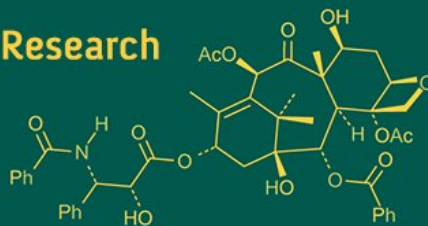
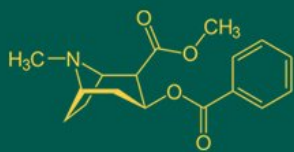


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Clinico-physiological response of dexmedetomidine and fentanyl citrate as premedicants to zolazepam-tiletamine-isoflurane anaesthesia in canine

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Abstract

The present study evaluated the clinico-physiological effects of dexmedetomidine and fentanyl citrate as premedicants to zolazepam-tiletamine-isoflurane anaesthesia in canines. Eighteen dogs were divided into three groups: atropine alone (Group I), atropine with dexmedetomidine (Group II) and atropine with fentanyl citrate (Group III). Dexmedetomidine produced significantly faster and deeper sedation, superior analgesia, earlier abolition of reflexes and shorter induction time ($p < 0.05$). It also reduced isoflurane requirement and prolonged duration of anaesthesia, but significantly delayed recovery. Fentanyl citrate showed moderate effects, whereas atropine alone was least effective. Physiological parameters revealed a decline in rectal temperature and respiration rate in all groups, with comparatively lower heart rate in the dexmedetomidine group. Haemodynamic parameters remained within normal limits. It was concluded that dexmedetomidine provides superior anaesthetic efficacy with marked isoflurane-sparing effect, though with prolonged recovery, making it the most effective protocol for balanced anaesthesia in canines.

Keywords: Dexmedetomidine, fentanyl citrate, zolazepam-tiletamine, isoflurane, canine anaesthesia, premedication, analgesia, sedation, clinico-physiological parameters

1. Introduction

Perfect anaesthesia is essential for successful surgical intervention, ensuring adequate hypnosis, analgesia and muscle relaxation. General anaesthesia is a reversible drug-induced depression of the central nervous system with loss of sensory, motor and autonomic functions (Tranquilli and Grimm, 2015) [75]. Balanced anaesthesia, achieved through the use of multiple drug combinations, enhances anaesthetic efficacy while minimizing individual drug side effects (Campagna *et al.*, 2003; Kumar *et al.*, 2012) [7, 43]. In veterinary practice, anaesthesia is induced using injectable agents and commonly maintained with inhalation anaesthetics like isoflurane due to better control and rapid recovery (McKenzie, 2008; Bustamante *et al.*, 2018) [6, 55]. Premedicants such as atropine, dexmedetomidine and fentanyl play a vital role in stabilizing physiological responses and improving analgesia (Lerche, 2015; Bloor *et al.*, 1992; Keating *et al.*, 2013) [4, 32, 51]. The tiletamine-zolazepam combination provides effective dissociative anaesthesia with muscle relaxation, while isoflurane ensures safe maintenance with minimal cardiopulmonary depression (Plumb, 2018; Matthews *et al.*, 2003) [54, 61]. However, limited studies in India have evaluated this combination; therefore, the present study was undertaken to assess the efficacy and suitability of tiletamine-zolazepam-isoflurane anaesthesia with different preanaesthetics in canine surgical patients.

2. Materials and Methods

The present study was conducted at the Department of Veterinary Surgery and Radiology and Teaching Veterinary Clinical Complex (TVCC), College of Veterinary Science and Animal Husbandry, Anjora, Durg (C.G.). A total of 18 mongrel dogs of either sex, weighing between 15-30 kg body weights, were selected for the study. All animals were dewormed prior to experimentation and randomly divided into three groups (Group I, II and III), each comprising six animals. The animals were fasted for 12 hours, with water withheld for 6

Hours before administration of anaesthesia. A pilot study was conducted to standardize the drug dosages, and the minimum effective doses were selected for the experiment. The animals were subjected to three different anaesthetic protocols.

In Group I, atropine sulphate (0.04 mg/kg IM) was used as premedication, followed by induction with zolazepam-tiletamine (3 mg/kg IV) and maintenance with 1.5-2% isoflurane in 100% oxygen. In Group II, atropine sulphate (0.04 mg/kg IM) was combined with dexmedetomidine (10 µg/kg IV), while in Group III, atropine sulphate (0.04 mg/kg IM) was combined with fentanyl citrate (4 µg/kg IV), with induction and maintenance protocols similar to Group I. Drug dosages were calculated based on body weight. Baseline values of all parameters were recorded prior to administration of premedicants. Following premedication, animals were allowed for onset of sedation. Intravenous access was established, and normal saline was administered at a rate of 5 ml/kg/h. Anaesthesia was induced 10 minutes after premedication using zolazepam-tiletamine administered intravenously until loss of pedal reflex. Endotracheal intubation was performed using appropriate-sized tubes, and anaesthesia was maintained with isoflurane (1.5-2%) in 100% oxygen for a duration of 90 minutes using a closed rebreathing system. After completion of the procedure, isoflurane was discontinued and oxygen was continued for an additional 5 minutes. Clinical parameters including onset and quality of sedation, induction time, quality of induction, reflex responses (jaw relaxation, palpebral and pedal reflex), and recovery characteristics such as extubation time, sternal recumbency time, standing time, complete recovery time and duration of anaesthesia were recorded using standardized scoring systems (Amarpal *et al.*, 1996; Carter *et al.*, 2013; Tamura *et al.*, 2014) [2, 9, 73].

Physiological parameters including rectal temperature (°F), respiration rate (breaths/min) and heart rate (beats/min) were recorded at predetermined intervals. Haemodynamic parameters including systolic, diastolic and mean arterial blood pressure were recorded using a non-invasive monitor, while capillary refill time was assessed manually. Mean blood pressure was calculated using the formula: $MBP = DBP + 1/3 (SBP - DBP)$.

3. Results

3.1 Assessment of anaesthesia

3.1.1 Onset of Sedation

The onset of anaesthesia in all the three groups has been shown in Table 1 and represented in Fig. 1.

Table 1: Mean±S.E. of Onset of sedation in different treatment groups in canine

Groups	Onset of sedation (min)
Group I	0a
Group II	5.50±0.42 ^b
Group III	8.83±0.47 ^c

Values bearing different superscript vary significantly ($P < 0.05$) between groups

The mean±S. E. onset of sedation was recorded as 0, 5.50±0.42 and 8.83±0.47 minutes in Group I, II and III, respectively, with significant differences between the groups ($p < 0.05$). No sedation was observed in Group I. Group II exhibited rapid and marked sedation with lateral recumbency, whereas Group III showed delayed and mild sedation. Overall, dexmedetomidine produced a faster and more pronounced sedative effect compared to fentanyl citrate.

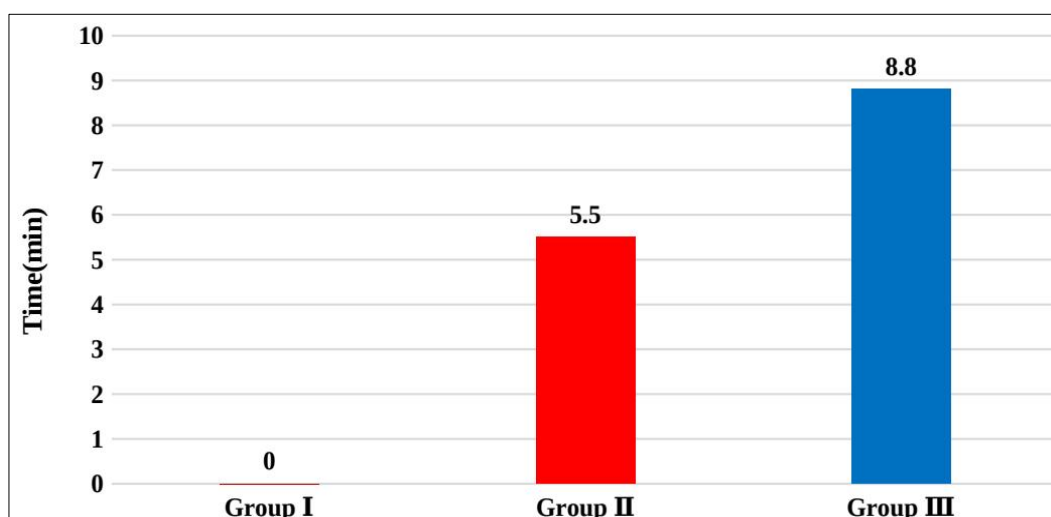


Fig 1: Bar diagram showing the Onset of sedation in different treatment groups in canines

3.1.2 Sedation score

The Sedation score in all the three groups has been shown in Table 2 and represented in Fig. 2.

Table 2: Mean±S.E. of Sedation score in different groups in canine

Groups	Sedation score
Group I	0a
Group II	3.5±0.22 ^c
Group III	2.5±0.22 ^b

Values bearing different superscript vary significantly ($P < 0.05$) between groups

The mean ± SE values of Sedation score after administration of preanaesthetics were recorded as 0, 3.5±0.22 and 2.5±0.22 minutes in group I, II and III respectively. The differences in Sedation score between group I and group II and between group II and group III were statistically significant ($p \leq 0.05$).

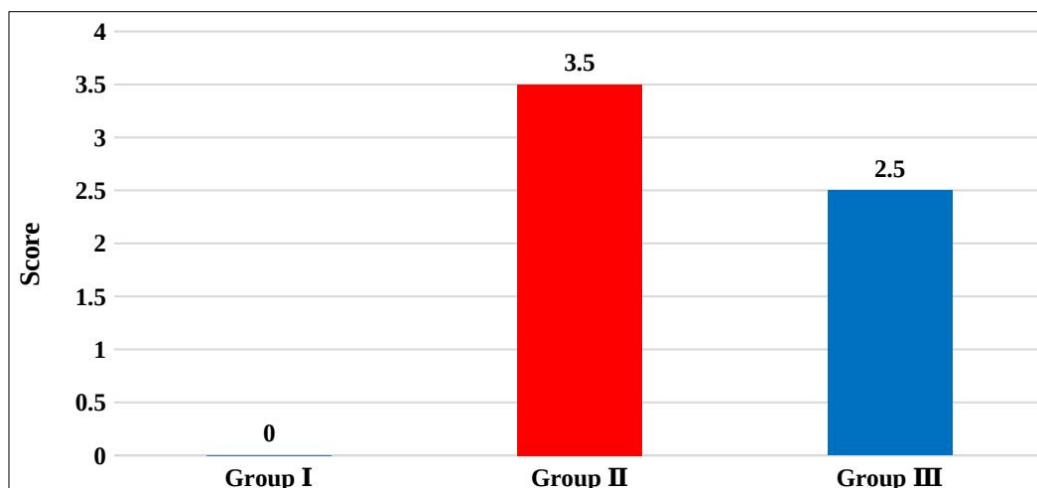


Fig 2: Bar diagram showing the sedation score in different treatment groups in canine

3.2 Record of various reflexes and responses

3.2.1 Palpebral reflex

The Mean±SE values of Palpebral reflex scoring at various

Intervals in all the three groups are depicted in Table 3 and Fig.3.

Table 3: Mean±S.E. of Palpebral reflex scoring in different treatment groups in canine

Group	Mean±SE									
	0 mins	5 min after Atropine	10min after Sedation	10 mins after induction	20 mins	30 mins	45 mins	60 mins	75 min	90 min
I	0.00±0.00 ^a	0.00±0.00 ^a	0.00±0.00 ^{Ab}	0.67±0.21 ^{Ab}	3.00±0.00 ^c	3.00±0.00 ^c	3.00±0.00 ^c	3.00±0.00 ^c	3.00±0.00 ^c	3.00±0.00 ^c
II	0.00±0.00 ^a	0.00±0.00 ^a	1.17±0.17 ^{Bb}	3.00±0.00 ^{Bc}	3.00±0.00 ^c	3.00±0.00 ^c	3.00±0.00 ^c	3.00±0.00 ^c	3.00±0.00 ^c	3.00±0.00 ^c
III	0.00±0.00 ^a	0.00±0.00 ^a	0.50±0.22 ^{Ab}	2.67±0.21 ^{Bc}	3.00±0.00 ^d	0.00±0.00 ^d	3.00±0.00 ^d	3.00±0.00 ^d	3.00±0.00 ^d	3.00±0.00 ^d

AB - Value bearing different superscript vary significantly ($p < 0.05$) between group

abc- Values bearing different superscript vary significantly ($p < 0.05$) within groups

0- Quick blink, 1- Slow blink, 2- Very slow and occasional blink, 3- No blink

The Mean ± S.E. values of palpebral reflex scores were 0.00 ± 0.00 at 0 min and after atropine administration in all the groups, indicating intact reflexes. In Group I, scores increased to 0.67 ± 0.21 at 10 min post-induction and reached 3.00 ± 0.00 by 20 min, remaining at this level up to 90 min, showing complete abolition of reflex. In Group II, scores increased significantly to 1.17 ± 0.17 after sedation and reached 3.00 ± 0.00 as early as 10 min post-induction, which

persisted up to 90 min. In Group III, scores increased to 0.50 ± 0.22 after sedation and 2.67 ± 0.21 at 10 min post-induction, with complete abolition (3.00 ± 0.00) from 20 min onwards. Within-group comparison revealed a significant ($p < 0.05$) increase in scores from baseline in all groups. Inter-group comparison indicated a significantly earlier abolition of palpebral reflex in Group II followed by Group III and Group I.

