Indian Journal of Animal Sciences **83** (7): 693–696, July 2013/Article

Blood gas, acid base and electrolyte changes during diazepam, midazolam premedication and halothane anaesthesia in buffaloes subjected to diaphragmatic herniorrhaphy

HARMANJEET SINGH[1], TARUNBIR SINGH[2], M RAGHUNATH[3], J MOHINDROO[4], PALLAVI VERMA[5], N S SAINI[6] and S S SINGH[7]

Guru Angad Dev Veterinary and Animal Sciences University, Ludhiana, Punjab 141 004 India

Received: 18 October 2012; Accepted: 27 February 2013

ABSTRACT

Present study was designed to evaluate blood gas, acid base and electrolyte changes in buffaloes subjected to general anaesthesia during diaphragmatic herniorrhaphy. The study was carried out on 12 animals divided randomly into 2 groups comprising 6 animals each. Diazepam and midazolam @ 0.2 mg/kg bwt were used as preanaesthetic agents in groups 1 and 2, respectively. Thiopental was administered for induction and halothane was used as maintenance agent. Heparinised blood samples from auricular artery were collected for estimation of blood gas, acid base and electrolyte status at varied intervals. Results showed that both anaesthetic combinations had no major alterations in blood electrolyte values, however, electrolyte balance was better maintained in group 2. Significant decrease in blood pH, PaO_2 and increase in $PaCO_2$ and HCO_3 noticed during the observation period primarily suggested respiratory acidosis. It was concluded that to prevent respiratory acidosis mechanical ventilation should be maintained throughout the surgical procedure.

Key words: Diaphragmatic hernia, Diazepam, Halothane, Midazolam

General anaesthesia is needed for major surgical interventions, which involves loss of consciousness, analgesia, suppression of reflex activity and muscle relaxation. Various combinations of preanaesthetics and anaesthetic agents were tested to achieve these properties (Thurmon *et al*. 1996, Hemming 2010). Diazepam, a benzodiazepine, enhances the effect of neurotransmitter gamma-aminobutyric acid, resulting in sedative, hypnotic, anxiolytic and muscle relaxant actions (Page *et al.* 2002). Midazolam, a short-acting imidazobenzodiazepine, is potent anxiolytic, hypnotic, anticonvulsant, skeletal muscle relaxant, sedative with cardiovascular sparing effects (Reves *et al.* 1985, Mandrioli *et al.* 2008, Olkkola and Ahonen 2008, Barash *et al*. 2009). Thiopentone sodium, a widely used ultrashort acting intravenous induction agent, was used in buffaloes for induction and maintenance of general anaesthesia (Singh *et al.* 1977, Krishnamurthy *et al.* 1980). Combination of thiopentone sodium with various preanaesthetics or tranquilizers reduces its induction and maintenance dose (Mirakhur *et al.* 1989).

Maintenance with intravenous anaesthetics may lead to drug over dose, increased recumbency and delayed recovery. Inhalant anaesthesia is considered safe for maintenance in long and risky procedures as it provides control on depth of anaesthesia, facilitates rapid recovery and is less toxic to the patients when compared with injectable anaesthetic agents (Kehlet and Dahl 1993). Halothane anaesthesia is used in cattle (Rugh *et al.* 1985, Matthews *et al.* 1986, Riazuddin *et al.* 2004). High chances of respiratory insufficiency in high risk patients, especially during recumbency and thoracotomy make monitoring of blood electrolyte and acid base changes important as any adverse alteration should be compensated at the earliest. Continuous monitoring of these parameters during the anaesthetic procedure may increase the safety of the procedure.

