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Behavioural and Sedative Study in Buffaloes Suffering from Diaphragmatic Hernia Treated with Various NSAIDS

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A B S T R A C T

The study was conducted in eighteen buffaloes categorised into three groups of six animals each. The drugs were used in following combinations: Glycopyrrolate–Xylazine–Meloxicam–Ketamine, Glycopyrrolate-Xylazine-Tolfenamic acid-Ketamine and Glycopyrrolate–Xylazine–Flunixin-meglumine–Ketamine. Glycopyrrolate was given @ 0.01 mg/kg body weight i/m, Xylazine @ 0.04 mg/kg body weight i/m, Meloxicam at 0.5 mg/kg body weight i/m, Tolfenamic acid 4 mg/kg body weight i/m, Flunixin-meglumine at 2.2 mg/kg body weight i/v and Xylazine and Ketamine @ 0.04 mg/kg body weight i/v and 1 mg/kg body weight i/v for induction and maintenance were given. Tolfenamic acid and Flunixin-meglumine groups produced comparable analgesia duration for 40.24±1.95 and 43.00 ±1.24 minutes respectively but analgesia duration for Meloxicam group was for 30.34±2.02 minutes comparatively lesser than Tolfenamic acid and Flunixin-meglumine groups. Anesthesia remained for comparable duration in Tolfenamic acid group (59.5±2.34 minutes), and Flunixin-meglumine group (58.83 ± 1.22 minutes) and shorter in Meloxicam group (54.66±2.45 minutes). Complete recovery was earliest in Meloxicam group in 85.66±2.02 minutes followed by Tolfenamic acid group in 91.33±2.89 minutes and Flunixin-meglumine group in 93.33±2.47 minute.

Introduction

Diaphramatic hernia is a serious thoraco-digestive disorder of buffaloes, in which a part of abdominal viscera "mainly reticulum" passed into the thoracic cavity through a congenital or acquired opening in the diaphragm causing chronic ruminaltympany, anorexia and displacement of the heart (Radostits *et al*., 2007). Its high prevalence reported especially from North India. In buffaloes herniation occurs mostly through right ventro-medial part of the diaphragm, which ruptures from the musculo-tendinous junction (Saini *et al*., 2000). The situation of diaphragmatic hernia is serious, as if it remains untreated causes death in 100% cases (Krishnamurthy *et al*., 1985).

Management of diaphragmatic hernia requires surgery in two stages. The first stage involves a laparo-rumenotomy that enables the surgeon to assess the location and extent of herniation, retract and remove foreign bodies. During the second stage of surgery, the repair of the diaphraghmatic defect is done under general anaesthesia along with controlled ventilation (Singh *et al*., 2006). There is severe pain during the time of diaphragmatic herniorrhaphy. To achieve anaesthesia and relieve the pain different analgesic drugs are used which act on peripheral and central nervous system.

General anaesthesia is a state of reversible unconsciousness produced by a process of controlled, reversible drug-induced intoxication of the central nervous system in which the patient neither perceives nor recalls noxious stimuli (Hall *et al*., 2001). It is not easy to select a drug or a combination of drugs for general anaesthesia especially in ruminants. Due to this reason, it becomes imperative to evaluate each sedative or preanaesthetic drug before clinical use.

Glycopyrrolateis a preanaesthetic drug which stimulates cardiac reflex and blocks vagus reflex, thus prevents or inhibits cardiac inhibitory effect of Xylazine. Xylazine administration produces profuse salivation in cattle as recorded by Kumar and Singh (1979). It produced tachycardia (Khan *et al.,* 2007a) in buffalo calves and that it when administered after Xylazine administration caused increased heart rate and mean arterial pressure (Khan *et al.,* 2007b).

Xylazine is typical α_2-adrenoceptor agonist and exerts its effect accordingly. There is marked variation in susceptibility to Xylazine's effect in various species of domestic animals.

