Bulgarian Journal of Veterinary Medicine, 2020, **23**, No 1, 89–101
ISSN 1311-1477; DOI: 10.15547/bjvm.2187

Original article

COMPARATIVE EVALUATION OF ELECTROCARDIOGRAPHIC EFFECTS OF DIFFERENT DOSES OF MEDETOMIDINE AND XYLAZINE IN CALF-CAMELS (*CAMELUS DROMEDARIUS*)

A. S. SAMIMI, E. SAKHAEE & F. IRANMANESH

Department of Clinical Science, Faculty of Veterinary Medicine,
Shahid Bahonar University of Kerman, Kerman, Iran

Summary

Samimi, A. S., E. Sakhaee & F. Iranmanesh, 2020. Comparative evaluation of electrocardiographic effects of different doses of medetomidine and xylazine in calf-camels (*Camelus dromedarius*). *Bulg. J. Vet. Med.,* **23**, No 1, 89–101.

This experimental, prospective, randomised, and blinded study aimed to perform comparative evaluation of electrocardiographic (ECG) effects of different doses xylazine and medetomidine in dromedary calves after intravenous (IV) administration. A total of twenty five clinically and paraclinically healthy male dromedary calves aged 15±2 weeks and weighing 95±5.5 kg were assigned randomly to five different groups (four experimental and one control). Groups XL and XH received a low (0.2 mg kg^{-1}) and high (0.4 mg kg^{-1}) dose of xylazine hydrochloride and groups ML and MH received a low (10 µg kg^{-1}) and high (20 µg kg^{-1}) dose of medetomidine hydrochloride once, IV. Finally, the control group (C) received normal saline in the same manner. ECG indices were evaluated on post treatment 0, 5, 10, 15, 30, 60, 90, 120 min, and 24 h. There was no significant difference in heart rate (HR) in all experimental groups at T90. HR was significantly lower after high doses than after low doses of medetomidine and xylazine at T120. HR was significantly lower in XH than in other groups of study at T24. At T90 QRS amplitude in XH was statistically lower than in control and XL groups. Analysis of P wave duration revealed that in MH and XH it was significantly longer than in ML, XL and control at T5. Duration of P wave in control group was significantly shorter than in all experimental groups from T10 to T90. RR interval duration was significantly shorter at T5 and T10 in control group compared to experimental groups. At T120, RR interval duration in MH and XH was considerably longer than that in ML, XL, and control. Compared with control group, cardiac arrhythmia scores were significantly lower than in all experimental groups from T5 to T60. At T90 and T120 in MH and XH, cardiac arrhythmia scores were significantly higher than those of XL, ML, and control. According to our findings, using low dose of medetomidine (10 µg kg^{-1}) and xylazine (0.2 mg kg^{-1}) was suggested in comparison with high dose of medetomidine (20 µg kg^{-1}) and xylazine (0.4 mg kg^{-1}) in dromedary calves with cardiac diseases in the field.

Key words: different doses, dromedary calves, electrocardiographic indices, medetomidine, xylazine

INTRODUCTION

Medetomidine and xylazine are imidazole α_2-adrenergic (α_2-adrenoreceptor) agonists that are white water-soluble crystalline substances. These compounds are non-narcotic, sedative (superficial and visceral), and analgesic drugs (Shah *et al.,* 2013; de Carvalho *et al.,* 2016). Adrenergic α-agonists are a class of sympathomimetic agents that selectively stimulate α-adrenergic receptors (El-Maghraby & Al-Qudah, 2005; Ismail, 2016a). The α-adrenergic receptors are two subgroups including α_1 and α_2. Alpha$_2$-adrenergic agonists are associated with sympatholytic properties. Different doses of α_2-adrenergic agonists are used to sedate animals for a variety of small operations (treatment of dental diseases and otitis, castration and some surgeries with local analgesia) and diagnostic procedures (such as restraint, radiologic, colonoscopic, endoscopic, intubation, and catheterisation) (Cardoso *et al.,* 2014; Duke-Novakovski *et al.,* 2015; Ismail, 2016b). Alpha$_2$-adrenergic agonists are dose-dependent sedative agents, used to decrease minimum alveolar concentration of inhaled anaesthetic agents, premedication prior to general anaesthesia and reduction of the required amount of injectable anaesthetic. Further positive activities that influence alpha$_2$-adrenergic agonists' use are analgesic properties and their synergistic action with opioids and anaesthetic drugs. In addition, α_2-adrenergic agonists are relatively safe substances and their effects are reversible by antagonists such as atipamezole and yohimbine (de Paiva *et al.,* 2014; Duke-Novakovski *et al.,* 2015; Azari *et al.,* 2017; Samimi & Azari, 2017).

The dromedary camels (*Camelus dromedarius*), because of their rarity, importance in transportation, beauty festival and riding races in some countries, have a unique place among all domesticated animals. They also have a high socioeconomic role because of wool, meat and milk (Azari *et al.,* 2012a). Nowadays, there is a large number of dromedaries in the Mediterranean regions including Africa, the Middle East, South America, and a smaller number in Australia as well as Iran (Samimi & Tajik, 2017; Samimi, 2018).

Animal health can be defined as the absence of disease determined by clinical examinations combined with various paraclinical tests. Analysis of electrocardiographic (ECG) variables is a necessary and reliable part of the evaluation of health, nutritional status, disease differential diagnosis and drugs pharmacodynamics in animals (Smith, 2015; Constable *et al.,* 2017; Samimi, 2018). ECG is a non-invasive, available, inexpensive and helpful diagnostic technique used to assess cardiac electrical activity (Samimi & Tajik, 2017). The importance of ECG parameters after administration of adrenergic α_2-agonist for specific species of animals has been emphasised (Azari *et al.,* 2012b; Samimi & Azari, 2017).

To the best knowledge of the authors, there is no published study documenting the comparison between effects of medetomidine and xylazine on ECG in camel calves. The aim of this study is to evaluate the effects of single intravenous (IV) administration of different doses of xylazine and medetomidine on ECG indices in dromedary calf-camels. Our hypothesis was that ECG indices following single administration of xylazine and medetomidine at various doses would be different in dromedary calves and that some unpredictable results in camel calves could occur.

