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## Clinical and physiological evaluation of midazolam-propofol and xylazine-propofol induction combination for isoflurane anaesthesia in cattle

**Basavaraj Muchalambe, Dilipkumar D, Shivaprakash BV, Venkatgiri and Manjunath patil**

#### Abstract

The study was conducted in 12 clinical cases presented to TVCC, Bidar. Twelve animals were randomly divided into two groups viz., Group-I and Group-II consisting of six animals in each group. Group-I animals received xylazine (0.08 mg/kg) intravenously, animals were then restrained in lateral recumbency and anaesthesia was induced by administering propofol (3mg/kg) intravenously. In the Group-II animals midazolam (0.4mg/kg) was administered intravenously, animals were then restrained in lateral recumbency and anaesthesia was induced by administering propofol (3mg/kg) intravenously. Maintenance of anaesthesia was done under isoflurane in both groups. Anaesthetic combinations were compared by clinical and physiological parameters. The induction and recovery were smooth and uneventful in both groups. Induction was quicker in Group- I animals. Recovery, sternal recumbancy time was quicker in Group- II. Excellent analgesia and moderate to extensive salivation was observed in both the groups. Physiological parameters like heart rate, respiratory rate, rectal temperature, fluctuated within the normal limits. Non-significant bradycardia in group- I. Intermittent apnoea was observed in all animals, frequency was higher in Group-I. Both the anaesthetic protocols in the present study provided satisfactory surgical plane of anaesthesia in cattle.

Part of Post-graduate Research work

**Keywords:** Clinical physiological evaluation of midazolam-propofol and xylazine-propofol induction

#### 1. Introduction

Cattle usually accept physical restraint well and that in conjunction with local or regional anaesthesia, is often sufficient to allow completion of many surgical procedures, however, many times in noncooperative animals and in diagnostic and surgical procedures that are more complex like diaphragmatic hernia, traumatic pericarditis, orthopedic surgery etc., where technical and anatomical aspects of the surgical procedure warrant absolute control of movement during surgery (Kumar *et al.*, 2013).

General anaesthesia in cattle involves complexities like regurgitation, bloat, respiratory complication, nerve paralysis etc., which are not often encountered in small animals however, carefully selected and properly managed general anaesthetic technique provide optimal conditions for surgery.

Xylazine is an  $\alpha_2$  adrenergic agonist drug used to induce tranquilization and or sedation, provides good muscle relaxation and analgesia during surgery, however, it carries the risk of suppressing the cardiovascular system.

Midazolam, water soluble benzodiazepine having sedative, hypnotic, anticonvulsant and muscle relaxant properties. It has been shown to have both analgesic and muscle relaxant effect (Ritcher, 1981) with minimum adverse effects on cardiovascular system (Jones *et al.*, 1979).

General anaesthesia in large ruminants is induced by either injectable or inhalation techniques, available drugs include thiobarbiturates, ketamine, geratesin, tiletamine – zolazepam, propofol, halothane, isoflurane and sevoflurane (Carroll and Hartsfield, 1996)<sup>[22]</sup>.

General anaesthesia in large ruminants is induced by either injectable or inhalation techniques, available drugs include thiobarbiturates, ketamine, geratesin, tiletamine – zolazepam, propofol, halothane, isoflurane and sevoflurane (Carroll and Hartsfield, 1996)<sup>[22]</sup>.

Currently ketamine is used as induction agent in cattle, along with several pre-anaesthetic agents, xylazine (Arai *et al.*, 2006)<sup>[10]</sup> diazepam (Riazuddin *et al.*, 2004a),

acepromazine (Kumar *et al.*, 2012) and guaifenesin (Riazuddin *et al.*, 2004b) under isoflurane anaesthesia. However, there is paucity of reports or studies on propofol anaesthesia in cattle in India. Therefore the present clinical study "Comparative evaluation of Midazolam – Propofol and Xylazine-Propofol induction combinations for isoflurane anaesthesia in cattle was undertaken.

## 2. Materials and methods

The study was conducted in 12 clinical cases presented to TVCC, Bidar, with various surgical conditions to evaluate clinical and physiological parameters under midazolam-propofol and xylazine-propofol induction combinations under isoflurane anaesthesia in cattle. Twelve clinical cases were randomly divided in two groups *viz.*, group-I and group-II with six animals in each group. The animals in Group-I received xylazine at the dose rate of 0.08mg/kg body weight intravenously, after tenminutes of xylazine administration, the animals were restrained in lateral recumbency and anaesthesia was induced by administering propofol, at the dose rate of 3mg/kg body weight intravenously, followed by immediate intubation, the animals were maintained on 5 per cent to 1 per cent of isoflurane. In the animals of Group-II, midazolam was administered at the dose rate of 0.4 mg per kg body weight intravenously, five minutes later the animals were restrained in lateral recumbency and anaesthesia was induced by administering propofol intravenously, at the dose rate of 3mg/kg body weight, followed by immediate intubation, the animals were maintained on 5 per cent to 1 per cent of isoflurane.