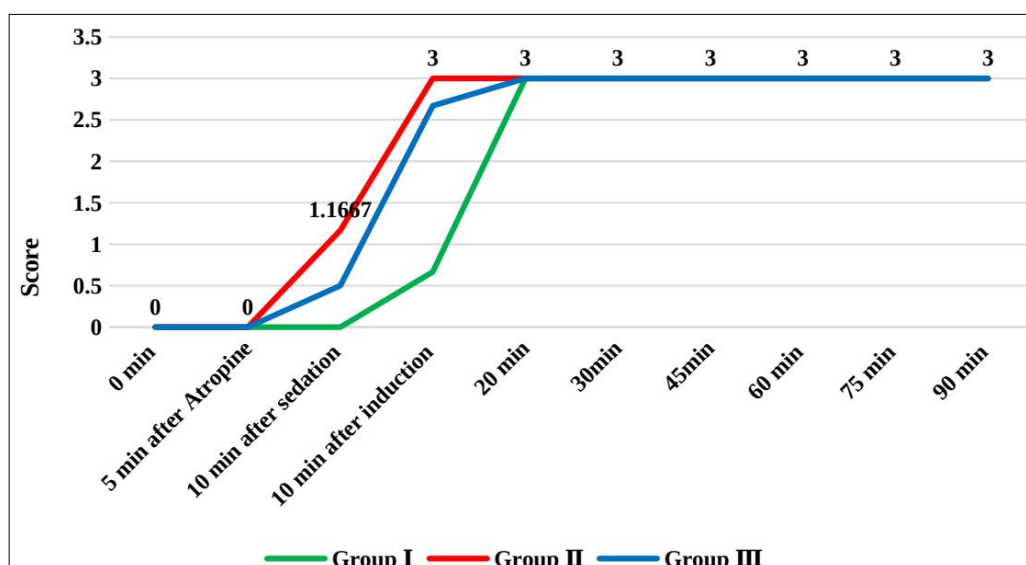


Fig 3: Graph showing the scoring of Palpebral reflex after different treatment groups in canine

3.2.2 Relaxation of jaw

The Mean±SE values of Relaxation of jaw score at various

Intervals in all the three groups are depicted in Table 4 and Fig.4.

Table 4: Mean±S.E. of Relaxation of jaw scoring in different treatment groups in canine

Mean±SE										
Group	0 mins	5 min after Atropine	10min after Sedation	10 mins after induction	20 mins	30 mins	45 mins	60 mins	75 min	90 min
I	0.00 ± 0.00 ^a	0.00±0.00 ^a	0.00± 0.00 ^{Aa}	2.33± 0.21 ^{Ab}	3.00 ± 0.00 ^c	3.00 ± 0.00 ^c	3.00 ± 0.00 ^c	3.00 ± 0.00 ^c	2.67 ± 0.21 ^c	2.50 ± 0.22 ^c
II	00.00 ± 0.00 ^a	0.00±0.00 ^a	1.33± 0.21 ^{Cb}	3.00± 0.00 ^{Bc}	3.00 ± 0.00 ^c	3.00 ± 0.00 ^c	3.00 ± 0.00 ^c	3.00 ± 0.00 ^c	3.00 ± 0.00 ^c	3.00 ± 0.00 ^c
III	0.00 ± 0.00 ^a	0.00±0.00 ^a	0.67± 0.21 ^{Bb}	2.50± 0.22 ^{ABc}	3.00 ± 0.00 ^d	3.00 ± 0.00 ^d	3.00 ± 0.00 ^d	3.00 ± 0.00 ^d	2.83 ± 0.17 ^d	2.67± 0.21 ^{cd}

AB-Values bearing different superscript vary significantly ($p<0.05$) between groups

abcd- Values bearing different superscript vary significantly ($p<0.05$) within groups

0- Not allowing to open the jaws, 1- Resistant to opening of the jaws and was be closed quickly, 2- Less resistance to opening of the jaws and was be closed slowly, 3- No resistance and jaws was remained open. The Mean±S.E. values of relaxation of jaw scores were 0.00±0.00 at 0 min and after atropine administration in all the groups, indicating absence of relaxation. In Group I, scores increased to 2.33±0.21 at 10 min post-induction and reached 3.00±0.00 by 20 min, remaining at this level up to 60 min, followed by a slight decrease at later intervals. In Group II, scores increased significantly to

1.33±0.21 after sedation and reached 3.00±0.00 as early as 10 min postinduction, which persisted up to 90 min. In Group III, scores increased to 0.67±0.21 after sedation and 2.50±0.22 at 10 min post-induction, with complete relaxation (3.00±0.00) from 20 min onwards, followed by a gradual decline at later intervals. Within-group comparison revealed a significant ($p<0.05$) increase in scores from baseline in all groups. Inter-group comparison indicated a significantly earlier and more sustained relaxation of jaw in Group II followed by Group III and Group I.

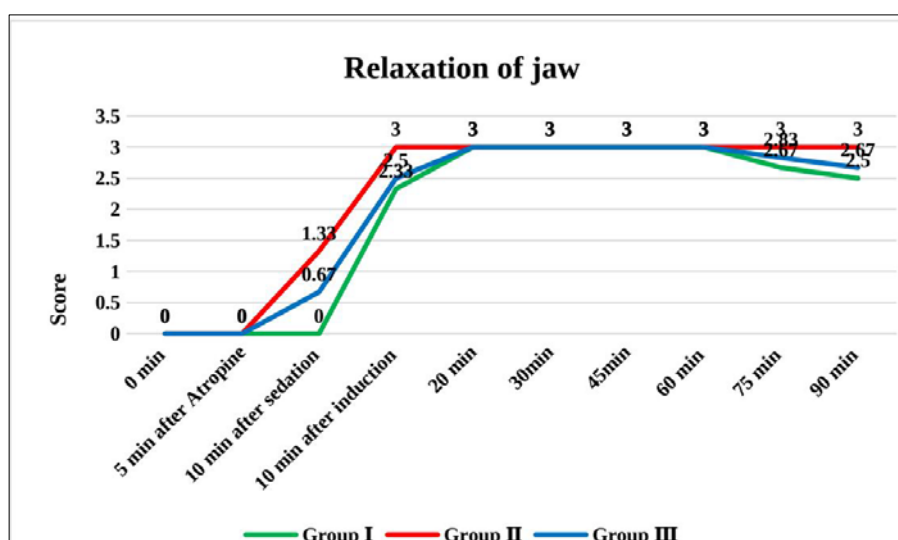


Fig 4: Graph showing the scoring of Relaxation of jaw in different treatment groups in canine

3.2.3 Pedal reflex

The Mean±SE values of Pedal reflex scoring at various

Intervals in all the three groups are depicted in Table 5 and Fig.5

Table 5: Mean±S.E. of Pedal Reflex scoring in different groups in different treatment groups in canine

Mean±SE										
Group	0 mins	5 min after Atropine	10min after Sedation	10 mins after induction	20 mins	30 mins	45 mins	60 mins	75 min	90 min
I	0.00 ± 0.00 ^a	0.00± 0.00 ^a	0.00± 0.00 ^{Aa}	1.33± 0.21 ^{Ab}	3.00 ± 0.00 ^c	3.00 ± 0.00 ^c	3.00 ± 0.00 ^c	3.00 ± 0.00 ^c	3.00 ± 0.00 ^c	3.00 ± 0.00 ^c
II	0.00 ± 0.00 ^a	0.00± 0.00 ^a	1.33± 0.21 ^{Cb}	3.00± 0.00 ^{Bc}	3.00 ± 0.00 ^c	3.00 ± 0.00 ^c	3.00 ± 0.00 ^c	3.00 ± 0.00 ^c	3.00 ± 0.00 ^c	3.00 ± 0.00 ^c
III	0.00 ± 0.00 ^a	0.00± 0.00 ^a	0.67± 0.21 ^{Bb}	2.66± 0.21 ^{Bc}	3.00 ± 0.00 ^d	3.00 ± 0.00 ^d	3.00 ± 0.00 ^d	3.00 ± 0.00 ^d	3.00 ± 0.00 ^d	3.00 ± 0.00 ^d

AB-Values bearing different superscript vary significantly ($p<0.05$) between groups

abcd- Values bearing different superscript vary significantly ($p<0.05$) within groups

0- Strong withdrawal, 1- Slow withdrawal, 2- occasional withdrawal, 3- No withdrawal.

The $\text{Me} \pm \text{S.E.}$ values of pedal reflex scores were 0.00 ± 0.00 at 0 min and after atropine administration in all the groups, indicating intact reflexes. In Group I, scores increased to 1.33 ± 0.21 at 10 min post-induction and reached 3.00 ± 0.00 by 20 min, remaining at this level up to 90 min, indicating complete abolition of reflex. In Group II, scores increased significantly to

1.33 ± 0.21 after sedation and reached 3.00 ± 0.00 as early as 10 min post-induction, which persisted up to 90 min. In Group III, scores increased to 0.67 ± 0.21 after sedation and 2.66 ± 0.21 at 10 min post-induction, with complete abolition (3.00 ± 0.00) from 20 min onwards. Within-group comparison revealed a significant ($p < 0.05$) increase in scores from baseline in all groups. Inter-group comparison indicated a significantly earlier abolition of pedal reflex in Group II followed by Group III and Group I.

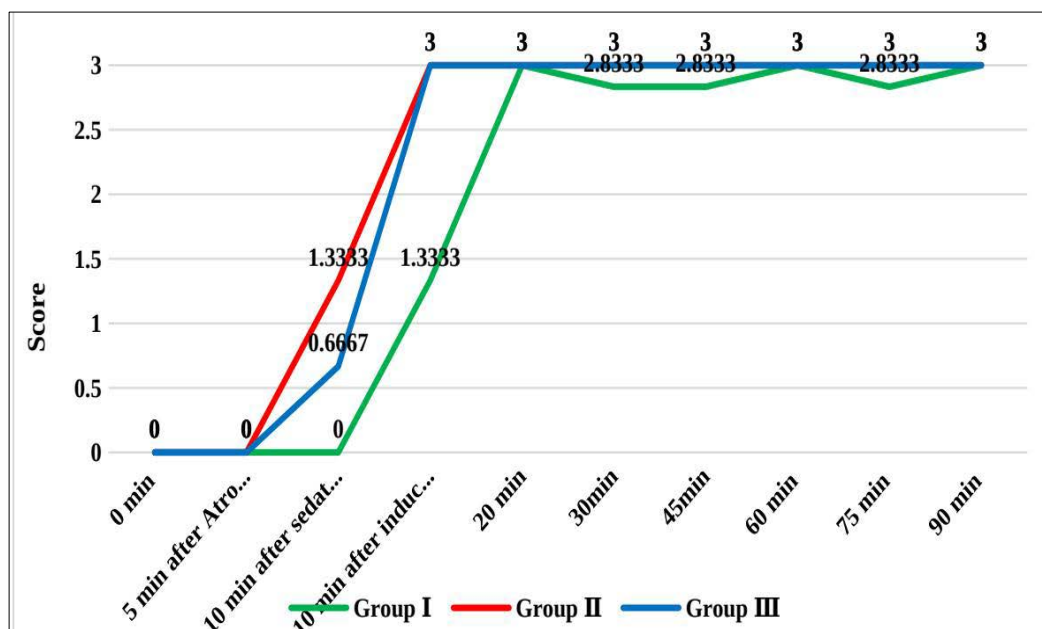


Fig 5: Graph showing the scoring of Pedal reflex in different treatment groups in canine

3.2.4 Analgesia

The $\text{Me} \pm \text{SE}$ values of Analgesia scoring at

Various intervals in all the three groups are depicted in Table 6 and Fig.6.

