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Evaluation of glycopyrrolate, fentanyl citrate, triflupromazine hydrochloride, midazolam and ketamine hydrochloride induction with isoflurane maintenance for the repair of tibial fractures in dogs

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Abstract
The objective of the study was to evaluate the efficacy of glycopyrrolate, fentanyl citrate, triflupromazine hydrochloride, midazolam and ketamine hydrochloride induction with isoflurane maintenance for the repair of tibial fractures in dogs. In the present study, a total of 12 dogs with tibial fractures were divided into 2 groups of 6 dogs each. The anaesthetic protocol used in group-I was glycopyrrolate, fentanyl citrate, triflupromazine hydrochloride and ketamine hydrochloride induction with isoflurane maintenance. In group-II, glycopyrrolate, fentanyl citrate, midazolam and ketamine hydrochloride induction with isoflurane maintenance was used. Qualitative parameters such as abolition of reflexes, degree of analgesia, degree of muscle relaxation and physiological parameters such as heart rate, respiratory rate and temperature were recorded at the 0th minute prior to induction and at the 15th, 30th, 60th and 90th minute after induction in both groups. Both the anaesthetic protocols provided safe and satisfactory anaesthesia in dogs undergoing tibial fracture repair. However, the dogs in group-II showed superior abolition of reflexes, analgesia and muscle relaxation as compared to group-I dogs at 15 minutes after induction. Thereafter, there was excellent analgesia and muscle relaxation with abolition of reflexes throughout the surgery in both groups.

Keywords: anaesthesia, fentanyl, tibia fracture, dogs

Introduction
Multimodal analgesia involves the use of different classes of analgesic agents to achieve synergistic effects and decrease adverse events [1]. The use of glycopyrrolate in conjunction with opioid administration, offset the potential bradycardic effects of the opioid [2]. Fentanyl is a pure μ agonist with a potency of around 50 times greater than morphine, enabling the use of small doses to produce profound analgesia [3]. Triflupromazine is a good pre-medicant with a quick sedative effect, long duration of anaesthesia with less induction dose of an anaesthetic and short recovery time [4]. The administration of midazolam provides for smooth induction and smooth tracheal intubation quality [5]. Ketamine produces a range of effects from sedation to anaesthesia. It is usually administered with a co-induction agent such as a benzodiazepine to avoid muscle rigidity, spontaneous movement and undesirable recoveries [6]. Isoflurane offers a fast induction and recovery. It also has a relative sparing effect on cardiovascular function and is hence preferred over other inhalant anaesthetics [7].

Materials and Methods
The study included 12 cases of tibia fractures in dogs which were stabilised using either the intramedullary pinning technique (group-I) or the intramedullary interlocking nailing technique (group-II). The dogs were kept off feed for 12 hours and off water for 6 hours prior to surgery. The anaesthetic protocol followed for dogs in group-I was pre-anaesthesia with glycopyrrolate [27] @ 0.01mg/kg subcutaneously, fentanyl citrate [28] @ 0.003mg/kg intravenously and triflupromazine HCl [29] @ 0.5mg/kg intravenously. Anaesthesia was induced with ketamine HCl [30] @ 6mg/kg intravenously and maintained with isoflurane [31] @ 2-3%. In group-II, the dogs were pre-anaesthetised with glycopyrrolate @ 0.01mg/kg subcutaneously, fentanyl citrate @ 0.003mg/kg intravenously and midazolam [32] @ 0.2mg/kg intravenously. Anaesthesia was induced with ketamine HCl @ 6mg/kg intravenously and maintained with isoflurane @ 2-3%. Following induction, the dogs were intubated with cuffed

endotracheal tubes of suitable sizes with the help of a laryngoscope in both groups. The endotracheal tubes were then connected to the small anaesthetic machine. To evaluate the efficacy of the anaesthetic protocols, the following parameters were recorded in both groups before the administration of pre-anaesthetics at the 0th minute and at the 15th, 30th, 60th and 90th minute after induction.

1. Abolition of reflexes: Abolition of pedal, palpebral and corneal reflexes were assessed and recorded.
2. Degree of analgesia: Analgesia was recorded by pinching of the digit or pad or by observing the animal's response to surgical stimulation.
3. Degree of muscle relaxation: Muscle relaxation was assessed by jaw tone and reduced resistance to passive flexion of the limb.
4. Physiological observations: Heart rate (beats/minute), respiratory rate (breaths/minute) and rectal temperature (°F) were recorded.
5. Type of recovery: This was determined by monitoring the animal during anaesthetic recovery.