MATERIALS AND METHODS

Animals

Twenty five male dromedary calf-camels (*Camelus dromedarius*) with a mean± standard deviation (SD) age of 15±2 weeks and mean±SD weight of 95±5.5 kg were used. Two months before commencing the experiments, animals were treated with albendazole 15 mg kg^{-1} orally (Dieverm600, Razak Pharmaceutical Co, Tehran, Iran) and Ivermectin 0.2 mg kg^{-1}, SC (Erfamectin1%; Erfan Pharmaceutical Co, Tehran, Iran) to control internal and external parasites. All calves were housed under the same husbandry and management conditions in the same group pen. The ration included mainly alfalfa hay and corn silage. Also, mineral supplements and fresh water were provided on a daily basis. Calves were checked to be in normal health based on clinical and paraclinical evaluations prior to the study. Prestudy paraclinical evaluation included haematological (haemoglobin, RBC, WBC, PCV, and differential leukocyte counts), biochemical (metabolic profile, electrolytes, renal and hepatic biomarkers), and faecal parasitologic examinations. Food was withheld for one day and water for 12 h prior to the beginning of the trials. The experiment was conducted in the morning. The ambient relative humidity and air temperature during the study were 12–15% and 18–22 ºC, respectively. Duration of experiment was 10 days. In one day, five calves of one group were moved to the experimental area and bound up (by the belt and rope) in a quiet sternal position on a soft and comfortable mattress, separately. The experimental area has been roofed and 5×6 m plots. The skin sites for attachment of ECG electrodes were aseptically prepared.

Experimental procedures

The calves were assigned randomly (by drawing of lots) to five different groups (four experimental and one control). Experimental groups were divided as followed. Groups XL and XH received a low (0.2 mg kg^{-1}) and high (0.4 mg kg^{-1}) dosage of xylazine hydrochloride (Xyla ®, 2%, Interchemie werken "De Adelaar, Venray, Holland) and groups ML and MH received a low (10 µg kg^{-1}) and high (20 µg kg^{-1}) dosage of medetomidine hydrochloride (Dorbene® vet, 0.1%, N-vet AB, Uppsala, Finland) once, IV. Finally, the control group (C), received normal saline in the same manner. Each drug was adjusted to 5 mL with 0.9% sodium chloride to comfort blinded IV administration via the jugular catheter.

Electrocardiography

The ECGs were obtained from each animal at 0, 5, 10, 15, 30, 60, 90, 120 min, and 24 h after treatments on a bipolar base-apex lead system using a multichannel ECG machine (Cardiocare-2000, Bionet Co., Ltd, Korea) with a calibration of 1 cm equal to 1 mV and speed of paper movement of 2.5 cm s^{-1} (Samimi & Tajik, 2017). In the base-apex lead system, the left hand lead (positive electrode with yellow colour), the right hand lead (negative electrode with red colour), and the wither's lead (earth electrode with black colour) were retained by alligator clips (after shaving and using ultrasonographic jelly) to the sixth intercostal space skin (behind the olecranon), the lower of the neck (on the jugular groove) and withers, respectively (Constable *et al.,* 2017; Samimi & Azari, 2017; Samimi, 2018). The precision of duration of interval was 0.02 sec and of its amplitude was 0.05 mV. A magnifier was used for measuring ECG indices. Intervals of each trace the heart

rate (HR) were calculated by measuring the average six RR. Cardiac rhythm was scored in each animal using a four-point scale, where cardiac rhythm scale corresponded to: 1 = normal rhythm; 2 = sinus arrhythmias; 3 = sinus bradycardia and 4 = sinus bradycardia plus sinus arrhythmias.

Statistical analysis

All statistical analyses were carried out by SPSS 23.0 (SPSS Inc, Chicago) and data were tested for normality using the Kolmogorov-Smirnov test. ECG indices and cardiac arrhythmia scores were compared among different groups and between two groups in each time using the non-parametric Kruskal-Wallis and U Mann-Whitney tests, respectively. Data were expressed as median scores (with minimum and maximum ranges) in non-parametric statistical analysis. Differences were considered statistically significant when the calculated P-value was less than 0.05.

RESULTS

All animals enrolled in the study completed the 120 min evaluation period, recovering without complications. Corneal and palpebral reflexes were normal during the experiment.

In comparison with control group, HR was significantly lower from T5 to T90 in all experimental groups ($P<0.05$) (Table 1). At T15, T30, and T60, HR was statistically insignificant in ML, XH, and MH and also in ML and XL. There was no significant difference in all experimental groups at T90 in HR. HR was significantly lower in high doses than low doses of medetomidine and xylazine at T120. It was significantly lower in XH than in other groups of study at T24 (Table 1).

The changes in several important ECG indices during the experiment in different groups are demonstrated in Tables 2 and 3. There were no statistically significant differences in T and P wave amplitude, PR and QT interval duration and duration of QRS wave in either comparison with a control group and among experimental groups from T0 to T24 h. At T90, QRS amplitude in XH was statistically lower than in control and XL groups. At this time, QRS wave amplitude was not statistically different in MH, XH, and ML. QRS wave amplitude in all experimental groups was statistically lower in comparison to the control group at T120, but there were no significant differences among MH, ML, and XL and also among XH, MH, and ML. T wave duration was significantly longer in MH than XL and control but there were no statistical differences among MH, XH, and ML at T60 and T90. Analysis of P wave duration revealed that in MH and XH it was significantly longer than in ML, XL and control at T5. Duration of P wave in control group was significantly shorter than in all experimental groups from T10 to T90. RR interval duration was significantly shorter at T5 and T10 in control group compared to experimental groups. At T15, T30 and T60 durations of RR interval were significantly shorter in control group compared to XL and in XL compared to ML, XH, and MH. In MH and XH, RR interval duration was significantly longer than in ML and XL, and also in XL and ML, it was longer vs control group at T90. At T120, RR interval duration in MH and XH was considerably longer than that in ML, XL, and control animals.

Compared with control group, cardiac arrhythmia scores were significantly lower than in all experimental groups from T5 to T60 (Table 1, Fig. 1 and 2). At T90 and

Table 1. Comparison of different doses of medetomidine and xylazine on heart rate and cardiac rhythm scores (median and ranges; n=5) in calf-camels (*Camelus dromedarius*) receiving a single IV dose of 0.2 mg kg^{-1} and 0.4 mg kg^{-1} xylazine hydrochloride respectively (groups XL and XH) and 10 µg kg^{-1} and 20 µg kg^{-1} medetomidine hydrochloride respectively (groups ML and MH). Calves in the control group were administered normal saline, IV

