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**Research Article**

# Clinico-physiological evaluation of xylazine-etomidate-isoflurane and dexmedetomidine-ketamine-isoflurane anaesthesia under guaifenesin premedication for various surgeries in cattle

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## Abstract

**The clinical study was conducted on 12 clinical cases of cattle of either sex, presented to the Department of Veterinary Surgery and Radiology, Veterinary College Bidar for various surgeries, which were randomly divided into two groups consisting of 6 animals each. In both the group, animals were premedicated with inj. guaifenesin (50 mg/kg I/V). The cattle in group-I were sedated with inj. xylazine (0.1 mg/kg I/V) and induced with inj. etomidate (0.5 mg/kg I/V). The cattle in group-II were sedated with inj. dexmedetomidine (2.5 µg/kg I/V) and induced with inj. ketamine (3 mg/kg I/V). Cattle of both groups were maintained under isoflurane anaesthesia. Quicker onset of sedation was noticed in group-II; however, quicker induction time, recovery time, recovery time to sternal position and standing position were earlier in group-I. Degree of analgesia and degree of muscle relaxation were slightly greater in dexmedetomidine premedicated group. Physiological parameters like respiratory rate, heart rate and rectal temperature decreased significantly in both groups. Anaesthetic complications like myoclonus were seen in two animals of group-I, while salivation and regurgitation were seen in one animal of group-I and two animals of group-II. Both the anaesthetic protocols provided an adequate surgical plane of anaesthesia for orthopaedic and soft tissue surgeries.**

**Keywords:** Etomidate, Isoflurane, Myoclonus, Regurgitation

## Highlights

- Induction of anaesthesia in cattle was smooth in both etomidate and ketamine anaesthesia except one cattle in which showed myoclonus during induction of anaesthesia with etomidate.
- Onset of sedation was significantly faster in dexmedetomidine sedated cattle, whereas induction of anaesthesia and recovery were earlier in etomidate induced cattle.
- Degree of analgesia was significantly higher in cattle sedated with dexmedetomidine, and degree of muscle relaxation was good to excellent in both xylazine and dexmedetomidine sedation.
- Physiological parameters such as respiratory rate and rectal temperature decreased significantly till the observation interval in both the etomidate and ketamine groups. However, the variations were within the normal physiological range.

## INTRODUCTION

General anaesthesia is an indispensable prerequisite for many major surgical procedures in cattle so that surgeons can perform surgical procedures with great precision and safety. Due to their large size, anatomy and complexities like regurgitation, bloat and nerve paralysis, cattle are not considered as good subjects for general anaesthesia. Cattle usually allow physical restraint well, and with local or regional anaesthesia, it is often sufficient to complete many simple surgical and diagnostic procedures; however, major surgical procedures like tibial fracture, femoral fracture, humerus fracture repair by internal fixation, diaphragmatic herniorrhaphy, celiotomy and tarsorrhaphy requires general anaesthesia.

Etomidate is a non-barbiturate intravenous general anaesthetic agent (Fresno *et al.*, 2008) which has a rapid onset of action and recovery (Nagel *et al.*, 1979). It is known for its cardiovascular stability compared to other induction agents (Rodríguez *et al.*, 2012; Saini *et al.*, 2020), however it lacks analgesic property (Reneman and Janssen, 1977). Ketamine is a dissociative anaesthetic agent that is used widely throughout veterinary anaesthesia (Hall *et al.*, 2014). It induces a ‘dissociative’ anaesthetic state (Pai and Heining, 2007), and it has a wide range of actions

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including analgesia, anaesthesia, hallucination, arterial hypertension, nystagmus, lachrymation and salivation (Pai and Heining, 2007). Dexmedetomidine is a highly specific and selective alpha-2 adrenoceptor agonist (Gertler *et al*., 2001). It has a quicker onset of sedation, good muscle relaxation and analgesia (Arunkumar *et al.*, 2017). Xylazine is the first alpha-2-adrenergic agonist used as a sedative and analgesic by veterinarians (Moolchand *et al*., 2014). It produces dose dependent recumbency in cattle (Abrahamsen, 2008), analgesia, respiratory depression and hypothermia (Sandhu and Rampal, 2006).

