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Research Article

DOSE SPARING EFFECTS OF FENTANYL CITRATE AND BUPRENORPHINE ON ISOFLURANE IN BUFFALOES UNDERGOING DIAPHRAGMATIC HERNIORRHAPHY

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ABSTRACT

Isoflurane is the most widely utilised maintenance agent in various procedures requiring general anaesthesia in buffaloes. Besides several advantages, isoflurane has a number of unfavourable effects during and after anaesthesia, including respiratory depression, hypotension, reduced cardiac output, and environmental pollution from its metabolites. The study was planned to achieve isoflurane dose sparing effect by using opioid analgesics in balanced anaesthetic combinations used for general anaesthesia given for longer duration surgery undergoing diaphragmatic herniorrhaphy in buffaloes. The study involved 15 female buffaloes aged between 2 to 9 years, suffering from diaphragmatic hernia and were randomly assigned to three groups, each with five animals. All animals were given (atropine (0.04 mg/kg) - xylazine (0.05 mg/kg) – propofol (till effect) - isoflurane). Group-I (control group-AXPI) received no analgesic and group-II (AXBPI) and group-III (AXFnPI) were given additional opioid analgesics, buprenorphine (0.006 mg/kg) and fentanyl citrate (2.0 mcg/kg), respectively. Haemato-biochemical analysis was conducted, at the time of presentation (pre-rumenotomy), before drug administration, at 5 minutes of induction of anaesthesia, at 15 minutes and 30 minutes of isoflurane administration, at the time of recovery from anaesthesia and 24 hours post-surgery. The mean volume of isoflurane (ml) utilized for group-I was (61.34±4.02) significantly higher than Group-II (46.27±2.96) and Group-III (38.55±1.81). No significant changes were observed in the physiological, haematological and biochemical profiles among these groups at different time intervals. Thus, it was concluded that opioid analgesics significantly reduce the quantity of isoflurane required in buffaloes.

Keywords: Atropine, Buffaloes, Buprenorphine, Diaphragmatic herniorrhaphy, Fentanyl Citrate, Isoflurane

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Diaphragmatic hernia (DH) is a typical example of internal herniation characterized by recurrent tympany not responding to medicinal treatment, reduced milk yield, scanty and pasty faeces and loss of condition owing to prolonged starvation. In the chronic condition, the reticulum is adhered to the hernial ring, which is thickened by fibrous tissue. Diaphragmatic hernia is a common sequel of foreign body syndrome in buffaloes (Sahu *et al.*, 2003). Varieties of surgical procedures in buffalo are preferably performed using combination of physical restraint, sedation and local or regional anaesthesia, but for complex surgical procedures like repair of diaphragmatic hernia (DH), general anaesthesia with an inhalant agent is necessary (Riazuddin *et al.*, 2004). Isoflurane is the most commonly used maintenance agent in balanced anaesthetic protocol for diaphragmatic herniorrhaphy in buffaloes (Chaudhary and Tayal, 2020). When isoflurane is employed as the sole anaesthetic agent, it may result in insufficient peri- and post-operative analgesia, as it is insufficient to eliminate adequately autonomic and nociceptive responses to the surgical stimulus on its own (Steffey and Mama, 2007). An ideal anaesthetic produces sleep, amnesia, analgesia and muscle relaxation. However, all these characteristics cannot be provided by a sole agent and therefore, a combination of drugs is used which is referred to as "balanced anaesthesia" (Thurmon and Short, 2007). The use of less isoflurane for sustaining general anaesthesia is significant since it reduces the common isoflurane side effects such as respiratory depression, hypotension, and lower cardiac output (Hikasa *et al.*, 2002). As a result, any reduction in isoflurane dose will benefit the patient, surgical team, and environment. Because of their powerful analgesic impact, opioid analgesics are said to have an inhalant sparing effect and minimise the minimum alveolar concentration (MAC) necessary to maintain surgical plain of anaesthesia (Tranqulii *et al.*, 2007). Administration of morphine, buprenorphine or butorphanol decreases the need for potent inhalant anaesthetics in cats and could potentially be beneficial in combination with inhalants (IIkiw *et al.*, 2002). Combined with its significant inhalant (MAC) sparing effect, cardiovascular function is further improved and its use as an adjunct in general anaesthesia has been strongly advocated (Ueyama *et al.*, 2009). The inclusion of butorphanol in the anaesthetic protocol had reduced isoflurane requirement in cattle (Senthilkumar *et al.*, 2013). Yadav (2020) reported that inclusion of opioid analgesic (butorphanol/pentazocine) significantly reduced the quantity of isoflurane required for maintenance of anaesthesia in buffaloes undergoing diaphragmatic herniorrhaphy anaesthetized by atropine-xylazine-