Groups	Time (minutes)								
	Baseline	5	10	15	30	60	90	120	24 hours
Heart rate (beats/min)									
Control	91 (71-81)	90 (68-90) [a]	92 (66-92) [a]	94 (69-94) [a]	89 (69-89) [a]	89 (71-89) [a]	71 (71-89) [a]	89 (66-89) [a]	93 (67-93) [a]
XL	84 (79-91)	41 (29-51) [b]	38 (31-50) [b]	37 (31-48) [b]	44 (34-52) [b]	41 (41-51) [b]	43 (41-49) [b]	51 (48-81) [b]	79 (73-89) [a]
ML	89 (59-89)	32 (27-36) [b]	35 (29-34) [b]	34 (30-34) [bc]	38 (29-41) [bc]	46 (37-49) [bc]	45 (40-51) [b]	51 (39-60) [b]	81 (59-85) [a]
XH	70 (70-91)	25 (23-62) [b]	26 (23-37) [b]	23 (23-38) [bc]	25 (25-38) [c]	28 (27-40) [c]	32 (32-43) [b]	26 (23-42) [c]	61 (53-66) [b]
MH	85 (71-89)	35 (21-35) [b]	32 (23-32) [b]	30 (21-32) [c]	28 (25-31) [c]	34 (29-39) [c]	36 (31-41) [b]	37 (37-41) [c]	75 (51-75) [a]
Cardiac rhythm									
Control	1 (1-2)	1 (1-2) [a]	1 (1-1) [a]	2 (1-2) [a]	2 (1-2) [a]	2 (1-2) [a]	2 (1-2) [a]	2 (1-2) [a]	1 (1-2)
XL	2 (1-2)	4 (4-4) [b]	4 (3-4) [b]	4 (3-4) [b]	3 (3-4) [b]	3 (3-4) [b]	2 (1-2) [a]	2 (1-2) [a]	2 (1-2)
ML	2 (1-2)	4 (4-4) [b]	4 (3-4) [b]	4 (3-4) [b]	3 (3-4) [b]	3 (3-4) [b]	1 (1-3) [a]	2 (1-2) [a]	2 (1-2)
XH	2 (1-2)	4 (4-4) [b]	3 (3-4) [b]	4 (3-4) [b]	3 (3-4) [b]	3 (3-4) [b]	4 (3-4) [b]	3 (3-4) [b]	1 (1-2)
MH	1 (1-2)	4 (4-4) [b]	4 (3-4) [b]	4 (3-4) [b]	3 (3-4) [b]	3 (3-4) [b]	4 (3-4) [b]	4 (3-4) [b]	1 (1-2)

Cardiac rhythm was scored in each animal using a four-point scale: 1 = normal rhythm; 2 = sinus arrhythmias; 3 = sinus bradycardia and 4 = sinus bradycardia plus sinus arrhythmias. For each parameter, different superscripts show a statistically significant difference between various groups at each time interval ($P<0.05$).

Table 2. Comparison of different doses of medetomidine and xylazine on duration and amplitude of electrocardiographic (ECG) indices (median and ranges; n=5) in calf-camels (*Camelus dromedarius*) receiving a single IV dose of 0.2 mg kg^{-1} and 0.4 mg kg^{-1} xylazine hydrochloride respectively (groups XL and XH) and 10 µg kg^{-1} and 20 µg kg^{-1} medetomidine hydrochloride respectively (groups ML and MH). Calves in the control group were administered normal saline, IV

Groups	Time (minutes)							
	Baseline	5	10	15	30	60	90	120	24 hours
P amplitude (mV)									
Control	0.09 (0.09-0.12) [a]	0.11 (0.09-0.12) [a]	0.1 (0.09-0.12) [a]	0.09 (0.07-0.11) [a]	0.1 (0.09-0.1) [a]	0.1 (0.09-0.11) [a]	0.11 (0.09-0.11) [a]	0.09 (0.09-0.11) [a]	0.11 (0.08-0.11) [a]
XL	0.11 (0.1-0.11) [a]	0.09 (0.07-0.09) [a]	0.09 (0.1-0.08) [a]	0.1 (0.07-0.11) [a]	0.1 (0.07-0.11) [a]	0.11 (0.09-0.12) [a]	0.11 (0.1-0.11) [a]	0.1 (0.1-0.13) [a]	0.09 (0.09-0.11) [a]
ML	0.11 (0.09-0.12) [a]	0.07 (0.06-0.08) [a]	0.07 (0.07-0.09) [a]	0.08 (0.08-0.09) [a]	0.08 (0.08-0.1) [a]	0.09 (0.08-0.11) [a]	0.1 (0.08-0.12) [a]	0.12 (0.09-0.12) [a]	0.12 (0.09-0.12) [a]
XH	0.12 (0.09-0.12) [a]	0.09 (0.08-0.11) [a]	0.09 (0.08-0.1) [a]	0.1 (0.07-0.11) [a]	0.11 (0.07-0.11) [a]	0.09 (0.06-0.09) [a]	0.07 (0.07-0.09) [a]	0.12 (0.08-0.12) [a]	0.11 (0.09-0.13) [a]
MH	0.11 (0.09-0.12) [a]	0.1 (0.09-0.11) [a]	0.09 (0.07-0.11) [a]	0.09 (0.07-0.1) [a]	0.08 (0.07-0.09) [a]	0.1 (0.09-0.1) [a]	0.11 (0.08-0.11) [a]	0.12 (0.1-0.13) [a]	0.11 (0.09-0.13) [a]
QRS amplitude (mV)									
Control	0.72 (0.7-0.75) [a]	0.62 (0.62-0.82) [a]	0.77 (0.74-0.8) [a]	0.74 (0.74-0.76) [a]	0.74 (0.7-0.78) [a]	0.78 (0.74-0.82) [a]	0.86 (0.7-0.9) [a]	0.86 (0.7-0.88) [a]	0.74 (0.71-0.74) [a]
XL	0.72 (0.69-0.74) [a]	0.71 (0.64-0.75) [a]	0.77 (0.71-0.80) [a]	0.8 (0.6-0.8) [a]	0.79 (0.7-0.79) [a]	0.81 (0.79-0.84) [a]	0.77 (0.74-0.92) [a]	0.68 (0.68-0.7) [b]	0.7 (0.68-0.71) [a]
ML	0.72 (0.68-0.75) [a]	0.69 (0.65-0.7) [a]	0.78 (0.74-0.8) [a]	0.67 (0.65-0.74) [a]	0.79 (0.71-0.81) [a]	0.85 (0.77-0.85) [a]	0.79 (0.68-0.79) [ab]	0.63 (0.63-0.7) [bc]	0.76 (0.65-0.76) [a]
XH	0.71 (0.71-0.74) [a]	0.59 (0.59-0.73) [a]	0.73 (0.69-0.77) [a]	0.75 (0.71-0.79) [a]	0.79 (0.72-0.79) [a]	0.8 (0.73-0.8) [a]	0.64 (0.63-0.67) [b]	0.59 (0.55-0.65) [c]	0.59 (0.59-0.73) [a]
MH	0.73 (0.7-0.73) [a]	0.7 (0.69-0.76) [a]	0.69 (0.68-0.74) [a]	0.69 (0.69-0.73) [a]	0.71 (0.65-0.75) [a]	0.83 (0.67-0.84) [a]	0.78 (0.65-0.79) [ab]	0.66 (0.74-0.67) [bc]	0.73 (0.72-0.75) [a]
T amplitude (mV)									
Control	0.19 (0.19-0.24) [a]	0.25 (0.19-0.25) [a]	0.23 (0.23-0.3) [a]	0.23 (0.21-0.26) [a]	0.27 (0.21-0.3) [a]	0.21 (0.21-0.26) [a]	0.23 (0.21-0.24) [a]	0.23 (0.2-0.24) [a]	0.26 (0.2-0.27) [a]
XL	0.24 (0.19-0.27) [a]	0.21 (0.17-0.26) [a]	0.22 (0.19-0.27) [a]	0.21 (0.21-0.25) [a]	0.24 (0.24-0.31) [a]	0.23 (0.22-0.26) [a]	0.21 (0.21-0.25) [a]	0.22 (0.21-0.27) [a]	0.27 (0.23-0.28) [a]
ML	0.28 (0.21-0.3) [a]	0.27 (0.18-0.31) [a]	0.26 (0.19-0.3) [a]	0.28 (0.21-0.29) [a]	0.27 (0.22-0.29) [a]	0.26 (0.21-0.3) [a]	0.25 (0.22-0.31) [a]	0.27 (0.23-0.31) [a]	0.28 (0.22-0.3) [a]
XH	0.27 (0.22-0.29) [a]	0.27 (0.21-0.28) [a]	0.25 (0.19-0.25) [a]	0.24 (0.19-0.25) [a]	0.26 (0.19-0.26) [a]	0.25 (0.21-0.25) [a]	0.23 (0.23-0.25) [a]	0.26 (0.22-0.26) [a]	0.19 (0.19-0.28) [a]
MH	0.28 (0.23-0.28) [a]	0.28 (0.22-0.28) [a]	0.26 (0.21-0.26) [a]	0.24 (0.19-0.25) [a]	0.25 (0.17-0.26) [a]	0.24 (0.18-0.27) [a]	0.26 (0.18-0.26) [a]	0.27 (0.21-0.27) [a]	0.27 (0.21-0.27) [a]