Ketamine is a dissociative anaesthetic that is used for induction/maintenance of anaesthesia in many species. It has the tendency to cause catalepsy and occasional seizers (Pageat, 1986). Propofol was found safe intravenous anaesthetic to induce general anaesthesia in buffaloes (Ratnesh, 2010).

Post-operative pain is commonly managed by Nonsteroidal anti-inflammatory drugs (NSAIDs)/ opioid (Dar *et al*., 2013). NSAIDs are used extensively in veterinary practice for their analgesic, anti-inflammatory and antipyretic effects. Nonsteroidal anti-inflammatory drugs (NSAIDs) have been reported to be extremely effective post-operative analgesics (Mathews, 2001).

Flunixin-meglumine is a carboxylic acid nonsteroidal anti-inflammatory drug and a potent inhibitor of cyclooxygenase (Semrad *et al*., 1985). In horses, Flunixin-meglumine is indicated for alleviation of inflammation and pain associated with musculoskeletal disorders and visceral pain associated with pain.

Tolfenamic acid belongs to the fenamate group and is a potent inhibitor of cyclo-oxygenase enzyme. It is efficient in treatment of chronic and acute painful locomoter syndromes in the dog (Lecoindre *et al*., 1995).

Meloxicam is an oxicam (enolic acid) derivative. Meloxicam has preferential COX-2 activity and is also a mild inhibitor of COX-1 in platelets and kidneys (Deneuche *et al.,* 2004). It is indicated for the management of inflammation and pain arising from acute and chronic diseases (Lascelles *et al.,* 2001).

Meloxicam, Tolfenamic acid and Flunixin-meglumine have not been tried earlier as pre-emptive analgesia in combination with Glycopyrrolate - Xylazine - Ketamine anaesthesia in buffaloes undergoing diaphragmatic harniorrhaphy (D.H.). Therefore, the present study was undertaken to evaluate the behavioural and sedative study in buffalo treated with the following drugs:

Group1 Glycopyrrolate - Xylazine - Meloxicam - Ketamine in buffaloes undergoing diaphragmatic herniorrhaphy.

Group2 Glycopyrrolate - Xylazine - Tolfenamic acid - Ketamine in buffaloes undergoing diaphragmatic herniorrhaphy.

Group 3 Glycopyrrolate -Xylazine - Flunixin-meglumine - Ketamine in buffalo undergoing diaphragmatic herniorrhaphy.

Materials and Methods

Eighteen clinical cases of buffaloes suffering from diaphramatic hernia presented to the Teaching Veterinary Clinical Complex, LUVAS, Hisar were taken in consideration for present study.

Diaphragmatic hernia was confirmed by radiography and rumenotomy. In positive cases, the ruminal contents were evacuated completely by laparo-rumenotomy and thereafter diaphragmatic hernia repair was done under general anaesthesia. Each animal was weighed before the diaphragmatic herniorraphy for calculating the proper dose of drugs used for general anaesthesia and kept off feed and water after laparo-rumenotomy and these animals were kept strictly on fluid therapy to avoid regurgitation during operation.

The animals were divided into three groups of six animals each. Pilot trials were done to standardize the dose rates and route of administration of different drugs.

Rectal temperature, heart rate (*by auscultation*) and respiration rate were recorded just before administration of the drug(s) along with the ambient temperature to form the base values. The blood samples were collected from jugular venipuncture before rumenotomy i.e before administration of the drugs, before diaphragmatic herniorraphy, 15 minutes after administration of Meloxicam/ Tolfenamic acid/ Flunixin-meglumine, 5 minutes after administration of Ketamine, after complete recovery from the effects of the drugs and at 24 hour after recovery. Various physiological parameters were recorded at before rumenotomy, before diaphragmatic herniorrhaphy, 15 minutes after Glycopyrrolate, 10 minutes after Xylazine, and 15 minutes after Meloxicam/Tolfenamic acid/Flunixin-meglumine administeration at recovery and 24 hours after diaphragmatic herniorrhaphy.