The degree of analgesia and muscle relaxation was graded based on the following criteria

0 – No analgesia or muscle relaxation
1 – Mild analgesia or muscle relaxation
2 – Moderate analgesia or muscle relaxation
3 – Excellent analgesia or muscle relaxation

After completion of the surgery, the isoflurane was stopped and oxygen was administered until the gag reflex was observed. After the gag reflex or swallowing reflex was observed, the anaesthetic machine was disconnected from the endotracheal tube and the endotracheal tube was deflated and removed. The data obtained was tabulated and statistically analysed using student's t-test.

Results and Discussion

Abolition of reflexes

Fifteen minutes after induction, the animals in group-II showed less response to stimuli when compared to the animals in group-I. At 30, 60 and 90 minutes after induction, the reflexes were absent in both groups. The reflexes were regained only after discontinuation of isoflurane. However, the animals in group-II showed signs of sedation for prolonged periods after anaesthesia.

The sedation and ataxia that was recorded in group-I could be due to the administration of triflupromazine hydrochloride [4, 8]. The delayed abolition of reflexes in group-I dogs might be due to the slow onset of sedation of triflupromazine hydrochloride [9]. In group-II, the abolition of pedal, palpebral and corneal reflexes could be due to the initial signs of profound weakness and ataxia as seen with midazolam [10]. The profound sedation followed by administration of midazolam in group-II, was due to the use of midazolam in combination with fentanyl and ketamine [11].

Degree of analgesia

The Mean ± SE analgesic scores of the dogs in group-I, before induction at the 0th minute and after induction at the 15th, 30th, 60th and 90th minute respectively were 0.00±0.00, 1.67±0.21, 3.00±0.00, 3.00±0.00 and 3.00±0.00. Mild to moderate analgesia was recorded 15 minutes after induction. The analgesia was excellent thereafter and throughout the surgery. The Mean ± SE scores of analgesia of the dogs in group-II, before induction at the 0th minute and after induction at the 15th, 30th, 60th and 90th minute respectively were 0.00±0.00, 2.83±0.17, 3.00±0.00, 3.00±0.00 and 3.00±0.00. Moderate to excellent analgesia was noticed 15 minutes after induction. Thereafter, the analgesia was excellent throughout the surgery.

Excellent analgesia was observed immediately after administration of fentanyl citrate [1, 4]. The duration of analgesia and anaesthesia was found to be long and was attributed to the administration fentanyl citrate in combination with ketamine hydrochloride [12]. The optimal analgesia throughout the period of anaesthesia was due to midazolam [13].

Degree of muscle relaxation

The Mean ± SE scores of muscle relaxation of the dogs in group-I, before induction at the 0th minute and after induction at the 15th, 30th, 60th and 90th minute respectively were 0.00±0.00, 1.50±0.22, 3.00±0.00, 3.00±0.00 and 3.00±0.00. Mild to moderate muscle relaxation was recorded 15 minutes after induction. The muscle relaxation was excellent thereafter and throughout the surgery. The Mean ± SE muscle relaxation scores of the dogs in group-II, before induction at the 0th minute and after induction at the 15th, 30th, 60th and 90th minute respectively were 0.00±0.00, 2.83±0.17, 3.00±0.00, 3.00±0.00 and 3.00±0.00. Moderate to excellent muscle relaxation was noticed 15 minutes after induction. The muscle relaxation was excellent throughout the surgery.

The excellent tranquilizing potency of triflupromazine hydrochloride could be associated with the excellent muscle relaxation in group-I [14]. In group-II, the optimal skeletal muscle relaxation throughout the period of anaesthesia was due to midazolam [13]. The smooth induction and endotracheal intubation in group-II dogs was due to the use midazolam as a pre-anaesthetic [5]. The undesired effects of ketamine such as muscle rigidity and spontaneous movement owing to the use of ketamine were avoided by the co-induction agent midazolam in group-II [6].

Heart rate (beats/minute)

In group-I, there was significant ($p \leq 0.01$) bradycardia between 15 to 90 minutes of the study, when compared to the pre-administration level (0 minute). In group-II, there was significant tachycardia ($p \leq 0.01$) at 15 minutes followed by bradycardia from 30 to 90 minutes. The bradycardia was statistically significant ($p \leq 0.05$) only at 30 minutes. However, there was non-significant ($p > 0.05$) tachycardia at 60 minutes followed by bradycardia at 90 minutes when compared to the before pre-medication level (0 minute). The comparison between groups revealed that group-I animals had a significantly ($p \leq 0.05$) higher heart rate compared to the group-II animals at all intervals of study except at the 15 minutes interval. The Mean ± SE values of heart rate (beats/minute) are given in figure 1 for both groups.