Table 2 (cont'd). Comparison of different doses of medetomidine and xylazine on duration and amplitude of electrocardiographic (ECG) indices (median and ranges; n=5) in calf-camels (*Camelus dromedarius*) receiving a single IV dose of 0.2 mg kg^{-1} and 0.4 mg kg^{-1} xylazine hydrochloride respectively (groups XL and XH) and 10 µg kg^{-1} and 20 µg kg^{-1} medetomidine hydrochloride respectively (groups ML and MH). Calves in the control group were administered normal saline, IV

Groups	Time (minutes)								
	Baseline	5	10	15	30	60	90	120	24 hours
P duration (sec)									
Control	0.07 (0.06-0.09) [a]	0.07 (0.06-0.09) [a]	0.06 (0.06- 0.09)[a]	0.07 (0.06-0.08) [a]	0.06 (0.06-0.07) [a]	0.07 (0.06-0.08) [a]	0.06 (0.06-0.08) [a]	0.07 (0.06-0.09) [a]	0.07 (0.07- 0.09) [a]
XL	0.08 (0.05-0.08) [a]	0.07 (0.06-0.07) [a]	0.11 (0.07-0.11) [b]	0.11 (0.08-0.11) [b]	0.12 (0.09-0.12) [b]	0.11 (0.08-0.11) [b]	0.09 (0.06-0.09) [b]	0.08 (0.06-0.1) [a]	0.11 (0.08-0.11) [a]
ML	0.08 (0.07-0.09) [a]	0.07 (0.06-0.08) [a]	0.09 (0.08-0.12) [b]	0.1 (0.09-0.11) [b]	0.11 (0.09-0.11) [b]	0.1 (0.09-0.11) [b]	0.09 (0.08-0.1) [b]	0.08 (0.08-0.1) [a]	0.08 (0.07-0.09) [a]
XH	0.08 (0.07-0.09) [a]	0.1 (0.08-0.1) [b]	0.13 (0.09-0.14) [b]	0.13 (0.11-0.13) [b]	0.12 (0.1-0.13) [b]	0.11 (0.1-0.12) [b]	0.1 (0.09-0.1) [b]	0.08 (0.08-0.1) [a]	0.09 (0.07-0.09) [a]
MH	0.05 (0.05-0.09) [a]	0.1 (0.08-0.1) [b]	0.12 (0.08-0.14) [b]	0.08 (0.08-0.14) [b]	0.11 (0.1-0.12) [b]	0.1 (0.09- 0.11) [b]	0.1 (0.09-0.1) [b]	0.09 (0.08-0.1) [a]	0.09 (0.06-0.09) [a]
QRS duration (sec)									
Control	0.1 (0.09-0.1) [a]	0.11 (0.09-0.11) [a]	0.06 (0.06-0.13) [a]	0.1 (0.08-0.12) [a]	0.1 (0.09-0.11) [a]	0.11 (0.09-0.13) [a]	0.09 (0.08-0.11) [a]	0.11 (0.08-0.11) [a]	0.09 (0.08-0.11) [a]
XL	0.12 (0.09-0.12) [a]	0.11 (0.09-0.13) [a]	0.1 (0.09-0.1) [a]	0.09 (0.09-0.1) [a]	0.1 (0.09-0.11) [a]	0.09 (0.09-0.12) [a]	0.11 (0.08-0.11) [a]	0.13 (0.08-0.13) [a]	0.09 (0.09-0.13) [a]
ML	0.09 (0.08-0.12) [a]	0.11 (0.09-0.12) [a]	0.13 (0.06-0.13) [a]	0.09 (0.07-0.11) [a]	0.09 (0.08-0.11) [a]	0.09 (0.08-0.11) [a]	0.06 (0.06-0.13) [a]	0.09 (0.07-0.13) [a]	0.09 (0.07-0.11) [a]
XH	0.09 (0.09-0.12) [a]	0.14 (0.11-0.14) [a]	0.05 (0.05-0.09) [a]	0.11 (0.08-0.12) [a]	0.12 (0.07-0.12) [a]	0.13 (0.09-0.13) [a]	0.07 (0.06-0.11) [a]	0.11 (0.09-0.12) [a]	0.13 (0.08-0.13) [a]
MH	0.11 (0.09-0.12) [a]	0.11 (0.08-0.11) [a]	0.08 (0.06-0.1) [a]	0.11 (0.08-0.12) [a]	0.12 (0.09-0.12) [a]	0.09 (0.09-0.11) [a]	0.08 (0.08-0.12) [a]	0.12 (0.07-0.12) [a]	0.12 (0.1-0.12) [a]
T duration(sec)									
Control	0.06 (0.06-0.08) [a]	0.09 (0.07-0.09) [a]	0.09 (0.07-0.11) [a]	0.08 (0.07-0.09) [a]	0.08 (0.07-0.09) [a]	0.08 (0.08-0.09) [a]	0.09 (0.08-0.1) [a]	0.1 (0.07-0.11) [a]	0.07 (0.07-0.09) [a]
XL	0.06 (0.06-0.08) [a]	0.07 (0.06-0.09) [a]	0.08 (0.07-0.09) [a]	0.09 (0.07-0.1) [a]	0.09 (0.07-0.09) [a]	0.08 (0.08-0.1) [a]	0.07 (0.07-0.11) [a]	0.08 (0.08-0.1) [a]	0.08 (0.08-0.1) [a]
ML	0.07 (0.05-0.08) [a]	0.05 (0.05-0.08) [a]	0.11 (0.09-0.12) [a]	0.09 (0.08-0.12) [a]	0.08 (0.08-0.1) [a]	0.11 (0.08-0.12)[ab]	0.1 (0.08-0.11) [ab]	0.1 (0.09-0.1) [a]	0.11 (0.08-0.11) [a]
XH	0.07 (0.07-0.08) [a]	0.07 (0.06-0.08) [a]	0.12 (0.08-0.12) [a]	0.07 (0.07-0.08) [a]	0.09 (0.07-0.1) [a]	0.1 (0.09-0.12)[ab]	0.11 (0.08-0.11)[ab]	0.11 (0.08-0.11) [a]	0.11 (0.08-0.11) [a]
MH	0.08 (0.06-0.08) [a]	0.07 (0.07-0.08) [a]	0.09 (0.07-0.09) [a]	0.08 (0.07-0.11) [a]	0.09 (0.07-0.11) [a]	0.09 (0.09-0.13)[b]	0.1 (0.09-0.12) [b]	0.11 (0.08-0.12) [a]	0.11 (0.08-0.12) [a]