The clinical parameters *viz.*, induction time, onset of sedation, analgesic score, degree of muscle relaxation, palpebral reflex score and recovery time were recorded before administration of any drug, immediately after induction (0 min) and then at every 15 minutes interval until recovery.

The heart rate, respiratory rate and rectal temperature were recorded before administration of any drug, immediately after induction (0 min) and then at every 15 minutes interval until recovery.

## 3. Results and discussion

### 3.1. Clinical Observation

#### 3.1.1. Induction Time (seconds)

In the Group-I animals, induction time ranged from 29 seconds to 34 seconds, with a mean induction time of  $32.00 \pm 0.85$  seconds. In the Group-II animals, induction time ranged from 37 seconds to 41 seconds, with a mean induction time of  $38.33 \pm 0.60$  seconds. The induction of anaesthesia was significantly earlier ( $P \leq 0.01$ ) in Group-I as compared to that in Group-II. The induction was significantly quick in the animals pre-medicated with xylazine – propofol combination, as compared to that in the animals pre-medicated with midazolam – propofol, whereas, Nain *et al.* (2010) observed that buffalo calves sedated with midazolam assumed sternal recumbency ( $34.0 \pm 15.85$  min) quicker than those sedated with acepromazine ( $74.16 \pm 22.28$  min). However, in the present study quick induction in Group-I animals might be attributed to administration of propofol after xylazine. Induction was smooth in both groups, which are in agreement with observations made by Kour and Singh (2004) who used midazolam-ketamine combination in buffalo. Riazuddin *et al.* (2004a) reported  $2.21 \pm 0.11$  minutes as induction time under xylazine-guaifenesin-ketamine anaesthesia as a triple drip in cattle. Nuh (2008) reported that the calves showed the first

signs of sedation (sunken head and reduced awareness)  $0.7 \pm 0.3$  min after the administration of detomidine-midazolam-ketamine anesthetic as a mixture in single syringe.

#### 3.1.2. Recovery Time (minutes)

In the Group-I animals, induction time ranged from 29 seconds to 34 seconds, with a mean induction time of  $32.00 \pm 0.85$  seconds. In the Group-II animals, induction time ranged from 37 seconds to 41 seconds, with a mean induction time of  $38.33 \pm 0.60$  seconds. The induction of anaesthesia was significantly earlier ( $P \leq 0.01$ ) in Group-I as compared to that in Group-II.

Statistically there was no significant difference between the groups in the time taken for the animals to recover after discontinuing the isoflurane. The Mean $\pm$ SE values of recovery time were;  $10.83 \pm 0.79$  and  $10.50 \pm 0.88$  minutes in Group-I and Group-II animals respectively. The recovery was smooth and uneventful in the animals of both groups, similar observations were reported in sheep during isoflurane anaesthesia by Mohamadnia *et al.* (2008). They observed that the mean time taken for the animals to make first attempt to swallow was 3.95 minutes.

#### 3.1.3. Sternal Recumbency Time (minutes)

In the Group-I animals, sternal recumbency time ranged from 14 minutes to 20 minutes, with a mean sternal recumbency time of  $17.60 \pm 0.93$  minutes. In the Group-II animals, sternal recumbency time ranged from 12 minutes to 18 minutes, with a mean sternal recumbency time of  $14.80 \pm 0.93$  minutes. The time taken to attain sternal recumbency after anaesthesia was significantly lesser ( $P \leq 0.05$ ) in Group-II as compared to that in Group-I.

The time taken for the animals to attain the sternal recumbency after discontinuing the isoflurane was significantly quicker in animals pre-medicated with midazolam - propofol as compared to animals pre-medicated with xylazine - propofol. In the present study Mean $\pm$ SE values of sternal recumbency time were;  $17.60 \pm 0.93$  and  $14.80 \pm 0.93$  minutes in Group-I and Group-II animals respectively. However, Cantalapiedra *et al.* (2000) <sup>[21]</sup> recorded that the cattle took only  $4.60 \pm 0.58$  minutes to attain sternal recumbency, after induction and maintenance of anaesthesia with isoflurane alone. The longer duration required to attain sternal recumbency in the present study might be due to pre-anesthetics and propofol used for induction.