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propofol combination. Clinically, one of the main issues concerning inhalant anaesthesia is the progressive cardiopulmonary depression related to delivery of high concentration of inhalant agents such as isoflurane (Gutierrez-Blanco *et al.*, 2013). This becomes even more important in patients with severe disease like diaphragmatic hernia. Therefore, a reduction in the dose of isoflurane by administration of adjunctive drugs such as buprenorphine, fentanyl, was planned to reduce the cardiopulmonary depression in buffaloes undergoing diaphragmatic herniorrhaphy (DH) premedicated with xylazine and atropine with propofol induction as it was hypothesized that buprenorphine and fentanyl citrate might spare the isoflurane significantly.

MATERIALS AND METHODS

Animals: After clinical examination, radiography, and rumenotomy, a total of 15 buffaloes with diaphragmatic hernia were chosen from those reported to the Veterinary Clinical Complex, LUVAS, Hisar between May 2020 and June 2021. The rumenotomy was followed with DH the next day. After rumenotomy, animals were maintained off feed and water and weighed before herniorrhaphy to calculate the dose of medications used for general anaesthesia. Blood samples were obtained from buffaloes before, during, and after surgery to analyse haematological and biochemical characteristics. The study used an unequal randomization procedure.

Procedure for anaesthesia: All buffaloes were given atropine (0.04 mg/kg; Atro (1.0 mg/mL); Prem Pharmaceuticals Ltd., Indore, Madhya Pradesh, India) and subsequently xylazine (0.05 mg/kg; specify route of administration Xylazin (20 mg/mL; Indian Immunologicals Ltd., Guntur, Andhra Pradesh, India) after 15 minutes. After fifteen minutes of xylazine treatment, buffaloes were easily confined in lateral recumbency for induction of anaesthesia. Then, in groups-II and III, buprenorphine (0.006 mg/kg; Bupregesic (100 mg/2mL; Neon Laboratories Ltd., Mumbai, India) or fentanyl citrate (2.0 mcg/kg; Trofentanyl (50 mcg/mL; Troika Pharmaceuticals Ltd., Thol., Gujarat, India) was given intravenously.

