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EVALUATION OF HALOTHANE ANAESTHESIA AFTER XYLAZINE/KETAMINE ADMINISTRATION IN DROMEDARY CAMELS (*Camelus dromedarius*)

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ABSTRACT

Objective was to evaluate halothane as an inhalation anaesthetic after premedication with xylazine and induction with ketamine in camels. Six healthy, adult female dromedary camels were used as prospective controlled study. Camels were premedicated with xylazine (0.2 mg/kg, IV). Twenty minutes later, anaesthesia was induced with ketamine (2 mg/kg, IV) and was maintained with halothane in 100% oxygen. Onset and duration of anaesthesia were recorded. Rectal temperature, respiratory rate, heart rate, oxygen haemoglobin saturation, and systolic, diastolic, and mean arterial blood pressure were measured before and 20 min after administration of xylazine and then every 10 min until recovery. Lead II electrocardiogram was used to constantly monitor camels for presence of arrhythmias. Depth of anaesthesia was determined by recording reflexes. Venous and arterial blood samples were taken for haematological examination and blood gases and pH, respectively, at the same intervals. Results revealed a significant decrease in respiratory rate after xylazine and ketamine administration and significant decrease in rectal temperature and arterial blood pressure during halothane anaesthesia. A noticeable increase in the heart and respiratory rates was observed during halothane anaesthesia if compared to xylazine/ketamine values. However, the percentage of oxygen haemoglobin saturation and arterial pO_2 increased significantly with significant decrease in arterial pH during halothane anaesthesia. There were non-significant changes in the CBC values. The quality of anaesthesia was good in the majority of camels and recovery ranged from marginal to excellent. In conclusions, halothane resulted in good maintenance of anaesthesia and marginal to excellent recovery in dromedary camels. Precautions should be taken to avoid ruminal regurgitation. Oxygen administration is recommended during early recovery.

Key words: Anaesthesia, camel, inhalation, halothane, ketamine

The use of inhalation anaesthetics such as halothane, isoflurane, and sevoflurane in large animals is increasing, especially for prolonged procedures. One advantage of maintenance with contemporary inhalation anaesthetics is that they are eliminated from the body, mainly through the respiratory tract, and do not accumulate during long procedures or require extensive metabolism for termination of their effects. Moreover, inhalation anaesthesia maximises effectiveness and safety, provided appropriate adaptations are made for fasting and positioning of ruminant animals. Sedation and induction of inhalation anaesthesia with injectable drugs are very important in large, aggressive animals. Xylazine is one of the α_2-adrenoreceptor agonists that are potent analgesics and reduce the minimum alveolar concentration of inhalational agents (Steffey and Pascoe, 1991). Ketamine hydrochloride is a relatively short-acting (dose-dependent) dissociative anaesthetic which produces anaesthesia with moderate analgesia in a number of species (Lin, 1996). Xylazine and ketamine have been used for premedication and induction, respectively, in horses (Clark-Price *et al,* 2008; Leece *et al,* 2008) and ruminants (Peshin *et al,* 1980; Waterman, 1981; Sellers *et al,* 2013). Intramuscularly injected xylazine and/or ketamine have been evaluated in dromedary camels under field conditions (White *et al,* 1987).

There are reports on the use of halothane anaesthesia in large ruminants like cattle (Steffey and Holand, 1979; Riazuddin *et al,* 2004) and buffaloes (Malik *et al,* 2011) and sheep (Lin *et al,* 1997). Although halothane has been reported as an inhalation anaesthetic agent in camels (White *et al,* 1986; Singh *et al,* 1994), it has not been fully investigated in

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such species. Considering the importance of this species and the scarcity of information, this study was designed to evaluate halothane anaesthesia after premedication with xylazine and induction with ketamine.

Materials and Methods

The experimental protocol was approved by the Ethics Committee for Animal Research of the Scientific Research Deanship, Qassim University, Saudi Arabia.

