Heighten Science PUBLICATIONS Corporation

ISSN
2576-9510

Research Article

Effects of carazolol on electrocadiographic and trace element status in sheeps

Remzi Gonul[1], Lora Koenhemsı[1], Handan Aydın Vural[2]*, Tevfik Gulyasar[3], Hasret Demırcan Yardıbı[4], Erman OR[1] and Bora Barutcu[5]

[1]Istanbul University, Faculty of Veterinary Medicine, Department of Internal Medicine, Turkey
[2]Istanbul University, Faculty of Veterinary Medicine, Department of Pharmacology and Toxicology, Turkey
[3]Trakya University, Medical School, Department of Biophysic, Turkey
[4]Istanbul University, Faculty of Veterinary Medicine, Department of Biochemistry, Turkey
[5]Istanbul University, Cerrahpasa Medical School, Department of Biophysic, Turkey

***Address for Correspondence:** Handan Aydın Vural, Istanbul University, Faculty of Veterinary Medicine, Department of Pharmacology and Toxicology, Turkey, Email: haydin@istanbul.edu.tr

Submitted: 27 March 2018
Approved: 06 April 2018
Published: 09 April 2018

Keywords: Carazolol; Sheep; Ecg; Trace elements

Abstract

Carazolol is a non-specific β-adrenargic reseptor blocking agent. It ıs structurally analogous to catecholamins, in that, when administered, it forms reversible bonds with β-adrenergic, however, induce adrenergic effects, and it inhibits the actions of the catecholamins in times of stres by saturing their sites of operation. The purpose of the research was to investigate the effects of carazolol on some serum enzymes, trace elements and cardiovascular status in sheep. Seven sheeps (age 6 months, 35 ± 10 kg) were used in this study. Carazolol administered by the intramuscular route at the dose of 0.01 mg/kg. Serum levels of urea, creatinin, ALT, AST, G-GT, LDH, T. protein, Ca, P, Mg, Cu, Fe, Zn, Se were investigated. Although all serum enzymes did not show any difference, serum Fe and Zn levels were decreased. Important results were obtained in electrocardiography (abnormal T wave and ST segment depression).

These results suggest that carazolol may increase incidence rate of myocardiyal ischemia risk in sheeps and it investigated by new researches.

Introduction

β-adrenargic receptor blockers have been used in the treatment of cardiovascular diseases such as arterial hypertension, coronary heart disease, supraventricular and ventricular tachyarrhytmias. Currently, there are many β-adrenargic receptor blockers for clinical use that differ with respect to pharmacokinetic and pharmacodynamic properties [1].

One of these, Carazolol, is a non-specific β-adrenargic receptor blocker agent having 1-(carbazol–4-yloxy)-3-isopropylamino-2-propanolol chemical structure [2]. It is a strong analogous of catecholamine (adrenalin-noradrenalin). It can bind to β receptors irreversibly. It is binding to β-adrenoreceptors are inhibited by the endogenous catecholamine secretion in stressed conditions [3]. Consequently, carazolol is used in the treatment of circulatory disorders caused by stress in many animals species including particulary pigs, also against neonatal mortality caused by weak uterine contractions, to reduce neonatal deaths by shortening the parturition time, milk withdrawal, semen collection in males, artificial insemination of females, in the treatment and preventation of retentio secundinarium caused by dystocia and in the treatment of endometritis in combination with other drugs in cattles [2].

How to cite this article: Gonul R, Koenhemsı L, Vural HA, Gulyasar T, Yardıbı HD, Erman OR, et al. Effects of carazolol on electrocadiographic and trace element status in sheeps. Insights Vet Sci. 2018; 2: 001-004. https://doi.org/10.29328/journal.ivs.1001007

However there is lack of studies performed for the acute effects of carazolol in the organism. Therefore, in this study we planned to investigate the effects of carazolol on electrocardiography, tension, oxygen saturation and some biochemical parameters in acute period in sheeps.

Material and Method

The study was carried on 7 Kivircik sheeps that were between 25-45 kg, non-pregnant, determined to be healthy after clinical examination, obtained from İ.Ü. Research and Application Farm. For this study, 0.01 mg/kg Carazolol was injected intramuscularly to each sheep. ECG, SpO2 ve blood pressure changes were investigated before and ½ hours after the administration of drug and changes on blood parameters and trace element levels were investigated after 2 hours.