In group-I, no opioid analgesic was administered. Induction was carried out with propofol (1.3 mg/kg; Neorof (10 mg mL; Neon Laboratories Ltd., Mumbai, India) after 5 minutes of analgesics administration. Intubation with a cuffed endotracheal tube (inner Diameter 20 mm, Surgivet, Smith medical firm, UK) was performed after induction and attached to a large animal anaesthetic machine (Vetland; Vetland Medical Sales and Services, Louisville, KY, USA). Isoflurane (Isotroy 250; Troikaa Pharmaceuticals Ltd., Gujarat, India) was administered via an agent-specific vaporizer (Drager, USA) in combination with oxygen via a semi-closed rebreathing system for maintenance. The oxygen flow rate was 10 L/minute during the first 3 minutes, then dropped to 6 L/minute with a variable vaporizer setting, and the surgical plane was kept consistent by monitoring body reflexes. For premedication quality, induction quality, maintenance quality, and recovery quality, number ratings ranging from 1 to 4 (1-poor, 2-fair, 3-good, 4-excellent) were assigned. The physical reaction of the treated animal to surgical stimulation during diaphragmatic herniorrhaphy was used to assess the drug's qualitative and subjective effects (sedation, analgesia, muscular relaxation). During the maintenance of anaesthesia, numerical values ranging from 0 to 3 (0-no effect, 1-mild effect, 2-moderate effect, 3-deep effect) were utilised for sedation, analgesia, and muscular relaxation. For DH, the animals were placed in dorsal recumbency and operated using a post-xiphoid trans-abdominal route. Throughout the procedure, all of the animals were given normal saline (10 mL/kg/hr; 0.9 percent NSS (1000 mL; Soxa Formulations and Research Pvt. Ltd., Gujarat, India). Isoflurane was stopped when the last skin suture was applied, but the animals were permitted to breathe oxygen until their swallowing and coughing reflexes recovered. Buffaloes were brought into the same room and placed in lateral recumbency before being moved to sternal recumbency when the endotracheal tube was removed. Post-operatively after recovery; Streptopenicillin [5g Animal; Dicrysticin-S (15,00,000 units Procaine Penicillin-G, I.P. and 5,00,000 units Penicillin G Sodium I.P., Streptomycin-2.5g); Zydus AHL - Cadila Healthcare Ltd., Vadodra, India] and Meloxicam (0.5 mg/kg; Meloxivet-20 (20 mg/mL); Carus Laboratories Pvt., India) were administered intramuscularly for five days along with antiseptic dressing of surgical wound.

Calculation of liquid isoflurane usage: The fresh gas flow rate (FGF) and vaporizer setting modifications were recorded at various periods. The quantity of isoflurane consumed in each group was determined using following formula (Senthilkumar *et al.*, 2013).

Isoflurane vapour delivered (mL) = Vapourizer setting (%) x FGF (Litre/minute) x Duration (minute) x 10

By aggregating the isoflurane vapour delivered for each of the FGF and vapourizer settings used, the total isoflurane vapour delivered (mL) during the complete duration of anaesthesia was computed. For statistical comparison, the total isoflurane vapour value obtained was equal to 400 kg body weight and a 40-minute operation duration:

Isoflurane vapour delivered for 400 kg and 40-minute

basis (mL) = (Total isoflurane vapour delivered (mL) x 400 x 40)/(Body weight x Duration of maintenance).

Using Avagadro's principle, the volume of liquid isoflurane consumed was determined, and correction factors were used to account for the effect of ambient temperature and atmospheric pressure in Operation Theatre.

= Isoflurane vapour delivered for 400 kg and 40 minute basis (ml) x 181.4 ¸ (ambient temp/273) x (760/ barometric pressure mm/Hg)

Haemato-Biochemical Parameters: Blood specimens were processed for hematological parameters using an automatic haematoanalyzer (MS4; Melet Schloesing Laboratories, Evalic, France) and plasma from heparinized blood was collected by centrifugation at 2500 rpm for 15 minutes for biochemical parameters using an automated random access blood chemistry analyzer (EM 200; Erba Mannheim, Germany) with commercially available kits.

Statistical evaluations: The two-way ANOVA with repeated measures was used to determine the significant difference between treatments and time points. The pair wise comparisons were done using Duncan's multiple range test (Duncan, 1955). The significance difference was considered if $P<0.05$.