Table 6: Mean $\pm$ S.E. of Analgesia Score in different treatment groups in canine

Mean $\pm$ SE										
Group	0 mins	5 min after Atropine	10 min after Sedation	10 mins after induction	20 mins	30 mins	45 mins	60 mins	75 min	90 min
I	0.00 ± 0.00^a	0.00 ± 0.00^a	0.00 ± 0.00^{Aa}	1.33 ± 0.21^{Ab}	3.00 ± 0.00^c	3.00 ± 0.00^c	3.00 ± 0.00^c	3.00 ± 0.00^c	3.00 ± 0.00^c	3.00 ± 0.00^c
II	0.00 ± 0.00^a	0.00 ± 0.00^a	1.50 ± 0.22^{Cb}	3.00 ± 0.00^{Bc}	3.00 ± 0.00^c	3.00 ± 0.00^c	3.00 ± 0.00^c	3.00 ± 0.00^c	3.00 ± 0.00^c	3.00 ± 0.00^c
III	0.00 ± 0.00^a	0.00 ± 0.00^a	0.67 ± 0.21^{Bb}	2.67 ± 0.21^{Bc}	3.00 ± 0.00^d	3.00 ± 0.00^d	3.00 ± 0.00^d	3.00 ± 0.00^d	3.00 ± 0.00^d	3.00 ± 0.00^d

ABC-Values bearing different superscript vary significantly ($P < 0.05$) between groups

abcd- Values bearing different superscript vary significantly ($P < 0.05$) within groups

0-Strong reaction to pinching of the inter-digital skin of the foot, 1- Weak responses to pinching of the inter-digital skin of foot, 2-Occasional response to pinching of the inter-digital skin of the foot, 3- No response to pinching of the inter-digital skin of the foot. The Mean $\pm$ S.E. values of analgesia scores were 0.00 ± 0.00 at 0 min and after atropine administration in all the groups, indicating absence of analgesia. In Group I, scores increased to 1.33 ± 0.21 at 10 min post-induction and reached 3.00 ± 0.00 by 20 min, remaining at this level up to 90 min, indicating complete

analgesia. In Group II, scores increased significantly to 1.50 ± 0.22 after sedation and reached 3.00 ± 0.00 as early as 10 min post-induction, which persisted up to 90 min. In Group III, scores increased to 0.67 ± 0.21 after sedation and 2.67 ± 0.21 at 10 min post-induction, with complete analgesia (3.00 ± 0.00) from 20 min onwards. Within-group comparison revealed a significant ($p < 0.05$) increase in scores from baseline in all groups. Inter-group comparison indicated a significantly earlier onset and deeper analgesia in Group II followed by Group III and Group I.

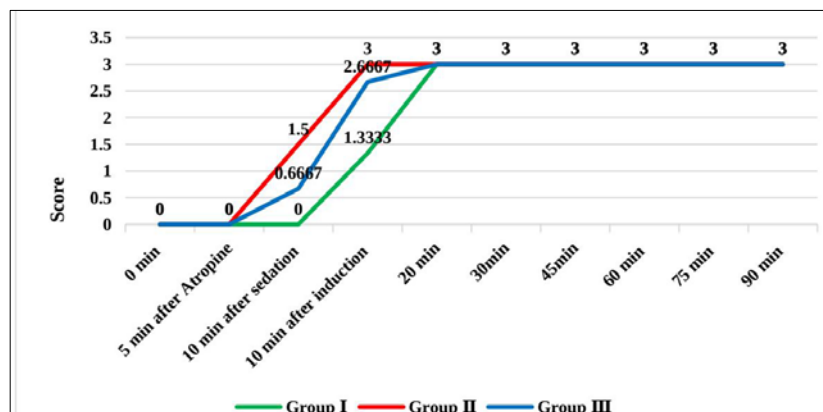


Fig 6: Graph showing the scoring of Analgesia in different treatment groups in canine

3.3 Induction of Anaesthesia

The mean±SE values of Induction of Anaesthesia (seconds) in all the three groups has been summarized in Table 7 and represented in Fig. 7.

Table 7: Mean±S.E. of Induction of anaesthesia in different groups in canine

Group	Induction of anaesthesia (Sec)
Group I	87.3±1.22 ^a
Group II	36.3±2.94 ^c
Group III	67.3±2.18 ^b

Values bearing different superscript vary significantly ($p < 0.05$) between groups

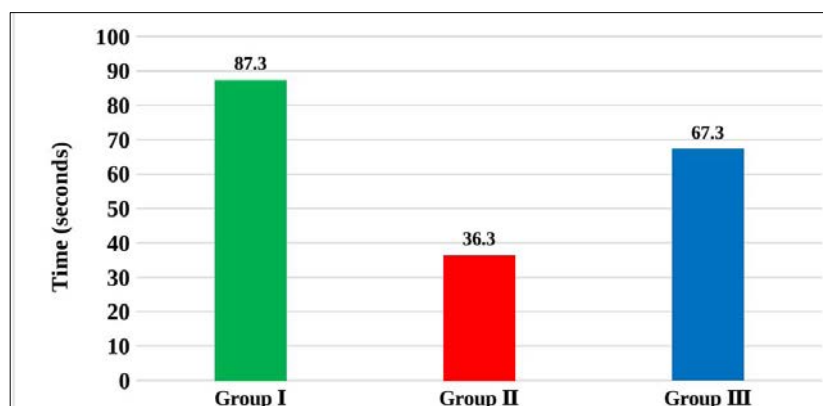


Fig 7: Bar diagram showing the time of Induction of anaesthesia in different treatment groups in canine

3.3.1 Quality of Anaesthetic induction

The mean±SE values of Quality of anaesthetic induction in different experimental groups have been depicted in Table 8.

Table 8: Mean±S.E. of Quality of Anaesthetic induction in different group in canine.

Group	Quality of anaesthetic induction
Group I	2.00±0.00 ^a
Group II	4.00±0.00 ^c
Group III	2.50±0.22 ^b

Values bearing different superscript vary significantly ($P < 0.05$) between group

The mean±SE scores of quality of anaesthetic induction was observed to be in 2.00±0.00, 4.00±0.00 and 2.50±0.22 in Group I, Group II and Group III respectively. Whereas induction was very smooth in Group II, quite smooth in Group III whereas moderately smooth induction was found in Group I. The quality of anaesthetic induction in Group II varied significantly ($p < 0.05$) as compared to groups I and III

In the present study induction of anaesthesia was recorded from the time of injection of Zolazepam-Tiletamine until pedal reflex was completely lost. After administration of Zolazepam-Tiletamine, the induction of anaesthesia was rapid, smooth and free from any untoward reactions like struggling and paddling in all the three groups. The mean anaesthetic induction time was 87.3±1.22, 36.3±2.94 and 67.3±2.18 sec. in groups I, II and III respectively. The induction time in group II was significantly ($p < 0.05$) rapid as compared to group I and group III.

3.4 Quality of Anaesthetic recovery

The mean±SE values of Quality of Anaesthetic Recovery in different experimental groups have been depicted in Table 9.

Table 9: Mean ± S.E. of Quality of Anaesthetic Recovery in different groups in canine

Group	Quality of Anaesthetic recovery
Group I	2.30±0.21 ^a
Group II	3.50±0.22 ^b
Group III	2.33±0.21 ^a

Values bearing different superscript vary significantly ($P < 0.05$) between groups

The mean±SE values of Quality of anaesthetic recovery was observed to be in 2.30±0.21, 3.50±0.22 and 2.33±0.21 in Group I, Group II and Group III respectively. The quality of anaesthetic recovery in Group II varied significantly ($p < 0.05$) compared to groups I and III.

3.4.1 Inhalant anaesthesia recovery Time (min)

The mean $\pm$ SE values of Inhalant anaesthesia recovery time

In different experimental groups have been depicted in Table 10 and Fig. 8.

Table 10: Mean $\pm$ S.E. of Inhalant anaesthesia recovery time (min) in different groups in different treatment groups in canine

Group	Inhalant anaesthesia recovery Time (min)
1	0.72 $\pm$ 0.20 ^a
2	14.17 $\pm$ 0.47 ^c
3	6.70 $\pm$ 0.78 ^b

Values bearing different superscript vary significantly ($P < 0.05$) between groups

The mean Inhalant anaesthesia recovery time in group II was significantly ($p < 0.05$) longer (14.17 $\pm$ 0.47 mins) than in group I

(0.72 $\pm$ 0.20 mins) and group III (6.70 $\pm$ 0.78 mins). A significant difference ($p < 0.05$) was observed between all the three groups.

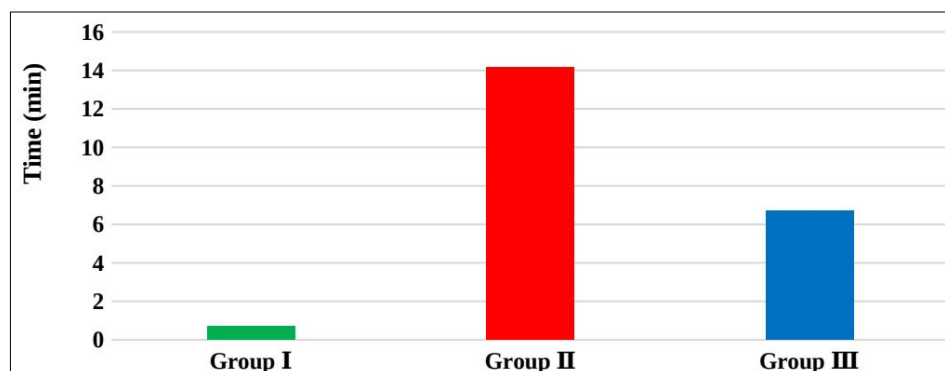


Fig 8: Bar diagram showing the Inhalant anaesthesia recovery time in different treatment groups in canine

3.5 Dose of Induction and Maintenance agent

Induction dose of Tiletamine-Zolazepam undertaken in the present study i.e., @ 3mg/kg b.wt. Was found to be sufficient for good induction and intubation amongst animals of all the three groups. However, evaluating the MAC% of Isoflurane somehow varied amongst the groups. In group I animals, it was found that three out of six animals required Isoflurane concentration 2.5- 3% after 45 minutes of anaesthesia for excellent maintenance. In group II, all the animals were efficiently maintained within 1.5 -2% MAC%. In group III animals, two out of six animals required Isoflurane concentration 2.1-2.5% for efficient maintenance of anaesthesia.

3.6 Extubation time (min)

The mean $\pm$ SE values of extubation time (min) in different

Experimental groups have been depicted in Table 11 and Fig. 9.

Table 11: Mean $\pm$ S.E. of Extubation time (min) in different treatment groups in canine

Group	Extubation time (min)
Group I	6.21 $\pm$ 0.47 ^a
Group II	8.82 $\pm$ 0.30 ^c
Group III	7.60 $\pm$ 0.33 ^b

Values bearing different superscript vary significantly ($P < 0.05$) between groups

The mean extubation time in group II was significantly ($p < 0.05$) longer (8.82 $\pm$ 0.30 mins) than in group I (6.21 $\pm$ 0.47 mins) and group III (7.60 $\pm$ 0.33 mins). A significant difference ($p < 0.05$) was observed between all the three groups.

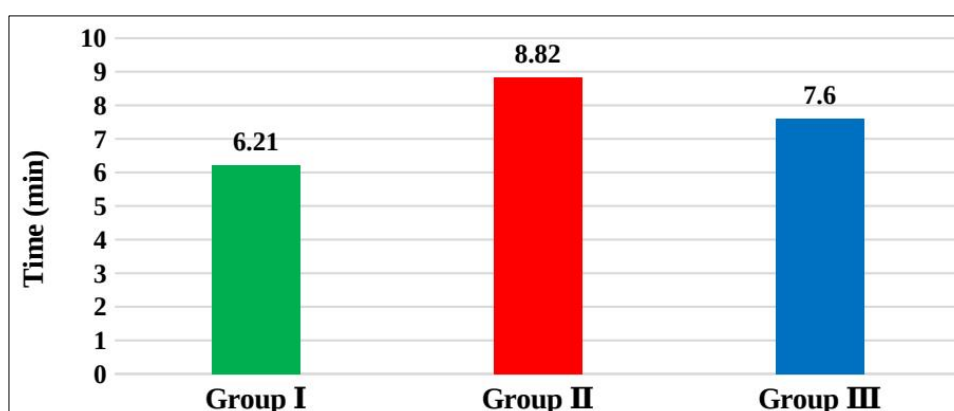


Fig 9: Bar diagram showing the Extubation time in different treatment groups in canine

3.7 Sternal recumbency time (min)

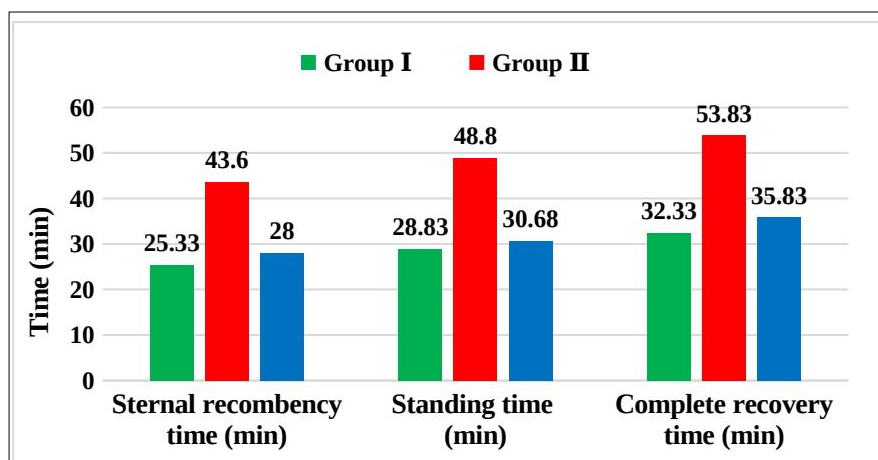
Time required by animals to regain sternal recumbency in all the three groups has been shown in Table 12 and represented in Fig. 10.