MATERIALS AND METHODS

The study was conducted in 12 clinical cases of buffaloes subjected to general anaesthesia for repair of diaphragmatic hernia. The history regarding age, sex, body weight,

Present address: [1]Captain, Remount and Veterinary Corpes, Government of India (harmanvets@gmail.com), [2] Assistant Scientist (tarunbir@gmail.com), [3,5] Assistant Professor (drraghupau@rediffmail.com, pallavivet@yahoo.com), [4] Associate Professor (jmohindroo@yahoo.co.in), [6,7] Professor (nssaini61 @rediffmail.com, simratgadvasu@rediffmail.com).

pregnancy and parturition status was recorded. Rumen was emptied completely by performing laparorumenotomy a day prior to repair of diaphragmatic hernia. No feed or water was given till surgery and the animals were maintained on intravenous fluids. Animals were randomly divided into 2 groups with 6 animals in each group. Animals were administered normal saline throughout the period of surgery and were restrained in lateral recumbency. Diazepam and midazolam @ 0.2 mg/kg bwt were used as preanaesthetic drugs in groups 1 and 2, respectively, 5% thiopental was administered 5 min after administration of preanaesthetic drugs in both groups. Initially one-third of the total calculated dose (@ 10mg/kg b.wt.) was given, which was topped up till effect. Animals were intubated with cuffed endotracheal tube of appropriate sizes and connected to the anaesthesia workstation. Halothane @ 2.5–3.5% was used initially followed by 1.5–2% for maintenance. After proper induction and intubation the animals were taken to dorsal recumbency for performing diaphragmatic herniorrhaphy. The respiration throughout the procedure was either spontaneous or was maintained by manual bagging of the rebreathing bag. Heparinised arterial blood samples (1 ml) from auricular artery were collected for estimation of acid base and electrolyte status at zero interval (base), 5 min after preanaesthetic administration (P5) and 5 min after induction of anaesthesia (I5). Thereafter, samples were taken at 15, 30, 45, 60, 90 and 240 min intervals. Acid base and electrolyte parameters like pH, PaO_2 (mm of Hg), $PaCO_2$ (mm of Hg), HCO_3^-(mmol/L), Na^+(mmol/L), K^+(mmol/L) and Cl^-(mmol/L) were estimated using blood gas analyzer.

Analysis of variance (ANOVA) and paired t test were used to compare the means among 2 groups at various time intervals and to compare the mean values at various intervals from their base values in each group (Snedecor and Cochran 1989).

RESULTS AND DISCUSSION

The animals presented were high risk patients having history of chronic tympany, anorexia and decreased milk yield. All animals under study were female buffaloes. They were either in advanced stages of pregnancy or had calved recently. The animals had a mean body weight of 304.50±18.39 kg and 340.00±16.58 kg, and mean age of 4.62±0.48 and 6.87±0.46 years in groups 1 and 2, respectively. Two animals were pregnant and 4 had recently calved in both groups.

Regurgitation and aspiration pneumonia are reported to be the most important complications in cattle subjected to halothane anaesthesia (Weaver 1971). However, in present study no such complications were observed. Complete emptying of rumen by laparorumenotomy might have helped in preventing these complications. Diazepam was used as preanaesthetic in combination with thiopental sodium (Mirakhur *et al.* 1989, Singh 2000) or with xylazine-ketamine (More *et al*. 1993) in previous studies. Midazolam was used as preanaesthetic along with thiopentone sodium in experimental calves (Bishnoi 2001) and buffaloes (Cheema 2002). Thiopentone sodium a rapid-onset ultra-short acting barbiturate is having anaesthetic, sedative, anxiolytic, anticonvulsant and hypnotic properties. However, it lacks analgesic effects (Francisco *et al.* 2005). For producing a balanced anaesthesia it may be combined with other agents. Combination anaesthetic protocols in both groups were satisfactory regarding induction, maintenance, muscle relaxation, ease to intubation and recovery.