RESULTS AND DISCUSSION

The buffaloes in the control group I(AXPI) used 61.34±4.02 mL of isoflurane on average. Group-II (AXBPI), on the other hand, used 46.27±2.96 mL of isoflurane, while group-III (AXFnPI) used 38.55±1.81 mL. AXBPI had a reduction of 24.57% and AXFnPI had a reduction of 37.16 % when compared to the control group (Table 1). In comparison to group-I, the volume of isoflurane used in groups-II and III was significantly lower. In induction, maintenance, recovery, CNS sedation, analgesia and muscle relaxation scores showed significant differences between groups, while there was no significant difference between premedications. Induction score was higher in animals receiving fentanyl than other groups. Maintenance score was highest in animals administered fentanyl followed by group administered buprenorphine than other group. Recovery score was significantly higher in group-III than group-I. Muscle relaxation was adequate in all the groups but it was significantly better in buffaloes given fentanyl and buprenorphine than the animals given no separate analgesic in their protocol (Table 2). The findings of this study back up previous findings that opioid analgesics have an inhalant sparing effect in diverse species (Tranqulii *et al.*, 2007; Senthilkumar *et al.*, 2013; Yadav, 2020). The percentage use of isoflurane was significantly lower in both groups when compared to the control group, however there was no significant difference between groups-II and III. Changes in nociceptive stimuli, surgeon variation, and anaesthetist variation may all influence the need for inhalant anaesthesia (Torske *et al.*, 1998). The same nociceptive stimuli (DH) were utilised in this clinical investigation, the procedures were conducted by the same surgeons, and the depth of anaesthesia was controlled by the same anaesthetist, reducing variability in isoflurane maintenance requirements.

Senthilkumar *et al.* (2013) found that premedicating bovine calves with opioids such butorphanol tartrate (0.02 mg/kg) and buprenorphine hydrochloride (0.006 mg/kg) reduced the MAC of isoflurane by 18.7% and 14.63%, respectively. In cats premedicated with butorphanol, Ilkiw

Table 1. Depicting amount of isoflurane utilized (on 400 kg and 40 min basis in ml) during diaphragmatic herniorrhaphy by different groups of buffaloes

Groups	Isoflurane liquid utilisized (ml)	Percentage isoflurane utilized of control group	Percentage reduction from control group
Group I	61.34 ± 4.02^{C}	100%	0%
Group II	46.27 ± 2.96^{AB}	75.43%	24.57%
Group III	38.55 ± 1.81^{A}	62.84%	37.16%

Means with different superscripts (A/B/C) in a column show significant difference between groups ($P<0.05$).

Table 2. Comparison of mean ± S.E. scores depicting quality of anaesthesia during different anaesthetic combinations in buffaloes undergoing diaphragmatic herniorrhaphy

Parameters	Group IAXPI	Group IIAXFPI	Group IIIAXLPI
Premedication	2.80 ± 0.37^{A}	2.80 ± 0.20^{A}	2.80 ± 0.20^{A}
Induction	2.80 ± 0.20^{AB}	3.20 ± 0.20^{BC}	3.60 ± 0.24^{C}
Maintenance	2.40 ± 0.24^{A}	3.60 ± 0.24^{B}	3.80 ± 0.20^{B}
Recovery	2.40 ± 0.24^{A}	3.40 ± 0.24^{BC}	3.80 ± 0.20^{C}
CNS Sedation	1.80 ± 0.20^{A}	3.00 ± 0.00^{C}	3.00 ± 0.00^{C}
Analgesia	1.80 ± 0.20^{A}	2.80 ± 0.20^{B}	3.00 ± 0.00^{B}
Muscle relaxation	1.60 ± 0.24^{A}	2.40 ± 0.24^{B}	2.60 ± 0.24^{B}

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

Table 3. Haematological parameters (Mean±Standard Error) of female buffaloes under study at different time intervals

Parameters	Group	Time Point		
		Before Rumenotomy	At 15 min of Isoflurane	At 24 Hours Recovery
Haemoglobin (g dL-1)	I	10.30 ± 0.72	9.78 ± 0.75	10.14 ± 0.88
	II	11.66 ± 0.67	10.0 ± 0.78	10.44 ± 0.49
	III	11.42 ± 0.42	10.42 ± 0.79	10.24 ± 0.62
Packed cell Volume (%)	I	25.60 ± 3.31	27.00 ± 3.77	26.80 ± 2.84
	II	32.64± 4.01	27.16 ± 4.29	24.90 ± 1.50
	III	32.40± 3.83	24.00 ± 0.75	31.00 ± 2.12
Total leukocyte Count ($x10^3$ mm-3)	I	9.90 ± 0.92	9.78 ± 0.95	8.35 ± 1.14
	II	7.86 ± 0.92	6.84 ± 0.54	7.17 ± 0.41
	III	10.61 ± 1.68	8.41 ± 0.95	8.81 ± 0.68