The mean $\pm$ SE of time taken by animals to regain sternal recumbency after last supply of isoflurane was calculated.

Table 12: Mean±S.E. of Sternal recumbency time (min) in different treatment groups in canine

Group	Sternal recumbency time (min)
Group I	25.33±2.30 ^a
Group II	43.60±4.07 ^b
Group III	28.00±2.99 ^a

Values bearing different superscript vary significantly ($p<0.05$) among groups. A significantly ($p<0.05$) longer sternal recumbency time was observed in Group II (43.60±4.07 min) followed by group III (28.00±2.99 min) as compared to group I (25.33±2.30 min). The Sternal recumbency time in Group II varies significantly ($p<0.05$) compared to Groups I and III

**Fig 10:** Bar diagram showing the Sternal recumbency time (min), Standing time (min) and complete recovery time (min) in different treatment groups in canine

3.8 Standing time (min)

Time required by animals to stand on its own in all the three

Groups has been shown in Table 13 and represented in Fig. 11

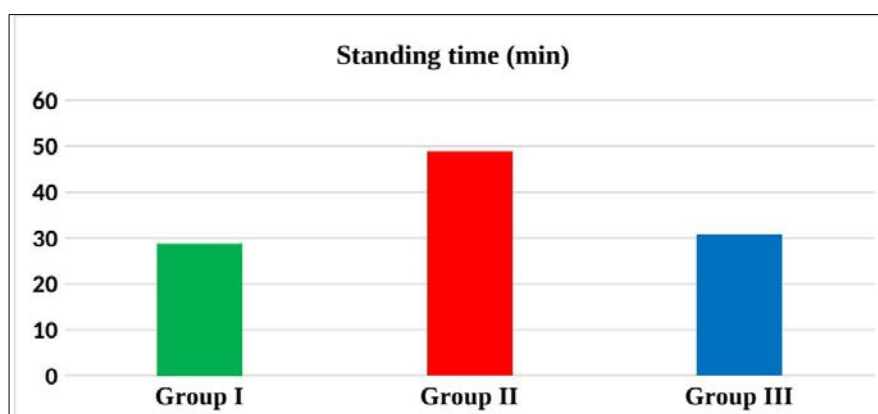
Table 13: Mean±S.E. of standing time (min) in different treatment groups in canine

Group	Standing time (min)
Group I	28.83±1.49 ^a
Group II	48.80±6.40 ^b
Group III	30.68±5.20 ^a

Values bearing different superscript vary significantly ($p<0.05$) among groups

The mean±SE of time taken by animals to stand on their own after last supply of isoflurane was calculated. A significantly ($p<0.05$) longer standing time

was observed in group II (48.80±6.40 mins) followed by group III (30.68±5.20 mins) as compared to group I (28.83±1.49 mins).

**Fig 11:** Bar diagram showing the Standing time (min) in different treatment groups in canine

3.9 Complete recovery time (min)

Time required by animals to stand on its own in all the three

Groups has been shown in Table 14 and represented in Fig. 12.

Table 14: Mean±S.E. of Complete recovery time (min) in different treatment groups in canine

Group	Complete recovery time (min)
Group I	32.33 ± 5.23 ^a
Group II	53.83 ± 3.52 ^b
Group III	35.83 ± 3.70 ^a

Values bearing different superscript vary significantly ($p<0.05$) between groups

The Mean±SE of time taken by animals for complete recovery after last supply of isoflurane was calculated. A significantly ($p<0.05$) longer duration was observed in

group II (53.83 ± 3.52 mins) followed by group III (35.83 ± 3.70 mins) and group I (32.33 ± 5.23 mins)

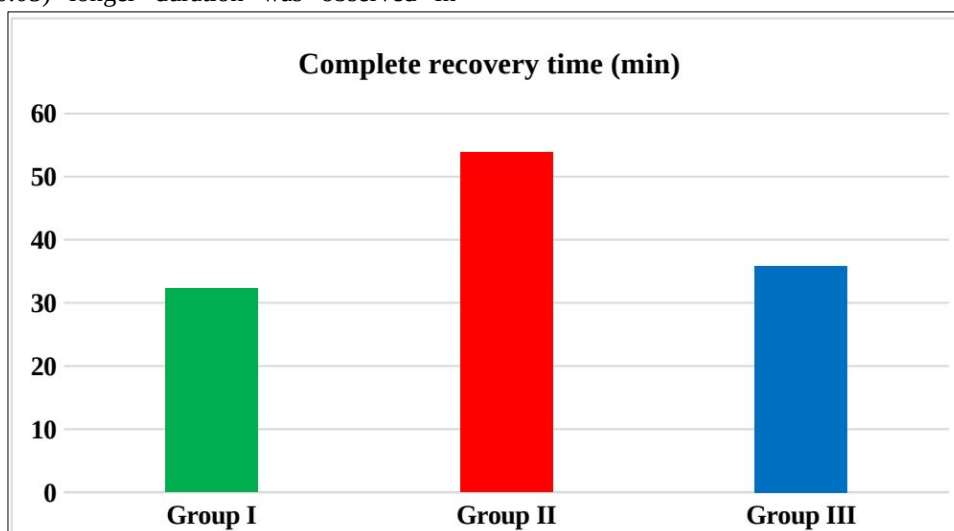


Fig 12: Bar diagram showing the complete recovery time (min) in different treatment groups in canine

3.10 Duration of anaesthesia (min)

Time required by animals to regain the pedal reflex from

Loss of pedal reflex in all the three groups has been shown in Table 15 and Fig.13.

Table 15: Mean±S.E. of Duration of anaesthesia (min) in different treatment groups in canine

Group	Duration of anaesthesia (min)
Group I	90.72 ± 0.20 ^a
Group II	104.17 ± 0.47 ^c
Group III	96.70 ± 0.78 ^b

Values bearing different superscript vary significantly ($P<0.05$) between groups

The Mean±SE of time taken by animals to regain pedal reflex from the loss of pedal reflex was calculated. A significant ($p<0.05$)

longer duration was observed in group II (104.17 ± 0.47) followed by group III (96.70 ± 0.78 mins) and group I (90.72 ± 0.20 mins).

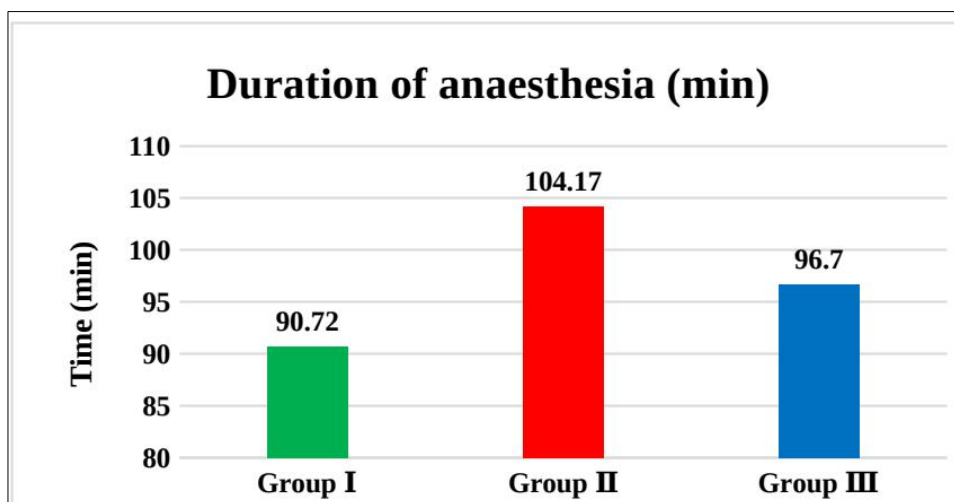


Fig 13: Bar diagram showing the Duration of anaesthesia (min) in different treatment groups in canine

3.10.1 Amount of Isoflurane consumed

Total amount of Isoflurane consumed by animals in all the

Three groups has been shown in Table 16 and Fig. 14.

Table 16: Mean±S.E. of Amount of Isoflurane consumed (ml) in different treatment groups in canine

Group	Amount of isoflurane (ml)
Group I	12.00 ± 0.58 ^c
Group II	5.58 ± 0.42 ^a
Group III	10.00 ± 0.58 ^b

Values bearing different superscript vary significantly ($p<0.05$) between groups

The $\text{Mean} \pm \text{SE}$ of Total amount of isoflurane consumed was calculated in each group. There was

significant ($p < 0.05$) difference in total amount of isoflurane consumed by group I compared to group and group. III II

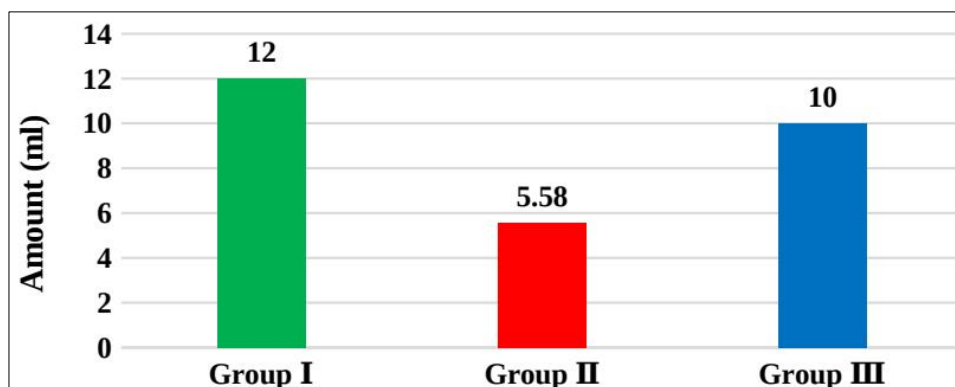


Fig 14: Bar diagram showing the Amount of isoflurane consumed (ml) in different treatment groups in canine

3.11 Physiological parameters

3.11.1 Rectal temperature (°F)

The $\text{mean} \pm \text{SE}$ values of Rectal temperature (°F) at various

Intervals in all the three groups are depicted in Table 22 and represented in Fig. 13.

Table 17: $\text{Mean} \pm \text{S.E.}$ of Rectal temperature (°F) in different treatment groups at various time interval in canine

Group	0 mins	5 min after Atropine	10 min after Sedation	10 mins after induction	20 mins	30 mins	45 mins	60 mins	75 min	90 min
I	101.5 $\pm$ 0.4 ^d _e	101.65 $\pm$ 0.42 _{de}	101.13 $\pm$ 1.5 ^e	100.81 $\pm$ 0.68 ^b _{cd}	100.26 $\pm$ 0.66 ^{ab} _{cd}	99.88 $\pm$ 0.64 ^{ab} _{cd}	99.43 $\pm$ 0.53 ^{Ba} _{bc}	99 $\pm$ 0.47 ^{Bab}	98.81 $\pm$ 0.30 ^{Bab}	98.46 $\pm$ 0.29 _{Ba}
II	100.9 $\pm$ 0.3 _{5g}	100.88 $\pm$ 0.34 _{fg}	100.46 $\pm$ 0.65 _{fg}	100.13 $\pm$ 0.38 ^e _f	99.28 $\pm$ 0.36 ^{de}	98.41 $\pm$ 0.43 ^{cd}	97.36 $\pm$ 0.46 ^{Ab} _c	96.8 $\pm$ 0.52 ^{Aab}	96.48 $\pm$ 0.77 ^{Aa} _b	95.48 $\pm$ 0.76 _{Aa}
III	101.2 $\pm$ 0.3 _{1g}	100.98 $\pm$ 0.26 _g	100.58 $\pm$ 0.26 _{fg}	100.13 $\pm$ 0.17 ^e _f	99.63 $\pm$ 0.21 ^{de}	99.01 $\pm$ 0.22 ^d	98.28 $\pm$ 0.21 ^{AB} _c	97.85 $\pm$ 0.17 ^{AB} _{bc}	97.53 $\pm$ 0.17 ^{AB} _{ab}	97.18 $\pm$ 0.09 _{Ba}

ABC- Values bearing different superscript vary significantly ($p < 0.05$) between groups. abcdefg- Values bearing different superscript vary significantly ($p < 0.05$) within groups

In Group I, rectal temperature showed a non-significant decrease from baseline up to 30 min, followed by a significant ($p < 0.05$) decrease from 45 min to 90 min, reaching 98.46 $\pm$ 0.29°F. In Group II, rectal temperature exhibited a non-significant decrease up to 10 min after sedation, followed by a significant ($p < 0.05$) decline from 10 min post-induction onwards, reaching the lowest value of 95.48 $\pm$ 0.76°F at 90 min. In Group III, a non-significant

decrease was observed up to 10 min after sedation, followed by a significant ($p < 0.05$) decrease from 10 min postinduction to 90 min, reaching 97.18 $\pm$ 0.09°F. Inter-group comparison revealed a significant ($p < 0.05$) difference in Groups II and III compared to Group I from 45 min to 90 min, with Group II showing the maximum decline followed by Group III.

