RESEARCH ARTICLE

Clinical Studies on Sedative Effect of Butorphanol and Buprenorphine in Bovine

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Abstract

The present clinical study was conducted on 24 bovines scheduled for major surgical procedures. The animals were randomly divided into four groups (n=6 each) to evaluate the preanaesthetic effect of Butorphanol and Buprenorphine. Animals in groups I and II, were premedicated with Butorphanol (0.02 mg/kg, IV), while in groups III and IV, Buprenorphine (0.006 mg/kg, IV) was used. Induction agent used in all 4 groups was a mixture of Ketamine HCl (1 gm) and Guaifenesin (25 gm) diluted in 500 mL of 5% dextrose and given intravenously "till effect". All animals were orotracheally intubated after induction of anaesthesia. In group I and III, Isoflurane and 100 % oxygen mixture was used as per demand of the cases, while a double drip of Ketamine and Guaifenesin mixture was given in groups II and IV to achieve the desired depth of surgical anaesthesia throughout the period of surgery. Evaluation of anaesthetic efficacy was made by determining the dose of induction agent (total dose), duration of maintenance anaesthesia (min), duration of surgery (min) and recovery time (min). A combination of Butorphanol and Buprenorphine provided good to excellent quality of sedation as compared to Butorphanol alone in bovine. Buprenorphine showed potent dose sparing effect on induction and maintenance dose of Ketamine and Guaifenesin or Isoflurane than Butorphanol in bovine.

Key words: Bovine, Buprenorphine, Butorphanol, Guaifenesin, Isoflurane, Ketamine.

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Introduction

Preanaesthetic drugs are vital components of anaesthesia management in bovines, helping to reduce stress, facilitate smooth induction, and enhance overall anaesthesia safety. Among various preanaesthetic agents, butorphanol and buprenorphine are widely used opioids with significant analgesic and sedative effects (Khattri *et al.,* 2013). Butorphanol is an opioid agonist-antagonist with good analgesic, antitussive and sedative effects. It is a synthetic drug that is chemically related to naloxone. It provides mild sedation, short duration of analgesia for minimally painful procedures and reduces the dose of intravenous induction agents (Khattri *et al.,* 2013) as well as inhalation anaesthetic drugs (Thurmon and Short, 2007). Respiratory depression and slow heart rate are the potential complications of opioid analgesics (Branson and Gross, 2001). Opioids are frequently included in balanced anaesthesia protocols for their strong analgesic and sedative effects (Lemke, 2007). In ruminants, butorphanol is valued for its pain-relieving properties, though it can also induce excitatory behavioral reactions (Jayakrishnan *et al.,* 2023).

Buprenorphine is a potent, semisynthetic opioid with mixed agonist-antagonist properties. It is a partial agonist at μ-opioid receptors and an antagonist at the κ-receptor. It is highly lipophilic and is derived from the thebaine (an alkaloid compound derived from the poppy flower) (Andaluz *et al.,* 2009). Its analgesic action may last as long as 7 to 24 h when given in a high dose. Due to its high lipolytic property, buprenorphine slowly associates from the opoid receptor as compared to morphine (Singh and Mahajan, 2016). It causes respiratory depression that can be reversed with naloxone or naltrexone. The dose of buprenorphine varies from 0.005 mg/kg to 0.01 mg/kg body weight, intramuscularly (Deepanshu, 2023). This study evaluated and compared the clinical effects of butorphanol and buprenorphine as preanaesthetic agents in bovines, focusing on their impact on sedation, analgesia, physiological stability, and overall anaesthetic outcomes.

