IJPT
1735-2657/08/72-157-160
IRANIAN JOURNAL OF PHARMACOLOGY & THERAPEUTICS
Copyright © 2006 by Razi Institute for Drug Research (RIDR)
IJPT 7:157-160, 2008

RIDR

RESEARCH ARTICLE

Effects of Tramadol on Electrocardiogram, Mean Electrical Axis and Respiration in Kagani Goats (*Capra hircus*)

R. RAINA, P. K. VERMA, N. K. PANKAJ, S. PRAWEZ and A. K. SRIVASTAVA

For author affiliations, see end of text.

Received January 18, 2008; Revised August 10, 2008; Accepted August 25, 2008

This paper is available online at *http://ijpt.iums.ac.ir*

ABSTRACT

The effects of tramadol on electrocardiogram (ECG), mean electrical axis and respiratory rates were studied in adult kagani goats after intramuscular administration of tramadol at 1 mg/kg b.wt as a prelude to its clinical use as an analgesic in veterinary practice. The ECG was monitored by standard bipolar leads and discernible electrocardiographic features were observed in lead II. The normal electrocardiographic parameters in healthy goats were; P-wave (0.04 ± 0.005 mV, 48 ± 4.29 ms), QRS complex (0.38 ± 0.037 mV, 84 ± 2.86 ms), T-wave (0.11 ± 0.005 mV, 76 ± 1.28 ms), PR, ST, QT intervals were 152 ± 5.72, 280 ± 7.29, 368 ± 18.60 ms, respectively. These parameters were not significantly different in goats up to 3h post treatment. Except significant reduction in T-wave amplitude (p<0.05) at 0.5h, no other significant change was observed. Reduction in T-wave indicates early re-polarization phenomenon and is indicative of some transient cardio-acceleratory effect of the drug. The mean electrical axis ($56.74^0 \pm 0.6^0$) before treatment didn't show significant differences up to 3h of post-treatment. The rate of respiration prior to treatment was observed 19.6 ± 2.57min^{-1} and administration of tramadol didn't produce any significant change on respiration up to 3h post treatment.

Keywords: *Tramadol, Electrocardiogram, Mean electrical axis, Respiration, Kagani goats*

Tramadol, a codeine analog, is a centrally acting synthetic analgesic and the drug owes its analgesic action to its weak opioid (μ) receptor agonist activity and inhibition of uptake of nor-epinephrine and serotonin. Tramadol is as effective as meperidine in the amelioration of labor pain and cause less respiratory depression in humans. The drug is also being considered to be a better alternative in comparison to other opioid analgesics in humans because of high analgesic potency and minimal respiratory depression at analgesic doses [1]. The analgesic activity of tramadol is due to both parent as well as its O-demethylated metabolite and this metabolite is 4-6 times more potent than the parent [2]. Tramadol is supplied as a racemic mixture, which is more effective than either of the enantiomer alone. The (+) enantiomer binds to the μ receptor and inhibit serotonin uptake whereas (-) enantiomer inhibit nor-epinephrine uptake and blocks α_2 receptors [3]. *In vitro* and *in vivo* studies also suggested that only (+)ve enantiomer of tramadol-induce vasodilatation at high doses indicating that tramadol can be used safely at therapeutic dose [4]. The vasodilation induced by tramadol is due to both nitric oxide production from endothelium and a direct effect on smooth muscle mediated via interaction with the μ receptors [4, 5].

Electrocardiographic studies are infrequently reported in animals [6, 7]. The electrocardiographic parameters have greatest value in recognizing and diagnosing arrhythmias in animals [8]. Variability in normal duration and amplitude of different electrocardiographic parameters are useful in evaluating the side effects of commonly used therapeutic drugs [9]. Mean electrical axis values (MEA) determine the site, size and direction of the conduction system of the heart, which is individual or a breed characteristic [10]. Studies on effects of tramadol on electrocardiographic parameters, mean electrical axis and respiration in goats are scarce. The study was pursued with the objective to determine different electrocardiographic parameters in normal goats and the effect of tramadol on these parameters at analgesic dose.