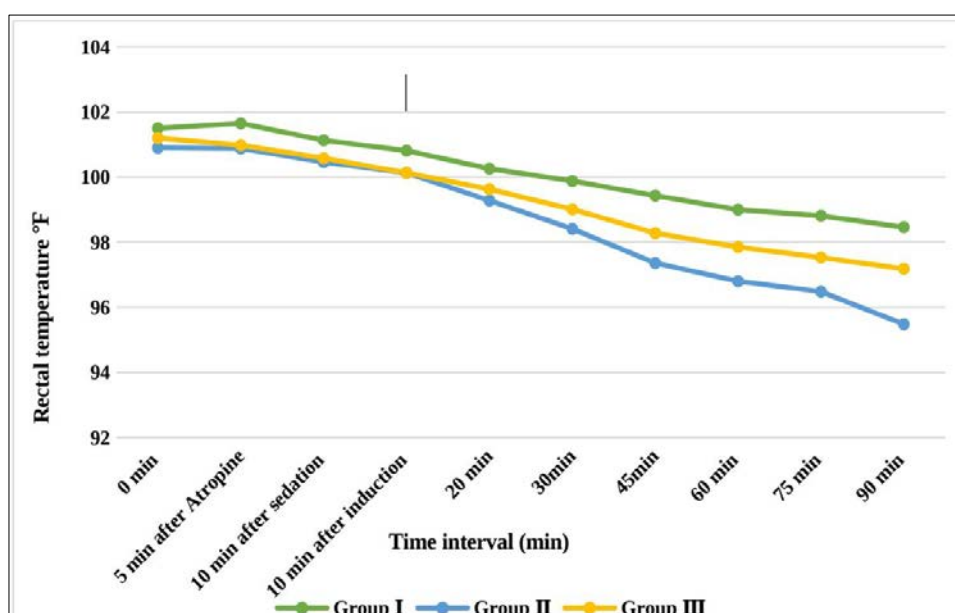


Fig 15: Graph showing the Rectal temperature (°F) at various intervals in different treatment groups in canine

3.11.2 Heart rate (beats/min)

The mean±SE values of Heart Rate (beats/minute) at various

Time intervals in all the three groups are depicted in Table 23 and represented in Fig 14.

Table 18: Mean±S.E. of Heart rate (beats/min) in different treatment groups at various intervals in canine

Group	0 mins	5 min after Atropine	10min after Sedation	10 mins after induction	20 mins	30 mins	45 mins	60 mins	75 min	90 min
I	88.00 ± 1.46 ^{Aa}	95.00 ± 1.03 ^{Ab}	96.67 ± 1.61 ^{Cb}	112.67 ± 2.62 ^{Ccde}	118.67 ± 2.62 ^{Bcde}	122.67 ± 2.62 ^{Be}	120.17 ± 3.37 ^{Bcd}	112.00 ± 2.78 ^{Bc}	103.17 ± 2.69 ^{Bb}	97.17 ± 2.56 ^b
II	87.50 ± 1.93 ^{Ab}	92.50 ± 1.67 ^{AC}	77.17 ± 2.09 ^{Aa}	93.00 ± 1.86 ^{Acde}	98.00 ± 1.65 ^{Acde}	103.00 ± 1.59 ^{Ae}	101.17 ± 1.56 ^{Ae}	100.17 ± 1.54 ^{Ae}	98.00 ± 1.51 ^{Ade}	94.67 ± 1.61 ^{cd}
III	85.33 ± 1.76 ^{Aab}	90.17 ± 1.90 ^{Abac}	83.33 ± 1.99 ^{Ba}	98.33 ± 2.01 ^{Bde}	102.50 ± 2.03 ^{Aef}	106.50 ± 2.03 ^{Af}	103.83 ± 1.90 ^{Aef}	100.33 ± 1.74 ^{Ade}	95.50 ± 1.91 ^{Acde}	92.50 ± 1.84 ^c

ABC - Value bearing different superscript vary significantly ($p < 0.05$) between group. abcdef - Value bearing different superscript vary significantly ($p < 0.05$) within group

In Group I, heart rate showed a significant ($p < 0.05$) increase following atropine administration and continued to increase significantly up to 30 min post-induction, reaching 122.67±2.62 beats/min. Thereafter, a gradual decrease was observed from 45 min to 90 min, returning near baseline values. In Group II, heart rate increased significantly ($p < 0.05$) after atropine administration, followed by a significant decrease after dexmedetomidine administration. Subsequently, heart rate increased significantly post-induction up to 30 min and then showed a gradual decline up to 90 min, approaching

baseline values. In Group III, heart rate increased significantly ($p < 0.05$) after atropine administration, followed by a non-significant decrease after fentanyl citrate administration. Post-induction, heart rate increased significantly up to 30 min and thereafter decreased gradually up to 90 min, returning towards baseline. Inter-group comparison revealed a significant ($p < 0.05$) difference in Group II at multiple intervals (10 min after sedation up to 75 min post-induction) when compared to Groups I and III, with comparatively lower heart rate values observed in Group II.

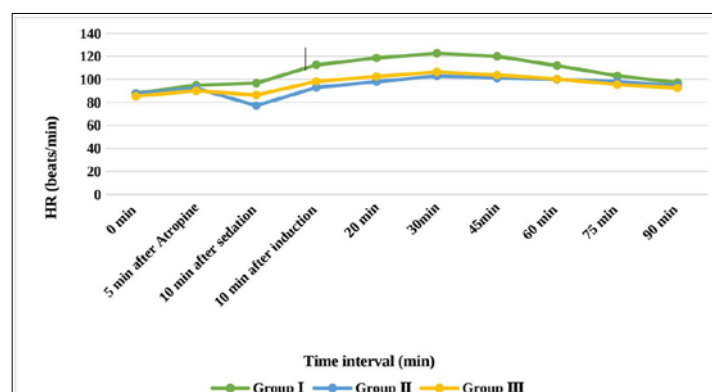


Fig 16: Graph showing the Heart rate (beats/min) at various intervals in different treatment groups in canine

3.11.3 Respiration rate (Breaths/min)

The mean±SE values of Respiration rate (Breaths/minute) at

Various time intervals in all the three groups are depicted in Table 24 and represented in Fig 15.

Table 19: Mean ± S.E. of Respiration rate (per/min) in different treatment groups at various intervals in canine

Group	0 mins	5 min after Atropine	10min after Sedation	10 mins after induction	20 mins	30 mins	45 mins	60 mins	75 min	90 min
I	30.17 ± 1.56 ^d	31.33 ± 1.67 ^d	30.83 ± 1.62 ^{Bd}	26.33 ± 0.92 ^{Cc}	24.00 ± 0.73 ^{Bbc}	22.00 ± 0.77 ^{ab}	19.83 ± 0.70 ^{ab}	19.67 ± 0.61 ^a	19.33 ± 0.42 ^{ab}	21.56 ± 0.44 ^{ab}
II	33.33 ± 4.52 ^b	35.67 ± 0.80 ^b	21.00 ± 0.73 ^{Aa}	18.83 ± 0.79 ^{Aa}	16.68 ± 0.43 ^{Aa}	16.53 ± 0.43 ^a	17.38 ± 0.50 ^a	17.20 ± 0.49 ^a	17.67 ± 2.03 ^a	18.10 ± 1.80 ^a
III	27.33 ± 2.72 ^d	32.83 ± 2.20 ^d	24.33 ± 0.28 ^{Ac}	22.33 ± 0.22 ^{Bc}	21.33 ± 1.33 ^{Ac}	20.67 ± 0.22 ^{ab}	18.33 ± 0.67 ^{ab}	19.67 ± 0.73 ^a	19.83 ± 0.45 ^{ab}	20.67 ± 1.31 ^{ab}

ABC - Value bearing different superscript vary significantly ($p < 0.05$) between group. abcdef - Value bearing different superscript vary significantly ($p < 0.05$) within group

The Mean±S. E. values of respiration rate (breaths/min) showed a declining trend following sedation and induction in all the groups. In Group I, respiration rate decreased significantly ($p < 0.05$) from 30.17±1.56 at baseline to 21.56±0.44 at 90 min. In Group II, a significant ($p < 0.05$) decrease was observed from 33.33±4.52 to 21.00±0.73 after sedation, further declining up to 16.53±0.43 and remaining below baseline up to 90 min. In

Group III, respiration rate decreased significantly ($p < 0.05$) from 27.33±2.72 to 24.33±0.28 after sedation and continued to decline up to 20.67±1.31 at 90 min. Within-group comparison revealed significant ($p < 0.05$) reduction in respiration rate over time in all groups. Inter-group comparison indicated significantly lower respiration rates in Group II at early intervals followed by Group III and Group I.

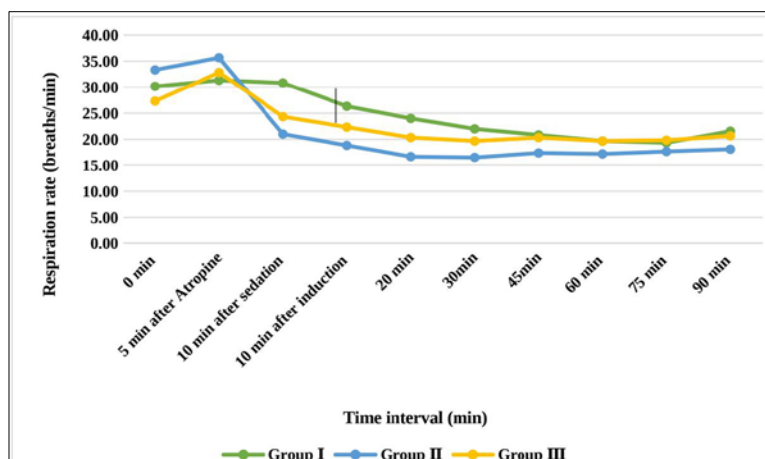


Fig 17: Graph showing the Respiration rate (breaths/min) at various intervals in different treatment groups in canine

3.12 Haemodynamic Parameters

3.12.1 Systolic blood pressure (mmHg)

The mean $\pm$ SE values of Systolic blood pressure (mmHg) at

Various time interval in all the three groups are depicted in Table 25 and represented in Fig 16.

