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Research Article

EVALUATION OF EFFICACY AND SAFETY OF GLYCOPYRROLATE - ACEPROMAZINE - BUTORPHANOL - PROPOFOL - SEVOFLURANE ANAESTHESIA IN BUFFALOES UNDERGOING DIAPHRAGMATIC HERNIORRHAPHY

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ABSTRACT

This study was undertaken for evaluation of efficacy and safety of glycopyrrolate-acepromazine-butorphanol-propofol-sevoflurane anaesthesia in buffaloes undergoing diaphragmatic herniorrhaphy. Six animals were included in the study. After premedication with glycopyrrolate (0.01 mg/kg), acepromazine (0.02 mg/kg) and butorphanol (0.03 mg/kg); induction and maintenance of anaesthesia was performed with propofol (1.3 mg/kg) and sevoflurane respectively. Scores for premedication, induction, maintenance and recovery were good while scores for sedation, analgesia and muscle relaxation were fair. No significant difference was recorded in physiological and haematological values. Significant increase in the diastolic and mean phase of non-invasive blood pressure was recorded at 30 minutes of sevoflurane administration compared to previous value. Significant increase in glucose, blood urea nitrogen and AST was observed on second day before any drug administration as compared to previous day.

Key words: Buffalo, Butorphanol, Diaphragmatic herniorrhaphy, Glycopyrrolate, Propofol, Sevoflurane, Xylazine

Diaphragmatic hernia is a serious acquired digestive disorder in buffaloes; which are predisposed due to indiscriminate feeding habits leading to the ingestion of foreign bodies (Radostits *et al.*, 2007) or in females due to increased intra-abdominal pressure in advanced stage of pregnancy (Krishnamurthy *et al.*, 1985) results in rupture of diaphragm. Inappetence, decreased or no rumination, history of recurrent tympany, black, hard and scanty faeces and decreased milk yield are the chief complaints. General anaesthesia and dorsal recumbency during transabdominal approach of diaphragmatic herniorrhaphy results in compromised ventilation-perfusion mismatch markedly due to pressure of the abdominal organs on the diaphragm, posterior vena cava and aorta. So, there is always a search for an anaesthetic regimen which provides eternal safety and possesses fewer side effects.

MATERIALS AND METHODS

The study was conducted in six buffaloes suffering from diaphragmatic hernia. During diaphragmatic herniorrhaphy, after premedication with glycopyrrolate (0.01 mg/kg, IM), acepromazine (0.02 mg/kg, IM) and butorphanol (0.03 mg/kg, IV); induction and maintenance of anaesthesia was performed with propofol (1.3 mg/kg, IV) and sevoflurane (1-6%), respectively. The observations included anamnesis and general clinical examinations, quality of anaesthesia, behavioural, physiological, haemodynamics, haematological and blood biochemical study.

Scoring for evaluation of quality of anaesthesia was done as blindfold study by a single observer to assign numerical values; starting from 1 to 4 (1-poor, 2-fair, 3-good, 4-excellent) for premedication, induction, maintenance and recovery quality and 0 to 3 (0-no effect, 1-mild effect, 2-moderate effect, 3-deep effect) for sedation, analgesia and muscle relaxation. Behavioural changes namely muzzle dryness, weak time, down time, various body reflexes and recovery time were observed. Rectal temperature, heart rate and respiratory rate, noninvasive blood pressure and SpO^2 were recorded at various time intervals. Blood samples were collected for haematology and blood biochemistry study from jugular venipuncture at various time intervals. The statistical analysis of data was done by one-way-ANOVA using Duncan's multiple range test (Duncan, 1955).

RESULTS AND DISCUSSION

Anamnesis and general clinical observations: All the animals were grouped in ASA Category IV of physical status having illness since 15 to 150 days (Mean 55.9±21.9 days). Inappetence, decreased to suspended rumination, history of tympany, black, hard and scanty faeces and decreased milk yield were the chief complaints. The mean age of buffaloes of this group was 6.5±0.43 years. Four out of six animals were in their 3rd lactation and one animal was in 2nd and another in 5th lactation. Two animals were non-pregnant and remaining four were pregnant (mean 5.13±0.43 month). The animals had a mean body weight of 365.00±14.08 kg after rumenotomy.