For each parameter, different superscripts show a statistically significant difference between various groups at each time interval ($P<0.05$).

Table 3. Comparison of different doses of medetomidine and xylazine on interval's duration of electrocardiographic (ECG) indices (median and ranges; n=5) in calf-camels (*Camelus dromedarius*) receiving a single IV dose of 0.2 mg kg^{-1} and 0.4 mg kg^{-1} xylazine hydrochloride respectively (groups XL and XH) and 10 µg kg^{-1} and 20 µg kg^{-1} medetomidine hydrochloride respectively (groups ML and MH) Calves in the control group were administered normal saline, IV

Groups	Time (minutes)								
	Baseline	5	10	15	30	60	90	120	24 hours
PR interval (sec)									
Control	0.18 (0.15-0.21) [a]	0.19 (0.19-0.31) [a]	0.24 (0.21-0.25) [a]	0.23 (0.19-0.26) [a]	0.2 (0.2-0.27) [a]	0.18 (0.18-0.23) [a]	0.23 (0.2-0.24) [a]	0.24 (0.21-0.24) [a]	0.18 (0.17-0.22) [a]
XL	0.17 (0.17-0.2) [a]	0.2 (0.19-0.26) [a]	0.22 (0.21-0.3) [a]	0.22 (0.22-0.28) [a]	0.21 (0.2-0.23) [a]	0.21 (0.2-0.22) [a]	0.19 (0.19-0.21) [a]	0.17 (0.17-0.24) [a]	0.18 (0.17-0.26) [a]
ML	0.19 (0.17-0.19) [a]	0.21 (0.2-0.23) [a]	0.23 (0.21-0.23) [a]	0.23 (0.21-0.23) [a]	0.21 (0.19-0.23) [a]	0.19 (0.18-0.23) [a]	0.22 (0.2-0.23) [a]	0.17 (0.17-0.2) [a]	0.18 (0.16-0.2) [a]
XH	0.18 (0.18-0.2) [a]	0.2 (0.2-0.24) [a]	0.22 (0.22-0.24) [a]	0.22 (0.22-0.24) [a]	0.2 (0.19-0.21) [a]	0.21 (0.18-0.21) [a]	0.2 (0.2-0.22) [a]	0.2 (0.18-0.21) [a]	0.17 (0.16-0.18) [a]
MH	0.17 (0.17-0.2) [a]	0.21 (0.2-0.21) [a]	0.22 (0.21-0.23) [a]	0.22 (0.21-0.23) [a]	0.19 (0.19-0.23) [a]	0.21 (0.2-0.23) [a]	0.2 (0.19-0.23) [a]	0.18 (0.17-0.22) [a]	0.17 (0.15-0.22) [a]
QT interval (sec)									
Control	0.4 (0.37-0.43) [a]	0.54 (0.37-0.54) [a]	0.51 (0.41-0.55) [a]	0.5 (0.43-0.5) [a]	0.45 (0.43-0.46) [a]	0.44 (0.42-0.45) [a]	0.49 (0.43-0.5) [a]	0.46 (0.46-0.48) [a]	0.48 (0.45-0.49) [a]
XL	0.41 (0.31-0.43) [a]	0.4 (0.35-0.51) [a]	0.41 (0.41-0.49) [a]	0.41 (0.41-0.49) [a]	0.42 (0.42-0.48) [a]	0.42 (0.34-0.47) [a]	0.44 (0.44-0.56) [a]	0.44 (0.44-0.49) [a]	0.43 (0.39-0.47) [a]
ML	0.41 (0.4-0.43) [a]	0.37 (0.37-0.41) [a]	0.46 (0.44-0.48) [a]	0.45 (0.44-0.48) [a]	0.44 (0.44-0.49) [a]	0.43 (0.43-0.49) [a]	0.55 (0.46-0.55) [a]	0.46 (0.41-0.48) [a]	0.48 (0.4-0.49) [a]
XH	0.36 (0.36-0.42) [a]	0.45 (0.43-0.51) [a]	0.46 (0.42-0.47) [a]	0.46 (0.43-0.47) [a]	0.45 (0.44-0.48) [a]	0.44 (0.44-0.48) [a]	0.54 (0.47-0.59) [a]	0.46 (0.4-0.48) [a]	0.48 (0.39-0.49) [a]
MH	0.39 (0.39-0.41) [a]	0.49 (0.44-0.5) [a]	0.45 (0.45-0.54) [a]	0.46 (0.45-0.55) [a]	0.34 (0.34-0.49) [a]	0.43 (0.43-0.48) [a]	0.55 (0.46-0.56) [a]	0.48 (0.4-0.48) [a]	0.42 (0.38-0.44) [a]
RR interval (sec)									
Control	0.66 (0.66-0.84) [a]	0.66 (0.66-0.88) [a]	0.65 (0.65-0.9) [a]	0.64 (0.64-0.87) [a]	0.67 (0.67-0.87) [a]	0.67 (0.67-0.84) [a]	0.84 (0.67-0.84) [a]	0.67 (0.67-0.9) [a]	0.64 (0.64-0.89) [a]
XL	0.71 (0.67-0.76) [a]	1.46 (1.17-2.06) [b]	1.58 (1.2-1.93) [b]	1.62 (1.25-1.93) [b]	1.36 (1.15-1.76) [b]	1.46 (1.17-1.46) [b]	1.39 (1.22-1.46) [b]	1.18 (0.74-1.25) [a]	1.01 (0.67-1.01) [a]
ML	0.67 (0.67-1.01) [a]	1.87 (1.66-2.22) [b]	1.71 (1.71-2.07) [b]	1.76 (1.76-2) [bc]	1.58 (1.46-2.07) [bc]	1.3 (1.22-1.62) [bc]	1.33 (1.18-1.5) [b]	1.18 (1-1.54) [a]	0.74 (0.7-1.04) [a]
XH	0.86 (0.66-0.86) [a]	2.4 (0.96-2.61) [b]	2.31 (1.62-2.61) [b]	2.6 (1.58-2.6) [bc]	2.4 (1.58-2.4) [c]	2.14 (1.5-2.22) [c]	1.87 (1.39-1.87) [c]	2.31 (1.43-2.61) [b]	0.98 (0.9-1.07) [a]
MH	0.76 (0.67-0.76) [a]	1.71 (1.71-2.86) [b]	1.87 (1.87-2.61) [b]	2 (1.87-2.86) [c]	2.14 (1.93-2.7) [c]	1.76 (1.54-1.82) [c]	1.66 (1.46-1.93) [c]	1.62 (1.46-1.62) [b]	0.8 (0.8-1.18) [a]

