ANESTHETIC EFFECTS OF KETAMINE-GUAIFENESIN AND ISOFLURANE ANESTHESIA FOR DIAPHRAGMATIC HERNIORRHAPHY IN BUFFALOES

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ABSTRACT

The study was undertaken on twelve buffaloes weighing 313 to 442 kg and age between 4 to 9 years to evaluate double drip of ketamine-guaifenesin and isoflurane anaesthesia for diaphragmatic herniorrhaphy. In Group I and II animals, anesthesia was induced with double drip of ketamine-guaifenesin (1000 mg of ketamine, 25 gm of guaifenesin in 500 ml Dextrose 5% solution) 1.5 ml/kg body weight. Double drip 2.5 mL/kg/h in Group I and 2% isoflurane in Group II was used for maintenance of anaesthesia. In both the groups, quality of induction of anaesthesia was good to excellent. The quality of maintenance was assessed by analgesia, muscle relaxation, corneal reflexes, palpebral reflexes, and position of eyeball. Four animals in each group showed excellent muscle relaxation and two animals showed good muscle relaxation during the observation period. Analgesia was excellent in both the groups. In Group I three animals showed smooth and fast recovery whereas smooth and prolonged in rest of the animals. In Group II, all the animals showed smooth and fast recovery. The combination was found suitable for diaphragmatic herniorrhaphy in buffaloes.

Keywords: *Bubalus bubalis*, buffaloes, diaphragmatic herniorrhaphy, ketamine, guaifenesin, double drip, isoflurane

INTRODUCTION

Ketamine is a commonly used dissociative anaesthetic with analgesic effect. It causes mild cardiovascular stimulation with maintenance of swallowing and cough reflexes (Quevedo and Bolanos, 2017). Ketamine provides poor muscle relaxation when used alone, it is therefore recommended to administer with other anaesthetic agents to improve muscle relaxation. Guaifenesin is a centrally acting muscle relaxant used in bovines which causes least changes on respiratory muscle activity and cardiac function at therapeutic doses (Lin and Walz, 2014). Ketamine causes increased tonic-clonic muscle activity in ruminants (Riebold, 1996; Hall *et al*., 2001). Hence, an adjunct to ketamine is essential to improve muscle relaxation (Stegmann, 1998). One of the commonly used combination is double drip. Double drip is created by adding ketamine (1000 mg)-guaifenesin (25 gm) in 5% dextrose solution which is used for inducing anaesthesia to be maintained with either double drip or inhalant anaesthesia which provide stable surgical plane of

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anesthesia in ruminants. Double drip may allow prolonged anaesthesia without bulky equipment (Davies and Jeanna, 1997). Use of isoflurane as a maintenance agent has been investigated by Stegmann (2004), Singh (2013); Bodh *et al.* (2014) in buffaloes. Depth of anaesthesia can be adjusted quickly, and faster recovery can be possible using inhalation anaesthesia. Use of volatile inhalant anesthetic agent as a sole anaesthetic may cause dose dependent cardiopulmonary depression. Therefore, balanced anaesthesia can be employed to decrease inhalent anaesthetic requirement which will maintain cardiovascular depressant effect and will provide adequate analgesia (Ringer *et al*., 2007; Araujo *et al*., 2014). Hence, the study was designed to evaluate the efficacy of ketamine-guaifenesin and isoflurane anaesthesia protocol for diaphragmatic herniorrhaphy.

MATERIALS AND METHODS

The study was conducted on twelve she buffaloes suffering from diaphragmatic hernia weighing 313 to 442 kg and age between 4 to 9 years. Left flank laparo-rumenotomy was done 24 h prior to herniorrhaphy to confirm the condition and to evacuate ruminal content to facilitate herniorrhaphy. Buffaloes were kept off feed for 24 h and were maintained on intravenous fluid therapy. Water was withheld for 12 h.