Camels

Six adult female healthy dromedary camels were used in this study. Their mean body weight was 378 kg (range = 321-503 kg) and their mean age was 7 year (range = 5-12 year). Food and water were withheld 48 h and 24 h, respectively, before the study. The experiments were performed in a temperature-controlled room maintained at 21–24°C.

Anaesthesia

Sixteen-gauge intravenous and 20-gauge intra-arterial catheters (Mais Co., Riyadh, Saudi Arabia) were placed in the left jugular vein and in the auricular artery (occasionally the radial artery), respectively, after clipping, surgical scrubbing and local infiltration of the skin with 1 ml lidocaine (Lidocaine 2%, Norbrook Laboratories, UK).

Xylazine HCl (Bomazine 10%, BOMAC Laboratories Ltd., New Zealand) was used as a pre-anaesthetic medication at 0.2 mg/kg IV. Twenty minutes later, anaesthesia was induced with ketamine (Ketamine 10% Alfasan, Woerden, Holland) at 2 mg/kg, IV.

Intubation (size 20 mm) was done in either sternal recumbency or in right lateral recumbency. Thereafter camel was moved onto a padded operating table and positioned in right lateral recumbency. The endotracheal tube was connected with a semiclosed-circle rebreathing anaesthetic machine (SurgiVet Foal Circuit Set, Smith Medical North America, Waukesha, WI, USA). Anaesthesia was maintained with halothane (Anestane®, HIKMA Pharmaceuticals, Amman, Jordan) in 100% oxygen at a flow rate of 6 L/min. Anaesthesia was discontinued after 1 h and the camels received supplemental oxygen (6 L/min) through the endotracheal tube. After tracheal extubation, oxygen was insufflated through a nasal tube until sternal recumbency was achieved.

Rectal temperature (RT), respiratory rate (RR), heart rate (HR), oxygen haemoglobin saturation (OHS), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial blood pressure (MBP) were measured before and 20 min after the administration of xylazine and then every 10 min until recovery. A pulse oximeter (504DX Digital Oximeter, Criticare Systems Inc., Waukesha, WI, USA) with a probe attached to the tongue was used to determine the concentration of OHS and the heart rate. The SBP, DBP, and MBP were indirectly measured with an oscillometric technique (Accutorr Plus™ Recorder, Datascope, Datascope Corp., Paramus, NJ 07652 USA), using a cuff placed around the tail. A lead II electrocardiogram (Kenz Cardico 302, Suzuken Co, Ltd., Japan) was used to constantly monitor the camels for the presence of arrhythmias. The depth of anaesthesia was determined by recording various reflexes, including the palpebral, jaw, tongue, ear and anal reflexes.

The time intervals between discontinuance of halothane and the time of first limb movement, time of regaining the swallowing reflex and extubation, and the time at which the animal regained sternal recumbency were recorded. Time to standing, and quality of recovery were also recorded. All camels were extubated when they regained swallowing reflexes. Subjective scores for overall quality of recovery (1 = poor; 2 = marginal; 3 = fair; 4 = good; 5 = excellent) from two observers were averaged to provide an overall recovery score. A score of 1 was associated with multiple, uncoordinated attempts to achieve sternal or standing posture resulting in a major or life-threatening injury. Score 2 was associated with excitement, paddling when recumbent, several attempts to stand, severe ataxia once standing, possible fall, and danger of self-inflicted injury. Score 3 showed some staggering and ataxia, a few unsuccessful attempts to stand, and ataxia immediately after standing up. Score 4 presented signs of slight ataxia and staggering, standing at 1st or 2nd attempt, and no serious instability. A score of 5 was associated with fewer than 3 quiet, coordinated efforts to sternal or standing posture.

Sampling

Jugular blood samples were collected from each camel into EDTA-containing vacutainer tubes (Venoject, Leuven, Belgium) immediately before and 20 min after the injection of xylazine and then every 10 min until complete recovery. The red blood cell counts (RBC), white blood cell counts (WBC), differential leukocytic counts (dWBC), packed cell volume (PCV), haemoglobin concentration (HB),

hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), and platelet counts (PLT) were determined by using an automated machine (Vet Scan HM5, ABAXIS, Union City, CA 94587 USA).