10cc blood without anticoagulant was taken from V. Jugularis for the serum blood analysis of sheeps. Biochemical blood parameters (ALT, ALP, GGT, Urea, Creatinin, LDH, T. Protein, Ca and P) were determined spectrophotometrically. Trace element calculations were made with atomic absorbtion device (Shimadzu AA-6800). Se calculations were performed with graphite furnace (Shimadzu Graphite Furnace Atomizer GFA-EX7).

Electrocardiographic records were taken as appropirate to technique with PETAŞ Kardiyopet 300 device. Blood pressure and oxygen saturation was measured with EDAN M9B bed-side monitor. For this purpose, non invasive blood pressure (diastolic, sistolic and mean) was taken from femoral or metatarsal artery depending on the size of animal. Oxygen saturation (SpO2), was determined from ear tip arterial blood of animals by measuring the hemoglobin oxygen saturation in arterial blood with plethysmogram by the device.

The mean values, standard deviations and statistical differences were performed by Student t test.

Results

No clinical difference was determined in the general conditions of animals 2 hours after the administration of drug.

No statistical difference was determined in biochemical parameters in blood analysis performed 2 hours after carazolol injection. The decrease in Fe and Zn was found statistically significant at $p<0.05$ level (Table 1).

SpO2 and blood pressure measurements performed 1/2 hour after the carazolol injection were found to increase, however these changes were not found statistically significant (Table 2).

Table 1: Changes in some blood parameters in sheeps 2 hours after carazolol administration

	0. Hour	2. Hour
	X± Sx	X± Sx
Urea (mg/dl)	6,3±2,4	5,7±2,4
Creatinin (mg/dl)	63±21,5	89,1±37,3
ALT (IU/L)	72,4±33,7	10,9±3,4
ALP (IU/L)	276,9±79,6	248,1±48,5
G-GT (IU/L)	12,4±4,1	15,1±6,7
LDH (IU/L)	61,7±15	61,2±12,8
T.protein (g/dl)	10,2±1,5	8,8±1
Ca (mg/dl)	11,4±3,4	5,8±1,4
P (mg/dl)	5,6±1,1	3,3±0,6
Mg (mg/dl)	1±0,04	1±0,02
Cu (µg/dl)	94,4±2,9	98,8±5,4
Fe (µg/dl)	348±26,2	194±28,9*
Zn (µg/dl)	114,9±4,2	84,2±3,9*

*p<0.05

Although no significant differences were observed in the measurements carried on electrocardiographic traces of ECG records obtained ½hours after injection (Table 3), abnormal T wave and ST segment depression changes were observed in two animals (Figure 1).

Table 2: Blood pressure and oxygen saturation changes in sheep ½ hours after carazolol administration.

	0.Hour	½ Hour
	X± Sx	X± Sx
Systolic (mmHg)	93,7±4,8	100,6±11,1
Mean (mmHg)	74,3±6,6	80,1±8,4
Diastolik (mmHg)	63,7±7	69±9,2
SpO_2 (%)	84,3±4,5	94±2,5

Table 3: Changes in II derivation of electrocardiographic parameters in sheep ½ hours after carazolol administration.

	O. Saat	½ Saat Sonra
	X± Sx	X± Sx
P Amplitude (mV)	0,1±0	0,1±0
P period (mm/sn)	0,04±0	0,04±0
PR interval(mm/sn)	0,09±0,02	0,1±0,04
QRS period (mm/sn)	0,04±0,004	0,05±0,006
R Amplitude (mV)	0,2±0,03	0,2±0,02
Q Amplitude (mV)	0,5±0,1	0,4±0,08
QT Interval (mV)	0,3±0,02	0,3±0,02
T Amplitude (mV)	0,2±0,06	0,3±0,07
T Period (mm/sn)	0,04±0,008	0,05±0,01

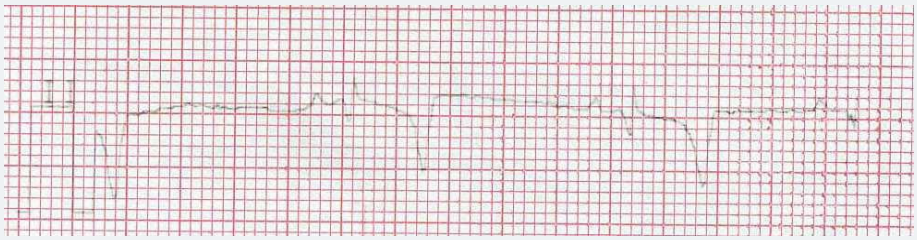

Figure 1: Changes in T wave and ST segment in ECG II. Derivation in sheep, ½ hours after carazolol administration.