The animals were observed to record the following behavioral and sedative changes:

1. *Spontaneous motor activity*
2. Onset of *salivation, urination, defaecation* and *lacrimation*
3. *Weak time*: time elapsed from administration of drug to onset of ataxia.
4. Qualitative and subjective *analgesic effect*(s) of drugs were judged by observing physical response of the medicated animal to pin prick/surgical response.
5. Recovery from effects of drugs was interpreted to have occurred as exhibited by:

a. *Sternal recumbency* and *head rightening reflex*

b. *Standing time* with ataxia.
Complete recovery without ataxia.

Results and Discussion

The study was conducted on eighteen clinical cases of diaphragmatic hernia presented in TVCC, Hisar and these were divided into three groups of six animals each. All the parameters listed below were observed/ recorded before the animals were operated for rumenotomy and were taken as base values. The results of study are presented in the following tables (Table 1–4).

Table.1 Group 1: Means and standard errors (±) in time format of minutes for different behavioural characteristics of onset of CNS depression and recovery from CNS depression induced by administration of Glycopyrrolate–Xylazine–Meloxicam–Ketamine combination

Reflexes		Mean time (minutes)	Standard error(±)
Muzzle dryness(after Glycopyrrolate administration)		14	**1.15**
Decreased spontaneous motor activity (SMA) (after Xylazine injection)		7.33	**0.55**
Ataxia /weak time (after Xylazine injection)		14.16	**0.54**
Swallowing reflex(after Ketamine administration)	Loss	2.33	**0.24**
	Regain	53.83	**1.40**
Regaining of Spontaneous respiration (after Ketamine administration)		39.66	**2.66**
Onset of analgesia (after Ketamine administration)	Fetlock	2	**0.22**
	Base of Horn	3.75	**0.30**
	Ribs	4.66	**0.33**
	Tail	3.08	**0.20**
Loss of analgesia (after Ketamine administration)	Fetlock	41.83	**2.40**
	Base of Horn	38	**2.36**
	Ribs	35	**2.35**
	Tail	37	**2.26**
Regaining of head rightening reflex (after Ketamine administration)		54.66	**2.45**
Return to sternal recumbency (after Ketamine administration)		61.66	**2.17**
Standing time with ataxia (after Ketamine administration)		72.66	**2.67**
Complete recovery (after Ketamine administration)		**85.66**	**2.02**

Table.2 Group:2 Means and standard errors (±) in time format of minutes for different behavioural characteristics of onset of CNS depression and recovery from CNS depression induced by administration of Glycopyrrolate–Xylazine–Tolfenamic acid–Ketamine combination

Reflexes		Mean time (minutes)	Standard error(±)
Muzzle dryness (after Glycopyrrolate administration)		14.83	**1.10**
Decreased spontaneous motor activity (SMA) (after Xylazine injection)		8.66	**0.88**
Ataxia /weak time (after Xylazine injection)		14.83	**0.87**
Swallowing reflex (after Ketamine administration)	Loss	2.16	**0.27**
	Regain	61.66	**2.20**
Regaining of Spontaneous respiration (after Ketamine administration)		43.66	**3.52**
Onset of analgesia (after Ketamine administration)	Fetlock	2.33	**0.21**
	Base of Horn	4.16	**0.65**
	Ribs	5.5	**0.61**
	Tail	3.08	**0.41**
Loss of analgesia (after Ketamine administration)	Fetlock	50.5	**2.43**
	Base of Horn	50.33	**2.83**
	Ribs	45.5	**2.56**
	Tail	49.5	**2.90**
Regaining of head rightening reflex (after Ketamine administration)		59.5	**2.34**
Return to sternal recumbency (after Ketamine administration)		66.33	**2.02**
Standing time with ataxia (after Ketamine administration)		76.16	**2.15**
Complete recovery (after Ketamine administration)		**91.33**	**2.89**