Quality of anaesthesia: The quality of premedication was good as the animals were calm, relaxed and easy to restrain

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Table1
Quality of anaesthesia in buffaloes undergoing diaphragmatic herniorrhaphy (Mean ± S.E.) (n=6)

Parameters	Pre-medi-cation (1-4)	Indu-ction (1-4)	Mainte-nance (1-4)	Reco-very (1-4)	Seda-tion (0-3)	Anal-gesia (0-3)	Muscle relax-ation (0-3)
Score	3.33 ±0.21	3.67 ±0.21	3.67 ±0.21	3.33 ±0.33	2.50 ±0.22	2.17 ±0.31	2.50 ±0.22

(Table 1). Acepromazine blocks dopamine receptors in the CNS and depresses the reticular-activating system (Baldessarini and Tarazi, 2005). Analgesic property was further improved by CNS depressant effect of propofol and sevoflurane. Induction and recovery scores was good as propofol results in rapid and smooth induction, rapid distribution, metabolism and elimination results in smooth recovery on intravenous administration. Propofol was found to be safe in buffalo calves for induction of general anaesthesia (Ratnesh *et al.*, 2014).

The maintenance quality was good as balanced anaesthetic combination was used results in moderate sedation, analgesic and muscle relaxation properties along with diminishing side effects of each other's. Although, sevoflurane alone had no significant direct effect on muscle relaxation (Ye *et al.*, 2015) but CNS depression caused by this drug potentiate the muscle relaxation efficiency of premedicated drugs.

Behavioural observations: After glycopyrrolate administration; muzzle and nostrils became dry in all the animals (Table 2) as glycopyrrolate is a non-selective muscarinic receptors antagonist (Lemke, 2007). Propofol induces depression by enhancing the effect of the inhibitory neurotransmitter GABA and decreasing the brain's metabolic activity resulting into loss of various reflexes (Concas *et al.*, 1991).

Intubation was performed after loss of tongue and swallowing reflex and relaxation of jaw. Vaporize setting during initial stage and during maintenance of anaesthesia was 5.00±0.65% and 2.81±0.39%, respectively. Acepromazine administration decreases the requirements of inhalant anaesthetics (Webb and O Brien, 1988). Initiation of recovery was manifested by regain of palpebral reflex with opening of eyelids after discontinuation of sevoflurane. Extubation was performed when animal started chewing endotracheal tube after regain of tongue reflex and swallowing reflex. Time required for the complete recovery by buffaloes was 36.83±7.92 min. (Table 2) as acepromazine when combined with opioid analgesics e.g. butorphanol results in enhanced level of sedation and analgesia with prolong recovery (Hall *et al.*, 2001).

Table 2
Behavioural characteristics of onset and recovery from CNS depression induced by anaesthetics in buffaloes undergoing diaphragmatic herniorrhaphy (Mean ± S.E.) (n=6)

Parameters	Min
Muzzle dryness*	11.20±2.44
Weak time**	9.17±1.60
Down time**	29.00±4.22
Loss of palpebral reflex!	3.83±0.40
Relaxation of jaw muscle!	2.83±0.31
Loss of tongue reflex!	3.17±0.48
Loss of swallowing reflex!	3.50±0.34
Intubation!	3.50±0.50
Extubation†	12.00±3.01
Regaining of muscle tone†	12.83±5.11
Regaining of head righting reflex†	15.00±5.05
Return to sternal recumbency†	18.33±5.96
Standing with ataxia†	26.33±7.40
Complete recovery†	36.83±7.92

*after administration of glycopyrrolate, **after administration of acepromazine, !after administration of propofol, †after discontinuation of sevoflurane

Physiological and Haemodynamics study: No significant changes were recorded in rectal temperature, heart rate and respiration rate during the entire period of anaesthesia (Table 3). Slight increase and decrease in heart rates were recorded after administration of glycopyrrolate and acepromazine. The mean non-invasive blood pressure (NIBP) increased significantly after glycopyrrolate as compared to base value. Hypotension produced by administration of propofol due to decreased myocardial contractility and arterial and venous vasodilation results in lesser arterial pressure (Ilkiw *et al.*, 1992). In addition, significant increase in the diastolic and mean non-invasive blood pressure was recorded at 30 minutes of sevoflurane administration as compared to values at 15 minutes of sevoflurane administration. This might be due to overall effect of increase in blood pressure due to dorsal recumbency and decrease due to use of anaesthetic drugs. Dunlop *et al.* (1994) recorded that compared with standing position, dorsal recumbency caused 50% increase in heart rate and 44% increase in arterial blood pressure in pregnant cows. Significant higher value of SpO^2 was noticed at 15 minutes of sevoflurane administration in both the groups is due to positive pressure ventilation.