For each parameter, different superscripts show a statistically significant difference between various groups at each time interval ($P<0.05$).

T120 cardiac arrhythmia scores in MH and XH, were significantly higher than in XL, ML, and control (Table 1, Fig. 3). However, no clinical signs of cardiac insufficiency or diseases were diagnosed in any animal.

DISCUSSION

ECG indices may provide a valid measure and an alternative means of monitoring animal health and drugs pharmacodynamics due to relatively systemic responses to an initiating stimulus at the time of drug injection in animals (Smith, 2015; Constable *et al.,* 2017). Research has been done to study various sedative effects of medetomidine in horses (Plumb, 2002), camels (Boardman *et al.,* 2014), sheep (Kastner *et al.,* 2003) and wild animals (Chittick *et al.,* 2001; de Paiva *et al.,* 2014). Although there are several reports on the effects of xylazine on ECG indices in adult dromedary camels, we could not find information on the effects of xylazine on ECG indices in dromedary calves. Moreover, equipotent doses of xylazine and medetomidine for calf-camels were reported in the literature. Consequently, the dose rates used in present study were based on studies comparing xylazine and medetomidine in ruminants. Moreover, camelids may be particularly susceptible

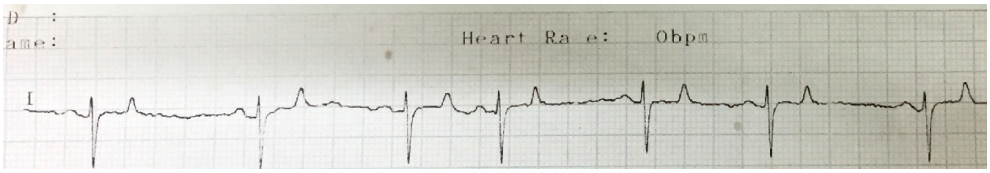

Fig. 1. Electrocardiogram (ECG) tracing (in base-apex lead system) from calf-camel (*Camelus dromedarius*) in low dosage medetomidine (ML) group (10 µg kg^{-1}) at T90 after IV administration, affected with sinus arrhythmia (paper speed: 25 mm s^{-1}; calibration: 10 mm mv^{-1}).

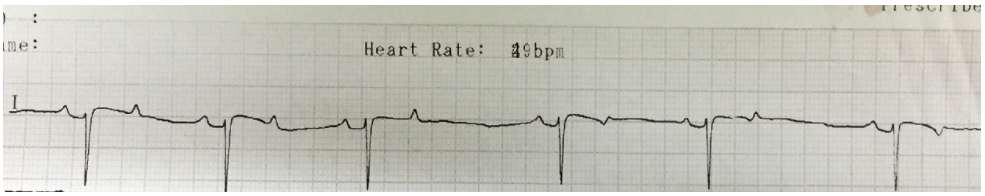

Fig. 2. Electrocardiogram (ECG) tracing (in base-apex lead system) from calf-camel (*Camelus dromedarius*) in high dosage xylazine (XH) group (0.4 mg kg^{-1}) at T90 after IV administration showing with sinus arrhythmia plus bradycardia (paper speed: 25 mm s^{-1}; calibration: 10 mm mv^{-1}).