Table.3 Group:3 Means and standard errors (±) in time format of minutes for different behavioural characteristics of onset of CNS depression and recovery from CNS depression induced by administration of Glycopyrrolate–Xylazine–Flunixin-meglumine–Ketamine combination

Reflexes		Mean time (minutes)	Standard error(±)
Muzzle dryness (after Glycopyrrolate administration)		15.83	**1.24**
Decreased spontaneous motor activity (SMA) (after Xylazine injection)		8.05	**0.23**
Ataxia /weak time(after Xylazine injection)		15.5	**0.84**
Swallowing reflex (after Ketamine administration)	Loss	2	**0.28**
	Regain	61.66	**2.64**
Regaining of Spontaneous respiration (after Ketamine administration)		49	**9.59**
Onset of analgesia (after Ketamine administration)	Fetlock	3	**0.34**
	Base of Horn	4.66	**0.42**
	Ribs	6.66	**0.42**
	Tail	3.33	**0.21**
Loss of analgesia (after Ketamine administration)	Fetlock	52.5	**1.87**
	Base of Horn	52.5	**2.14**
	Ribs	49.66	**1.66**
	Tail	48.33	**0.84**
Regaining of head rightening reflex (after Ketamine administration)		58.83	**1.22**
Return to sternal recumbency (after Ketamine administration)		63.33	**1.14**
Standing time with ataxia (after Ketamine administration)		78.83	**1.83**
Complete recovery (after Ketamine administration)		**93.33**	**2.47**

Table.4 Means and standard errors (±) in time format of minutes for different behavioural characteristics of different groups

Reflexes		Mean time (minutes) GXMK	Mean time (minutes) GXTAK	Mean time (minutes) GXFMK
Muzzle dryness(after Glycopyrrolate administration)		14±1.15	14.83±1.10	**15.83±1.24**
Decreased spontaneous motor activity (SMA) (after Xylazine injection)		7.33±0.55	8.66±0.88	**8.05±0.23**
Ataxia /weak time (after Xylazine injection)		14.16±0.54	14.83±0.83	**15.5±0.84**
Swallowing reflex (after Ketamine administration)	Loss	2.33±0.24	2.16±0.27	**2.00±0.28**
	Regain	53.83±1.40	61.66±2.20	**61.66±2.64**
Regaining of Spontaneous respiration (after Ketamine administration)		39.66±2.66	43.66±3.52	**49±9.59**
Onset of analgesia (after Ketamine administration)	Fetlock	2.00±0.22	2.33±0.21	**3.00±0.34**
	Base of Horn	3.75±0.30	4.16±0.65	**4.66±0.42**
	Ribs	4.66±0.33	5.5±0.61	**6.66±0.42**
	Tail	3.08±0. 20	3.08±0.41	**3.33±0.21**
Loss of analgesia (after Ketamine administration)	Fetlock	41.83±2.40	50.5±2.43	**52.5±1.85**
	Base of Horn	38.00±2.36	50.33±2.83	**52.5±2.14**
	Ribs	35.00±2.35	45.5±2.56	**49.66±1.66**
	Tail	37±2.26	49.5±2.90	**48.33±0.84**
Regaining of head rightening reflex (after Ketamine administration)		54.66±2.45	59.5±2.34	**58.83±1.22**
Return to sternal recumbency (after Ketamine administration)		61.66±2.17	66.33±2.02	**63.33±1.14**
Standing time with ataxia (after Ketamine administration)		72.66±2.67	76.16±2.15	**78.83±1.83**
Complete recovery (after Ketamine administration)		**85.66±2.02**	**91.33±2.89**	**93.33±2.47**