Table 20: Mean $\pm$ S.E. of Systolic blood pressure (mmHg) in different treatment groups at various intervals in canine

Group	0 mins	5 min after Atropine	10min after Sedation	10 mins after induction	20 mins	30 mins	45 mins	60 mins	75 min	90 min
I	139.67 $\pm$ 5.52 ^a	140.17 $\pm$ 3.51 ^a	135.17 $\pm$ 3.04 ^{Aa}	135.83 $\pm$ 7.90 ^a	135.17 $\pm$ 8.63 ^a	132.67 $\pm$ 8.46 ^{Aa}	130.50 $\pm$ 8.48 ^{Aa}	128.33 $\pm$ 8.50 ^{Aa}	130.50 $\pm$ 8.48 ^a	135.17 $\pm$ 8.28 ^a
II	132.67 $\pm$ 2.36 ^{ab}	138.67 $\pm$ 2.36 ^{abc}	151.00 $\pm$ 2.48 ^{Bd}	146.17 $\pm$ 5.00 ^{cd}	146.83 $\pm$ 3.49 ^{cd}	142.00 $\pm$ 2.24 ^{Bbcd}	140.67 $\pm$ 3.89 ^{Bbc}	139.17 $\pm$ 3.04 ^{Babc}	136.00 $\pm$ 2.21 ^{ab}	130.17 $\pm$ 2.20 ^a
III	136.67 $\pm$ 2.25 ^{ab}	140.83 $\pm$ 2.06 ^{ab}	146.00 $\pm$ 3.43 ^{Bb}	143.50 $\pm$ 3.46 ^{ab}	141.17 $\pm$ 3.32 ^{ab}	140.67 $\pm$ 6.64 ^{Bab}	140.00 $\pm$ 7.25 ^{Bab}	133.83 $\pm$ 5.19 ^{Ba}	135.33 $\pm$ 5.25 ^a	136.83 $\pm$ 5.33 ^{ab}

ABC - Value bearing different superscript vary significantly ($p < 0.05$) between group. abc - Value bearing different superscript vary significantly ($p < 0.05$) within group

In animals of Group I, systolic blood pressure showed a non-significant increase from baseline (0 min) to after premedication (139.67 $\pm$ 5.52 to 140.17 $\pm$ 3.51). It then decreased nonsignificantly ($p > 0.05$) at 60 minutes (128.33 $\pm$ 8.50) before rising non-significantly again to (135.17 $\pm$ 8.28) at 90 minutes when compared to the baseline values. In animals of Group II, systolic blood pressure increased significantly $\leq$ ft ($p < 0.05$) from baseline (0 min) to 10 min. after sedation (132.67 $\pm$ 2.36 to 151.00 $\pm$ 2.48). Following ZT induction, it decreased significantly ($p < 0.05$) over the next 20 minutes and non-significantly

from 30 min. to 90 min. reaching to 130.17 $\pm$ 2.20mmHg when compared to the baseline values. In animals of Group I, I, I systolic blood pressure increased non-significantly ($p > 0.05$) from baseline (0 min) to 10 min after sedation (136.67 $\pm$ 2.25 to 146.00 $\pm$ 3.43). Following ZT induction, it decreased nonsignificantly ($p > 0.05$) over the next 90 minutes, reaching 136.83 $\pm$ 5.33. compared to baseline values. Comparison between the groups showed significant ($p < 0.05$) difference in Group II (at 10 min after sedation, 20 min, 30 min and 60 min post induction) when compared to group I and non-significant difference with group III

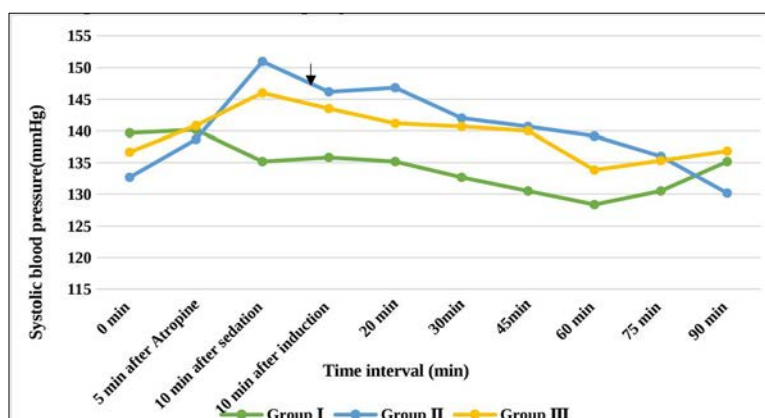


Fig 18: Graph showing the Systolic blood pressure (mmHg) at various intervals in different treatment groups in canine

3.12.2 Diastolic blood pressure (mmHg)

The mean $\pm$ SE values of Diastolic blood pressure (mmHg) at

Various time interval in all the three groups are depicted in Table 26 and represented in Fig 17.

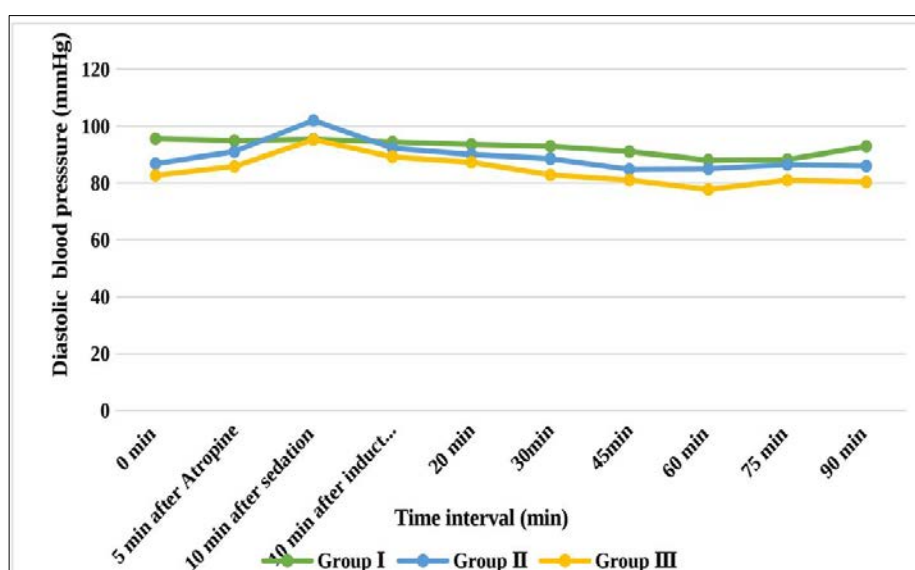
Table 21: Mean $\pm$ S.E. of Diastolic Blood Pressure (mmHg) in different treatment groups in canine

Group	0 mins	5 min after Atropine	10min after Sedation	10 mins after induction	20 mins	30 mins	45 mins	60 mins	75 min	90 min
I	95.50 $\pm$ 5.37 ^{Ba}	94.83 $\pm$ 5.27 ^a	95.33 $\pm$ 4.38 ^a	94.33 $\pm$ 5.81 ^a	93.50 $\pm$ 8.50 ^a	92.83 $\pm$ 8.03 ^{Ba}	91.00 $\pm$ 3.37 ^a	88.00 $\pm$ 3.29 ^a	88.17 $\pm$ 2.20 ^{Ba}	92.83 $\pm$ 3.66 ^{Ba}
II	86.83 $\pm$ 1.47 ^{ABa}	91.00 $\pm$ 1.53 ^a	102.00 $\pm$ 3.50 ^b	92.17 $\pm$ 1.42 ^a	90.00 $\pm$ 1.44 ^a	88.50 $\pm$ 2.00 ^{ABa}	84.83 $\pm$ 2.40 ^a	85.00 $\pm$ 3.94 ^a	86.50 $\pm$ 1.45 ^{ABa}	86.00 $\pm$ 1.57 ^{ABa}
III	82.67 $\pm$ 2.12 ^{Aab}	85.83 $\pm$ 1.05 ^{ab}	95.17 $\pm$ 3.98 ^c	89.17 $\pm$ 3.36 ^{bc}	87.33 $\pm$ 3.28 ^{bc}	82.83 $\pm$ 2.41 ^{Aab}	81.00 $\pm$ 4.09 ^{ab}	77.67 $\pm$ 1.50 ^a	81.00 $\pm$ 1.37 ^{Aab}	80.33 $\pm$ 2.04 ^{Aab}

ABC - Value bearing different superscript vary significantly ($p < 0.05$) between group. abc - Value bearing different superscript vary significantly ($p < 0.05$) within group

The Mean $\pm$ S. E. Values of diastolic blood pressure (mmHg) showed mild variations across time intervals in all the groups. In Group I, values showed a non-significant change from baseline (95.50 $\pm$ 5.37) and gradually decreased to 92.83 $\pm$ 3.66 at 90 min. In Group II, diastolic pressure increased significantly ($p < 0.05$) to 102.00 $\pm$ 3.50 after sedation, followed by a nonsignificant decline up to 86.00 $\pm$ 1.57 at 90 min. In Group III,

values increased significantly ($p < 0.05$) to 95.17 $\pm$ 3.98 after sedation and then decreased non-significantly to 80.33 $\pm$ 2.04 at 90 min. Within-group comparison revealed significant ($p < 0.05$) changes mainly after sedation in Groups II and III, while inter-group comparison indicated significant differences ($p < 0.05$) in Group II at certain intervals compared to Groups I and III.

**Fig 19:** Graph showing the Diastolic blood pressure (mmHg) at various intervals in different treatment groups in canine

3.12.3 Mean blood pressure (mmHg)

The Mean $\pm$ SE values of Mean blood pressure (mmHg) at

Various time interval in all the three groups are depicted in Table 27 and represented in Fig 18.

Table 22: Mean $\pm$ S.E. of Mean Blood Pressure (mmHg) in different treatment groups in canine

Group	0 mins	5 min after Atropine	10min after Sedation	10 mins after induction	20 mins	30 mins	45 mins	60 mins	75 min	90 min
I	98.50 $\pm$ 2.38 ^{ba}	104.50 $\pm$ 1.38 ^{cA}	105.33 $\pm$ 1.31 ^{bcA}	93.67 $\pm$ 1.48 ^{bA}	92.17 $\pm$ 1.47 ^{abA}	91.17 $\pm$ 1.47 ^{abA}	90.00 $\pm$ 1.48 ^{abA}	89.00 $\pm$ 1.48 ^{aA}	87.83 $\pm$ 1.54 ^{aA}	87.50 $\pm$ 1.65 ^{aA}
II	107.33 $\pm$ 2.55 ^{Bde}	109.00 $\pm$ 1.53 ^{Bde}	119.50 $\pm$ 1.26 ^{Cf}	111.17 $\pm$ 1.42 ^{Be}	107.50 $\pm$ 1.26 ^{de}	106.50 $\pm$ 1.18 ^{Bcd}	102.83 $\pm$ 0.60 ^{bc}	103.00 $\pm$ 0.97 ^{Bbc}	102.33 $\pm$ 0.88 ^{Bb}	98.33 $\pm$ 0.80 ^{Aa}
III	99.50 $\pm$ 3.09 ^{Aab}	103.00 $\pm$ 1.32 ^{Aab}	112.33 $\pm$ 1.20 ^{Bb}	111.00 $\pm$ 1.53 ^{Ab}	107.83 $\pm$ 0.95 ^b	103.00 $\pm$ 1.06 ^{Aab}	91.50 $\pm$ 14.72 ^a	96.67 $\pm$ 0.49 ^{Aab}	99.50 $\pm$ 0.76 ^{Aab}	102.00 $\pm$ 0.89 ^{Bab}

ABC - Value bearing different superscript vary significantly ($p < 0.05$) between group. abcdef - Value bearing different superscript vary significantly ($p < 0.05$) within group

The Mean $\pm$ S.E. values of mean blood pressure (mmHg) showed an initial increase following atropine and sedation, followed by a gradual decline during maintenance in all the groups. In Group I, mean blood pressure increased up to 105.33 $\pm$ 1.31 and then decreased significantly ($p < 0.05$) from 93.67 $\pm$ 1.48 at 10 min post-induction to 87.50 $\pm$ 1.65 at 90 min. In Group II, values increased significantly ($p < 0.05$) to 119.50 $\pm$ 1.26 after sedation,

followed by a gradual decline up to 98.33 $\pm$ 0.80 at 90 min. In Group III, a non-significant increase was observed up to 112.33 $\pm$ 1.20 after sedation, followed by a gradual decline with slight rise at 90 min. Within-group comparison revealed significant ($p < 0.05$) changes over time, while inter-group comparison indicated significantly higher mean blood pressure values in Group II at most intervals compared to Groups I and III.

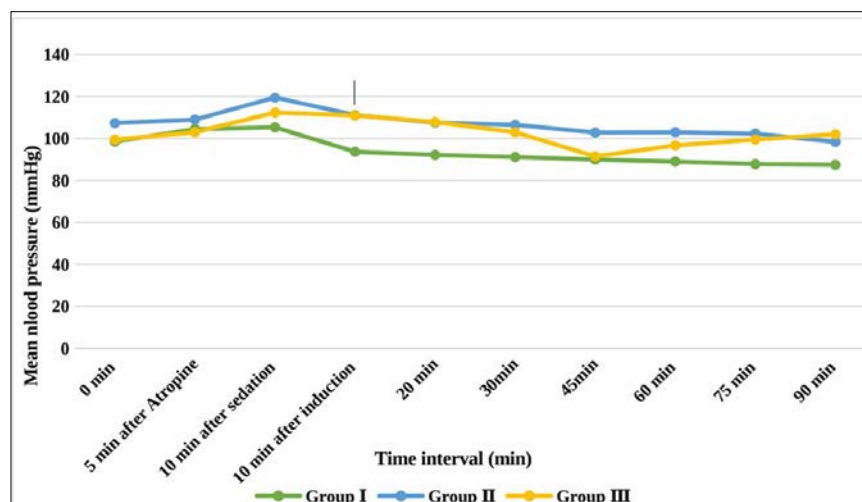


Fig 20: Graph showing the Mean blood pressure (mmHg) at various intervals in different treatment groups in canine

3.13 Capillary Refill Time (seconds)

Capillary refill time remained unchanged amongst all the groups at different time intervals despite using different preanaesthetic combinations and it remained stable between 1-2 seconds throughout the anaesthesia. Capillary refill time shown in present study did not show any significant ($P < 0.05$) change throughout the study period.