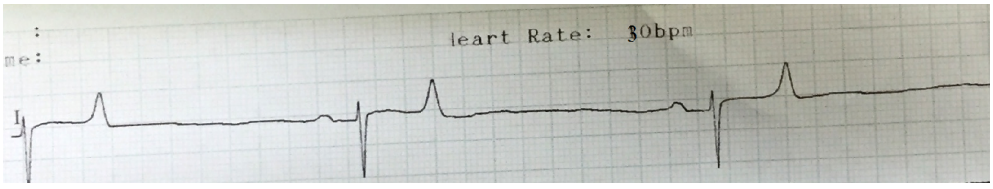

Fig. 3. Electrocardiogram (ECG) tracing (in base-apex lead system) from calf-camel (*Camelus dromedarius*) in high dosage medetomidine (MH) group (20 µg kg^{-1}) at T90 after IV administration demonstrating sinus bradycardia (paper speed: 25 mm s^{-1}; calibration: 10 mm mv^{-1}).

to mentioned drugs intoxication by doses harmless for other ruminants (Plumb, 2002; Pereira *et al.,* 2006; Azari *et al.,* 2012b; de Carvalho *et al.,* 2016). Chosen time course of 24 h was based on what is known about the pharmacokinetic characteristic of α_2-adrenergic agonist drugs in ruminants (Plumb, 2002). Lack of information about ECG effects and comparison of α_2-adrenergic agonist drugs such as xylazine and medetomidine in camel calves can lead to failure in diagnostic procedures. Furthermore, this study compared the effects of medetomidine and xylazine at low and high doses on ECG indices in dromedary calves. According to previous published articles, high dose of α_2-adrenergic agonists compared to low dose resulted in higher antinociception grade (Azari *et al.,* 2012b; de Carvalho *et al.,* 2016).

In cattle, camel and buffalo calves, the HR was reported within 75 to 95 beats min^{-1} (Smith, 2015; Constable *et al.,* 2017). Our results showed similar findings in all groups of study at T0. According to our results, all of the animals showed bradycardia 5 min after xylazine and medetomidine (low and high dose) injection. Similar findings have been reported in other species after sedation with α_2-adrenergic agonists in goats (Shah *et al.,* 2013), sheep (de Carvalho *et al.,* 2016), horses (Duke-Novakovski *et al.,* 2015), dogs (Cardoso *et al.,* 2014), and adult camels (Samimi & Azari, 2017). Sinus bradycardia occurred due to a significant decrease in HR below the normal range (Constable *et al.,* 2017). During sedation by adrenergic α_2-agonists as a result of bradycardia following decreased HR, a decrease in CNS activity and sympathetic output occurred. In our study, HR was statistically lower after high doses than after low doses of medetomidine and xylazine at T120 ($P<0.05$). de Carvalho *et al*. (2016) reported that after 120 min (in IV administration of 0.1 mg kg^{-1} xylazine) HR did not return to the normal value in sheep. Samimi & Azari (2017) and Duke-Novakovski *et al.* (2015) showed that HR returned to normal level after 90 min in IV administration of 50 µg kg^{-1} detomidine in camels and 1.5 µg kg^{-1} dexmedetomidine in horses. In our study, HR was significantly lower in XH than other groups at T24. It may be due to hepatic insufficiency for drug metabolisation, a higher proportion of water to total body weight, and unpredictable responses to experimental studies in calves (versus adults), which has been considered in pediatric anaesthesiology (Smith, 2015; Grimm *et al.,* 2015; Constable *et al.,* 2017).

Our results revealed that at T90, the QRS amplitude in XH was statistically lower than in control and XL groups. At this time, QRS wave amplitude was not significantly different in MH, XH, and ML. During sedation periods in animals, as a result of a decrease in cardiac contractility following decreased QRS wave amplitude, cardiac output and blood flow to tissues was reduced. Moreover, there is a positive correlation between ECG wave's amplitude and cardiac contractility (Zarifi *et al.,* 2012, Constable *et al.,* 2017). In conditions such as cardiac and circulatory failure, hypotension, and anaemia cases, the low dose of xylazine was suitable for use in calf-camels.

There were negative correlations between ECG wave's indices (such as duration of P waves and RR intervals) and HR (Constable *et al.,* 2017). In our study, duration of T waves and RR intervals were longer in MH and XH during different times of study after drug administration. In conditions such as pathological arrhythmia, myocarditis, endocarditis,

hypothyroidism, and electrolyte imbalances, high dose of medetomidine and xylazine was not recommended for sedation in calf-camels. Also, beta-blockers and antiarrhythmic drugs may limit the use of high dose of xylazine and medetomidine in calf-camels.

The increase in QT and RR interval durations (a less than twice increase in the normal value in QT and RR interval durations), increase in RR interval and a decrease in HR below normal value showed the presence of sinus arrhythmias and sinus bradycardia, respectively. Pathological (myocardial disease, acid-base, and electrolytes imbalances) and physiological conditions (variation in autonomic nervous system discharge) can affect the rhythm and rate of heart (Constable *et al.,* 2017). In the present study, at T90 and T120 in MH and HX, cardiac arrhythmia scores were significantly higher than XL, ML, and control. However, no clinical signs of cardiac insufficiency or diseases (e.g., jugular engorgement and pulsation, ascites, submandibular edema in observation, and cardiac murmur in auscultation) were diagnosed in any animal. Pourjafar *et al.* (2011) reported sinus bradycardia and sinus arrhythmia that could be accepted as physiological arrhythmias without clinical signs of a cardiac problem in camelids (Pourjafar *et al.,* 2011). In the current study, changes in ECG indices probably were no related with serum concentrations of electrolytes and acid-base imbalances during 120 min after drug administration in camel calves. Moreover, these changes could be due to stimulation of autonomic nervous system (α_2-adrenoreceptor mediate sedation) and decreased output from the sympathetic nervous system by α_2-adrenergic agonists. At the same time, α_2-adrenergic agonists produced bradycardia accompanied often by the development of sinus arrhythmias, first degree sinoatrial block, and occasionally second degree of atrioventricular block (Samimi & Azari, 2017), which could be the result of vagal reflex (Plumb, 2002; Berton & Horspool, 2004; Constable *et al.,* 2017). Endocarditis, myocarditis, pericarditis, and cardiac failure may limit the use of systemic α_2-adrenergic agonists for sedation in calf-camels.

It was concluded that a single high dose of either medetomidine (20 µg kg^{-1}) or xylazine (0.4 mg kg^{-1}) showed more cardiac dysrhythmia and imbalances in ECG indices which may be categorised as side effects, compared to a low dose after IV administration in dromedary calf-camels. According to our findings, low doses of medetomidine (10 µg kg^{-1}) and xylazine (0.4 mg kg^{-1}) are suggested in comparison with high doses in dromedary calves with cardiac diseases in the field.

REFERENCES

Azari, O., M. M. Molaei, L. Emadi, E. Sakhaee & M. Esmaeili, 2012a. Epidural ketamine in the dromedary camel. *Veterinary Anaesthesia and Analgesia*, **39**, 291–295.

Azari, O, M. M. Molae, L. Emadi, E. Sakhaee, H. Sharifi & S. Mehdizadeh, 2012b. Haematological and biochemical alterations caused by epidural and intramuscular administration of xylazine hydrochloride in dromedary camels (*Camelus dromedarius*). *Veterinaria Italiana*, **48**, 313–321.