Arterial blood samples were collected at the same intervals as the venous blood samples in heparinised Vacutainer tubes for immediate measurements of pO_2, pCO_2 and pH using a blood gas analyser (GEM® Premier 3000, Instrumentation Laboratory Co., Bedford, MA 01730-2443 USA).

Statistical analyses

The data were expressed as mean ±SEM and were analysed with a commercial statistical software package (SPSS, Statistical Package for Social Sciences, SPSS Inc., Chicago, IL, USA, Copyright© for Windows, version 18.0). A repeated measures analysis of variance was used as the statistical model to evaluate the differences over time in the dependent variables, including the parameters of physiological and haematological functions. The Duncan test was used to calculate multiple comparisons. Results were considered significant at $P<0.05$.

Results

The camels showed lowering of the head and neck, dropping of the lower lip, and protrusion of the tongue after xylazine administration. These signs appeared 11 ±2.4 min after administration of xylazine. Although the camels assured sternal recumbency, the head and neck were lowered and rested on the floor after 8 ± 2.1 min of ketamine administration. The head was kept in straight position and intubation was done in sternal recumbency in 5 animals and lateral recumbency in one.

The palpebral reflex disappeared in 3 camels (50%) after 10 min and in 5 of the camels (83.3%) after 20 and 30 min of halothane anaesthesia. After discontinuing halothane, the reflex returned in all camels (100%) after 10 min. The eyeball was centrally positioned in all camels during halothane anaesthesia. Tongue protrusion occurred in all 6 (100%) of the camels after 10 min of xylazine administration, while the ear reflex and muscle relaxation disappeared in all 6 (100%) of the camels after 10 min of ketamine administration and continued to be absent during the anaesthesia. Upon discontinuing the halothane anaesthesia, these reflexes appeared after 20 min in all camels (100%). The anal reflex disappeared in three camels (50%) after 10 min of anaesthesia. The anus was dilated with exposure of rectal mucosa in all 6 (100%) of the camels after 20 min of anaesthesia and the anal reflex reappeared in all 6 (100%) of the animals after 20 min of recovery. Ruminal regurgitation occurred in 1 camel (16.7%) 20 min after halothane anaesthesia. The quality of anaesthesia was good in 4 (66.7%) and excellent in 2 (33.3%) camels. The mean set value of the isoflurane vaporiser was 3.03% (range 1.5-4%).

There was non-significant decrease ($p>0.05$) in heart rate after ketamine administration when compared to 0 time. The heart rate increased non-significantly during halothane anaesthesia if compared to values during xylazine administration (Fig 1).

However, the respiratory rate decreased significantly ($p= 0.036$) after xylazine administration with non-significant increase during halothane anaesthesia (Fig 1). Again, respiratory rate decreased highly significantly ($p=0.009$) 40 min of recovery and the decrease was significant 50 min ($p=0.036$) and 70 min ($p=0.047$) of recovery.

Rectal temperature decreased significantly ($p = 0.013$) 10 min after halothane anaesthesia and later a highly significant ($p = 0.0001$) decrease during anaesthesia and during the recovery period (Fig 1). Blood pressure (systolic, mean and diastolic) showed a highly significant ($p = 0.0001$) lowering during anaesthesia and a significant ($p = 0.02$) elevation during the late recovery period (Fig 1). Systolic blood pressure decreased significantly ($p = 0.03$) after xylazine and ketamine administration (Fig 1).

The increase in the percentage of oxygen haemoglobin saturation was highly significant ($p = 0.0001$) during halothane anaesthesia and the early recovery period (Fig 1).

The mean values (±SEM) of the complete blood count (CBC) after xylazine and ketamine administration, during halothane anaesthesia, and during recovery are illustrated in Table 1.

There were non-significant changes in the CBC values during this study. However, there were significant ($p=0.04$) decrease in HB after xylazine administration and highly significant ($p=0.0001$) decrease after ketamine administration, during halothane anaesthesia and during recovery (Table 1).