Buffaloes were randomly divided into two equal groups based on maintenance agent used *viz.* Group I and II. Induction of anaesthesia was done by intravenous double drip of ketamine and guaifenesin (GK) at 1.5 mL/kg body weight in both the groups. Following abolishment of gag reflexes, endotracheal intubation by 18 mm internal diameter endotracheal tube was done by blind technique. Maintenance of anaesthesia was done by using double drip solution at 2.5 mL/kg/h in Group I and by 2% isoflurane in Group II via a semi closed rebreathing system (Mallard Medical Inc 2800c-Large animal anesthesia machine). Oxygen flow rate was set to 4 to 6 L/minutes. Depth of anaesthesia was maintained by adjusting vapourizer setting by continuous monitoring patients reflexes and painful response to surgical stimulation. Intermittent positive pressure ventilation was initiated with the setting of 9 breaths/minutes, I:E ratio of 1:3 after 15 minutes of maintenance in both the groups.

The anesthetic parameters *viz*. quality of induction, induction time, analgesia, muscle relaxation, reflexes, eyeball position, maintenance dose, duration of anaesthesia, recovery time and quality of recovery at 0, 15, 30, 45, 60 minutes interval during anaesthesia were studied. The quality of induction was assessed by following grades as shown in Table 1.

The time interval (minutes) between intravenous injection of double drip solution to disappearance of all the reflexes was considered as induction time. Analgesia was evaluated by observing the animal's response after a deep pin prick at the coronary band with a 22 G needle. The grades of analgesia are shown in Table 2.

Muscle relaxation was judged by jaw relaxation and as per subjective assessment of the surgeon which is graded as shown in Table 3.

Palpebral and corneal reflexes were recorded as a measure of depth of sedation. Palpebral reflexes were assessed by observing the blink of eyelids by tapping at the medial canthus of eye and graded on a 0 to 3 score scale (Table 4).

Corneal reflex was recorded as a measure for depth of anaesthesia and was assessed by observing the blink of eyelids on touching the

cornea with index finger. Position of the eye ball was noted as central, downward or ventro-medial rotation. Maintenance dose of anaesthetic was measured as total dose of double drip administered during maintenance upto completion of the surgical procedure in Group I and was calculated in mililitre. In Group II, percentage of isoflurane required for maintenance of anaesthesia was noted. Duration of anaesthesia (minute) was recorded as the time recorded from the time of abolition of pinprick reflex to the time of reappearance of the pinprick reflex. The quality of recovery was evaluated in grades as shown in Table 5.

The time (minute) taken from the discontinuation of intravenous/inhalation anaesthetic agent to the first head righting reflex was considered as lateral recumbency with head up, spontaneous regaining of sternal recumbency was considered as sternal recumbency time and spontaneous regaining of standing position was considered as standing time.

Diaphragmatic herniorrhaphy was done by transabdominal approach as per the standard surgical technique in supine position. After regaining spontaneous breathing, IPPV was stopped and on completion of surgical procedure double drip of ketamine-guaifenesin in Group I and isoflurane administration in Group II was discontinued.

The data of this investigation was statistically analyzed using complete randomized design one way analysis of variance (ANOVA) for anaesthetic parameters as per Snedecor and Cochran (1994)

RESULTS AND DISCUSSION

Induction quality was excellent (60%) to good (40%) in both the groups with double drip solution. Easy, quick and safe endotracheal intubation, absence of pinprick reflexes indicated the analgesic effect of ketamine and complete muscle relaxation effect of guaifenesin. Tadmor *et al.* (1979); Pathak *et al.* (1982); Stegmannn (1998); Ninu *et al.* (2015) used ketamine successfully as an induction agent in buffaloes. Abrahamsen (2008) stated that induction was more gradual with ketamine-guaifenesin (double drip) and when used correctly it can be the most benign method of anesthetic induction for ruminant patients at 1.7 to 2.2 mL/kg body weight. Dhawle (2018) observed good (50%) to moderate (50%) quality of induction after double drip administration in severely compromised uremic patients.