## MATERIALS AND METHODS

The clinical study was conducted on 12 clinical cases of cattle presented to the Department of Veterinary Surgery and Radiology, Veterinary College, Bidar for surgical treatments. They were randomly divided into two groups of six cattle in each group. The animals were fasted for 24 to 48 hours and deprived of water for 12 to 18 hours prior to anaesthesia. The clinical status of each animal was assessed by recording heart rate, respiratory rate, rectal temperature and haemato-biochemical examinations prior to anaesthesia. Pre-operative fluid therapy was given to all the animals as per requirement. All the animals in the group I and II were premedicated with inj. 5% guaifenesin at the dose rate of 50 mg/kg body weight intravenously. After 5 minutes, inj. xylazine hydrochloride at the dose rate of 0.10 mg/kg and dexmedetomidine at the dose rate of 2.50 µg/kg were administered intravenously to group-I and II animals, respectively. Cattle in group-I were induced with inj. etomidate at the dose rate of 0.50 mg/kg intravenously, 10 minutes after the administration of inj. xylazine hydrochloride, and cattle in group-II were induced with inj. ketamine hydrochloride at the dose rate of 3 mg/kg intravenously, 10 minutes after the administration of inj. dexmedetomidine. 1.50-2.50% isoflurane was used for maintenance of surgical plane of anaesthesia as per the requirement of animals in each group.

Clinical parameters like sedation time (minutes), induction time (seconds), recovery time (minutes), recovery time to sternal position (minutes), recovery time to standing position (minutes), degree of analgesia and degree of muscle relaxation were recorded before induction (0 minute) and 10 minutes after sedation and after induction at $10^{th}$, $30^{th}$, $60^{th}$ and $120^{th}$ minutes interval of general anaesthesia. Other clinical parameters like type of induction and type of recovery were also recorded.

The time taken from administration of sedative agent to the development of ataxia, drooping of eyelids and drowsiness in animals was recorded as sedation time. The time taken to induce general anaesthesia after administration of induction agent was recorded as induction time. The time from discontinuation of the inhalant agent (isoflurane) to the first spontaneous movement of any body part was recorded as recovery time. Time taken by the cattle from discontinuation of inhalant agent to sternal position was recorded as recovery time to sternal position, and time taken by the cattle from discontinuation of inhalant agent to standing position was recorded as recovery time to standing position.

Degree of analgesia was recorded by observing cattle response to deep prick at tail, perineum, inguinal region, upper part of hind limb, digits, thorax and lower abdomen and was graded on 0 to 3 scale (Gautam *et al.*, 2017). Degree of analgesia was recorded before premedication (0 minute), 10 minutes after sedation and after induction at $10^{th}$, $30^{th}$, $60^{th}$ and $120^{th}$ minutes interval of general anaesthesia.

The degree of muscle relaxation was assessed by observing abdominal muscles and reduced resistance to passive flexion of the limb and relaxation of head, neck and limb muscles and was graded on grade A to grade D score (Agivale *et al*., 2019). This was observed before induction (0 minute) and 10 minutes after sedation and after induction at $10^{th}$, $30^{th}$, $60^{th}$ and $120^{th}$ minutes interval of general anaesthesia.

**Table 1. Assessment of degree of analgesia**

| Scale | Description |
|---|---|
| 0 | No analgesia: Strong reaction to pin pricks |
| 1 | Mild: Weak reaction to needle pricks |
| 2 | Moderate: Occasional response to needle pricks |
| 3 | Complete analgesia |

**Table 2. Assessment of degree of muscle relaxation**

| Score | Quality | Character |
|---|---|---|
| Grade A | Excellent | Complete relaxation |
| Grade B | Good | Adequate muscle relaxation for surgical procedure |
| Grade C | Moderate | Partial relaxation of head, neck and limb muscles |
| Grade D | Poor | Rigidity in muscles of head, neck and limb |

Physiological parameters viz., heart rate (beats/minute), respiratory rate (breaths/minute) and rectal temperature (°F) were recorded before premedication (0 minute), 10 minutes after sedation and after induction at $10^{th}$, $30^{th}$, $60^{th}$ and $120^{th}$ minutes interval of general anaesthesia.

## RESULTS

The details of all the clinical and physiological parameters recorded in the present clinical study are given in the table 3 and 4, respectively.