Arterial blood pH decreased highly significantly ($p=0.001$) 40 and 60 min of halothane anaesthesia (Table 1). Arterial pO_2 increased highly significantly

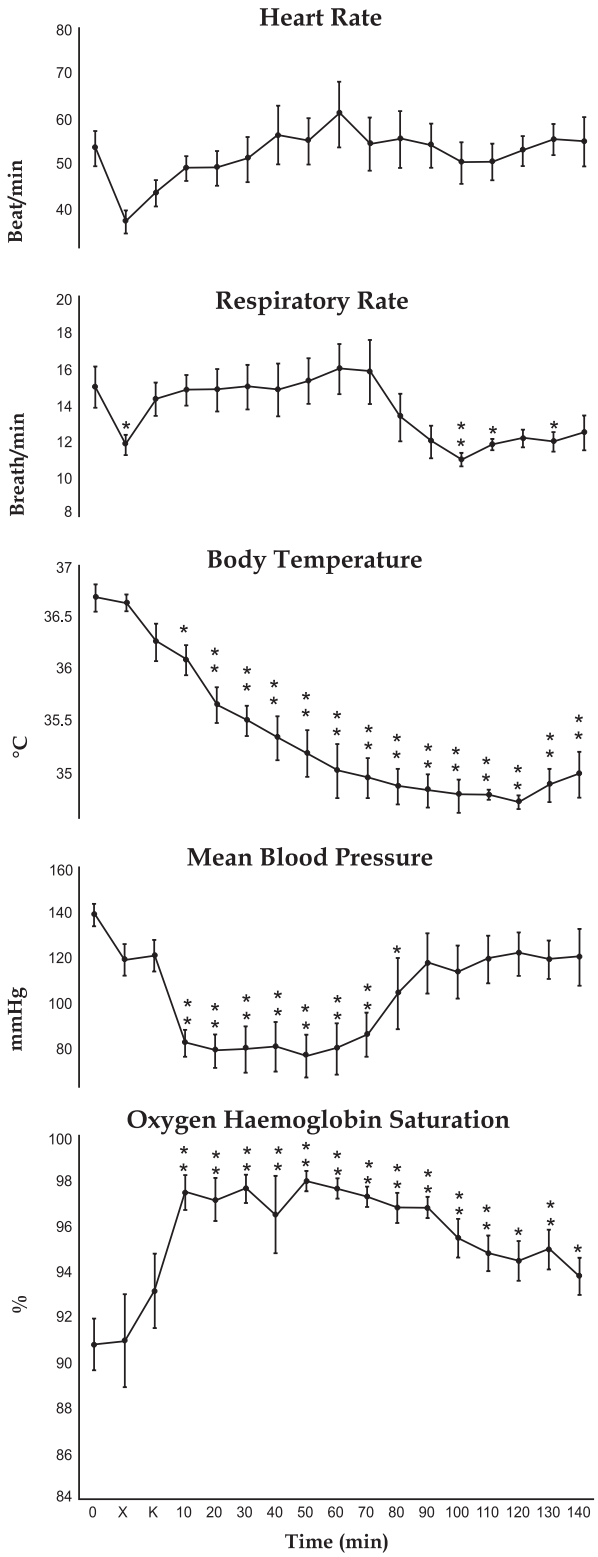

Fig 1. Changes in physiological parameters in dromedary camels (n=6) at 0 time, after xylazine and ketamine administration, during halothane anaesthesia, and during recovery[a].

[a]X=xylazine, K= ketamine, *Value is significantly different from the 0 time value, **Value is highly significantly different from the 0 time value.

(p=0.001) during halothane anaesthesia and during early recovery period (Table 1).

Electrocardiograph showed a normal sinus rhythm before premedication in all camels. Bradyarrhythmia with increased PR and ST interval were recorded after xylaxine administration; however, a relative tachyarrythmia was observed after ketamine administration. Moreover, an inverted T wave was noticed during the whole study in all the camels. A decrease in QRS and T wave amplitudes with an increase in PR interval were recorded during halothane anaesthesia and during early recovery period.