The mean induction time was 3.75±0.37 and 3.67±0.20 min in Group I and II respectively. Thangadurai *et al.* (2016) recorded induction time of 1.64±0.09 minutes with diazepam premedication and induction using guaifenesin (50 mg/kg b.wt IV) and ketamine hydrochloride (4 mg/kg b.wt IV). Gnanasekar *et al.* (2013) reported induction time of 2.50±0.35 minutes after detomidine-ketamine-guaifenesin administration.

Pin prick response was abolished after 13.33±0.49 minutes in Group I and 10.66±0.49 minutes in Group II. Mean time of onset of analgesia for fetlock, abdomen, base of horn and ribs was 10.16±0.03, 11.16±0.51, 12.16±0.40 and 13.33±0.49 minutes, respectively, in Group I which was significantly different within group. The onset of analgesia was 8.66±0.37, 9.33±0.4, 10.00±0.32 and 10.66±0.49 minutes for fetlock, abdomen, base of horn and ribs, respectively in Group II. Non-significant change was observed in onset of analgesia when compared between the groups. The N-methyl-Daspartate receptor involved in pain processing, including central and peripheral

sensitization and visceral pain (Riviere and Papich, 2009; Pal *et al*., 2016). In the present study, the excellent analgesia produced in Group I might be due to antagonistic effect of ketamine on NMDA receptor. Lin and Walz (2014) enlisted various mechanisms of analgesic action of ketamine *viz*. 1) Spinoreticular tracts blockade 2) Depression of nucleus of medial medullary reticular formation 3) Suppression of spinal cord lamina at dorsal horn and 4) CNS interaction on opiate receptors of spinal cord along with antagonism of NMDA receptor.

Mean duration for loss of analgesia for different body parts *viz*. ribs, base of horn, abdomen, fetlock was 63.33±0.84 minutes, 63.33±0.84 minutes, 63.5±0.87 minutes and 63.83±0.84 minutes, respectively of Group I, whereas in Group II, it was 62.66±0.87 minutes, 62.66±0.87 minutes, 63.50±0.73 minutes and 63.66±0.87 minutes, respectively. There was no significant difference in mean duration for loss of analgesia of different body parts in both the groups. However, non-significant changes were noted within the groups. Kumar *et al.* (2014) noticed loss of analgesia at ribs, base of horn, abdomen, fetlock at 39.72±1.42, 43.37±1.80, 42.95±1.70, 43.95±1.83 minutes respectively after diazepam-ketamine administration in buffalo calves. Lokesh *et al.* (2018) noticed loss of analgesia by needle prick at fetlock, base of horn, ribs, base of tail at 41.83±2.40, 38±2.36, 35±2.35, 37±2.26 minutes respectively after ketamine (1 mg/kg) administration for diaphragmatic herniorrhaphy in buffaloes. Excellent analgesia achieved in present study in Group II was thought to be due to the adjunct effect of ketamine and isoflurane.

In both the groups, four animals (66.66%) showed excellent muscle relaxation and two animals (33.33%) showed good muscle relaxation throughout the observation period. Excellent muscle relaxation observed in Group I which might be due to selective depression of transmission of nerve impulse at internuncial neurons of spinal cord, brain stem and subcortical areas due to use of guaifenesin as reported by Singh *et al.* (1990); Kandpal and Kumar (1998). Complete relaxation of the muscles of the jaw, rectum and penis after guaifenesin administration was reported by Singh *et al.* (1981) in buffalo calves. Kumar *et al.* (2014c) noticed mild relaxation of jaws up to the end of anaesthetic period after dexmedetomidine-ketamine administration. In the present study, the muscle tonicity caused by ketamine hydrochloride was might be counteracted by guaifenesin due to its muscle relaxant property. Eger (1984); Kumandas and Ertugrul (2015) stated that isoflurane induces faster anesthetic induction with good muscle relaxation. Therefore, excellent muscle relaxation produced in buffaloes with isoflurane maintenance might be due to long lasting muscle relaxing effect of guaifenesin and CNS depressant action of isoflurane.