[Downloaded from ijpt.iums.ac.ir on 2026-10-13]

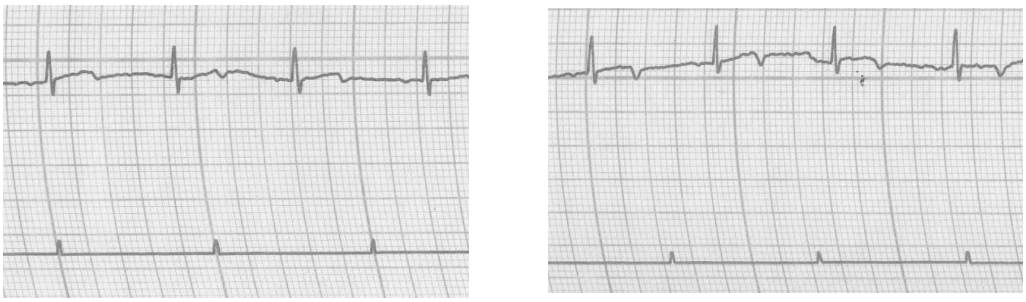

Fig 1 a. Electrocardiograms of Lead II of goat before (A) and after 0.5h (B) tramadol treatment, using physiograph Medicaid, Chandigah, India. Sensitivity 500µv and chart speed, 2.5 cm per second.

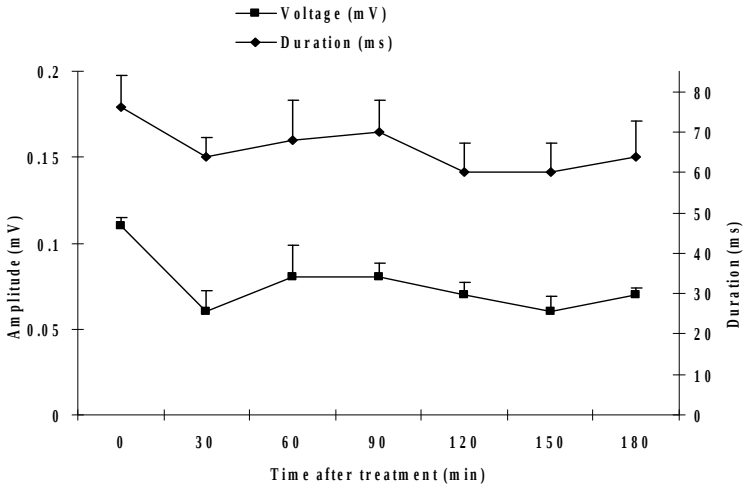

Fig 1 b. Graphical representation amplitude (mV) and duration (ms) of T-wave before and after administration of tramadol

MATERIALS AND METHODS

Healthy kagani goats (*Capra hircus*) of either sex aged 2-3 years were selected for the study. The animals were housed in the animal shed of Faculty of Veterinary Sciences, at R.S. Pura, Jammu (INDIA). All animals were maintained under standard condition of feeding and management. The animals were fed green fodder and concentrates at standard rates and free access to water. The studies were conducted in the month April-June when ambient temperature varied in between 35 - 400C. During recording of electrocardiogram (ECG) goats were made to stand on wooden plane. Needle electrodes were inserted subcutaneously proximal to the olecranon on the caudal aspect of the right and left forelegs for the right and left arm wires, respectively and in the external aspect of the stifle joint of the right and left leg wires, respectively [11]. The three standard bipolar limb leads (I, II, and III) and augmented unipolar limb leads (aVR, aVL and aVF) were recorded on paper using a three channel physiograph (Medicaid, Chandigah, India). A commercial human pharmaceutical preparation of Tramadol (Cadilla Health Care, Ahmadabad, India) was administered intramuscularly at the dose rate of 1mg kg-1body wt. Recording of ECG parameters were done before and after the administration of drug. Most of the opioids like pentazocine provide effective analgesia for (1-6 h) when they are used in a dose range of 0.4-2mg kg-1 intramuscularly [12]. Therefore, a dose of 1mg kg-1 body wt. was selected. The reported half life of drug in dogs is 0.80±0.12h [2]. Therefore the recording of ECG parameters and respiration were done at different pre-determined time intervals up to 3h of post administration. The mean electrical axis was calculated by the method of described by Dragutin and coworkers in 1999 [13]. The results obtained were analyzed statistically using paired t-test between mean obtained before and after treatment [14].