The first limb movement was noticed within 8.5 (±1.7) min (range=5-15 min) of discontinuing halothane anaesthesia. The swallowing reflex returned after a mean time of 19.3 ± 4.6 min (range = 8-37 min) after which the endotracheal tube was deflated and extubated. Sternal recumbency occurred after 69 ± 10 min (range=44-116 min), while time to standing was 111.3 ± 9.2 min (range=87-153 min) after discontinuing halothane anaesthesia. The quality of recovery was marginal (score 3) in 2 (33.3%), good (score 4) in 1 (16.7%) and excellent (score 5) in 3 (50%) camels.

Discussion

A significant decrease in respiratory rate after xylazine and ketamine administration and significant decreases in rectal temperature and arterial blood pressure were recorded in the camels during halothane anaesthesia. A noticeable increase in the heart and respiratory rates was observed during halothane anaesthesia if compared to xylazine/ketamine values. However, the percentage of oxygen haemoglobin saturation and arterial pO_2 increased significantly with significant decrease in arterial pH during halothane anaesthesia. There were non-significant changes in the CBC values. The quality of anaesthesia was good in the majority of camels. Recovery was graded marginal to excellent.

Signs of sedation and relaxation were recorded in the present camels after xylazine and ketamine administration. In another study (Peshin *et al,* 1980), xylazine at a dose of 0.4 mg/kg caused mild salivation, drooping of lower lips, and relaxation of the neck in camels which were similar to the results of the current study. Xylazine has also been found to decrease the heart rate, cardiac output and arterial blood pressure in different animal species (Hoffman, 1974; Campbell *et al,* 1979; Haskins *et al,* 1986). The effects of intramuscular xylazine and/or ketamine

Table 1. Mean (±SEM) values of CBC and arterial blood gases and pH in dromedary camels (n=6) after xylazine and ketamine administration and during halothane anaesthesia.

Time (min)	Mean(±SEM)									
	RBCs (X1012/L)	WBCs (X109/L)	PLT (X109/L)	HB(g/dL)	MCV (fL)	HCT (%)	MCH (pg)	MCHC (g/dL)	pH	pCO_2 (mmHg)	pO_2 (mmHg)
0	6.2(1.4)	12.3(2.3)	875.2(297.7)	18(0.7)	19.9(5.2)	12.3(4.2)	18.5(0.8)	59.6(10.6)	7.44(0.01)	44.7(1.9)	82.3(18)
X	5.4(1.3)	12.7(2.6)	218.8(15.7)	16.5(0.6)*	24.4(0.5)	13(3.1)	30.5(11.8)	59.7(10.7)	7.4(0.02)	47.2(3.8)	87(17.8)
K	4.8(1.0)	12.6(2.0)	366(192.2)	15(0.3)**	28(3.8)	10.3(3.1)	37.3(9.1)	51.9(9.1)	7.4(0.02)	54.3(1.1)	130.7(23.4)
20	4.6(1.1)	13.1(2.3)	831.7(3.04.4)	15.7(0.4) **	36.7(5.2)	8.6(3.2)	27.7(5.7)	55(11.9)	7.39(0.02)	58.5(3.9)	224.3(37.9) **
40	4.7(1.2)	11.6(1.9)	983(391.7)	15.3(0.6) **	37.2(5.5)	9.3(3.2)	26.3(7.4)	53.1(10.9)	7.31(0.04)**	62(8.1)	218.2(33.1) **
60	4.6(1.0)	11.9(1.5)	318.3(192.8)	14.7(0.4) **	28.2(4.0)	9.6(3.1)	40.1(9.4)	51.6(9.9)	7.3(0.04)**	67.3(10.9)	226(21.8) **
80	4.9(0.9)	12(1.6)	382.7(209.4)	15.5(0.5) **	28.5(3.8)	9.3(2.9)	43.2(10.4)	52.6(10.5)	7.38(0.03)	56.8(7.8)	208(22)**
100	4.3(1.0)	12.9(1.5)	149.7(19.4)	15(0.5) **	23.7(0.4)	10.4(2.9)	45(8.3)	50.7(9.5)	7.38(0.02)	51.2(5.9)	163.8(53)*
120	3.9(1.2)	13.2(1.6)	1060.5(368.3)	15.7(0.5) **	37.5(5.6)	8.9(2.9)	26.2(7.4)	53.2(10.9)	7.4(0.02)	52.7(5.7)	102.3(15.4)
140	4.9(0.9)	15.2(1.4)	457.5(252.6)	16(0.4) **	28.3(4.3)	10.5(2.9)	39(9.5)	52.1(10.2)	7.43(0.03)	50.2(3.1)	93.5(11.9)