Arterial blood samples showed no significant alterations

Table 1. Mean±SE blood electrolyte (mmol/L) profile in different groups at various intervals

		Time (min)								
		Base		Induction		Maintenance				Recovery
	Group	0	5 (P_5)	10 (I_5)	15	30	45	60	90	240
Na	1	137.67 ±1.11	134.67[a] ±1.11	136.67 ±1.11	134.67 [a] ±1.47	135.67 [a] ±1.11	136.67 [a] ±1.11	134.67 [a] ±1.47	134.67 [a] ±1.11	137.67 ±1.11
	2	139.83 ±1.64	142.83 [b] ±1.64	140.83 ±1.64	139.83 [b] ±1.64	142.83 [b] ±1.56	142.83 [b] ±1.56	142.83 [b] ±1.55	139.83 [b] ±1.64	140.83 ±1.64
K	1	4.12 ±0.22	3.99 ±0.22	4.27 ±0.22	4.09 ±0.22	4.57 ±0.34	4.52 ±0.34	4.40 ±0.34	4.38 ±0.35	4.25 ±0.34
	2	4.22 ±0.21	4.37 ±0.21	4.50 ±0.21	4.56 ±0.21	4.60 ±0.2	4.56 ±0.21	4.45 ±0.21	4.40 ±0.20	4.34 ±0.21
Cl	1	106.50 ±1.38	106.17 ±1.78	104.50 ±1.82	102.50 ±0.85	103.83 ±0.87	104.17 ±1.74	103.50 ±1.18	104.50 ±1.36	103.50 ±1.59
	2	107.17 ±0.83	106.00 ±1.21	104.33 ±0.71	102.67 ±1.43	104.17 ±1.33	103.83 ±1.25	104.83 ±1.33	105.00 ±1.91	105.92 ±0.97

Asterisked values differ significantly from the base value of the group (*P<0.05; **P<0.01; ***P<0.001). Values with different alphabets differ significantly between the groups at the corresponding intervals (P<0.05)

Table 2. Mean±SE blood acid base profile in different groups at various intervals

		Time (min)								
		Base		Induction		Maintenance				Recovery
	Group	0	5 (P_5)	10 (I_5)	15	30	45	60	90	240
pH	1	7.42	7.30 [a]	7.21 [a]*	7.20***	7.17***	7.09***	7.10***	7.08***	7.38
		±0.02	±0.07	±0.07	±0.02	±0.02	±0.05	±0.02	±0.02	±0.02
	2	7.41	7.39 b	7.35 [b]*	7.18***	7.12***	7.11***	7.09***	7.08***	7.36
		±0.03	±0.02	±0.02	±0.05	±0.03	±0.04	±0.03	±0.03	±0.05
PaO_2	1	78.33	75.83	62.33[a]*	59.00 [a]*	64.00	66.00	69.17	76.50	74.67
		±2.60	±2.62	±2.68	±1.59	±2.97	±2.67	±2.83	±5.20	±5.04
	2	80.00	79.33	74.50[b]	71.50 [b]	67.50*	62.83 *	76.00	78.50	79.83
		±0.73	±0.80	±2.03	±0.99	±0.99	±3.24	±2.11	±0.99	±0.79
$PaCO_2$	1	41.83	39.83	47.00 *	53.83 [a]***	55.83 ***	52.00 ***	49.33*	48.00*	44.83
		±0.87	±1.16	±1.09	±1.16	±1.16	±3.41	±2.17	±1.09	±1.16
	2	41.50	44.50	47.50	56.50 [b]***	58.50 ***	55.50 ***	50.00***	46.66*	42.33
		±0.76	±0.76	±0.76	±0.76	±0.76	±0.76	±2.93	±2.66	±0.88
HCO_3	1	22.83	24.33	25.67**	26.83***	25.67**	24.67	26.67***	26.83***	25.83*
mmol/L		±0.87	±0.56	±0.33	±0.70	±0.84	±0.67	±0.71	±0.79	±0.31
	2	22.17	23.33	25.33*	24.67	24.00	25.17*	24.83	25.00*	24.00
		±1.40	±0.92	±0.95	±0.92	±0.77	±0.87	±0.65	±0.73	±0.73

Asterisked values differ significantly from the base value of the group (*P<0.05; **P<0.01; ***P<0.001). Values with different alphabets differ significantly between the groups at the corresponding intervals (P<0.05).