Table 4. Biochemical parameters (Mean ± Standard Deviation) of female buffaloes under study at different time intervals

Parameters	Group	Time Point		
		Before Rumenotomy	At 15 min of Isoflurane	At 24 Hours Recovery
Total proteins (g dL-1)	I	6.81 ± 0.46	7.23 ± 0.32	7.01 ± 0.31
	II	6.97 ± 0.16	6.92 ± 0.12	7.28 ± 0.20
	III	7.12 ± 0.13	7.16 ± 0.16	7.20 ± 0.15
Albumin (g dL-1)	I	4.69 ± 0.59	5.10 ± 0.32	4.96 ± 0.38
	II	4.83 ± 0.39	4.76 ± 0.25	5.17 ± 0.30
	III	4.81 ± 0.33	5.10 ± 0.29	5.16 ± 0.16
Globulin (g dL-1)	I	0.49 ± 0.09	0.43 ± 0.05	0.44 ± 0.09
	II	0.47 ± 0.11	0.52 ± 0.08	0.43 ± 0.10
	III	0.50 ± 0.08	0.40 ± 0.05	0.40 ± 0.05
Blood Glucose (mg dL-1)	I	66.6 ± 8.27	185.8 ± 41.97	76.6 ± 11.74
	II	123.2 ± 11.3	162.8 ± 21.09	105.00 ± 11.0
	III	112.2 ± 22.54	129.00 ± 35.26	95.2 ± 51.5
Urea (mg dL-1)	I	39.38 ± 7.83	51.18 ± 3.62	50.34 ± 5.34
	II	39.80 ± 7.45	34.78 ± 2.53	39.48 ± 4.25
	III	35.12 ± 5.02	46.22 ± 10.82	55.14 ± 6.68
Creatinine (mg dL-1)	I	0.70 ± 0.11	0.62 ± 0.17	0.73 ± 0.13
	II	1.14 ± 0.13	0.82 ± 0.13	1.28 ± 0.13
	III	1.16 ± 0.27	2.20 ± 0.34	3.14 ± 0.71
Aspartate amino transferase (IU L-1)	I	173.46 ± 18.74	135.14 ±9.68	193.2 ± 31.35
	II	163.32 ± 33.84	162.26 ± 41.72	200.82 ± 27.73
	III	164.54 ± 15.93	209.42 ± 22.38	356.74 ± 77.89
'Alanine amino transferase (IU L-1)	I	106.78 ± 21.14	69.56 ± 6.45	69.40 ± 15.38
	II	110.38 ± 12.89	133.24 ± 9.47	138.26 ± 11.80
	III	102.42 ± 5.79	144.96 ± 17.14	143.52 ± 7.76
Sodium (mmol L-1)	I	134.84 ± 1.26	133.06 ± 0.65	136.14 ± 1.38
	II	131.00 ± 2.32	137.16 ± 2.33	135.8 ± 1.61
	III	127.94 ± 1.46	134.18 ±1.75	133.24 ± 1.80
Potassium (mmol L-1)	I	60 ± 0.35	3.68 ± 0.64	4.78 ± 0.19
	II	4.20 ± 0.33	3.67 ± 0.59	4.04 ± 0.27
	III	4.59 ± 0.46	4.02 ± 0.31	4.33 ± 0.25
Cortisol (µg dL-1)	I	16.54 ± 2.54	27.88 ± 8.61	45.97 ± 12.84
	II	31.52 ± 14.45	35.03 ± 17.94	40.28 ± 22.30
	III	10.17 ± 3.20	18.20 ± 6.52	11.77 ± 1.95