Group 1

CNS depression was observed after intramuscular administration of Xylazine as all the animals showed decrease in spontaneous motor activity at 7.33±0.55 minutes, ataxia at 13.5±1.47 minutes followed by lateral recumbency. In cattle administration of Xylazine (0.5 mg/kg, IM) produced deep sedation with animal going into lateral recumbency (Hall and Clarke, 1969). Dropping of head and ataxia was seen in horses given premedication with Xylazine (Butera *et al*., 1980). A moderate amount of salivation with good sedation and muscle relaxation was observed following Xylazine administration in buffalo calves (Peshin and Kumar, 1979). Palpebral and corneal reflexes and tongue movements (curling) were abolished in four animals during the period of anaesthesia. Swallowing reflex was abolished after 2.33±0.24 minutes of Ketamine administration. This finding holds well to the findings in goats given an intravenous dose of midazolam followed by Ketamine (Singh, 2004) and by Kumar and Thurmon (1977), in goats given acepromazine-Ketamine anasesthesia and by Singh (2008) in buffalo calves given an intravenous dose of Xylazine and Ketamine, but the findings are contrary with the reports of Ghanawat and Mantra, (1996) in cats given Xylazine-Ketamine and in buffalo calves given Ketamine @ 2.0 mg/kg by intravenous drip, Ketamine anaesthesia showed intact palpebral and corneal reflexes. There was complete analgesia at fetlock, base of tail, abdomen, ribs periosteum and base of horn after administration of Ketamine. Analgesia remained for 30.34±2.02 minutes at ribs periosteum. Leece *et al.*, (2005) concluded that meloxicam provided satisfactory analgesia for 72 hours following ovariohysterectomy in dogs. Post-operative analgesic effect of Meloxicam and Butorphanol were considered adequate in African buffaloes following Midazolam-Ketamine-Isoflurane anaesthesia (Stegmann, 2004). Pre-operative administration of meloxicam immediately before induction was also found safe and effective method of controlling post operative pain for upto 24 hours in dogs (Mathews 2001 and Deneuche *et al*., 2004). Mathews *et al.*, (2001) studied the analgesic efficacy of meloxicam after various soft tissue surgical procedures and reported that meloxicam provides excellent analgesia for upto 24 hours after administration as compared to Butorphenol.

Anaesthesia remained for a mean time of 54.66±2.45minutes. Ketamine provides profound analgesia (Evers and Crowder, 2001) and agrees with findings in calves given intravenous Xylazine-Ketamine (Singh, 2008); in goats given midazolam-Ketamine intravenously (Singh, 2004). Singh (2004) reported that good analgesia commenced 5 minutes after Ketamine administration and remained till 30 minutes. In present study head rightening reflex was observed at 54.66±2.45 minutes indicating the start of recovery period followed by sternal recumbency at 61.66±2.17 minutes and standing of animals with ataxia occurred at 72.66±2.67 minutes with complete recovery without ataxia at 85.66±2.02 minutes of Ketamine injection.

Group 2

Onset of CNS depression started after intramuscular administration of Xylazine as all the animals showed decrease in spontaneous motor activity at 8.66±0.88 minutes, ataxia at 14.83±0.87 minutes followed by lateral recumbency. In cattle administration of Xylazine (0.5 mg/kg, IM) produced deep sedation with animal going into lateral recumbency (Hall and Clarke, 1969). Dropping of head and ataxia was seen in horses given premedication with Xylazine

(Butera *et al*., 1980). Onset of salivation was observed in two animals. A moderate amount of salivation with good sedation and muscle relaxation was observed following Xylazine administration in buffalo calves (Peshin and Kumar, 1979). Palpebral and corneal reflexes and tongue movements (curling) were abolished in two animals during the period of anaesthesia. Swallowing reflex was abolished after 2.16±0.27 minutes of Ketamine administration. This finding holds well to the findings in goats given an intravenous dose of midazolam followed by Ketamine (Singh, 2004) and by Kumar and Thurmon (1977), in goats given acepromazine-Ketamine anaesthesia and by Singh (2008) in buffalo calves given an intravenous dose of Xylazine and Ketamine, but the findings are contrary with the reports of Ghanawat and Mantra, (1996) in cats given Xylazine-Ketamine and in buffalo calves given Ketamine @ 2.0 mg/kg by intravenous drip, Ketamine anaesthesia showed intact palpebral and corneal reflexes. There was complete analgesia at fetlock, base of tail, abdomen, ribs periosteum and base of horn after administration of Ketamine. Analgesia remained for 40.24±1.95 minutes at ribs periosteum. Tolfenamic acid was found effective for post operative analgesia in dogs undergoing orthopaedic surgery (Grandemange *et al.*, 2007).