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Materials and Method

The study was conducted at the Department of Veterinary Surgery and Radiology, College of Veterinary Science & A.H., Kamdhenu University, Junagadh, Gujarat (India). Twenty-four clinical cases of bovine presented for major surgical procedures were included in the study. All these animals were

randomly allotted to four different groups, consisting of six animals in each group, irrespective of age, breed, sex, body weight and surgical procedure. In animals of groups I and II, premedication was carried out with Butorphanol (0.02 mg/kg, IV), while in groups III and IV, Buprenorphine (0.006 mg/kg, IV) was used. Induction agent used in all 4 groups was a mixture of Ketamine HCl (1 gm) and Guaifenesin (25 gm) diluted in 500 mL of 5% dextrose and given intravenously "till effect".

All animals were orotracheally intubated after induction of anaesthesia. In group I and III, Isoflurane and 100 % oxygen mixture was used as per demand of the cases, while a double drip of Ketamine and Guaifenesin mixture was given in groups II and IV to achieve the desired depth of surgical anaesthesia throughout the period of surgery. Evaluation of anaesthetic efficacy was done by determining the dose of induction agent (total dose), duration of maintenance anaesthesia (min), duration of surgery (min) and recovery time (min). Quality of anaesthesia was assessed by the quality of sedation, induction, maintenance and recovery. Following parameters like palpebral reflex, corneal reflex, pedal reflex, jaw tone and eyeball position were evaluated before administration of any drug (base), 5 min after premedication and at 5^{th}, 15^{th}, 30^{th}, 45^{th}, 60^{th}, 90^{th} and 120^{th} min time interval after the induction of anaesthesia. The quality of anaesthesia was scored as per the scoring scale given by Bodh (2011). The data generated was statistically analyzed using one-way analysis of variance and the period effect was compared by the Duncan's *post-hoc* test at $p<0.05$ (Snedecor and Cochran, 1994).

Results and Discussion

The mean ± SE values of sedation quality were noticed as 2.67 ± 0.21, 2.67 ± 0.21, 3.00 ± 0.00 and 2.83 ± 0.16 for group I, II, III and IV, respectively. Following premedication, animals exhibited reduced responsiveness to external stimuli, drooping eyelids, and ataxia, indicating effective sedation. The level of sedation was graded as fair to good across all groups, with no significant differences observed between groups. None of the animals sedated with butorphanol or buprenorphine exhibited excitement or distress prior to induction of anaesthesia. All animals remained calm and manageable with minimal restraint, displaying partial eyelid closure and a slowed palpebral reflex. These findings aligned with those stated by Hall *et al.* (2014), who emphasized that opioid sedatives improve induction of anaesthesia and reduce the amount of injectable anaesthetics required. Overall, sedation in all groups was smooth and predictable, with butorphanol and buprenorphine both demonstrating effective sedative effects. These results confirm that both preanaesthetic agents facilitate an optimal level of sedation for induction and maintenance of anaesthesia in bovine surgery.

In this study, Ketamine and Guaifenesin combination was used in all groups for induction. During the study, mean ± SE values of induction doses of agents were calculated and compared with the actual doses required in 4 groups (Table 1). There was apparent decrease in the actually required induction dose of double drip of ketamine and guaifenesin combination when compared with the calculated doses in all 4 groups, but statistically the difference was significant only in groups III and IV. The results suggest that premedication in bovine effectively reduces the required induction doses of the ketamine-guaifenesin combination. Similar findings have been reported in earlier studies by Riazuddin *et al.* (2004), Neelkanth (2021), Khyum *et al. (*2021), and Thavardas *et al.* (2022).

Table 1: Induction doses of calculated and actually required anaesthesia for different groups of preanaesthetic agents (Mean ± SE)

Groups (n=6)	Induction dose	
	Calculated dose (mL)	Required dose (mL)
Group I	625 ± 86.7[a]	416 ± 57.8[a]
Group II	550 ± 95.6[a]	367 ± 63.7[a]
Group III	584 ± 33.5[a]	389 ± 22.3[b]
Group IV	522 ± 31.4[a]	348 ± 20.9[b]

Mean ± SE bearing different superscripts within the group differ significantly ($p<0.05$)