The palpebral reflexes were intact and strong up to 15 minutes of induction which later on depressed and remained intact but weak in rest of the observation period in Group I. The findings of the present study are in aggregation with Singh *et al.* (1981); Pal *et al.* (2016); Lokesh *et al.* (2018) after administration of guaifenesin, acepromazine-ketamine and ketamine alone respectively in buffalo calves. This was in contrary to the findings of Kumar *et al.* (2014b); Singh *et al*. (2011); Malik *et al.* (2012). The palpebral reflexes remained completely abolished during isoflurane maintenance in Group II as inhalant agents produce complete suppression of patient's reflexes. Similar findings were noticed by Singh *et al*. (2013) and Singh (2014).

In Group I, intact corneal reflexes were observed throughout anesthesia and mild to

moderate response was observed occasionally at some time interval in few animals. Similar findings were observed by Rings and Muir (1982) in calves and Ninu *et al.* (2015) after ketamine administration. This was in contrary to the findings in buffalo calves under guaifenesin anesthesia (Sarma and Kumar, 1998; Singh *et al*., 1981), midazolam-ketamine (Kumar *et al*., 2014b) and xylazine-ketamine (Singh *et al*., 2011) where corneal reflexes were completely abolished. Corneal reflexes were completely abolished at all intervals during isoflurane maintenance in Group II which might be due to total suppression of patients reflexes as evidenced by Singh *et al.* (2013). Eyeball position during general anesthesia is a reliable indicator of the depth of anesthesia in ruminants (Reibald, 2007). Eyeball remained in central position in three animals and ventromedial in rest three animals of Group I after ketamine-guaifenesin induction. Central rotation of eyeball was noticed by Ninu *et al.* (2015) after ketamine induction. Downward rotation of eyeball was noticed during isoflurane maintenance in Group II at most of the time interval. These findings were in accordance with Rugh *et al.* (1985) in cattle and Singh (2011) in buffaloes.

The required mean maintenance dose of double drip in Group I animals was 392.50±66.65 mL which was found to be lower i.e., half of the calculated dose. Abrahamsen (2008) stated that a constant-rate infusion of Double Drip 2.5 mL/kg/h was sufficient to provide stable plane of surgical anesthesia in ruminants. Dzikiti (2013) stated that the rate of administration of intravenous drugs for maintenance of general anesthesia should be guided by the signs of anaesthetic depth displayed by individual patients and not necessarily by known theoretical infusion rates. Also, buffaloes in the present study were chronically affected with DH that might have knocked them down at low doses. Concentration of isoflurane required to maintain adequate depth of anesthesia in Group II was 1.5 to 2.5%. Similar concentration of isoflurane has been used by Gencelep *et al*. (2004); Chandran (2010); Offinger *et al*. (2012); Singh *et al*. (2013); Bodh *et al*. (2014); Thangadurai *et al.* (2016) for anaesthetic maintenance.

Mean duration of anesthesia was 59.83±1.56 minutes and 58.83±1.38 minutes in Group I and II, respectively. There was no significant difference in duration of anesthesia within and between the groups. Kumar *et al.* (2014a) used diazepam-ketamine combination and observed anesthesia of duration 37.72 minutes with least adverse effects on cardiopulmonary parameters. Kastner *et al.* (2001) reported duration of anesthesia 102.6 minutes after dexmedetomidine premedication, ketamine induction and isoflurane maintenance in sheep whereas Vettorato *et al.* (2012) noticed anaesthetic time of 214±45 minutes in isoflurane maintenance.