4. Discussion

4.1 Assessment of anaesthesia

4.1.1 Onset of sedation

In the present study, animals of Group II receiving dexmedetomidine exhibited an earlier and more profound onset of sedation compared to other groups. Atropine alone did not produce any sedative effect, whereas fentanyl citrate induced mild to moderate sedation within approximately 7-8 minutes. Dexmedetomidine produced marked sedation characterized by ataxia, muscle relaxation, recumbency, head lowering and eyelid closure, thereby facilitating easier handling of animals. These findings are consistent with previous reports describing similar sedative effects of α_2 -adrenergic agonists in dogs (Kuusela *et al.*, 2001, 2003) [46]. The onset of sedation observed in this study aligns with earlier findings of 5-15 minutes following dexmedetomidine administration (Granhölm *et al.*, 2007) [16], while Ahmad *et al.* (2013) [1] reported a mean onset time of 4.5 ± 0.96 minutes. The higher sedative potency of dexmedetomidine compared to medetomidine has also been well documented (Kuusela *et al.*, 2000) [45]. In contrast, fentanyl citrate produced only mild sedation, supporting previous observations that opioid analgesics induce moderate central nervous system depression in dogs (Branson *et al.*, 2001) [5], with onset of action reported within 4-7 minutes (Hall *et al.*, 2001a) [19].

4.1.2 Sedation score

In the present study, animals of Group I receiving atropine sulphate did not exhibit any sedation, whereas those in Group II administered dexmedetomidine showed profound sedation. In contrast, Group III animals receiving fentanyl citrate exhibited only mild sedation. These findings are in agreement with Dent *et al.* (2019) [11], who reported a sedation score of 3 ± 0.8 for dexmedetomidine irrespective of the route of administration. Similar observations were reported by Singh *et al.* (2013a), who documented a

sedation score of 3 ± 0.09 with dexmedetomidine alone or in combination with fentanyl citrate. Kuusela *et al.* (2001) [46] also reported deep sedation at higher doses of medetomidine/dexmedetomidine, while lower doses produced only mild sedative effects. In the present study, fentanyl citrate induced mild sedation (score 0-1), which is consistent with Hamad *et al.* (2022) [20]. Additionally, moderate salivation, nasal secretions and panting were observed in some animals, with onset of panting around 7 minutes post-administration, corroborating the findings of Hughes and Nolan (1999) [25].

4.2 Record of various reflexes

4.2.1 Palpebral reflex

In the present study, intact and strong palpebral reflex was observed in Groups I and III following premedication with atropine sulphate and atropine-fentanyl, respectively, whereas Group II (atropine-dexmedetomidine) showed a weak and sluggish reflex. Following induction with zolazepam-tiletamine, the palpebral reflex became markedly reduced but was not completely abolished, while complete abolition was observed during maintenance with isoflurane in all groups. These findings are consistent with Lin *et al.* (1993) [53] and Ko *et al.* (1998) [37], who reported variable palpebral reflex responses following TZ administration. Dexmedetomidine has been reported to cause a moderate to marked reduction in palpebral reflex, with eyelids relaxed but reflex remaining sluggish (Sabbe *et al.*, 1994; Kuusela *et al.*, 2001) [46, 65]. Greater suppression of the reflex with drug combinations compared to dexmedetomidine alone has also been documented (Ahmad *et al.*, 2013) [1], indicating synergistic effects. Similar observations of mild depression during sedation and complete abolition after induction have been reported by Khattri *et al.* (2013) [33] and Carroll *et al.* (1998) [8].

4.2.2 Relaxation of Jaw

In the present study, animals of Groups I and III did not allow opening of the jaw following premedication with atropine sulphate and atropine-fentanyl, respectively, whereas Group II (atropine-dexmedetomidine) showed mild resistance with quick closure of the jaw. Following induction and maintenance, excellent jaw relaxation was observed in all groups. Tiletamine-zolazepam administered alone is known to provide inadequate muscle relaxation and

may cause muscle rigidity and spontaneous movements (Dugassa *et al.*, 2018; Gomez *et al.*, 2013) ^[13]; however, such effects were not evident in the present study, likely due to the muscle relaxant effect of isoflurane masking these responses. Previous studies have also reported inadequate muscle relaxation with TZ alone (Lin *et al.*, 1993) ^[53], whereas improved relaxation has been observed with the use of α_2 -agonists (Sinclair, 2003) ^[69]. The findings of good to excellent muscle relaxation in the present study are in agreement with earlier reports using similar drug combinations (Jadon *et al.*, 1995; Ksenija *et al.*, 2012; Santosh *et al.*, 2013; Khattri *et al.*, 2013) ^[27, 33, 39, 67], suggesting a synergistic effect of the anaesthetic agents.

4.2.3 Pedal reflex

In the present study, animals of Groups I and III exhibited intact and strong pedal reflex following premedication with atropine sulphate and atropine-fentanyl, respectively, whereas Group II (atropine-dexmedetomidine) showed a weak and sluggish pedal reflex. Complete abolition of pedal reflex was achieved after induction with zolazepam-tiletamine and during maintenance with isoflurane in all groups. However, the reflex returned earlier in groups receiving TZ alone, indicating comparatively shorter duration of analgesia. These findings are in agreement with Wilson *et al.* (1993) ^[77], who reported inadequate analgesia with TZ alone, which can be enhanced by α_2 -agonists due to synergistic action at central and spinal receptors. Dexmedetomidine provides analgesia through spinal and supraspinal mechanisms (Sinclair, 2003; Murrell and Hellebrekers, 2005) ^[56, 69], resulting in prolonged suppression of pedal reflex. Similar prolonged abolition of pedal reflex with drug combinations has been reported by Chen *et al.* (2005) ^[10] and Ahmad *et al.* (2013) ^[1]. In contrast, fentanyl citrate produced only partial analgesia, as evidenced by slow withdrawal response, which may be attributed to its opioid-mediated analgesic effect (Wagner, 2002) ^[76].

4.2.4 Analgesia

In the present study, Group II animals receiving dexmedetomidine-tiletamine-zolazepam exhibited superior quality and longer duration of analgesia compared to Groups I and III. This prolonged analgesic effect may be attributed to dexmedetomidine, which acts primarily at the spinal level by inhibiting nociceptive transmission in the dorsal horn (Kuusela *et al.*, 2000; Talukdar and Hikas, 2009) ^[45]. Similar findings of enhanced and prolonged analgesia with α_2 -agonist combinations have been reported by Chen *et al.* (2005) ^[10] and Ko *et al.* (2007) ^[33]. Previous studies have also demonstrated moderate to prolonged analgesia with tiletamine-zolazepam combinations (Won *et al.*, 2010; Ksenija *et al.*, 2012) ^[39, 78], with further enhancement when combined with other agents (Hampton *et al.*, 2019; Ratnu *et al.*, 2021; Koli *et al.*, 2021) ^[21, 38, 63]. In contrast, fentanyl citrate in Group III produced only mild analgesia (score 0-1), possibly due to the lower dose used, although its analgesic effect persisted for approximately 45 minutes, in agreement with Hall *et al.* (2001) ^[19]. While fentanyl is a potent μ -opioid agonist, peak analgesic effects may vary depending on dose and timing (Stoelting and Hillier, 1999; Gutstein *et al.*, 2001; Hamad *et al.*, 2022) ^[17, 20, 71]. Overall, dexmedetomidine and fentanyl contributed to improved analgesia during induction and maintenance with tiletamine-

zolazepam and isoflurane.

4.3 Induction of Anaesthesia

In the present study, Group II exhibited a significantly $\leq$ ft ($p < 0.05$ right) shorter induction time compared to Groups I and III, which may be attributed to the sedative effects of dexmedetomidine facilitating rapid induction. Tiletamine-zolazepam administered intravenously is known to induce anaesthesia within 60-90 seconds (Kastner, 2007; Lin, 1991) ^[30, 52], with induction times decreasing at higher doses (11.2 ± 3.2 to 16.0 ± 4.8 seconds) (Hellyer *et al.*, 1989) ^[24]. Similar rapid induction has been reported with dexmedetomidine-based protocols, including 57.33 ± 0.99 seconds (Arunkumar *et al.*, 2017) ^[3] and 33.10 ± 2.59 seconds (Koli *et al.*, 2021) ^[38], supporting the present findings. These results are further corroborated by studies of Rafee *et al.* (2015a), Hafez *et al.* (2017) ^[18], Karasu *et al.* (2018) ^[29] and Ratnu *et al.* (2021) ^[63], indicating that α_2 -agonists significantly enhance the efficiency of anaesthetic induction.

4.3.1 Quality of Anaesthetic induction

In Group II, induction quality was excellent, with most animals allowing smooth endotracheal intubation on the first attempt. This may be attributed to effective preanaesthetic sedation with atropine and dexmedetomidine, resulting in reduced salivation and adequate muscle relaxation. In contrast, Groups I and III showed comparatively poorer induction quality, with persistence of pharyngeal reflexes and requirement of multiple intubation attempts, likely due to insufficient analgesia leading to coughing, excitement and movement during induction. These findings are in agreement with Hafez *et al.* (2017) ^[18] and Hampton *et al.* (2019) ^[21], who reported similar variations in induction quality and intubation ease under comparable protocols. Post-induction apnoea and transient respiratory depression were observed following rapid intravenous administration of the TZ combination, which resolved spontaneously within a few minutes. Similar observations have been reported by Savvas *et al.* (2005) ^[68] and Hampton *et al.* (2019).

4.4 Quality of Anaesthetic recovery

Recovery quality was smooth in the majority of animals, with Group II showing comparatively better recovery than Groups I and III. In Groups I and III, transient emergence delirium was observed, characterized by hyperactive motor activity such as paddling, flailing, vocalization and excitation during the immediate post-anaesthetic period. This rough recovery may be attributed to the longer duration of action of tiletamine compared to zolazepam, leading to residual dissociative effects such as muscle rigidity, sympathetic stimulation and delirium (Landry and Maza, 2020) ^[49]. The smoother recovery observed in Group II could be due to the sedative and calming effects of dexmedetomidine. Isoflurane may further improve recovery quality by attenuating the excitatory effects of tiletamine during prolonged anaesthesia. These findings are in agreement with Pablo and Bailey (1999) ^[58] and Hampton *et al.* (2019a).

4.4.1 Inhalant anaesthesia recovery time

Inhalant anaesthesia recovery time, assessed by reappearance of pedal reflex, was shortest in Group I (TZ-isoflurane alone) and longest in the dexmedetomidine

premedicated group, followed by the fentanyl premedicated group. The prolonged recovery in the dexmedetomidine group may be attributed to its potent sedative and CNS depressant effects, which delay return of reflexes. These findings are consistent with previous reports by Nam *et al.* (2013) [57] and Hampton *et al.* (2019) [21]. Ko *et al.* (1998) [37] also noted that recovery time decreases when lower doses of TZ are combined with sedatives, whereas Santosh *et al.* (2012) [66] reported prolonged recovery with increasing doses of dexmedetomidine.

4.5 Extubation time (min)

In the present study, all *dogs* were extubated within 10 minutes after discontinuation of anaesthesia. Extubation time was comparatively longer in the dexmedetomidine premedicated group (Group II) than in the fentanyl group (Group III), likely due to the prolonged sedative effects of dexmedetomidine. These findings are in agreement with Di Franco *et al.* (2024) [12] and Jarosinski *et al.* (2021) [28]. Group III animals showed shorter extubation time compared to Group I, which may be attributed to the additive effects of opioids in reducing anaesthetic requirements and facilitating faster recovery (Hunt *et al.*, 2014) [26]. Prolonged extubation with higher doses of dexmedetomidine has also been reported by Kuusela *et al.* (2001) [46]. Variations in extubation time across studies may be due to differences in anaesthetic protocols and agents used, as also observed by Gomez *et al.* (2006) and Hampton *et al.* (2019) [21].

4.6 Sternal recumbency time (min)

Preanaesthetic administration of dexmedetomidine significantly prolonged sternal recumbency time (SRT) in Group II compared to Groups I and III. This may be attributed to the enhanced sedative and synergistic effects of dexmedetomidine with tiletamine-zolazepam, leading to delayed recovery and redistribution of drugs. These findings are in agreement with Kwon *et al.* (2003) [48] and Hellyer *et al.* (1989) [24], who reported prolonged SRT with α_2 -agonist combinations and higher doses of TZ, respectively. Santosh *et al.* (2012) [66] also observed increased SRT with higher doses of dexmedetomidine. In contrast, shorter SRT reported by Pereira *et al.* (2019) [60] may be due to lower drug dosages. Overall, dexmedetomidine significantly prolongs SRT due to its potent sedative effects.