Glycopyrrolate did not cause ventricular arrhythmias and prevented sinus bradycardia [15, 16, 17]. Glycopyrrolate produced initial tachycardia in group-II [18]. Severe bradycardia due to fentanyl citrate was not observed and was attributed to the use of glycopyrrolate as a pre-medicant in both groups. The mild bradycardia observed after induction could be associated with the administration of fentanyl citrate in both groups [2, 12].

Respiratory rate (breaths/minute)

In both groups, there was significant bradypnoea ($p \leq 0.01$) at all intervals of study when compared to the pre-medication status. Comparison between groups revealed that group-II animals had a higher ($p \leq 0.05$) respiratory rate before pre-medication when compared to group-I animals, whereas, significant ($p \leq 0.05$) bradypnoea was observed in group-II animals compared to group-I animals at 15 minutes of study. However, there was a non-significant difference ($p > 0.05$) in the respiratory rate at 30, 60 and 90 minutes of the study between the two groups. The Mean ± SE values for respiratory rate (breaths/minute) are given in figure 2 for both groups.

Fentanyl citrate produced bradypnoea, however, did not cause apnoea in any of the 12 cases [12]. The respiratory depression observed in group-II dogs could be attributed to the administration of a combination of ketamine and midazolam [19]. The marked respiratory depression in both groups was attributed to the use of isoflurane as a maintenance agent [20].

Rectal temperature (°F)

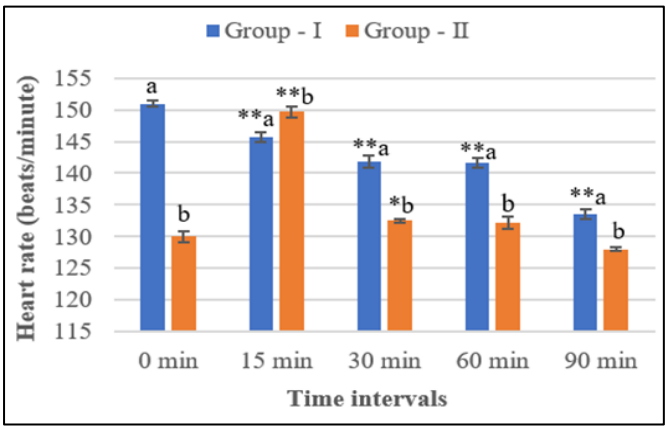
In group-I animals, the rectal temperature decreased from 15 minutes to 90 minutes when compared to the pre-administration level. Hypothermia was significant ($p \leq 0.05$) only at the 90 minutes interval when compared to pre-anaesthetic level. In group-II animals, there was an overall decrease in rectal temperature ($p > 0.05$) when compared to the pre-administration level. However, there was a slight increase ($p > 0.05$) in rectal temperature at 60 minutes, as compared to the 30 minutes interval. Comparison between groups revealed that there was no statistical difference between group-I and group-II animals at all intervals of study. However, statistically non-significant slightly higher rectal temperature was observed in group-II animals when compared to group-I animals at all the intervals of study. The Mean ± SE values for rectal temperature (°F) are given in figure 3 for both groups.

Decrease in body temperature was noticed in both groups after induction of anaesthesia and could be mildly associated with the administration of fentanyl citrate [12, 21]. The decrease in rectal temperature could be due to the use of triflupromazine in the anaesthetic protocol [8]. The decrease in rectal temperature observed in both groups was due to the administration of ketamine coupled with pre-anaesthetics [22].

Type of recovery

The recovery in both groups of dogs, was smooth and uneventful.

Smooth recovery was noted in all cases and could be partially attributed to fentanyl citrate [23]. In group-I, the smooth, short and satisfactory recovery might have been due to the use of triflupromazine hydrochloride as a pre-medicant [4, 24]. The smooth recovery followed by prolonged light sedation in group-II dogs was due to the administration of midazolam [25]. In group-II dogs, the undesirable recovery associated with ketamine was abolished due to the co-induction agent midazolam [6, 26]. The quick recovery recorded in both groups was due to the maintenance with isoflurane [7, 20].