Azari, O., S. Seyyedin, M. M. Molaei, H. Hassibi & B. Hashemi Madani, 2017. Analgesic and sedative effects of caudal epidural tramadol in dromedary camels. *Bulgarian Journal of Veterinary Medicine,* doi: 10.15547/bjvm.2052

Berton, J. J. & J. I. L. Horspool, 2004. Equine Clinical Pharmacology, 1st edn, WB Saunders, London.

Boardman, W. S., M. R. Lethbridge, J. O. Hampton, I. Smith, A. P. Woolnough, M-M. McEwen, G. W. J. Miller & C. G. Caraguel, 2014. Evaluation of medetomidine-ketamine and medetomidine-ketamine-butorphanol for the field anesthesia of free-ranging dromedary camels (*Camelus dromedarius*) in Australia. *Journal of Wildlife Diseases*, **50**, 873–882.

Cardoso, C. G., D. R. Marques, T. H. Silva & E. Mattos-junior, 2014. Cardiorespiratory, sedative and antinociceptive effects of dexmedetomidine alone or in combination with methadone, morphine or tramadol in dogs. *Veterinary Anaesthesia and Analgesia*, **41**, 636–643.

Chittick, E, W. Horne, B. Wolfe, K. Sladky & M. Loomis, 2001. Cardiopulmonary assessment of medetomidine, ketamine, and butorphanol anesthesia in captive Thomson's gazelles (*Gazella thomsoni*). *Journal of Zoo and Wildlife Medicine,* **32**, 168–175.

Constable, P. D., K. W. Hinchcliff, S. H. Done & W. Grunberg, 2017. Veterinary Medicine: A Textbook of the Diseases of Cattle, Horses, Sheep, Pigs and Goats, 11th edn, Elsevier, London.

de Carvalho, L. L., L. T. Nishimura, L. P. Borges, S. A. Cerejo, I. O. Villela, A. Auckburally & E. de Mattos-Junior, 2016. Sedative and cardiopulmonary effects of xylazine alone or in combination with methadone, morphine or tramadol in sheep. *Veterinary Anaesthesia and Analgesia*, **43**, 179–188.

de Paiva, A. L., T. L. Nunes, M. G. de Oliveira, A. M. de Morais, E. A. dos Santos, A. R. Silva, M. F. de Oliveira & V. V. de Paula, 2014. Effects of atipamezole and medetomidine administration on seminal variables and functions of erection and ejaculation of the collared peccary (*Tayassu tajacu*) after electroejaculation. *BMC Veteterinary Research*, **10**, 170–176.

Duke-Novakovski, T., C. Palacios-Jimenez, T. Wetzel, L. Rymes & A. F. Sanches-Teran, 2015. Cardiopulmonary effects of dexmedetomidine and ketamine infusions with either propofol infusion or isoflurane for anesthesia in horses. *Veterinary Anaesthesia and Analgesia*, **42**, 39–49.

El-Maghraby, H. M. & K. Al-Qudah, 2005. Sedative and analgesic effects of detomidine in camels (*Camelus dromedarius*). *Journal of Camel Practice and Research*, **12**, 41–45.

Grimm, K. A., L. A. Lamont, W. J. Tranquilli, S. A. Greene & S. A. Robertson, 2015. Lumb & Jones' Veterinary Anesthesia and Analgesia, 5th edn, Wiley Blackwell, Iowa.

Ismail, Z. B., 2016a. A review of anaesthetic drugs used for premedication, sedation, induction and maintenance in camels (*Camelus dromedarius*) in field situations. *Journal of Camel Practice and Research*, **23**, 207–211.

Ismail, Z. B., 2016b. Epidural analgesia in cattle, buffalo, and camels. *Veterinary World,* **9**, 1450–1455.

Kastner, S. B. R., P. Wapf, K. Feige, D. Demuth, R. Bettschart-Wolfensberger, M. K. Akens & M. Huhtinen, 2003. Pharmacokinetics and sedative effects of intramuscular medetomidine in domestic sheep. *Journal of Veterinary Pharmacology and Therapeutics*, **26**, 271–276.

Pereira, F. L. G., S. A. Greene, M.-M. McEwen & R. Keegan, 2006. Analgesia and anesthesia in camelids. *Small Ruminant Research*, **61**, 227–233.

Plumb, D. C., 2002. Veterinary drug handbook, 4th edn, Iowa state university press, Iowa.

Pourjafar, M., K. Badiei, A. Chalmeh & H. Pourmirzaei, 2011. Standard electrocardiographic parameters of base apex lead system in different age groups of clinically healthy dromedary camel (*Camelus dromedarius*). *Journal of Camel Practice and Research*, **18**, 79–82.

Samimi, A. S. & J. Tajik, 2017. Second-degree atrioventricular block in a diarrheic calf-

camel (*Camelus dromedarius*). *Comparative Clinical Pathology*, **26**, 3–7.

Samimi, A. S. & O. Azari, 2017. The effect of detomidine on clinical signs, serum electrolytes, electrocardiographic indices, and cardiac arrhythmias in *Camelus dromedarius*. *Comparative Clinical Pathology*, **26**, 707–712.

Samimi, A. S., 2018. Electrocardiographic and clinico-paraclinical evaluation of a dromedary camel suffered from theileriosis. *Comparative Clinical Pathology*, **27**, 1409–1415.

Shah, Z., A. B. Kalhore, A. B. Kachiwal, I. Ahmad, H, Sattar, M. A. Khan, Z. U. Rehman, F. A. Khan, T. Hussain & H. A. Ullah, 2013. Comparative studies on sedative and analgesic effects of xylazine and detomidine in goats. *The Journal of Animal Plant and Sciences*, **23**, 39–42.

Smith, B. P., 2015. Large Animal Internal Medicine, 5th edn, Elsevier, St. Louis.

Zarifi, M., S. Buczinski, A. Rezakhani, M. R. M. Dezfouli & A. KhonshA, 2012. Effect of lactation on functional and morphological echocardiographic variables in adult dairy cows. *Journal of Veterinary Cardiology*, **14**, 415–421.

Paper received 24.06.2018; accepted for publication 05.11.2018

Correspondence:

Amir Saeed Samimi, DVM, DVSc
Department of Clinical Science,
Faculty of Veterinary Medicine,
Shahid Bahonar University of Kerman,
Kerman, Iran, Postal code: 7616914111
Tel.: +983433257447
Fax: +983433257447
E-mail address: Samimi@uk.ac.ir
ORCID: orcid.org/0000-0003-4568-6619