RESULTS AND DISCUSSION

Present investigation employed human technique of Einthoven's triangle in ventral plane quite successfully in goats in standing position [15]. It was observed that various components were quite discernible in unipolar and bi-polar limb leads. Therefore, comparisons were based on lead II electrocardiogram. Table 1 depicts the recorded values during the experiments on goats on duration and amplitude of P wave, duration of the QRS complex, mean electrical axis, duration of PR and QT intervals, S-T segment and respiration before and at different predetermined time intervals post administration of tramadol.

[Downloaded from ijpt.iums.ac.ir on 2026-10-13]

Table 1. Comparative electrocardiographic parameter and respiration in Kagani goat and effect of Tramadol hydrochloride @ 1mg.kg-1 intramuscular administration

Parameter		Control	After Treatment (min.)					
			30	60	90	120	150	180
P - wave	Voltage (mV)	0.04±0.005	0.06±0.007	0.045±0.003	0.045±0.007	0.04±0.005	0.04±0.005	0.04±0.005
	Duration (ms)	48±4.29	40±1.78	44±6.44	40±3.57	40±1.78	44±2.86	40±3.57
QRS complex	Voltage (mV)	0.38±0.037	0.40±0.047	0.39±0.029	0.37±0.031	0.375±0.049	0.37±0.0375	0.37±0.044
	Duration (ms)	84±2.86	80±1.78	76±2.86	88±5.72	82±3.22	82±3.22	82±3.22
T - wave	Voltage (mV)	0.11±0.005	0.06±0.012*	0.09±0.019	0.08±0.008	0.07±0.007	0.06±0.009	0.07±0.004
	Duration (ms)	76±7.85	64±1.76	68±10.0	72±7.87	60±7.15	60±715	64±8.58
PR interval (ms)		152±5.72	176±8.58	160±7.15	176±8.58	168±5.72	168±11.4	192±5.72
ST interval (ms)		280±7.29	292±11.4	280±7.15	284±4.65	264±8.58	284±2.86	272±5.72
QT interval (ms)		368±18.60	360±7.15	360±7.15	364±4.65	344±8.58	352±5.72	344±8.58
Mean Electrical Axis		56.74±3.6	55.52±2.64	57.1±4.6	56.9±2.46	57.3±4.4	56.36±3.02	56.52±4.78
Respiration (min^{-1})		19.6±2.57	18.6±3.57	17±1.71	19.8±2.28	20.2±3.50	20±3.35	20±4.17

Values are expressed as mean ± S.E. of recording six adult animals
Mean treatment values are different from the mean control values at 5% (p<0.05)

In present study prior to treatment the amplitude and duration of P-wave signifying atrial depolarization were 0.04±0.005 mV and 48±4.29 ms, respectively which is comparable with kids and lambs [5] but lesser than 0.229±0.06 mV reported for dogs [16]. The administration of tramadol didn't produce significant changes in the amplitude and duration of P-wave up to 3 h post administration.