The mean ± SE values of induction quality scores were 3.17 ± 0.17, 3.67 ± 0.21, 3.50 ± 0.22 and 3.83 ± 0.17 in groups I, II, III and IV, respectively. There was no significant difference between groups, however buprenorphine preanaesthetic demonstrated superior induction quality as compared to butorphanol. After administration of preanaesthetic drugs, double drip mixture was used for induction of anaesthetia in all groups. Endotracheal intubation was easily facilitated in all groups following the induction. The current smooth and rapid induction, easy and quick tracheal intubation without regurgitation in all four groups concurred with earlier studies. Kerr *et al.* (2007) administered GKX @ 0.57 ± 0.18 mL/kg body weight to calves which exhibited high-quality induction. Similarly, Ninu *et al.* (2015) reported ketamine induction as highly safe for buffaloes undergoing diaphragmatic herniorrhaphy. Dhawale (2018) observed induction quality ranging from excellent to good in cattle anaesthetized using triple drip (Xylazine, Ketamine and Guaifenesin) and double drip (Ketamine and Guaifenesin) protocols. However, a significantly earlier onset of anaesthesia was observed in the triple drip group compared to the double drip group. Kherkar (2019) reported that double drip anaesthesia in buffaloes undergoing diaphragmatic herniorrhaphy resulted in excellent induction in 60% of cases and good induction in the remaining 40%.

In group I and III, maintenance was achieved using an isoflurane-oxygen mixture, while in groups II and IV, maintenance was achieved using a double-drip solution of ketamine and guaifenesin. The recommended maintenance anaesthesia dose, as per the existing literature, is 2.50 mL/kg/h utilizing a double-drip solution containing Guaifenesin (50 mg/mL) and Ketamine (2.00 mg/mL). The mean ± SE values of isoflurane used as maintenance anaesthesia were 2.19 ± 0.06 % and 2.08 ± 0.08 % in groups I and III, respectively, while

required dose of double drip of ketamine and guaifenesin combination for maintenance in group II and IV was 1127.67 ± 83.10 mL (1.61 mL/kg/h) and 1027.67 ± 89.13 mL (1.37 mL/kg/h), respectively. Statistical analysis revealed no significant difference in the maintenance anaesthesia doses between the groups. Regarding inhalational anesthesia, Doherty *et al.* (2002) observed that the pre-administration of butorphanol (0.05 mg/kg) significantly reduced the minimum alveolar concentration (MAC) of halothane in ponies and isoflurane in bovine. Similarly, Senthilkumar *et al.* (2013) found that butorphanol reduced the requirement of isoflurane by 40.70% during maintenance anesthesia in cattle.

The effectiveness of maintenance anaesthesia in different groups was determined by evaluating jaw tone, palpebral reflex, pedal reflex and eyeball position at multiple time points. All the reflexes were completely abolished following induction and remained suppressed thought out the maintenance anaesthesia with a consistent mean score of 4.0 ± 0.00 in all four groups. Observations indicated that jaw tone was completely abolished, allowing easy mouth opening without resistance in all groups. Similarly, pedal and palpebral reflexes were absent throughout the maintenance period, suggesting adequate depth of anaesthesia. Eyeball position remained ventro-medial in Groups I and III, whereas central positioning was observed in Groups II and IV. This observations aligned with previous research findings that isoflurane induces ventromedial eye rotation, while ketamine maintains a centrally positioned eyeball due to its dissociative effects (Lin *et al.,* 1997; Stegmann, 1998). No significant fluctuations in anaesthetic depth were observed across all groups, confirming the stability of maintenance anaesthesia protocols. These findings supported prior studies of Kumar *et al.* (2014) and Kherkar (2019), which documented similar responses to inhalant and intravenous anaesthetic maintenance in ruminants.

The mean (± SE) duration of surgery, duration of maintenance anaesthesia, and total duration of anesthesia in the 4 groups did not vary significantly (Table 2), although these varied depending on the type of surgical conditions and procedures employed during the study. The variations observed in duration of maintenance anaesthesia were likely due to the different surgical procedures performed in each group.