Recovery from anesthesia was smooth but prolonged in 50% animals and smooth and fast in rest 50% animals of Group I, whereas, in Group II, all animals showed smooth and fast recovery. In Group I, the average time taken for lateral recumbency, sternal recumbency and for standing were 35.17±1.36, 41.83±1.79 and 65.50±1.30 minutes, which were significantly higher than Group II animals and were 11.00±0.71, 14.33±1.07 and 27.50±0.63 minutes respectively. Quevedo and Bolanos (2017) observed total recovery time of 45.50±2.50 minutes after detomidine (30 µg/kg b.wt) premedication, double drip induction and maintenance. Singh *et al*. (1985) observed lateral recumbency at 58.8±6.8 minutes with standing time of 77.9±7.1 minutes and complete recovery at 97.2±7.5 minutes after administration of guaifenesin alone. Faster recovery observed

Table 1. Grades of induction quality.

Grade	Clinical signs
A	Excellent, smooth and rapid induction, good depth of anesthesia without any complications, loss of gag reflex, easy and quick endotracheal intubation, regular respiratory movements, unresponsive to all reflexes.
B	Good, no excitement, satisfactory depth of anaesthesia with slight voluntary/involuntary movements, reflex response to intubation, absence of reflex to pin-prick, little response to palpebral reflexes
C	Moderate, mild excitement, longer tracheal intubation time, slightly prolonged induction and a few characteristic signs which interferes with the course of anaesthesia, period of slight apnoea, variation in heart beats, respiration and leg movements
D	Poor, obvious excitement, attempt to stand after recumbency, inability to intubate trachea, absence of the characteristic signs of anaesthesia, apnea with severe convulsions, arrhythmia, leg movements.

Table 2. Grades of analgesia.

Grades	Clinical signs
+ (no analgesia)	Strong response to pin prick
++ (mild analgesia)	Weak reaction to pin prick
+++ (moderate analgesia)	Occasional response to pin prick
++++ (excellent analgesia)	No response to pin prick

Table 3. Grades of muscle relaxation.

Grade	Clinical signs
Poor	Tightly closed jaws and stiff limbs, no flaccidity of abdomen, high pain sensation lead to movement of animal during surgery.
Moderate	Moderate resistance to opening of jaws and flexion of limbs, no flaccidity of abdomen, moderate pain sensation indicated by the movement of the animal during surgery.
Good	Mild resistance to opening of jaws and flexion of limbs, no flaccidity of abdomen, no signs of pain and discomfort, little movement of animal during surgery.
Excellent	No resistance to jaw opening and limb flexion, flaccid abdomen, no signs of pain and discomfort, no movement of animal during surgery.

Table 4. Grades of reflexes.

Grade	Clinical signs
0	Intact but strong reflex (quick blink).
1	Intact and weak reflex (slow response).
2	Very weak reflex (very slow and occasional).
3	Abolished reflex.

Table 5. Grades of quality of recovery.

Clinical signs	Grade
Smooth and fast recovery.	++++
Smooth and prolonged recovery.	+++
Struggling and fast recovery.	++
Struggling and prolonged recovery.	+

in Group II animals was in accordance with Cantalapeidra *et al*. (2000); Bodh *et al*. (2014) with isoflurane maintenance. Better cardiovascular function, less stress response, lower blood gas partition coefficient, faster changes in minimum alveolar concentration, minimum alteration in hepatic blood flow and quicker elimination might have lead to faster recovery as stated by Riazuddin *et al*. (2004).

CONCLUSION

Easy and safe endotracheal intubation can be possible by double drip (50 mg/mL guaifenesin and 2.0 mg/mL ketamine in 500 mL D 5% solution) 1.5 mL/kg body weight in buffaloes. Double drip (GK) induction and isoflurane maintenance provided better clinical, physiological and haemodynamic stability for diaphragmatic heriorraphy in buffaloes. Double drip (GK) induction and maintenance was found suitable for diaphragmatic heriorraphy in buffaloes despite of initial cardiopulmonary depression and longer recovery time.

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