#### 3.1.4. Standing Time (minutes)

In the Group-I animals, standing time ranged from 28 minutes to 44 minutes, with mean standing time of  $35.40 \pm 3.07$  minutes. In the Group-II animals, standing time ranged from 25 minutes to 41 minutes, with a mean standing time of  $37.60 \pm 5.02$  minutes. The comparison between the groups revealed that there was no statistically significant ( $P > 0.05$ ) difference in the standing time.

Statistically there was no significant difference between the groups in the time taken for the animals to stand after discontinuing the isoflurane. The findings are in agreement with earlier study by Nain *et al.* (2010). The mean $\pm$ SE values of standing time were;  $35.40 \pm 3.07$  and  $37.60 \pm 5.02$  minutes in Group-I and Group-II animals respectively. However, the standing time was only  $6.70 \pm 1.02$  minutes when only isoflurane is used to anesthetize cattle (Cantalapiedra *et al.*, 2000) <sup>[21]</sup>. The longer standing time in the present study could

be due to xylazine and midazolam used as pre-anaesthetics and propofol as induction agent.

### 3.1.5. Analgesia

The mean±SE analgesia score in Group-I animals, before induction, immediately after induction (0 minute), 15 minutes, 30 minutes, 45 minutes and 60 minutes after induction were; 0.00±0.00, 2.33±0.33, 3.00±0.00, 2.50±0.43, 2.17±0.31 and 2.50±0.22 respectively.

The mean±SE analgesia score in Group-II animals, before induction, immediately after induction (0 minute), 15 minutes, 30 minutes, 45 minutes and 60 minutes after induction were; 0.00±0.00, 1.17±0.17, 2.00±0.00, 2.33±0.33, 2.83±0.60 and 2.67±0.56 respectively.

An excellent analgesia was recorded at maximum depth of anaesthesia in both the groups. Pain was significantly abolished from 0 to 60 minutes in both the groups. There was non-significant difference in the analgesia level produced between the groups at all the intervals of study. The similar findings were recorded after detomidine-diazepam-ketamine anaesthesia in buffalo (Pawde *et al.*, 2000) and after midazolam-ketamine anaesthesia in sheep (Al-Redah, 2011) [6].

### 3.1.6. Palpebral reflex

The present study showed that in both the groups of animals, the palpebral reflex was brisk and present before induction of anaesthesia. A sluggish palpebral reflex was present even after induction in all animals, similar observations were recorded, xylazine-ketamine anaesthesia in buffalo calves (Chandrashekhar *et al.*, 2003) [23] and after midazolam-ketamine induction in buffalo (Amandeep and Singh, 2004) [7]. However, three to six minutes after starting administration of isoflurane set at 3 to 5 per cent, the palpebral reflex started testing negative in most of the animals. At the maximum depth of anaesthesia most of the animals tested negative or only mild palpebral reflex was present. However, after about five minutes of withdrawal of isoflurane inhalation in all the animals across the groups, the reflexes started reappearing. Similar observations during maintenance of anaesthesia with isoflurane, was recorded by Singh *et al.* (2013) after thiopental induction in buffalo.

### 3.1.7. Salivation

Moderate to extensive salivation was observed in all the animals across the groups throughout anaesthesia. Hikasa *et al.* (2000) recorded only mild salivation under isoflurane anaesthesia without any pre-medication in sheep, however, moderate to profuse salivation was recorded in buffaloes in which anaesthesia was induced by thiopental but maintained under isoflurane (Singh *et al.*, 2013). Profuse salivation was reported after midazolam administration in sheep (Stegmann, 1998). Increased salivation recorded during present study might be due to decreased swallowing reflex.

## 3.2. Physiological Observations

### 3.2.1. Heart Rate (beats/minutes)

The heart rate (Mean±SE) in Group-I animals before anaesthesia, immediately after induction (0 minute), and then at 15 minutes, 30 minutes, 45 minutes and 60 minutes after induction were; 65.90±2.47, 78.80±3.12, 65.20±0.97, 65.00±1.91, 62.00±1.73 and 60.20±3.06 respectively. The heart rate (Mean±SE) in Group-II animals before anaesthesia, immediately after induction (0 minute), and then at 15

minutes, 30 minutes, 45 minutes and 60 minutes after induction were; 69.40±4.86, 73.60±8.07, 58.40±4.30, 57.20±4.27, 56.00±4.21 and 58.00±7.05 respectively.