The mean ± SE values of recovery time in groups I, II, III and IV Presented in Table 2 revealed significant differences between the groups. Animals maintained on isoflurane and oxygen mixture in group I and III recovered significantly earlier as compared to group II and IV where double drip of ketamine and guaifenesin combination was used. The findings of the study were similar to Thakur *et al.* (2011), Coelho *et al.* (2014), Dhawale (2018), Khyum *et al.* (2021), Neelkanth (2021) and Thavardas *et al.* (2022). Relatively low solubility, lower blood-gas partition coefficient, and quicker alveolar concentration adjustments during isoflurane anesthesia likely contributed to this rapid recovery. Additionally, Riazuddin *et al.* (2004) attributed early recovery to improved cardiovascular stability, reduced stress response, minimal hepatic blood flow alterations, and faster elimination. These findings suggest that isoflurane provides a smooth and rapid recovery, particularly when used with butorphanol or buprenorphine as preanesthetic agents. The rapid recovery is also attributed to isoflurane's lower blood-gas solubility, which allows for faster elimination and emergence from anesthesia (Cantalapiedra *et al.,* 2000; Bodh *et al.,* 2014). Conversely, double-drip anesthesia resulted in prolonged recovery due to slower redistribution of ketamine and guaifenesin.

All animals across the four groups recovered smoothly and uneventfully from anaesthesia, exhibiting no excitement, staggering, or paddling. The mean score values of quality of recovery were 3.66 ± 0.21, 3.50 ± 0.22, 3.33 ± 0.21 and 3.50 ± 0.22 in groups I, II, III and IV, respectively, with no statistical difference. Sakata *et al.* (2007) stated that hyperventilation aids in faster anaesthetic elimination, further explaining the shortened recovery time observed with isoflurane. Additionally, Riazuddin *et al.* (2004) associated the faster recovery following isoflurane anaesthesia with improved cardiovascular stability, a diminished stress response, and minimal hepatic metabolism. The findings of this study regarding quality of recovery aligned with previous studies by Prassinos *et al.* (2005) and Quevedo and Bolanos (2017). Singh *et al.* (1985) reported smooth recovery with inhalant as well as double drip anaesthesia. Both isoflurane and double-drip anaesthesia effectively maintained a stable anaesthetic depth, with isoflurane demonstrating superior recovery characteristics. The results confirm that isoflurane anaesthesia allows for quicker emergence, whereas double drip anaesthesia provides sustained effects with longer but smooth recovery. These findings emphasize the importance of tailoring anaesthetic protocols based on procedural requirements and post-operative monitoring needs.

Table 2: Mean (± SE) duration of surgery, maintenance and total duration of anaesthesia (min) in different groups

Groups (n=6)	Duration of surgery (min)	Duration of maintenance anaesthesia (min)	Total duration of anaesthesia (min)	Recovery time (min)
I	71.17±6.35^{a}	64.67±6.28^{a}	67.89±6.20^{a}	11.00±0.96^{a}
II	109.67±5.28^{a}	102.3±5.19^{a}	114.45±6.38^{a}	22.00±1.46^{b}
III	98.67±12.76^{a}	93.33±12.7^{a}	87.33±8.98^{a}	10.30±1.50^{a}
IV	111.33±7.42^{a}	105.3±7.52^{a}	108.33±7.32^{a}	29.70±1.65^{b}

Means ± SEs bearing same superscript within and between the groups do not differ significantly (p>0.05).

Conclusion

The study concluded that a combination of Butorphanol and Buprenorphine provided good to excellent quality of sedation as compared to Butorphanol alone in bovine. Buprenorphine showed potent dose sparing effect on induction and maintenance dose of Ketamine and Guaifenesin or Isoflurane than Butorphanol in bovine.

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