**Clinical parameters:** In group-I, the onset of sedation ranged from 3.30 to 4.50 minutes, with a mean of 4.05±0.28 minutes. In group-II, the onset of sedation ranged from 2.66 to 2.94 minutes, with a mean of 2.76±0.17 minutes. Time for sedation was significantly quicker ($p \leq 0.05$) in group-II as compared to that of group-I. In group-I, the time for induction ranged from 55 to 70 seconds, with a mean of 61.66±2.17 seconds. In group-II, time for induction ranged from 57 to 75 seconds, with the mean of 64.16±2.67 seconds. Induction time was non-significantly quicker in group-I as compared to that of group-II. In group-I, the type of induction was rapid, and the quality of induction was satisfactory; however, two cattle showed myoclonus during induction, where it was for a short, transient period. With mild jaw tone, all cattle quickly assumed lateral recumbency. The induction in group-II was rapid and smooth, with the presence of a palpebral reflex and a mild jaw tone. The cattle did not show any adverse effects after induction. In group-I, recovery time ranged from 9 to 14 minutes, with a mean of 11.41±0.75 minutes. In group-II, recovery time ranged from 13 to 27 minutes, with a mean of 17.66±2.30 minutes. Recovery time was significantly ($p \leq 0.05$) quicker in group-I as compared to that of group-II. In group-I, recovery time to the sternal position ranged from 38 to 65 minutes, with a mean of 50.50±4.13 minutes. In group-II, recovery time ranged from 37 to 73 minutes, with a mean of 53.83±5.02 minutes. Comparison between the groups showed non-significant differences between the groups. In group-I, the recovery time to standing position ranged from 70 to 215 minutes, and the mean was 160.00±20.20 minutes. In group-II, recovery time ranged from 80 to 218 minutes, and the mean was 168.16±22.75 minutes. Comparison between the groups showed non-

**Table 3. Clinical parameters in both the groups (Mean±SE)**

| Parameters | Groups | Mean±SE |
|---|---|---|
| Onset of sedation (minutes) | Group-I | $4.05^{a}\pm0.28$ |
| | Group-II | $2.76^{b}\pm0.17$ |
| Induction for time (seconds) | Group-I | 61.66±2.71 |
| | Group-II | 64.16±2.67 |
| Recovery time (minutes) | Group-I | $11.41^{a}\pm0.75$ |
| | Group-II | $17.66^{b}\pm2.30$ |
| Recovery time to sternal position (minutes) | Group-I | 50.50±4.13 |
| | Group-II | 53.83±5.02 |
| Recovery time to standing position (minutes) | Group-I | 160.00±20.20 |
| | Group-II | 168.00±22.75 |

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

**Table 4. Physiological parameters in both the groups (Mean±SE)**

| Parameters | Groups | Time intervals (minutes) | | | | | |
|---|---|---|---|---|---|---|---|
| | | 0 min | 10 min sedation | 10 min induction | 30 min induction | 60 min induction | 120 min induction |
| Degree of analgesia | Group-I | 00.00 ±00.00 | $1.16^{**a}$ ±0.16 | $1.33^{**a}$ ±0.21 | $2.66^{**}$ ±0.21 | $2.66^{**}$ ±0.53 | $2.50^{**}$ ±0.22 |
| | Group-II | 00.00 ±00.00 | $1.83^{**b}$ ±0.16 | $2.66^{**b}$ ±0.21 | $2.83^{**}$ ±0.16 | $2.83^{**}$ ±0.16 | $2.66^{**}$ ±0.21 |
| Respiratory rate (breaths/minute) | Group-I | $26.83^{*}$ ±2.15 | $20.33^{*}$ ±1.33 | 22.66 ±1.35 | $21.50^{*}$ ±0.42 | $21.33^{*}$ ±0.71 | $21.66^{*}$ ±0.61 |
| | Group-II | 28.50 ±2.89 | 25.50 ±2.56 | 26.83 ±1.30 | $21.50^{*}$ ±0.84 | $21.50^{*}$ ±0.88 | $21.16^{*}$ ±0.30 |
| Heart rate (beats/minute) | Group-I | $63.50^{*}$ ±3.87 | $51.66^{*}$ ±3.32 | $55.33^{a}$ ±3.30 | $46.66^{**a}$ ±2.93 | $47.33^{**a}$ ±2.67 | $46.50^{**a}$ ±3.05 |
| | Group-II | $61.83^{*}$ ±2.82 | $49.83^{*}$ ±3.19 | $74.66^{*b}$ ±3.82 | $66.16^{b}$ ±2.61 | $64.50^{b}$ ±2.21 | $69.00^{b}$ ±4.43 |
| Rectal temperature ($^{O}$F) | Group-I | 101.31 ±0.17 | 100.90 ±0.14 | $100.00^{**}$ ±0.13 | $99.48^{**}$ ±0.21 | $99.25^{**}$ ±0.21 | $98.60^{**}$ ±0.51 |
| | Group-II | 101.03 ±0.36 | 100.45 ±0.32 | 100.26 ±0.19 | $99.90^{*}$ ±0.26 | $99.68^{*}$ ±0.33 | $99.90^{*}$ ±0.28 |