X=xylazine, K= ketamine, * Value is significantly different from the 0 time value, **Value is highly significantly d different from the 0 time value.

on physiological parameters and muscle relaxation have been studied in the dromedary camel (White *et al,* 1987). Hypotension which was not correlated with bradycardia has occurred in camels 30 to 60 min after xylazine administration (Peshin *et al,* 1980).

Ketamine has been widely used for intravenous induction and maintenance of general anaesthesia in horses because of its analgesic properties (Correll *et al,* 2004) but has not been recommended as the sole intravenous agent (Greene *et al,* 1986). Ketamine has been reported to cause increase in heart rate and arterial blood pressure as a result of direct stimulation of the CNS (Wong and Jenkins, 1974). Unexpectedly, there was a non-significant decrease in the heart rate of the camels in the current study. This might have been due to the action of xylazine that masks the action of ketamine. A mixture of xylazine and ketamine was found to be superior to either drug used alone in camels (White *et al,* 1987).

Endotracheal intubation has been cited as being difficult in camels because of the narrow oral space (White *et al,* 1987), the spatula-shaped tongue with a well-developed dorsum, the wide epiglottis that overlapping the soft palate, and the presence of the palatine diverticulum (Singh *et al,* 1994). However, muscle relaxation and analgesia resulting from the xylazine and ketamine administration was helpful in the intubation of the camels in the present study. A modified technique for intubation was used in the camels of this study. To facilitate intubation, the anaesthetist introduced his right hand in order to locate the epiglottis and used the other hand to push the larynx from outside towards the oral cavity. The endotracheal tube was then introduced by the help of an assistant; therefore, in the present study, a stylette was not needed to help intubate the camels. In another study (Singh *et al,* 1994), a moderately stiff polyethylene cord of 15 mm diameter was introduced into the trachea to facilitate intubation in camels.

The effect of inhalation anaesthetics on heart rate has been shown to be variable and dependent on the agent and species (Steffey, 1996). Although within the base values, non-significant increase in the heart and respiratory rates were recorded in the camels of study if compared to xylazine/ ketamine values. In another study, heart and respiratory rates have been reported to remain above the base values during halothane anaesthesia in camels with respiration being shallow and rapid (White *et al,* 1986; Singh *et al,* 1994). This increase in the heart rate might be attributed to the marked tachycardia caused by the induction with (Singh *et al,* 1994). A significant increase in respiratory rate during halothane anaesthesia has been also recorded in water buffaloes (Malik *et al,* 2011). Similar findings of tachycardia have also been reported in cattle anesthetised with halothane

(Gates *et al,* 1971). By contrast, bradycardia has been shown to develop after halothane anaesthesia in cattle calves and no change in heart rate was reported when it was used at clinical doses in these animals (Stoelting, 1991). However, halothane, like most other inhalant anaesthetic agents, has been reported to cause respiratory depression, hypotension and reduced cardiac output in a dose-dependent pattern (Antognini and Eisele, 1993; Steffey, 2001; Hikasa *et al,* 2002). It has also been reported that a significant bradycardia was observed after premedication with medetomidine and butorphanol combination and during halothane anaesthesia in water buffaloes (Malik *et al,* 2011).