Table 5. Weight and period of anaesthesia of female buffaloes under study

Animal	Group-I (AXPI)		Group-II (AXBPI)		Group-III (AXFnPI)	
	Wt. (kg)	Time (min.)	Wt. (kg)	Time (min.)	Wt. (kg)	Time (min.)
A	257	54	336	53	310	46
B	311	58	265	55	400	48
C	249	54	340	47	363	46
D	384	56	420	49	344	50
E	341	53	325	54	250	51

et al. (2002) found a 19% reduction in the need for isoflurane. Both buprenorphine and butorphanol had an isoflurane sparing effect in cattle anaesthetized with a midazolam (0.3 mg/kg) - ketamine (11 mg/kg) mixture, according to Ramakrishnan *et al.* (2019), but butorphanol (0.4 mg/kg) had a larger isoflurane sparing effect than buprenorphine (0.01 mg/kg). According to Yadav *et al.* (2020), the minimum alveolar concentration of isoflurane fell by 41.2% after IV administration of butorphanol (0.03 mg/kg) and 37.5% after IV administration of pentazocine (0.75mg/kg).

Other analgesics may also be useful in lowering the use of isoflurane during surgery. As a result, the goal of this study was to see if fentanyl citrate and buprenorphine had any dose-sparing effects on isoflurane in buffaloes undergoing Diaphragmatic herniorrhaphy. More research, particularly for large animals, is required in this sector in the near future.

There were no significant differences in haematological parameters of buffaloes between the three groups. The

variation was similar in all groups and followed the mean of preoperative values in similar pattern. The variations in TLC might be attributed to individual disease pathology but not due to anaesthesia, hence of no clinical importance. The decrease in PCV during anaesthesia or sedation may have been caused by the shifting of fluid from the extravascular compartment in order to maintain normal cardiac output.

There were no significant differences in biochemical parameters (total proteins, albumin, globulin, aspartate amino transferase, alanine amino transferase). Urea level increased during procedure with significant variation but remained within clinical range. The creatinine level was significantly different (statistically) at pre-operative level due to their individual differences of duration of illness, therapies provided and physical status but there were no clinically significant differences between different groups. The levels of plasma sodium in this study remained within the normal limit for buffaloes even at 24 hours of recovery. The diet of ruminants is rich in potassium. Therefore, inappetence and subsequent development of anorexia for several days would cause plasma potassium concentration to fall below normal. There was least change in the level of cortisol peri and post-operatively in buffaloes given opioids than in buffaloes given either NSAIDs or no analgesic. Increase in plasma glucose after xylazine administration was reported in water buffalo (Singh *et al.*, 2013). Also, relaxation of body muscles during anaesthesia might have lowered the utilization of glucose at tissue level, leading to hyperglycaemia (Table 3 and 4). Table 4 shows the weight and duration of anaesthesia of the female buffaloes under study.

CONCLUSION

Opioid analgesics (buprenorphine/fentanyl citrate) have significant sparing effecton isoflurane necessary for maintenance of surgical anaesthesia in buffaloes undergoing diaphragmatic herniorrhaphy anaesthetized with atropine-xylazine-propofol combination. Fentanyl Citrate has more isoflurane sparing effect (37.16%) than Buprenorphine (24.57%).

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REFERENCES

Chaudhary, R.N. and Tayal, R. (2020). Evaluation of sevoflurane and isoflurane as maintenance agent in buffaloes after glycopyrrolate-xylazine-butorphanol-propofol anaesthesia. *Indian J. Anim. Res.* **54(2)**: 209-215.

Duncan, D.B. (1955). Multiple range and multiple F test. *Biometerics.* **11**: 15-18.

Gutierrez-Blanco, E., Victoria-Mora, J.M., Ibancovichi-Camarillo, J.A., Sauri-Arceo, C.H., Bolio-González, M.E., Acevedo-Arcique, C.M., Marin-Cano, G. and Steagall, P.V. (2013). Evaluation of the isoflurane-sparing effects of fentanyl, lidocaine, ketamine, dexmedetomidine, or the combination lidocaine- ketamine-dexmedetomidine during ovariohysterectomy in dogs. *Vet. Anaesth. Analg.* **40**: 599-609.