in sodium levels (Table 1) throughout the anaesthetic period. Comparison among 2 groups showed significant (P<0.05) low values of sodium during most of the time in group 1, in comparison to group 2. Blood potassium levels (Table 1) were elevated throughout the maintenance period. However, the increase was not statistically significant and the values remained within the normal range throughout the observation period. Chloride levels (Table 1) showed a nonsignificant decrease in animals of both groups. The changes in electrolyte concentration showed no significant variations in all the groups thereby indicating that both combinations did not have appreciable untoward effects on the blood electrolyte values. Similar observations were reported after using thiopental-halothane (Singh 1988), and diazepam-thiopental combination (Mirakhur *et al.* 1988) in cattle. However, Rassam and Counsell (2005) reported sodium and water retention in animals subjected to anaesthesia and surgery during the perioperative period.

Arterial blood pH values showed a nonsignificant fall (Table 2) immediately after administration of preanaesthetics in both groups. After induction, pH decreased significantly (P<0.05) in both groups. A highly significant (P<0.001) decrease in pH from base value was observed during 15 to 90 min of anaesthesia. The values returned towards the base levels by end of the observation period. Simeonova *et al.* (2005) have also recorded similar decrease in blood pH values in dogs subjected to halothane anaesthesia. Trends in arterial O_2 saturation were similar to pH. PaO_2 values (Table 2) showed a decrease during anaesthetic procedure. PaO_2 decreased nonsignificantly after premedication. A significant (P<0.05) decrease in PaO_2 was observed after induction in group 1 (P<0.05). In group 2, the decrease in PaO_2 after induction was statistically nonsignificant. During maintenance, significant (P<0.05) decrease in PaO_2 was observed between 10 and 15 min interval in group 1 and at 45 min interval in group 2. An improvement in PaO_2 values was observed after 30 to 45 min, however, the PaO_2 values remained below the base values throughout the observation period. Comparison among 2 groups revealed significant (P<0.05) depression in PaO_2 in group 1 from 5 to 10 min after induction with thiopental. It showed better maintenance of PaO_2 in the animals receiving midazolam. $PaCO_2$ in the animals of 2 groups (Table 2) showed significant increase from 10 min to 90 min interval. However, at 240 min the values were near the base levels. Comparison among 2 groups showed no significant differences in $PaCO_2$ throughout the study period. Bicarbonate (HCO_3^-) levels (Table 2) showed nonsignificant increase after premedication in both groups. This increase was statistically significant throughout the maintenance period in group 1 and during most of time in group 2. Decreased pH, PaO_2 and increase in $PaCO_2$, HCO_3 levels during anaesthetic period are important findings as they indicate the changes in blood pH to be of respiratory origin. Lateral and dorsal recumbency and opening of thorax might have been responsible for respiratory acidosis. Ruminants are generally prone to hypoxemia in lateral and dorsal recumbency. Large animal species tend to develop a big imbalance in the distribution of ventilation relative to pulmonary blood flow. This results in a large alveolar to arterial oxygen tension difference (Tagawa *et al*. 1994).

Ventilation/perfusion mismatch during dorsal recumbency might have led to respiratory compromise. The findings are in corroboration with the observations of Fujimoto *et al.* (1985) who reported decreased pH, decreased pO_2 and increased pCO_2 during halothane anesthesia in sheep. Thielscher *et al.* (1994) had recorded a decrease of PaO_2 by 77% and increase of $PaCO_2$ by 11% above the initial level 10 min after starting the barbiturate anaesthesia in pigs. Therefore, it is desirable that buffaloes being administered general anaesthesia should be mechanically ventilated to avoid hypercapnoea. Depressant effect of the anaesthetic agents on respiratory centres might be another factor responsible for acidosis. Positive pressure artificial respiration has to be performed to maintain respiratory acid base balance throughout the operation to sustain the animal under such coniesditions.

Comparing 2 preanaesthetic agents the electrolyte balance was better maintained by midazolam. However, maintenance of acid base balance in both groups was not adequate. Thus forced ventilation throughout the anaesthetic procedure is recommended in bovine.

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