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Research Article

CLINICAL EVALUATION OF NITROUS OXIDE SUPPLEMENTATION DURING ISOFLURANE ANAESTHESIA IN BUFFALOES UNDERGOING DIAPHRAGMATIC HERNIORRHAPHY

SHIVANSH MEHRA[1]*, SANDEEP POTLIYA[2], R.S. BISLA[2] and YOGESH BANGAR[3]
[1]Department of Veterinary Surgery and Radiology, [2]HPVK, Karnal,
[3]Department of Animal Genetics and Breeding, College of Veterinary Sciences,
Lala Lajpat Rai University of Veterinary and Animal Sciences, Hisar-125004, India

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ABSTRACT

The present study was undertaken to evaluate clinical characteristics of nitrous oxide supplementation during atropine-xylazine-ketamine-isoflurane anaesthesia in 12 buffaloes undergoing diaphragmatic herniorrhaphy. Buffaloes were randomly divided in two groups having six animals in each group. All the animals were induced with combination of xylazine (0.1 mg/kg) and ketamine (0.25 mg/kg) intravenously after fifteen minutes of pre- medication (atropine @ 0.04 mg/kg, IM and xylazine @ 0.04 mg/kg, IM) in both the groups. Isoflurane was used as sole inhalation anaesthetic agent for maintenance anaesthesia along with 100% oxygen in group-I (AXKI); while, isoflurane along with N_2O-Oxygen (50% N_2O - 50% O_2) admixture was used for maintenance anaesthesia in group-II (AXKI-N_2O). Clinical and behavioral changes were observed during and after anaesthesia. For clinical observation, a fixed criterion was followed for evaluation of quality of anaesthesia and scoring was done to assign numerical values. Result of study found that quality of anaesthesia was significantly better, predominantly with significantly higher recovery score in Group-II than in Group-I. There was significantly early regain of eye and jaw reflexes and early extubation in Group-II than in Group-I showing early recovery from anaesthetic effects. Supplementation of nitrous oxide in atropine-xylazine-ketamine-isoflurane anaesthetic protocol provided better quality of maintenance anaesthesia with early and smooth recovery in buffaloes undergoing diaphragmatic herniorrhaphy.

Keywords: Buffalo, Diaphragmatic herniorrhaphy, Isoflurane, Nitrous oxide

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Bovine surgery presents a series of challenges to accompany under humanitarian considerations. The humane handling of animals is performed by combination of minimum physical restraint, sedation and local or regional anaesthesia to avoid complications of general anaesthesia. But, for major surgical procedures like repair of diaphragmatic hernia, maintenance of anaesthesia for a longer period is needed; for which either intravenous or inhalant anaesthetic agents are used. Repeated dose of intravenous anaesthesia in ruminants is associated with complications like cardiopulmonary depression, prolonged recovery and recumbency. These disadvantages of intravenous anaesthesia can be minimized by induction with injectable agent and inhalant agent for maintenance (Thurmon *et al.*, 1996). But when a single inhalation agent is used as sole anaesthetic it is often not sufficient to abolish appropriately autonomic and nociceptive responses to the surgical stimulus, potentially leading to inadequate peri- and post-operative analgesia (Steffey and Mama, 2007). Nitrous oxide was recommended as an analgesic adjuvant for 'balanced anesthesia' technique and to reduce volatile anesthetic agent requirement (Ilkiw, 1999). Nitrous oxide has been routinely used in human being (Swan *et al.*, 1999) but its use in veterinary patients is very scarce (Steffey and Howland, 1978; DeYoung and Sawyer, 1980; Hikasa *et al.*, 1996). However there is little or no information on use of nitrous oxide in bovine.

*Corresponding author: sunnymehra316@gmail.com

MATERIALS AND METHODS

The study was conducted on twelve buffaloes suffering from diaphragmatic hernia reported to the Veterinary Clinical Complex, Haryana Pashu Vigyan Kendra, Karnal. After clinical examination diaphragmatic hernia was diagnosed by radiography and confirmed by exploratory laparo-rumenotomy. Animals were kept off feed and water withdrawal after laparo-rumenotomy and weighed before doing herniorrhaphy (on next day) for calculating the dose of drugs used for general anaesthesia. Following drugs were used in different combinations for general anaesthesia during herniorrhaphy:

Table 1. Aneasthetic protocols of buffaloes undergoing diaphragmatic herniorrhaphy

Group	Preanaesthetic agent	Induction agent	Maintenance agent
I (AXKI) (n=6)	Atropine sulphate@ 0.04 mg/kg b.wt. i/m	Ketamine@ 0.25 mg/kg b.wt. i/v+	Isoflurane with 100% oxygen
II (AXKI-N_2O) (n=6)	+ Xylazine@ 0.04 mg/kg b.wt. i/m	Xylazine@ 0.1 mg/kg b.wt. i/v	Isoflurane+Oxygen (50%): Nitrous Oxide (50 %)

Animals were randomly divided in to two groups having six animals in each group.