Haematological and Blood Biochemical study: No significant difference was recorded in haematological values (Table 4). Similar results were observed by (Potliya, 2012) in buffalo calves. Increase in glucose was observed after 24 hours of rumenotomy which might be due to restraining of animals resulted in increased stimulation of

Table 3
Effects of anaesthetics on Physiological and Haemodynamic parametersin buffaloes undergoing diaphragmatic herniorrhaphy (Mean ± S.E.) (n=6)

Time	Ambient Temperature (°C)	Rectal Temperature (°C)	Heart rate (beats/min.)	Respiratory rate (breaths/min.)	Non-invasive blood pressure (mmHg)			SpO^2 (%)
					Systole	Diastole	Mean	
Before Rumenotomy	18.30^{a}±0.96	37.48^{a}±0.37	44.67^{a}±1.50	15.17^{a}±1.01	-	-	-	-
Before drug admn.	19.70^{b}±0.73	37.42^{a}±0.09	48.00^{a}±5.39	13.50^{a}±0.56	139.50^{a}±9.37	100.17^{abc}±5.22	114.33^{bc}±6.04	91.67^{ac}±1.89
At 5 min. of glycopyrrolate	19.70^{b}±0.73	37.48^{a}±0.14	47.67^{a}±5.52	14.50^{a}±0.67	141.00^{a}±12.35	92.83^{ac}±7.10	109.50^{bc}±7.89	91.83^{a}±1.08
At 10 min. of glycopyrrolate	19.70^{b}±0.73	37.55^{a}±0.16	49.00^{a}±5.51	14.67^{a}±0.80	150.83^{a}±9.95	100.33^{abc}±5.63	116.83^{ac}±6.46	92.50^{ac}±1.23
At 15 min. of glycopyrrolate	19.70^{b}±0.73	37.57^{a}±0.18	51.67^{a}±5.81	15.33^{a}±0.84	158.17^{a}±9.95	115.50^{b}±8.63	132.17^{b}±7.24	92.67^{ac}±1.31
At 5 min. of acepromazine	19.70^{b}±0.73	37.55^{a}±0.20	50.00^{a}±4.93	14.83^{a}±0.75	149.83^{a}±9.60	107.50^{abc}±7.83	123.00^{abc}±7.80	92.00^{ac}±1.48
At 10 min. of acepromazine	19.70^{b}±0.73	37.15^{a}±0.06	49.00^{a}±4.12	14.17^{a}±0.54	155.83^{a}±9.46	107.00^{abc}±7.50	123.50^{abc}±8.43	90.00^{a}±0.73
At 15 min. of acepromazine	19.70^{b}±0.73	37.15^{a}±0.05	46.33^{a}±4.71	13.67^{a}±0.67	148.67^{a}±11.79	103.50^{abc}±7.97	118.67^{abc}±9.13	92.17^{a}±0.95
At 15 min. of sevoflurane	20.05^{b}±0.69	37.40^{a}±0.16	53.50^{a}±5.70	23.67^{a}±5.67	111.50^{a}±10.49	79.67^{a}±9.42	90.50^{a}±9.74	96.67^{b}±0.76
At 30 min. of sevoflurane	20.05^{b}±0.69	37.32^{a}±0.14	51.33^{a}±5.10	19.33^{a}±2.88	144.00^{a}±12.38	110.00^{b}±9.99	122.17^{bc}±10.27	95.33^{abc}±2.23
At recovery	19.70^{b}±0.73	37.23^{a}±0.06	48.67^{a}±6.51	15.17^{a}±1.76	171.33^{a}±19.51	129.50^{bc}±15.62	143.67^{bc}±16.00	95.50^{bc}±0.50

Means with different superscripts vary significantly ($p<0.05$) within columns

Table 4
Effects of anaesthetics on haematological and biochemical parameters in buffaloes undergoing diaphragmatic herniorrhaphy (Mean ± S.E.) (n=6)