Control values of ventricular depolarization represented by amplitude of QRS complex is 0.38±0.037 mV which is higher than the reported values of (0.17±0.086mV) in kids but is comparable to cats (0.427±0.25mV) [5, 17]. The higher QRS amplitude in goats in the present study indicates higher systolic pressure [17]. In the present study duration of QRS complex was 84±2.86ms is lower than in kids (93±7ms) but higher than reported values in dogs (54±0.01ms), cats (32±0.007ms) and llamas (50.0±8.00ms) [16,17,18]. Administration of tramadol didn't effect duration and amplitude of QRS complex. Tilley, 1985 has suggested that longer QRS complex duration to be a resultant of a heart block or enlargement of either of ventricle or both ventricles.

Significant reduction in T-wave amplitude (0.06±0.009mV) at 0.5h post administration was observed as compared to control (0.11±0.005mV) and representative recording is shown in fig.1a and b. However, no such significant reduction in duration of T-wave was observed. The decrease prominence T-wave indicate re-polarization phenomenon of the ventricles particularly basal part is rather rapid and the next cardiac cycle begins quickly thereby indicative of cardio accelerator effect of tramadol. The control duration of ST and QT intervals are higher than the reported values of kids 220±12ms, 313±13ms, but comparable with llamas 230±46, 360±60ms respectively [7, 18]. However no significant change was observed in these intervals up to 3h of post treatment compared to pretreatment values. Determination of electrical axis of heart is an important aid for understanding deviation of impulse conduction in the heart and can help in diagnosis of pathological conditions of heart. In the present study tramadol didn't significantly affect the mean electrical axis values ($56.74^0 \pm 0.6^0$) in goats. The respiration rates reported for goats are in the range of 12-25 min^{-1} [19] and tramadol didn't affect significantly respiration rates (19.6±2.57 min^{-1}). Conversely opiate substitutes like, pentazocine causes significant reduction in respiration in kids [7]. Finding also suggested that tramadol also provides a cardio-protective effect against myocardial ischemia-reperfusion in isolated rat heart [20].

From the results it can be concluded that at the dose rate 1mg kg^{-1} in goats, tramadol is a safe analgesic due to its mild and transient effect on ECG events without effecting respiration.

REFERENCES

1. Zahedi, H. Comparison of tremadol and pethidine for post-anesthetic shivering in elective cataract surgery, *Journal Research of Medical Science*, 2004; 5, 37-41.
2. Raimundo, J.M., Sudo, R.T., Pontes, L.B., Antunes, F., Trachez, M.M., Zapata-Sudo. G. *In vitro* and *in vivo* vasodilator activity of racemic tramadol and its enantiomers in Wistar rats. *European Journal of Pharmacology*, 2006; 530, 117-123.
3. Kaya, T., Gursoy, S., Karadas, B., Sarac, B., Fafali, H., Soydan, A.S. High-concentration tramadol-induced vasodilation in rabbit aorta is mediated by both endothelium-dependent and -independent mechanisms. *Acta Pharmacol Sin*, 2003; 24, 385-389.
4. Kukanich, B., Papich, M.G. Pharmacokinetics of tramadol and the metabolite O- desmethyltramadol in dogs, *Journal Veterinary Pharmacology Therapeutics*, 2004; 27 239-246.
5. Grond, S., Meuser, T., Uragg, H., Stahlberg H.J., Lehmann, K.A. Serum concentration of tramadol enantiomers during pa-

[Downloaded from ijpt.iums.ac.ir on 2026-10-13]

tient controlled analgesia, *British Journal Clinical Pharmacology*, 1995; 48, 254-257.