4.7 Standing time (min)

In the present study, animals in Groups I and III required considerable effort to attain standing, often showing excitement, paddling and flailing, with multiple attempts needed to achieve sternal recumbency and standing. These findings are in agreement with Hampton *et al.* (2019a). In contrast, Group II animals exhibited delayed but smoother standing without such excitatory signs, likely due to the sedative effects of dexmedetomidine. However, standing time was prolonged in this group, consistent with reports by Singh *et al.* (2013a) and Santosh *et al.* (2013) [67], indicating that α_2 -agonists such as dexmedetomidine increase recovery and standing time.

4.8 Complete recovery time (min)

Complete recovery time (CRT) was significantly lower when tiletamine-zolazepam (TZ) was administered alone. However, TZ at doses of 5-10 mg/kg IV may produce inadequate anaesthesia with prolonged and sometimes rough

recovery (Gomez *et al.*, 2013). CRT was comparatively higher in animals premedicated with dexmedetomidine than with fentanyl citrate, likely due to the prolonged sedative and tranquilizing effects of mathtt α_2 - ag on is ts. These findings are consistent with Kwon *et al.* (2003) [48], who reported increased recovery times with xylazine and medetomidine combinations compared to TZ alone. Recovery was smoother in mathtt α_2 - ag on is t groups due to their sustained tranquilizing effects, which aligns with the present observations using dexmedetomidine. In contrast, tiletamine-zolazepam alone may result in less smooth recovery, possibly due to the longer half-life of tiletamine relative to zolazepam (Chen *et al.*, 2005) [10].

4.9 Duration of anaesthesia (min)

Duration of anaesthesia was comparatively shorter when tiletamine-zolazepam (TZ) was used alone or in combination with fentanyl citrate, whereas it was highest in the dexmedetomidine-TZ- isoflurane group. The shorter duration with TZ alone may be due to its limited anaesthetic effect at standard doses, although increasing the dose can prolong surgical anaesthesia (Hellyer *et al.*, 1989) [24]. The prolonged duration observed with dexmedetomidine may be attributed to its potent sedative, analgesic and muscle relaxant effects, enhancing the depth and duration of anaesthesia. Similar findings have been reported by Kwon *et al.* (2003) [48], who observed longer anaesthetic duration with α_2 -agonist combinations, and by Koli *et al.* (2021) [38], Pablo and Bailey (1999) [58], and Hampton *et al.* (2019) [21], supporting the prolongation of anaesthesia with such combinations.

4.10 Amount of Isoflurane consumed

In the present study, the total isoflurane consumption was highest in Group I, likely due to the absence of preanaesthetic medication and inadequate depth of anaesthesia achieved with Zoletil alone, resulting in a higher MAC requirement. In contrast, Group III showed comparatively lower isoflurane consumption, which may be attributed to the analgesic effect of fentanyl citrate, known to reduce MAC (Hellyer *et al.*, 2001) [23]. Group II exhibited the least isoflurane requirement, possibly due to the combined sedative, analgesic and muscle relaxant effects of dexmedetomidine, leading to a pronounced MAC-sparing effect. These findings are in agreement with previous reports indicating reduced isoflurane requirement following administration of α_2 -agonists such as dexmedetomidine and medetomidine (Kuusela *et al.*, 2001; Kastner *et al.*, 2006; Singh *et al.*, 2013a) [46, 70].

4.11 Physiological Parameters

4.11.1 Rectal Temperature (°F)

Rectal temperature (RT) decreased non-significantly following administration of atropine and other preanaesthetics in all groups, and showed a significant decline after induction with zolazepam-tiletamine and maintenance with isoflurane, remaining below baseline throughout the 90-minute observation period. In Group I, RT decreased non-significantly up to 30 minutes postinduction, followed by a significant decline until 90 minutes. The reduction in RT may be attributed to the combined effects of anaesthetic agents causing CNS depression, muscle relaxation and decreased metabolic rate. Dexmedetomidine-induced hypothermia is associated with

reduced muscular activity and central depression (Sinclair, 2003; Kumar *et al.*, 2018) [42, 69]. Fentanyl citrate produced a mild, non-significant decrease in temperature, likely due to reduced basal metabolic rate and increased heat loss through panting (Hamad *et al.*, 2022; Haskins, 2013) [20, 22]. Additionally, anaesthesia impairs thermoregulation, further contributing to hypothermia (Ko and Krimins, 2014) [36]. Similar observations have been reported by Lemke (2007) [50].

4.11.2 Heart rate (beats/min)

Heart rate (HR) increased significantly in all groups following atropine administration due to its vagolytic action blocking parasympathetic influence on the heart (Ko *et al.*, 2001) [35]. Subsequent administration of dexmedetomidine and fentanyl citrate resulted in a significant and nonsignificant decrease in HR in Groups II and III, respectively. Induction with Zoletil (tiletamine- zolazepam) caused a significant increase in HR up to 30 minutes, followed by a gradual decline from 45 to 90 minutes during maintenance with isoflurane anaesthesia. The tachycardia observed with Zoletil may be attributed to its sympathetic-stimulating effect along with the vagolytic action of atropine, as reported by Dugassa *et al.* (2018) [13], Hellyer *et al.* (1989) [24] and Tarraga *et al.* (2000) [74]. Isoflurane further contributed to increased HR, possibly as a compensatory response to decreased peripheral vascular resistance and negative inotropic effects (Eger, 1984; Hellebrekers, 1986). Dexmedetomidine-induced bradycardia may be due to α_2 -adrenoceptor-mediated vasoconstriction, reflex vagal stimulation and reduced cardiac output (Lemke, 2007; Murrell and Hellebrekers, 1986; Nam *et al.*, 2013) [50, 57]. Fentanyl citrate produced a mild, non-significant decrease in HR, likely due to suppression of sympathetic tone and enhanced vagal activity acting on the sinoatrial node (Loeb *et al.*, 1984), although some studies have reported minimal or no effect (Arndt *et al.*, 1984; Grimm *et al.*, 2005). Overall, HR changes observed in the present study reflect the combined pharmacodynamic effects of atropine, Zoletil, dexmedetomidine, fentanyl and isoflurane.

4.11.3 Respiration rate (breaths/min)

Respiration rate (RR) showed a non-significant increase in all groups following atropine administration, followed by a significant decrease in Groups II and III after administration of dexmedetomidine and fentanyl citrate, respectively. Subsequently, RR further decreased in all groups after zolazepam-tiletamine administration and during maintenance with isoflurane anaesthesia. The initial increase may be attributed to the stimulatory effect of atropine on the cardiopulmonary system (Robaj *et al.*, 2014) [64], whereas the subsequent decrease is likely due to central nervous system depression caused by α_2 -agonists and opioids (Kuusela *et al.*, 2001; Ahmad *et al.*, 2013; Nishimura *et al.*, 2018) [1, 46]. Similar reductions in RR with dexmedetomidine-based protocols have been reported by Santosh *et al.* (2013) [67] and Ratnu *et al.* (2021) [63]. Fentanyl-induced respiratory depression may be due to its action on pontine and medullary respiratory centres (Bailey *et al.*, 1990), with reports of apnoea and reduced respiratory activity during fentanyl- isoflurane anaesthesia (Keating *et al.*, 2013; Bufalari *et al.*, 2007) [32]. The overall decrease in RR observed in the present study may be attributed to the

combined depressant effects of tiletamine- zolazepam and isoflurane (Hellyer *et al.*, 1989; Lin *et al.*, 1989) [24].

4.12. Haemodynamic Parameters

4.12.1 Systolic blood pressure (mmHg)

Systolic blood pressure (SBP) showed a non-significant increase in all groups following atropine administration, with a significant ($p < 0.05$) rise in Group II and a non-significant increase in Group III at 10 minutes post-sedation. Thereafter, SBP decreased non-significantly following administration of zolazepam-tiletamine and remained stable during maintenance with isoflurane. The initial increase in SBP may be attributed to atropine and peripheral α_2 -adrenoceptor-mediated vasoconstriction induced by dexmedetomidine (Vainio *et al.*, 1989; Bisht *et al.*, 2018a, 2018b), while the subsequent decline may be due to reduced peripheral vascular resistance following tiletamine-zolazepam administration (Hellyer *et al.*, 1989) [24]. Similar biphasic changes in SBP with α_2 -agonists have been reported by Gomez-Villamandos *et al.* (2005) and Akbar *et al.* (2014). In Group III, the non-significant increase in SBP may be associated with increased systemic vascular resistance due to fentanyl (Simoes *et al.*, 2016; Hamad *et al.*, 2022; Hendrix *et al.*, 1995) [20]. The subsequent decrease in SBP during maintenance may be attributed to the combined effects of tiletamine-zolazepam and isoflurane, which has also been reported in previous studies (Keating *et al.*, 2013; Liehmann *et al.*, 2006) [32].

4.12.2 Diastolic blood pressure (mmHg)

Diastolic blood pressure (DBP) showed a significant ($p < 0.05$) increase in Groups II and III following atropine administration up to 10 minutes post-sedation, followed by a non-significant decrease after administration of tiletamine-zolazepam and during maintenance with isoflurane. The initial rise in DBP may be attributed to peripheral α_2 -adrenoceptor-mediated vasoconstriction induced by dexmedetomidine, whereas the subsequent decline reflects reduced sympathetic tone and decreased peripheral vascular resistance (Zornow *et al.*, 1989; Sinclair, 2003) [69]. Similar biphasic responses have been reported by Rafee *et al.* (2015) [62]. The decrease in DBP following tiletamine-zolazepam administration is consistent with Hellyer *et al.* (1989) [24], who attributed it to reduced vascular resistance. In Group III, fentanyl-induced increase in DBP may be due to increased systemic vascular resistance (Grimm *et al.*, 2005), with a transient rise followed by gradual decline as reported by Hamad *et al.* (2022) [20]. However, contrasting findings of decreased or non-significant changes in DBP with fentanyl combinations have also been documented (Keating *et al.*, 2013; Gardocki and Yelnosky, 1964; Hughes *et al.*, 1999) [25, 32].

4.12.3 Mean blood pressure (mmHg)

Mean blood pressure (MBP) showed a significant ($p < 0.05$) increase in Group II and a nonsignificant increase in Group III following atropine administration up to 10 minutes post-sedation. Thereafter, MBP decreased significantly $\leq$ ft ($p < 0.05$ right) in Group II and non-significantly $\leq$ ft ($p > 0.05$ right) in Group III following administration of tiletamine-zolazepam and during maintenance with isoflurane. The initial rise in MBP may be attributed to the effects of atropine and peripheral α_2 -adrenoceptor stimulation by dexmedetomidine (Vainio *et al.*, 1989; Bisht *et al.*, 2018a, 2018b), whereas the subsequent decline

reflects reduced peripheral vascular resistance and the biphasic response of α_2 -agonists, characterized by transient hypertension followed by prolonged hypotension (Hellyer *et al.*, 1989; Ruffolo *et al.*, 1993; Tibirica *et al.*, 1991) [24]. Isoflurane further contributed to the decrease in MBP by reducing peripheral vascular resistance (Hikasa *et al.*, 2000). In Group III, the non-significant changes in MBP may be associated with the variable cardiovascular effects of fentanyl, including transient increases in vascular resistance followed by mild hypotension. Similar reductions in MBP during isoflurane-opioid anaesthesia have been reported by Liehmann *et al.* (2006) and Grimm *et al.* (2005), although variable responses with fentanyl have also been documented (Hamad *et al.*, 2022) [20].

4.13 Capillary Refill Time (seconds)

Capillary refill time (CRT) did not show any significant change ($p < 0.05$) throughout the observation period in any of the groups. CRT, an indicator of peripheral perfusion, normally remains below 2 seconds and prolongs in cases of circulatory compromise (Kumar *et al.*, 2013) [41]. In the present study, consistent CRT values and normal mucosal coloration indicated adequate peripheral circulation, suggesting that the anaesthetic protocols did not adversely affect haemodynamic stability. Similar findings have been reported by Kumar *et al.* (2013) in dogs.

5. Conclusion

Dexmedetomidine as a premedicant with zolazepam-tiletamine-isoflurane provided superior sedation, analgesia, smoother induction and reduced isoflurane requirement, though with prolonged recovery. Fentanyl citrate showed moderate effects, while atropine alone was inadequate. All protocols were physiologically safe; however, dexmedetomidine-based anaesthesia was found to be the most effective for balanced anaesthesia in *canines*.

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7. Conflict of Interest

The authors affirm that there is no conflict of interest related to the publication of this research.

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