Discussion

In veterinary medicine, carazolol has been used to decrease cardiovascular responses arising from catecholamine usage, in stress related disorders, in the area of veterinary artificial insemination and gynecology [3].

No studies were found regarding to side effects however the drug has been used widely recently. In our study, urea, creatinin, ALT, ALP, GGT, LDH, Ca, P, T.Protein, Mg, Cu levels in blood serum parameters were found to be in normal level however statistical decrease in $p<0.5$ level on serum Fe, Zn levels was determined after Carazolol injection.Moreover, all other values were reported to be within referance values.

Some behavioural,physiological, haemotologic and neurohormonal changes can occur in animal body depending on the stress [4-8]. Most of the trace elements were known to be function as a part of enzym, hormon and vitamins [4,9]. For this reason, we think that stress factors must be taken into consideration in the evaluation of changes observed in sheeps after carazolol injection and new studies should be done relating to this subject.

Researchers [5,7,9] have also reported that several hormons that play role in stress cause elevation in cardiac rhythm and blood pressure, increase in plasma catecholamine and behavioral changes. In our study, elevation in systolic, mean and diastolic arterial blood pressure were not found statistically significant after carazolol

injection to sheeps. Nevertheless, this condition is thought to be result of stress that was created during administration as well as the detection of changes in the second controls after injection suggesting the stress and side effects of drug.

When the acute effects of drug to the heart were evaluated no findings were observed except abnormal T wave and depression in ST segment formed in two animals. We have observed that the drug may cause some biochemical and cardiovascular effects, although the drug has been used more recently. We think that these should also be taken into consideration when using the drug and the side effects of the drug must be further investigated.

References

1. Borchard U. Pharmacological properties of β-adrenoreseptor blocking drugs. J Clin Bas Cardiol. 1998; 1-5.
2. Bademkıran S, Horozkaya H. İneklerde güç doğuma bağlı şekillenen retensiyo sekundinaryumun engellenmesinde beta blokörlerin (carazolol) ve PGF2α'nın etkilerinin karşılaştırılması. 2016. **Ref.:** https://goo.gl/WZzSrd
3. Aydın H, Gündüz MC, Yardibi H. Effects os carazolol on plasma malondialdehyde, superoxide dismutase and catalase in sheeps. J Animal Veterinary Advances. 2009; 8: 771-773. **Ref.:** https://goo.gl/UzsKR5
4. Carlson GP. Clinical Chemistry Tests. In: Large Animal Internal Medicine. Edit by Smith B.P. Third ed. Part IV. Mosby Company. 1990; 389-412. **Ref.:** https://goo.gl/C5F5F2
5. Cook CJ. Glucocorticoid feedback increases the sensitivity of the limbic system to stress. Physiology Behavior. 2002; 75: 455-464. **Ref.:** https://goo.gl/3TbN2c
6. Dakka AA, Abdel-Aal TS. Studies on minerals picture in the blood sera of egyptian Sheep. Assiut Veterinary Medicine J. 1992; 28: 242-249.
7. Fazio E, Ferlazzo A. Evaluation of stress during transport. Vet Res Commun. 2003; 27: 519-524. **Ref.:** https://goo.gl/Vd3yuc
8. Sharma MC, Chinmay J, Pathak NN, Kaur H. Copper status and enzyme. hormone, vitamin and immune functions in heifers. Res Vet Sci. 2005; 79: 113-123. **Ref.:** https://goo.gl/ZmwH7S
9. Weisinger RS, Blair-West JR, Burs P, Denton DA, Purcell B, et al. Cardiovascular effects of long-term central and peripheraladministration of urocortin, corticotropin-releasing factor, and adrenocorticotropin in sheep. Endocrinology. 2004; 145: 5598-5604. **Ref.:** https://goo.gl/1p736h