Means bearing superscript $^{**}$ differ significantly ($p \leq 0.01$) from interval before within the group to different interval; Means bearing superscript $^{*}$ differ significantly ($p \leq 0.05$) from interval before within the group to different interval; Means bearing superscript $^{a,\,b}$ differ significantly ($p \leq 0.05$) between the groups at corresponding different intervals significant differences between the groups. In cattle of group-I, analgesia was mild to moderate at 10 minutes after sedation and 10 minutes after induction. It was moderate to complete analgesia at 30 minutes after induction, and it continued to be excellent till 120 minutes. In cattle of group-II, analgesia was mild to moderate at 10 minutes after sedation, and it was excellent at 10 minutes after induction, and it continued to be excellent up to 120 minutes. Comparison between the groups showed a significant ($p \leq 0.05$) difference between the groups at 10 minutes after sedation and 10 minutes after induction. In group-I cattle, muscle relaxation was moderate to good at 10 minutes after premedication, and it continued up to 10 minutes after induction. Muscle relaxation was excellent at 30 minutes after post-induction, and it continued up to 120 minutes. In group-II, muscle relaxation was moderate to good at 10 minutes after premedication, and it continued up to 10 minutes after induction, and muscle relaxation was excellent at 30 minutes of post-induction, and it continued up to 120 minutes. However, muscle relaxation was slightly higher in group-II cattle sedated with dexmedetomidine when compared to group-I.

**Physiological parameters:** Respiratory rate decreased significantly ($p \leq 0.05$) at 10 minutes after premedication with xylazine and 30, 60 and 120 minutes after induction in group-I cattle. The respiratory rate decreased significantly ($p \leq 0.05$) at 30, 60 and 120 minutes after induction, and it decreased non-significantly at 10 minutes after sedation in group-II cattle. Comparison between the groups revealed that there was no significant difference between the groups at all the corresponding intervals. Heart rate decreased significantly ($p \leq 0.05$) at 10 minutes after premedication and 10 minutes after induction. There was a significant ($p \leq 0.01$) decrease in heart rate at 30 minutes, 60 minutes and 120 minutes when compared with the mean of 0 minute. Heart rate decreased significantly ($p \leq 0.05$) at 10 minutes after premedication and which then increased significantly ($p \leq 0.05$) at 10 minutes after administration of ketamine. From 30 minutes of post-induction, the heart rate decreased towards normal. The decrease in heart rate at 10 minutes after premedication was significantly ($p \leq 0.05$) more in cattle premedicated with dexmedetomidine (group-II) compared to cattle premedicated with xylazine. Comparison between the groups revealed that group-II cattle had a significantly ($p \leq 0.05$) higher heart rate compared to group-I cattle at 10, 30, 60 and 120 minutes of post-induction. Rectal temperature decreased significantly ($p \leq 0.01$) at 10, 30, 60 and 120 minutes of post-induction in group-I cattle. There was a significant ($p \leq 0.05$) decrease in rectal temperature at 30, 60 and 120 minutes after induction when compared with a mean of 0 minutes, and there was a non-significant decrease in rectal temperature at 10 minutes after sedation and 10 minutes after induction in group-II. Comparison between the groups revealed that there was no significant difference between the groups at all the intervals of the study.

**Anaesthetic complications:** One animal in group I showed myoclonus during induction of anaesthesia, and regurgitation and salivation were observed in one animal in group I and two animals in group II.