The heart rate tachycardia was observed at 0 minute in both the groups of animals and it was statistically significant ( $p \leq 0.01$ ) only in group-II animals. Thereafter gradual bradycardia was observed upto 60 minutes in both the groups of animals. However, bradycardia was statistically non-significant from 15 to 60 minutes in both the groups of animals. The result is in agreement with earlier study by Haskins *et al.* (1985) in dogs and by Stegmann (1998) and Abu-Ahmed (2013) [2] in goats.

### 3.2.2. Respiratory Rate (Breaths/minute)

The respiratory rate (Mean±SE) in Group-I animals before anaesthesia, immediately after induction (0 minute), and then at 15 minutes, 30 minutes, 45 minutes and 60 minutes after induction were; 21.60±0.46, 25.20±1.87, 19.00±0.64, 16.20±0.18, 16.20±0.67 and 15.00±0.40 respectively. The respiratory rate (Mean±SE) in Group-II animals before anaesthesia, immediately after induction (0 minute), and then at 15 minutes, 30 minutes, 45 minutes and 60 minutes after induction were; 21.80±1.53, 24.00±0.50, 22.60±1.34, 16.60±0.68, 15.60±0.79 and 15.40±0.68 respectively.

In the Group-I animals there was non-significant decrease in respiratory rate up to 15 minutes after induction. The bradypnoea statistically significant between 15 to 60 minutes of study. The respiratory rate showed declining trend from 15 to 60 minutes

The result is in agreement with earlier study by Al-Redah (2011) [6] in sheep, and by Abu-Ahmed (2013) [2] in goats under midazolam-ketamine anaesthesia. However, Nuh (2008) reported significantly increased respiratory rate under detomidine-midazolam-ketamine anaesthesia in calves. In Group-II animals the respiratory rate gradually increased up to 15 minutes after induction, The respiratory rate showed declining trend from 15 to 60 minutes. The bradypnoea statistically significant between 15 to 60 minutes of study. The result is in agreement with earlier study by Baniadam *et al.* (2007) [11] who observed increased respiratory rate followed by decreased respiratory rate in sheep under acepromazine-ketamine anaesthesia. However, Nain *et al.* (2010) reported significantly increased respiratory rate under midazolam sedation and non-significant change under acepromazine sedation in the buffalo calves, which is not in agreement with the observations made in the present study.

### 3.2.3. Rectal Temperature (°F)

The rectal temperature (Mean±SE) in Group-I animals before anaesthesia, immediately after induction (0 minute), and then at 15 minutes, 30 minutes, 45 minutes and 60 minutes after induction were; 101.46±0.13, 101.67±0.07, 99.92±0.33, 99.48±0.38, 99.56±0.41 and 99.26±0.22 respectively. The rectal temperature (Mean±SE) in Group-II animals before anaesthesia, immediately after induction (0 minute), and then at 15 minutes, 30 minutes, 45 minutes and 60 minutes after induction were; 101.80±0.27, 101.62±0.16, 100.20±0.35, 100.67±0.52, 99.98±0.48 and 99.68±0.31 respectively.

Statistically there was no significant difference between the groups. Declining trend from 0 to 60 minute in both the groups of animals. Hypothermia was statistically significant between 30 to 50 minute in group I animal whereas, it was significant only between 45 to 60 minutes in Group II. The rectal temperature increased immediately after induction in

both groups, the increase was significant in Group-I animals. The similar findings have also been reported after ketamine administration in dogs by Haskins *et al.* (1985). Similar findings had also been reported by Parry *et al.* (1982) after acepromazine administration in horses, by Baniadam *et al.* (2007) [11] after acepromazine-ketamine administration in sheep and by Nuh (2008) after detomidine-midazolam-ketamine anaesthesia in calves. The decrease in the rectal temperature might be attributed to a decrease in the skeletal muscle tone, reduced metabolic rates and muscle relaxation, along with depression of thermoregulatory centers. A significant decrease in the rectal temperature was reported by Singh *et al.* (2012) and Singh *et al.* (2013) in water buffalo after fentanyl-medetomidine-thiopental-isoflurane anaesthesia.

In conclusion, anaesthetic combinations were compared by clinical and physiological parameters. The induction and recovery were smooth and uneventful in both groups. Induction was quicker in Group- I animals. Recovery, sternal recumbancy time was quicker in Group- II. Excellent analgesia and moderate to extensive salivation was observed in both the groups. Physiological parameters like heart rate, respiratory rate, rectal temperature, fluctuated within the normal limits. Non-significant bradycardia in group-I. Intermittent apnoea was observed in all animals, frequency was higher in Group-I. Both the anaesthetic protocols in the present study provided satisfactory surgical plane of anaesthesia in cattle.

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