After pre-anaesthetic medication with atropine (0.04 mg/kg, IM) and xylazine (0.04 mg/kg, IM); each animal was restrained in lateral recumbency for induction of anaesthesia. Fifteen minutes after pre-anaesthetic medication induction was done using a combination of

xylazine-ketamine (mixed in a syringe) administered intravenously. After induction, intubation was performed with cuffed endotracheal tube and connected to Vetland® large animal anaesthetic machine. For maintenance of anaesthesia, isoflurane was used as sole anaesthetic agent in Group-I (AXKI) through agent specific vaporizer and along with 100% oxygen through a semi-closed rebreathing system. While in Group-II (AXKI-N_2O), Nitrous Oxide was given in 50:50 ratios with oxygen along with isoflurane. Animals were positioned in dorsal recumbency for surgery through post-xiphoid trans-abdominal approach for diaphragmatic herniorrhaphy. Initially vaporizer was set at 1 and 0.8% in group-I and in group-II, respectively; then reduced to maintain between 0-1% during the herniorrhaphy and uniform surgical plane of anaesthesia was maintained. Clinical and behavioral changes were observed during and after anaesthesia.

For clinical observation, a fixed criterion was followed for evaluation of quality of anaesthesia and scoring was done to assign numerical values; starting from 1 to 4 (1-poor, 2-moderate, 3-good, 4-excellent) for premedication quality, induction quality, maintenance quality and recovery quality. Qualitative and subjective effects (sedation, analgesia, muscle relaxation, jaw relaxation and epiglottis relaxation) of drugs were judged by observing physical response of the medicated animal to surgical stimulation during diaphragmatic herniorrhaphy. Numerical values starting from 0 to 3 (0-no effect, 1-mild effect, 2-moderate effect, 3-deep effect) was used for sedation, analgesia and muscle relaxation during maintenance of anaesthesia and palpebral reflex, corneal reflex, extent of salivation were judge according to (-) completely abolished, (+) mild response, (++) moderate response, (+++) good response, (++++), excellent response. These all observations were made through blind fold study by a single person (Potliya *et al.*, 2016).

In behavioural observations, animals were observed to record the loss of various body reflexes (loss of palpebral reflex, loss of tongue reflex, loss of jaw tone and loss of swallowing reflex) and recovery from effect of drugs was taken to have occurred by regain of body reflexes (alar reflex, swallowing reflex, regaining of head righting reflex, return to sternal recumbency, standing time with ataxia, browsing time and complete recovery without ataxia).

The statistical analysis of data was done by the mean along with standard errors of each parameters were obtained using descriptive statistics. The independent t-test was used to determine significant ($P<0.05$) difference between two groups.

RESULTS AND DISCUSSION

The comparisons between mean scores of quality of anaesthesia during different anaesthetic combinations are shown in Table 1. In premedication, induction, maintenance, sedation, analgesia and muscle relaxation; no significant differences were observed between groups while there was significant difference observed in recovery score between groups. All the buffaloes were subjected to the same premedication and induction protocol as per their body weights, so no significant differences were observed in premedication and induction.Mechanism of action of nitrous oxide by acting supraspinal and spinal receptors by non-competitive NMDA inhibition (Jevtovic-Todorovic *et al.*, 1998) and, analgesic effects are like morphine occurs through the release of endogenous opioids that act on opioid receptors. The anxiolytic effects are through GABA-A activation (Zhang *et al.*, 1999). Accordingly, deep analgesia and moderate sedation was observed during herniorrhaphy in buffaloes of Group II (AXKI-N_2O) compared to Group I (AXKI). The difference was not statistically significant but marked on clinical observation.Nitrous oxide releases proenkephalin in the CNS. While single agent 66–70% nitrous oxide provides an analgesic effect similar to a whole blood concentration of remifentanil of 2 ng/ml (Lee *et al.*, 2005).Maintenance of anaesthesia with halothane was not smooth due to less analgesia with atropine-xylazine-propofol-halothane anaesthesia (Potliya *et al.*, 2016). Muscle relaxation was adequate in both the groups with no significant difference between them. Unlike other volatile anesthetics, nitrous oxide has no muscle relaxation properties. Potliya *et al.* (2015) also reported good muscle relaxation in buffaloes with atropine-xylazine-propofol/ ketamine–isoflurane anaesthesia in buffaloes undergoing diaphragmatic herniorrhaphy. A significantly higher recovery score was obtained in Group-II (AXKI-N_2O) than in Group-I (AXKI). Nitrous oxide has a low blood solubility (blood-gas partition coefficient of 0.47), because of its high lipid solubility transfers across the alveolus rapidly leading to a quick onset and offset due to concentration effect for additionally administered volatile agents in the lungs and is known as the second gas effect (Hellams *et al.*, 2018).