A significant hypothermia was recorded in camels of the present study that was similar to other studies (Singh *et al,* 1994; Malik *et al,* 2011). The decrease in the basal metabolic rate might be the cause of the decrease in rectal temperature.

Blood pressure (systolic, diastolic and mean) decreased significantly in the present camels during halothane anaesthesia, which was similar to the findings of other studies in camel (Singh *et al,* 1994), cattle (Thurmon and Benson, 1993) and water buffaloes (Malik *et al,* 2011). Hypotension in the present camels was possibly due to peripheral vasodilation and myocardial depression.

The significant increase in the percentage of oxygen haemoglobin saturation in the camels might be due to the inhalation of isoflurane in 100% oxygen. This increase was associated with marked decrease in arterial blood pH and increase in arterial pO_2. These findings might be suggestive of respiratory acidosis. In contrast, haemoglobin oxygen saturation has been decreased during halothane anaesthesia in water buffaloes (Malik *et al,* 2011). The most frequently used index of respiratory system response to general anaesthetics has proved to be the arterial pCO_2 (Steffey, 1996). All inhalation anaesthetics have been found to depress alveolar ventilation and, as a consequence, increase arterial pCO_2 in a dose-related fashion. Arterial pCO_2 has been reported to have a direct depressant action on the heart and on the smooth muscle of the peripheral blood vessels and to cause indirect stimulation of circulatory function (Steffey, 1996). The changes in the CBC values during this study were minimum which was similar to other findings in camels (Singh *et al,* 1994).

The testing reflexes (palpebral, tongue, jaw muscles, ear, and anal) in the camels were suitable for monitoring the quality of anaesthesia. Such reflexes have been used before to monitor the quality of inhalation anaesthesia in animals (Hikasa *et al,* 2000; Singh *et al,* 2013). The position of the eyeball in the camels of the present study was central, unlike that of cattle, in which the eyeball is ventrally rotated and partially or completely hidden under the lower eyelid (Thurmon and Benson, 1993).

ECG findings of the camels revealed bradyarrhythmia after xylaxine administration and inverted and decreased intensity of T waves after ketamine administration, during halothane during recovery. Similar changes in the ECG have been reported in buffaloes (Malik *et al,* 2011).

Moreover, a change in the polarity of T wave has been recorded in camels during halothane anaesthesia (Singh *et al,* 1994). It has been reported that alpha2-agonists cause heart block and bradyarrhythmia (Muir and Manson, 1996). The most commonly encountered arrhythmogenic effects of xylazine include sinoatrial block, atrioventricular block, bradycardia, 1st and 2nd degree heart block, AV dissociation, and sinus arrhythmia (Dunkle *et al,* 1986; Greene and Thurmon, 1988). Electrocardiography has revealed first-degree atrioventricular block, sinoatrial block, sinus arrhythmia, and wandering pacemaker in the sinoatrial node (Peshin *et al,* 1980). Moreover, the configuration and magnitude of the T wave have varied considerably between species (Muir and Manson, 1996).

It has been reported that rapid recovery from anaesthesia is advantageous in ruminants in order to reduce the risk of regurgitation (Mohamadnia *et al,* 2008). The quality of recovery ranged from marginal to excellent in camels of the present study. In another study, recovery of halothane anaesthesia has been reported to be uneventful (Singh *et al,* 1994). Ruminal regurgitation was recorded in one camel of the present study after food and water were withheld 48 and 24 h, respectively. In another study in cattle, the same management did not prevent ruminal regurgitation (Cantalapiedra *et al,* 2000).

Conclusion

In conclusion, a slight modification facilitated intubation in camels after induction with ketamine. Marked decreases in rectal temperature and blood pressure were associated with halothane anaesthesia with significant increase in the percentage of oxygen haemoglobin saturation. The changes in the CBC values were minimum with marked changes in arterial pH and pO_2 during this study. The quality

of anaesthesia was good in all camels with evidence of ruminal regurgitation in one camel. Recovery was marginal to excellent with supplementation of oxygen is being recommended during early recovery.

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