## DISCUSSION

Quicker onset of sedation in group-II might be due to dexmedetomidine being highly specific, more potent and selective alpha-2-adrenoceptor agonist, as opined by Gertler *et al.* (2001). Ragab *et al.* (2022) reported a faster onset of sedation in goats after the administration of dexmedetomidine. Vigneshwaran *et al.* (2020) reported good quality of sedation in cattle sedated with dexmedetomidine. Sharma *et al.* (2019) reported good sedation in buffaloes sedated with xylazine. Quicker onset of induction in group-I might be due to etomidate being an ultra-short acting hypnotic agent (Reneman and Janssen, 1977) which acts via enhancing GABA receptors (Forman and Warner, 2011) and it has a rapid onset of action (Nagel *et al.*, 1979). Kumar *et al.* (2020) and Saini *et al.* (2020) reported excellent quality and quicker induction of anaesthesia with etomidate in dogs. Liu *et al.* (2018) reported myoclonus during induction in dogs induced with etomidate. Mama *et al.* (2005) reported good to excellent quality of induction in horses induced with ketamine. Early recovery in group-I might be due to shorter elimination half-life in xylazine as compared to dexmedetomidine (Cagnardi *et al.*, 2017) and also be due to etomidate being an ultrashort acting agent (Reneman and Janssen, 1977) with short elimination half-life (3.88±1.11 hours) and rapid clearance (954±178 mL/min) (Giese and Stanley, 1983). Early recovery in dogs induced with etomidate was reported by Saini *et al.* (2020). Chaudhary *et al.* (2017) evaluated anaesthetic combination of glycopyrrolate-xylazine-butorphanol-thiopentone-isoflurane in buffaloes and reported recovery time was 3.00±0.45 minutes. Vigneshwaran *et al.* (2020) observed good analgesia in cattle administered with dexmedetomidine, and Sekhar *et al.* (2020) reported rapid onset and longer duration of analgesia in cattle with epidural dexmedetomidine and ropivacaine anaesthesia. Vigneshwaran *et al.* (2020) reported adequate muscle relaxation in cattle with an anaesthetic combination of glycopyrolate-dexmedetomidine-ketamine-isoflurane anaesthesia. Thavardas *et al.* (2022) reported excellent quality of muscle relaxation in cattle with guaifenesin and ketamine anaesthesia in the form of continuous drip. Respiratory depression was slightly higher in xylazine premedicated cattle compared to dexmedetomidine premedicated cattle. This might be due to xylazine, which inhibits locus coeruleus, producing respiratory depression. Similar findings were observed by Jaiswal *et al.* (2016) in buffalo calves and Sekhar *et al.* (2020) in cattle after dexmedetomidine administration. A significant decrease in the respiratory rate after xylazine premedication was observed by Ghurashi *et al.* (2016) in donkeys and Venkatgiri *et al.* (2017), and Muchalambe *et al.* (2018) in cattle. Respiratory rate was nonsignificantly greater in cattle induced with ketamine (group-II) compared to cattle induced with etomidate (group-I). This might be due to bronchodilation caused by ketamine (Sinner and Graf, 2008). Similar findings were observed by Molinaro Coelho *et al.* (2014) in donkeys with ketamine-propofol anaesthesia. Hikasa *et al.* (2000) observed a decrease in the respiratory rate in sheep during isoflurane anaesthesia. Khattri *et al.* (2013) and Ragab *et al.* (2022) observed a significant decrease in heart rate after dexmedetomidine in buffaloes and goats, respectively. Neelakant *et al.* (2021) observed a significant increase in heart rate in cattle with guaifenesin-ketamine- isoflurane anaesthesia. Kumar *et al.* (2014) reported a significant decrease in rectal temperature with dexmedetomidine and ketamine anaesthesia. Ghurashi *et al.* (2016) reported decreased rectal temperature in donkeys after administration of xylazine and ketamine. Liu *et al.* (2018) and Kamble *et al.* (2021) reported decreased rectal temperature in dog with dexmedetomidine and etomidate anaesthesia. Onmaz *et al.* (2009) reported a significant decrease in rectal temperature in sheep during isoflurane maintenance anaesthesia.

Anaesthetic complications like myoclonus might be due to subcortical disinhibition (Isitemiz *et al*., 2014). Liu *et al.* (2018) reported that myoclonus was induced in dogs with etomidate. Regurgitation and salivation in both groups might be due to a decrease in gastro-oesophageal sphincter pressure by alpha2 adrenoceptor agonists and stimulation of salivation by ketamine (Sandhu and Rampal, 2006). Gunderson *et al*. (2013) observed salivation in dogs during induction of anaesthesia with etomidate. Khattri *et al.* (2013) observed mild salivation in buffalo after premedication with dexmedetomidine. Muchalambe *et al.* (2018) reported moderate to extensive salivation in cattle premedicated with xylazine. Shivasharanappa (2022) reported excessive salivation and regurgitation in cattle induced with ketamine and maintained under isoflurane anaesthesia.

In the present clinical study, both the anaesthetic protocols provided adequate surgical plane of anaesthesia with good analgesia and muscle relaxation for orthopaedic and soft tissue surgeries. In both groups, physiological parameters such as respiratory rate and rectal temperature decreased significantly till the observation interval. However, the variations were within the normal physiological range and did not indicate any anaesthetic emergencies. Both protocols can be used for surgeries which are prolonged for more than two hours in a compromised patient. However, etomidate can be used safely as an induction agent in cardiac-compromised cattle or in surgeries like diaphragmatic herniorrhaphy, even though it is not commonly used in cattle.

**Conflict of interest:** Authors have no conflict of interest in the study.

**Author's contribution:** NMR, B: Conception and designing of the research and conducted the research work; NMR, DK: Statistical analysis of the data and technical support; NMR, S: Interpretation of the results; V: Technical support.

**Data availability statement:** All the data supporting the research findings have been presented in this paper. The corresponding author is willing to provide the raw data upon reasonable request.

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