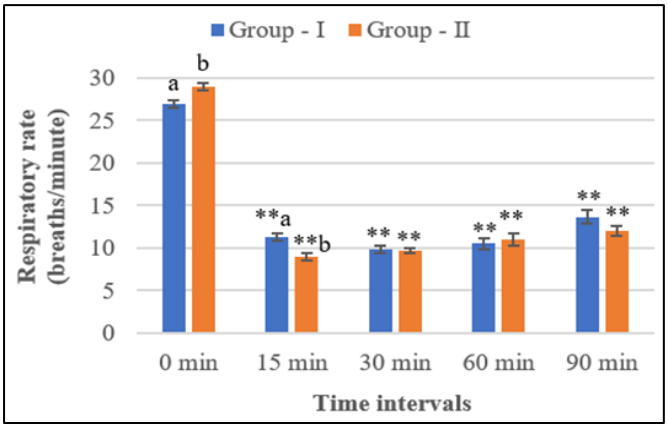


Means bearing superscript* differ significantly ($p \leq 0.05$) from interval 'before (0 min)' within the group

Means bearing superscript** differ significantly ($p \leq 0.01$) from interval 'before (0 min)' within the group

Means bearing superscript a, b differ significantly ($p \leq 0.05$) between the groups at corresponding intervals

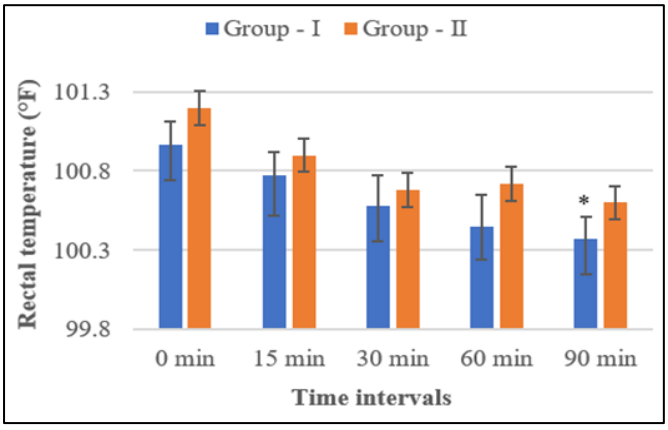
Fig 1: Mean ± SE of heart rate (beats/minute) at different intervals during anaesthesia in both groups of dogs



Means bearing superscript** differ significantly ($p \leq 0.01$) from interval 'before (0 min)' within the group

Means bearing superscript a, b differ significantly ($p \leq 0.05$) between the groups at corresponding intervals

Fig 2: Mean ± SE of respiratory rate (breaths/minute) at different intervals during anaesthesia in both groups of dogs



Means bearing superscript* differ significantly ($p \leq 0.05$) from interval 'before (0 min)' within the group

Fig 3: Mean ± SE of rectal temperature (°F) at different intervals during anaesthesia in both groups of dogs

Conclusions

In conclusion, both the anaesthetic protocols provided safe and satisfactory anaesthesia in dogs. However, the dogs in group-II showed superior abolition of reflexes, analgesia and muscle relaxation as compared to group-I dogs at 15 minutes after induction.