Hikasa, Y., Hokushin, S., Takase, K. and Ogasawara, S. (2002). Cardiopulmonary, haematological, serum biochemical and behavioural effects of sevoflurane compared with isoflurane or halothane in spontaneously ventilating goats. *Small Rumi Res.* **43**: 167-178.

Ilkiw, J.E., Pascoe, P.J. and Tripp, L.D. (2002). Effects of morphine, butorphanol, buprenorphine and U50488H on the minimum alveolar concentration of isoflurane in cats. *Am. J. Vet Res.* **63**: 1198-1202.

Ramakrishnan, K.S., Dharmaceelan, S., Senthilkumar, S., Vijayakumar, G. and Rajendran, N. (2019). Analgesic and isoflurane sparing effect of buprenorphine and butorphanol in cats anaesthetized with midazolam-ketamine-isoflurane. *Indian J. Anim. Res.* **53(8)**: 1094-1096.

Riazuddin, M., William, B.J. and Ameerjan, K. (2004). Studies on halothane, isoflurane anaesthesia in dorsal and lateral recumbency in cattle. *Indian J. Vet. Surg.* **25**: 75-76.

Sahu, A., Chawla, S.K., Krishnamurthy, D., Tayal, R., Behl, S.M. and Singh, J. (2003). Diaphragmatic herniorrhaphy in buffaloes: clinical evaluation of 72 cases. *Indian J. Vet. Surg.* **24(1)**: 33-34.

Senthilkumar, S., Rajendran, N., Dharmaceelan, S., Kathirvel, S., Subramanian, M. and Selvaraj, P. (2013). Fresh gas flow reduction and isoflurane sparing effect of butorphanol and buprenorphine during low flow isoflurane anesthetic in cattle. *Adv. Anim. Vet. Sci.* **1(2)**: 29-32.

Singh, G.D., Kinjavedkar, P., Amarpal, Aithal, H.P., Pawde, A.M., Zama, M.M.S., Singh, J. and Tiwary, R. (2013) Clinicophysiological and haemodynamic effects of fentanyl with xylazine, medetomidine and dexmedetomidine in isoflurane-anaesthetized water buffaloes (*Bubalus bubalis*). *J. South African Vet. Assoc*. **84(1)**: 1-11.

Steffey, E.P. and Mama, K.R. (2007). Inhalation anaesthetics. In: Lumb and Jones' Veterinary Anaesthesia and Analgesia. (4th Edn.), (Edts.) Tranquilli W.J., Thurmon J.C. and Grimm K.A.) Blackwell publishing Ames, Iowa, USA. pp. 355-393.

Thurmon, J.C. and Short, C.E. (2007). History and overview of veterinary anesthesia. In: Tranquilli W.J., Thurmon J.C., Grimm K.A. (Edtrs.). Lumb & Jones' Veterinary Anesthesia and Analgesia. (4th Edn.), Blackwell Publishing Ltd, Oxford. pp. 3-6.

Torske, K.E., Dyson, D.H. and Pettifer, G. (1998). End tidal halothane concentration and postoperative analgesia requirements in dogs: a comparison between intravenous oxymorphone and epidural bupivacaine alone and in combination with oxymorphone. *Can. Vet. J.* **39**: 361-369.

Tranquilli, W.J., Thurmon, J.C. and Grimm, K.A. (2007). Lumb and Jones' Veterinary anesthesia and analgesia. (4th Edn.), Considerations for general anesthesia baltimore: Williams and Wilkins, Blackwell Publishing Ltd., Oxford. pp. 9-47.

Ueyama, Y., Lerche, P., Eppler, M. and Muir, W.W. (2009). Effects of intravenous administration of perzinfotel, fentanyl and a combination of both drugs on the minimum alveolar concentration of isoflurane in dogs. *Am. J. Vet. Res.* **70**: 1459-1464.

Yadav, P. (2020). Isoflurane sparing effect of pentazocine, butorphanol and meloxicam to propofol induction and isoflurane maintenance in buffaloes. M.V.Sc. thesis submitted to Lala Lajpat Rai University of Veterinary and Animal Sciences, Hisar.