6. Tovar, P., Santisteban, R. Effects of maturational changes upon the orientation of auricular activation vector in sheep, *Journal Veterinary Medicine*, 1987a; 34, 18-24.
7. Mir, S.A., Nazki, A.R., Raina, R. Comparative electrocardiographic studies, and differing effects of Pentazocine on ECG, heart and respiratory rates in young sheep and goats, *Small Ruminant Research*, 2000; 3, 13-17.
8. Miller, R.H., Lehmkuhl, L.B., Bonagura, J.D., Beall, M.J. Retrospective analysis of the clinical utility of ambulatory electrocardiographic (Holter) recordings in syncopal dogs: 44 cases (1991-1995), *Journal Veterinary Internal Medicine*, 1999. 13, 111-122.
9. Smith, F.W.K., Hadlock, D.J. Electrocardiography. In: Manual of canine and feline cardiology, 2nd ed. (M. S. Miller, L. P. Tilley, Eds.). W. B. Saunders. Philadelphia, 1995.
10. Tilley, L.P. Essentials of canine and feline electrocardiography: Interpretation and treatment. Lea & Febiger. Philadelphia, 1985.
11. Nahas, K., Geffray, B. QT interval measurement in the dog: chest lead versus limb lead, *Journal Pharmacology. Toxicology Methods*, 2004; 50, 201-207.
12. Gerring, E.L. Equine colic cause diagnosis and treatment in: Bogan JA, Lee P, Yoxall AT (Eds.). Pharmacological basis of large animal medicine, Blackwell Scientific Publication Oxford, 1983.
13. Dragutin, N., Noll, G., Luscher T.F. Corrected Formula for the Calculation of the Electrical Heart Axis. *Croatian Medical Journal*, 1999; 40, 1-4.
14. Shedecor, G.W., Cochran, W.G. Statistical methods. Oxford and IBM publishing Co., Bombay India, 1967.
15. Montoya, A.J.R, Ponce, V.J. Normal cardiac rhythm in goats. Medicine Veterinaria, 1986; 3, 227-31.
16. Kovacevic, A., Duras, M., Gonercic, T. Contribution of standardization of heart rate electrocardiographic values in Doberman pinschers, *Veterinarski Archiv*, 1999; 69 211-219.
17. Pereira, G.G., Larsson, M.H., Yamaki, F.L., Soares, C.E., Yamato, J.R., Neto, L.M., Froes, R.T., Bastos, V.L. Effects of propofol on the electrocardiogram and systolic blood pressure of healthy cats pre- medicated with Acepromazine, *Veterinary Anesthesia and analgesia*, 2004; 31, 235-238.
18. Marc, S., K., Clay, A.C, Alan, W.S., Kathryn, M.M., David, E.A. Determination of electrocardiographic parameters in healthy llamas and alpacas, *American Journal Veterinary Research*, 2004; 65, 1719-1723.
19. Miller, W.C., West, G.P. Black's Veterinary Dictionary, Adam and Charies Black, London, 1972.
20. Bilir, A., Erkasap, N., Koken, T., Gulec, S., Kaygisiz, Z., Tanriverdi, B., Kurt, I.Effects of tramadol on myocardial ischemia-reperfusion injury. *Scand Cardiovascular Journal*, 2007; 41, 242-247.

CURRENT AUTHOR ADDRESSES

R. Raina, Division of Pharmacology & Toxicology, Faculty of Veterinary Sciences & Animal Husbandry, SKUAST-J, R.S. Pura 181102, Jammu (J & K), INDIA. E-mial: drpawankv@yahoo.co.in (Corresponding author)

P. K. Verma, Junior Scientist, Division of Pharmacology and Toxicology, Faculty of Veterinary Sciences and Animal Husbandry, R.S. Pura, Jammu (J&K), INDIA.

N. K. Pankaj, Junior Scientist, Division of Pharmacology and Toxicology, Faculty of Veterinary Sciences and Animal Husbandry, R.S. Pura, Jammu (J&K), INDIA.

S. Prawez, Junior Scientist, Division of Pharmacology and Toxicology, Faculty of Veterinary Sciences and Animal Husbandry, R.S. Pura, Jammu (J&K), INDIA.

A. K. Srivastava, Director, National Dairy Research Institute, Karnal Haryana, INDIA.

[Downloaded from ijpt.iums.ac.ir on 2026-10-13]