The comparison between effects of administration of both anaesthetic combinations on behavioral parameters in buffaloes undergoing diaphragmatic herniorrhaphy is shown in Table 2. There was no significant difference observed in loss of various reflexes between two groups as premedication and induction was done with same protocol in both groups.

Table 2. Mean±S.E score values of different quality parameters of buffaloes (Group-I and II) undergoing diaphragmatic herniorrhaphy

Quality Parameters	Group I (n=6)	Group II (n=6)
Premedication	2.50±0.22	2.50±0.34
Induction anaesthesia	3.17±0.31	3.50±0.22
Maintenance anaesthesia	3.33±0.33	3.83±0.17
Recovery	2.17 ± 0.40^{A}	3.50 ± 0.22^{B}
Sedation	2.83±0.17	3.00±0.00
Analgesia	2.33±0.33	2.83±0.17
Muscle relaxation	2.67±0.21	3.00±0.00

Means with different superscripts (A/B) in a row show significant difference between groups (P<0.05)

Table 3. Mean±S.E values of different behavioral parameters of buffaloes (Group-I & II) undergoing diaphragmatic herniorrhaphy

Behavioural Parameters	Group I (n=6) (Minute)	Group II (n=6) (Minute)
Muzzle dryness°	7.67±0.49	8.33±1.15
Down time°°	18.67±2.32	18.17±7.08
Loss of swallowing reflex*	2.50±0.43	3.83±0.70
Intubation*	2.83±0.48	2.83±0.48
Relaxation of jaw muscle*	2.83±0.65	3.17±0.87
Loss of tongue reflex*	3.50±1.31	3.50±0.67
Drooping of eyelids*	6.83±1.17	5.17±1.28
Loss of palpebral reflex*	7.33±1.56	5.83±1.49
Regain of alar reflex†	13.67±4.39	9.17±2.74
Regain of corneal reflex†	18.17±6.82	9.83±3.09
Regain of palpebral reflex†	23.17 ± 7.74^{B}	11.17 ± 3.40^{A}
Eyes open†	13.67±4.91	10.17±3.01
Regain of Jaw reflex†	27.17 ± 5.76^{B}	19.50 ± 2.98^{A}
Regain of tongue reflex†	24.83±5.17	17.33±4.62
Regain of swallowing reflex†	27.83±5.16	19.83±4.48
Extubation†	38.17 ± 5.12^{B}	22.17 ± 2.93^{A}
Regaining of muscle tone†	29.83±8.07	18.83±3.31
Regaining of head righting reflex†	36.67±7.44	22.17±2.92
Return to sternal recumbency†	45.33±5.55	31.83±3.81
Standing with ataxia†	87.67±21.41	42.00±4.76
Browsing†	107.50±20.29	59.67±16.02
Complete recovery†	142.33±23.56	83.67±27.28

°after administration of atropine; °°after administration of xylazine
*after administration of xylazine+ketamine; †after discontinuation of inhalation
Means with different superscripts (A/B) in a row show significant difference between groups (P<0.05)

But there was significantly early regain of eye and jaw reflexes and early extubation in Group-II (AXKI-N_2O) than in Group-I (AXKI) showing early recovery from anaesthetic effects. Adding N_2O during the last 30 min of anisoflurane-based inhalational anesthetic reduced the time to extubation, eye opening, and orientation (Mraovic *et al.*, 2018). Standing time with ataxia and complete recovery was not significantly different in both groups but comparatively lesser in group-II (AXKI-N_2O). Addition of N_2O to isoflurane anaesthesia resulted in a better recovery with lower incidence of adverse behaviour and marginally faster recovery in dogs anaesthetized with propofol (Laing *et al.*, 2009).

CONCLUSION

Atropine-xylazine-ketamine-isoflurane in addition with nitrous oxide and oxygen (50:50%) anaesthetized buffaloes provided better maintenance anaesthesia with proper analgesia and muscle relaxation sedation alongwith significant early recovery from anaesthesia during diaphragmatic herniorrhaphy.

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