Anaesthesia remained for a mean time of 59.5±2.34minutes. Ketamine provides profound analgesia (Evers and Crowder, 2001) and agrees with findings in calves given intravenous Xylazine-Ketamine (Singh, 2008); in goats given midazolam-Ketamine intravenously (Singh, 2004). Singh (2004) reported that good analgesia commenced 5 minutes after Ketamine administration and remained till 30 minutes. In present study head rightening reflex was observed at 59.5±2.34 minutes indicating the start of recovery period followed by sternal recumbency at 66.33±2.02 minutes and standing of animals with ataxia occurred at 76.16±2.15 minutes with complete recovery without ataxia at 91.33±2.89 minutes of Ketamine injection.

Group 3

After intramuscular administration of Xylazine CNS depression was observed as all the animals showed decrease in spontaneous motor activity at 8.05±0.23 minutes, ataxia at 15.5±0.84 minutes followed by lateral recumbency. In cattle administration of Xylazine (0.5 mg/kg, IM) produced deep sedation with animal going into lateral recumbency (Hall and Clarke, 1969). Dropping of head and ataxia was seen in horses given premedication with Xylazine (Butera *et al*., 1980). Onset of salivation was observed in two animals. A moderate amount of salivation with good sedation and muscle relaxation was observed following Xylazine administration in buffalo calves (Peshin and Kumar, 1979). Palpebral and corneal reflexes and tongue movements (curling) were observed in four animals during the period of anaesthesia. Swallowing reflex was abolished after 2.16±0.27 minutes of Ketamine administration. This finding holds well to the findings in goats given an intravenous dose of midazolam followed by Ketamine (Singh, 2004) and by Kumar and Thurmon (1977), in goats given acepromazine-Ketamine anaesthesia and by Singh (2008) in buffalo calves given an intravenous dose of Xylazine and Ketamine, but the findings are contrary with the reports of Ghanawat and Mantra, (1996) in cats given Xylazine-Ketamine and in buffalo calves given Ketamine @ 2.0 mg/kg by intravenous drip, Ketamine anaesthesia showed intact palpebral and corneal reflexes. There was complete analgesia at fetlock, base of tail, abdomen, ribs periosteum and base of horn after administration of Ketamine. Analgesia

remained for 43±1.24 minutes at ribs periosteum. In horses, Flunixin-meglumine is indicated for alleviation of inflammation and pain associated with musculoskeletal disorders and visceral pain associated with colic. Flunixin-meglumine is a drug that is approved by US Food and Drug Administration for therapy for colic and musculoskeletal disorders (Houdeshell and Hennessey, 1977; Vernilimer and Hennessey, 1977). Anaesthesia remained for a mean time of 58.83±1.22 minutes. Ketamine provides profound analgesia (Evers and Crowder, 2001) and agrees with findings in calves given intravenous Xylazine-Ketamine (Singh, 2008); in goats given midazolam-Ketamine intravenously (Singh, 2004). Singh (2004) reported that good analgesia commenced 5 minutes after Ketamine administration and remained till 30 minutes. In present study head rightening reflex was observed at 58.83±1.22 minutes indicating the start of recovery period followed by sternal recumbency at 63.33±1.14 minutes and standing of animals with ataxia occurred at 78.83±1.83 minutes with complete recovery without ataxia at 93.33±2.47 minutes of Ketamine injection.

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