Parameters (Units)	Before rumenotomy	Diaphragmatic Herniorrhaphy					At 24 hrs. of recovery
		Before drug administration	At 5 min. of propofol	At 15 min. of sevoflurane	At 30 min. of sevoflurane	At recovery	
Haemoglobin (g/dl)	8.68^{a}±0.62	9.20^{a}±0.65	8.43^{a}±0.86	8.38^{a}±0.70	7.88^{a}±0.86	8.30^{a}±0.95	8.40^{a}±0.69
Packed cell volume (%)	34.45^{a}±3.10	36.07^{a}±3.13	34.07^{a}±2.13	33.62^{a}±2.50	33.03^{a}±3.52	30.82^{a}±3.87	35.60^{a}±1.77
TEC (x106/mm3)	5.53^{a}±0.41	5.91^{a}±0.28	5.43^{a}±0.23	5.52^{a}±0.14	5.32^{a}±0.46	5.34^{a}±0.20	5.67^{a}±0.14
TLC (x103 /mm3)	7.77^{a}±1.06	5.95^{a}±1.01	5.34^{a}±0.61	5.08^{a}±0.65	5.50^{a}±0.67	6.08^{a}±0.76	4.86^{a}±0.66
L (%)	40.33^{a}±5.35	34.67^{a}±4.51	33.83^{a}±4.96	32.67^{a}±5.01	36.50^{a}±4.30	38.67^{a}±2.94	33.67^{a}±3.70
M (%)	1.50^{a}±0.22	1.33^{a}±0.21	1.33^{a}±0.21	1.33^{a}±0.21	1.33^{a}±0.21	1.17^{a}±0.27	1.50^{a}±0.22
N (%)	58.17^{a}±5.41	63.83^{a}±4.54	64.83^{a}±5.06	66.00^{a}±5.07	62.33^{a}±4.36	60.00^{a}±3.06	64.83^{a}±3.74
GLC (mg/dL)	71.75^{a}±13.62	101.23^{bc}±13.9	104.57^{b}±10.14	99.53^{b}±8.48	100.57^{bc}±9.68	96.33^{bc}±11.09	83.28^{ac}±8.29
Cortisol (nmol/L)	136.42^{ac}±35.73	157.01^{abc}±46.37	137.38^{ac}±32.7	120.71^{abc}±43.87	228.82^{b}±29.8	177.81^{bc}±21.52	98.76^{a}±29.11
LDH (U/L)	1973.00^{a} ±304.12	2208.00^{a} ±288.41	2270.17^{a} ±295.57	2131.83^{a} ±319.52	2096.00^{a} ±350.37	2175.67^{a} ±341.52	2278.83^{a} ±339.75
AST (U/L)	299.78^{a} ±86.58	458.98^{b} ±126.15	443.83^{b} ±109.8	436.85^{b} ±115.95	432.53^{b} ±121.12	408.48^{b} ±100.76	431.55^{b} ±105.72
Bilirubin T (mg/dL)	1.16^{ab}±0.18	2.98^{ab}±1.78	1.27^{b}±0.18	1.06^{ab}±0.17	0.90^{a}±0.10	0.91^{a}±0.12	1.12^{ab}±0.16
BUN (mg/dL)	52.43^{a}±2.09	64.73^{b}±3.85	65.32^{b}±4.05	62.63^{b}±5.16	64.00^{b}±4.05	63.83^{b}±5.30	66.50^{b}±4.55
Creatinine (mg/dL)	1.79^{a}±0.05	2.16^{ab}±0.14	2.17^{ab}±0.18	2.06^{ab}±0.23	2.15^{ab}±0.18	2.15^{ab}±0.22	2.30^{b}±0.18

Means with different superscripts vary significantly ($p<0.05$) within rows.

sympathetic nervous system causing increased secretions of adrenocortical hormones (Mirakhur *et al.*, 1984). Higher cortisol level may be due to long term stress period in these animals. Yan *et al.* (2016) concluded that chronic stress was associated with insulin resistance. Surgical and anaesthetic stress to the body may be responsible for significant higher value of cortisol at 30 minutes of sevoflurane administration in buffaloes. Pre-operative higher values of some parameters like AST, ALT, LDH, ALP and GGT; comparatively lower values of total protein, albumin and globulin suggest that buffaloes suffering from diaphragmatic herniorrhaphy also had some liver affection. The LDH and AST level was increased non-significantly and significantly, respectively after rumenotomy that might be due to cutting of muscles during rumenotomy and herniorrhaphy and restraining the buffaloes in lateral and dorsal recumbency for long time during herniorrhaphy might be the cause of rise in LDH level. Similar observation was observed by Potliya (2015) and Chaudhary (2016). Increase in BUN and creatinine values were seen after 24 hours of rumenotomy as the animals were chronically ill and were kept off-feed and off-water after rumenotomy.

On the basis of above observations it was concluded that balanced anaesthetic combination of glycopyrrolate-acepromazine-butorphanol-propofol-sevoflurane is effective as well as safe for buffaloes undergoing diaphragmatic herniorrhaphy.

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