References

1. Monteiro BP, Steagall PV. Pain management in a dog undergoing orthopedic surgery. Clinicians Brief, 2017, 60-62.
2. Bednarski R, Grimm K, Harvey R, Lukasik, VM, Penn S, Sargent B, *et al*. AAHA anaesthesia guidelines for dogs and cats. Journal of the American Animal Hospital Association. 2011;47(6):377-385.
3. Borer-Weir K. Veterinary Analgesia. Edn 11, Saunders Elsevier, Philadelphia, 2014, 114.
4. Suresha L, Ranganath BN, Vasanth MS, Ranganath L. Haemato-biochemical studies on triflupromazine HCl and diazepam premedication for propofol anaesthesia in dogs. Veterinary World. 2012;5(11):672-675.
5. Le Chevallier D, Slingsby L, Murrell JC. The use of midazolam in combination with medetomidine for pre-medication in healthy dogs. Veterinary Anaesthesia and Analgesia. 2018;46(1):5-11.
6. Berry SH. Veterinary Anaesthesia and Analgesia. Edn 5, Wiley Blackwell, New Jersey, 2015, 285.
7. Ludders JW. Advantages and guidelines for using isoflurane. Veterinary Clinics of North America: Small Animal Practice. 1992;22(2):328-331.
8. High JP, Hassert Jr. GL, Rubin B, Piala, JJ, Burke JC, Craver BN. Pharmacology of fluphenazine (prolixin). Toxicology and Applied Pharmacology. 1960;2(5):540-552.
9. Arunkumar S, Dilipkumar D, Shivaprakash BV. Clinical and physiological evaluation of dexmedetomidine, xylazine and triflupromazine as pre-anaesthetics with propofol-isoflurane anaesthesia for various surgeries in dogs. The Pharma Innovation Journal. 2017;6(8):100-105.
10. Court MH, Greenblatt DJ. Pharmacokinetics and preliminary observations of behavioural changes following administration of midazolam to dogs. Journal of Veterinary Pharmacology and Therapeutics. 1992;15(4):343-350.
11. Plumb DC. Plumb's veterinary drug handbook. Edn 6, Blackwell Publishing, New Jersey. 2008, 616-618.
12. Sharabiyani AK, Moghadam MT. Clinical assessment of anesthesia caused by combination protocol of acepromazine-fentanyl-ketamine in dogs. Open Access Journal of Biomedical Science. 2019;1(2):60-66.
13. Verstegen J, Petcho A. Medetomidine-butorphanol-midazolam for anaesthesia in dogs and its reversal by atipamezole. Veterinary Record. 1993;132(14):353-357.
14. Singh K, Kumar A, Kumar S, Potliya S, Singh S. Evaluation of triflupromazine-propofol as an anaesthetic combination in buffalo calves. The Haryana Veterinarian. 2014;53(2):79-83.
15. Lemke KA, Tranquilli WJ, Thurmon JC, Benson GJ, Olson WA. Hemodynamic effects of atropine and glycopyrrolate in isoflurane-xylazine-anesthetised dogs. Veterinary Surgery. 1993;22(2):163-169.
16. Lemke KA. Electrocardiographic and cardiopulmonary effects of intramuscular administration of glycopyrrolate and romifidine in conscious beagle dogs. Veterinary Anaesthesia and Analgesia. 2001;28:75-86.
17. Lockhead K. Overview of anesthetic drugs: review, applications, contraindications (Proceedings), 2009; DVM 360.
18. Sinclair MD, Mcdonell WN, O'Grady M, Pettifer G, The cardiopulmonary effects of romifidine in dogs with and without prior or concurrent administration of glycopyrrolate. Veterinary Anaesthesia and Analgesia. 2002;29:1-13.
19. Jacobson JD, Hartsfield SM. Cardiorespiratory effects of intravenous bolus administration and infusion of ketamine-midazolam in dogs. American Journal of Veterinary Research. 1993;54(10):1710-1714.
20. Hellebrekers LJ. Comparison of isoflurane and halothane as inhalation anaesthetics in the dog. Veterinary Quarterly. 1986;8(3):183-188.
21. Kukanich B, Clark TP. The history and pharmacology of fentanyl: Relevance to a novel, long-acting transdermal fentanyl solution newly approved for use in dogs. Journal of Veterinary Pharmacology and Therapeutics. 2012;35(2):3-19.
22. Gioeni D, Di Cesare F, D'Urso ES, Rabbogliatti V, Ravasio G. Ketamine-dexmedetomidine combination and controlled mild hypothermia for the treatment of long-lasting and super-refractory status epilepticus in 3 dogs suffering from idiopathic epilepsy. Journal of Veterinary Emergency and Critical Care. 2020;30(4):455-460.
23. Andreoni V, Hughes JML. Propofol and fentanyl infusions in dogs of various breeds undergoing surgery. Veterinary Anaesthesia and Analgesia. 2009;36:523-531.
24. Van Der Veen RR. The use of triflupromazine: Case reports. Journal of the South African Veterinary Association. 1961;32(1):97-98.
25. Kojima K, Nishimura R, Mutoh T, Hong SH, Mochizuki M, Sasaki N. Effects of medetomidine-midazolam, acepromazine-butorphanol and midazolam-butorphanol on induction dose of thiopental and propofol and on cardiopulmonary changes in dogs. American Journal of Veterinary Research. 2002;63(12):1671-1679.
26. Reed RA, Quandt JE, Brainard BM, Copeland JE, Hofmeister EH. The effect of induction with propofol or ketamine and diazepam on quality of anaesthetic recovery in dogs. Journal of Small Animal Practice. 2019;60(10):589-593.
27. Inj. Pyrolate, Neon Laboratories Ltd., Thane
28. Inj. Fenstud, Rusan Pharma Ltd., Mumbai
29. Inj. Siquil, Zydus Animal Health and Investments Ltd., Gujarat
30. Inj. Aneket, Neon Laboratories Ltd., Thane
31. Sosrane, Neon Laboratories Ltd., Thane
32. Inj. Mezolam, Neon Laboratories Ltd., Mumbai