance of TZ in the absence of dexmedetomidine. The α2-agonist may have further influenced recovery in group B by enhancing sedation or prolonging zolazepam elimination (Dewangan *et al.*, 2025) [10]. Comparable prolongation of standing time after TZ anaesthesia was reported by Ukkali (2022) [40], while Singh (2021) noted extended sternal recumbency, standing time and total recovery duration in calves given tiletamine-zolazepam compared with ketamine-midazolam. Animals in groups A and C of the present study regained standing more quickly. The inclusion of dexmedetomidine in group B likely accounted for the lengthened recovery, consistent with its known capacity to deepen and extend anaesthesia.

Animals premedicated with butorphanol displayed brief agitation such as restlessness, excessive sniffing, and exaggerated tail movement along with a shorter recovery phase. This pattern aligns with earlier reports that opioids can induce central nervous system stimulation in ruminants (Dzikiti *et al.*, 2016; Delgado *et al.*, 2021) [9, 12]. Overall, recovery from dexmedetomidine-TZ and TZ alone was smooth and uncomplicated, whereas butorphanol-TZ anaesthesia produced transient behavioural abnormalities. Statistical comparison among the groups confirmed a significant ($P<0.05$) difference in recovery times.

Administration of TZ produced excellent anaesthetic quality across all three groups, marked by rapid induction, strong muscle relaxation, and effective analgesia. These effects are consistent with the rapid CNS uptake of TZ following intravenous administration, followed by swift redistribution and efficient metabolic clearance (Ko *et al.*, 2007) [18]. Complete abolition of reflexes in all groups after induction confirmed attainment of a surgical plane of anaesthesia. Among the treatment protocols, dexmedetomidine premedication resulted in the best overall anaesthetic quality, with group B maintaining optimal anaesthesia for up to 30 minutes, whereas groups C and A exhibited excellent anaesthesia for approximately 15 minutes. Although TZ alone provided good muscle relaxation, its duration was shorter, likely reflecting the central muscle-relaxant action of zolazepam, as seen in group A. The enhanced and prolonged muscle relaxation observed in the dexmedetomidine group suggests that the α2-agonist augmented TZ-induced sedation and muscle relaxation, findings that are in line with observations reported by Singh *et al.* (2021).

The decline in rectal temperature across groups can be attributed to reduced basal metabolic rate, decreased muscular activity, and depression of the hypothalamic thermoregulatory centre (Kumar *et al.*, 2014) [19]. The changes were consistent with indicating hypothermia with α2-agonists due to CNS depression and reduced skeletal muscle tone. Dexmedetomidine-induced hypothermia has been similarly attributed to α2-adrenergic stimulation, lowered metabolic rate, and muscle relaxation (Tranquilli, 2015) [39]. The initial tachycardia observed in Groups A and C aligns with the known sympathomimetic properties of tiletamine and the excitatory, κ-receptor-mediated CNS stimulation seen with butorphanol. Tiletamine enhances cardiac output through increased sympathetic tone and catecholamine release, explaining the marked elevation in

heart rate **(**Abalos *et al.*, 2016) [1]. Similarly, butorphanol is recognized to induce behavioural excitement and sympathetic activation, contributing to persistent tachycardia during the early anaesthetic period (Maidanskaia *et al.*, 2023) [25]. Conversely, dexmedetomidine induced significant bradycardia in Group B due to its potent α2-adrenergic agonist action, decreasing norepinephrine release and increasing vagal tone (Pawde *et al.*, 2000) [26]. Following tiletamine-zolazepam induction, however, a compensatory increase in heart rate occurred, reflecting the opposing sympathomimetic action of tiletamine **(**Lin *et al.*, 1989) [22]. The respiratory depression following tiletamine-zolazepam was consistent with its pharmacological actions. Zolazepam potentiates GABAergic inhibition, reducing respiratory centre responsiveness, while tiletamine's NMDA antagonism suppresses medullary respiratory neurons, contributing to apneustic and irregular breathing (Chang *et al.*, 2024) [8]. The marked decrease in respiration rate in dexmedetomidine-treated animals aligns with α_2-agonist-induced central depression of respiratory centres and diminished chemoreceptor sensitivity (Cagnardi *et al.*, 2017) [6]. In contrast, butorphanol initially increased respiration rate due to κ-opioid receptor-mediated CNS excitation and sympathetic activation (Maidanskaia *et al.*, 2023) [25], before the depressant influence of tiletamine-zolazepam emerged. Overall, all the physiological alterations in all the groups were transient, values returning towards baseline by 120 minutes. All values were within acceptable physiological limits, indicating a wide margin of safety of these drug combinations.

Conclusion

Intravenous administration of tiletamine-zolazepam @ 2.5 mg/kg body weight produced a short, safe anaesthetic period with smooth recoveries, whereas premedication with dexmedetomidine @2 µg/kg body weight I/V prior to induction provided superior anaesthetic quality, characterized by rapid and smooth onset, profound analgesia, excellent muscle relaxation, and prolonged duration without any complications. Butorphanol premedication @0.075 mg/kg body weight I/V yielded adequate analgesia and moderate muscle relaxation with a comparatively shorter anaesthetic duration, although transient excitatory behaviour was noted during sedation and recovery in some calves. Among the protocols evaluated, the glycopyrrolate-dexmedetomidine-tiletamine-zolazepam combination was proved to be the most balanced and effective regimen, as compared to glycopyrrolate-butorphanol-TZ and TZ alone in overall anaesthetic quality, duration, and recovery characteristics. All the physiological changes remained within normal limits and were of transient nature which were compensated by 120 min, indicating that all the three protocols were clinically safe and there was uneventful recovery without any complications in buffalo calves.

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Conflict of Interest

The authors declare no conflict of interest.

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