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Assessment of amiodarone effects on intact cats' electrocardiograms

Farzad GOUYA[1], Ali Shabestari ASL[2,*]

[1]Tabriz Branch, Islamic Azad University, Tabriz, Iran

[2]Department of Clinical Sciences, Faculty of Veterinary Medicine, Tabriz Branch, Islamic Azad University, Tabriz, Iran

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Abstract: Amiodarone can be used for treatment of ventricular and supraventricular arrhythmias in canine medicine, but its exact role in feline electrocardiography and its side effects have not been proven. The aim of this study was the evaluation of amiodarone and its different dosages' effects on intact feline heart electrocardiograms. Eight healthy stray cats were selected and control electrocardiogram was obtained. Amiodarone tablets were prescribed twice daily at 10 mg/kg for 7 days. The same protocol was repeated with doses of 15 and 25 mg/kg. Hexagonal electrocardiograms were obtained at the end of each stage. Electrocardiograms were evaluated for P amplitude and duration, QRS duration, R amplitude, QT interval, PR interval, and heart rate changes. All data were compared with the control and between groups' electrocardiograms. Obvious changes were seen in PR interval, QT interval, and heart rates in all dosages but P duration changes were seen only with the 25 mg/kg dosage. We used the same doses that were recommended in canine medicine. This study showed that 10 mg/kg of amiodarone has no visible changes in cats' electrocardiograms, but a toxic dose and even the dose of 15 mg/kg produced some obvious changes. Therefore, more studies are necessary to find the proper amiodarone doses in cats.

Key words: Amiodarone, electrocardiogram, cat

1. Introduction

Amiodarone, the second most common human antiarrhythmic medication, can be used in the treatment of canine ventricular and supraventricular arrhythmias (1–4). Different mechanisms have been described for antiarrhythmic effects of amiodarone, but principally it is classified as a third-class antiarrhythmic agent because it has been pronounced as having potassium channel blockage properties. Additionally, it acts as a sodium (Na^+) and calcium (Ca^{2+}) channel blocker, as well as a nonselective β-blocker (2,4–6). In addition to vasodilatation and a decrease in cardiac after load pressure (4), amiodarone lengthens the repolarization time and the effective refractory period (1,2,7–9); therefore, it causes a delay in the induction of new action potential (2). Thus, amiodarone acts as a broad-spectrum antiarrhythmic drug and it shows the properties of all classes of antiarrhythmic agents (2,3,4,9).

The beneficial effects of amiodarone on the refractory period and the treatment of resistant ventricular arrhythmias were reported (2,7–14). Despite the advantages of amiodarone in treatment of different ventricular and supraventricular arrhythmias, its use in veterinary medicine is restricted (4,15). Similar to human medicine, liver damage, lack of appetite, gastrointestinal (GI) dysfunctions, positive Coombs test, cardiac toxemia, and hypo- or hyperthyroidism were reported in canine medicine (4,15). However, the exact role of amiodarone in feline electrocardiograms (ECGs) and its side effects were not yet proven in feline medicine (4,16,17).

The aims of this study were: 1) the evaluation of amiodarone effects on intact feline ECGs, and 2) study of the effects of different amiodarone dosages on feline heart ECGs.

2. Materials and methods

Eight healthy and intact stray cats were selected randomly. All of them were short-hair cats, of both sexes and of 3–4 kg in weight, and none of them had infectious diseases. All cats were kept in separated boxes and after adaptation to the new environment, control ECGs were obtained without use of any analgesic drugs. Amiodarone tablets (Shahre Daru, 200 mg, Iran) were prescribed twice daily with 10 mg/kg as the starting dose, as described in canine medicine (4,16,17). With attention to the amiodarone pharmacokinetics and pharmacodynamics, all cats were treated for at least 7 days by the selected doses. Treatment with 10 mg/kg of oral amiodarone was continued for 7 days and then ECGs (Siemens, Germany) were obtained.

* Correspondence: shabestari@iaut.ac.ir

The same protocol was repeated with doses of 15 and 25 mg/kg twice daily. Hexagonal leads were used for the obtaining of ECGs and lead 2 (Long II) was studied for ECG changes. All ECGs were checked for P amplitude and duration, QRS duration, R amplitude, QT interval, PR interval, and heart rates. All data were compared with the control and between groups' ECGs. Finally, the given data were examined by one-way ANOVA and Student's t-test by SPSS 13.

3. Results

3.1 P amplitudes results

There were no differences between controls and the different dosages of amiodarone as well as between dissimilar dosages ($P > 0.05$, Figure 1).

3.2 P duration results

Obvious delaying in the P wave duration was seen only at 25 mg/kg and significant differences were seen between this dose and the control ECGs ($P < 0.05$, Figure 2).

3.3 R amplitude and QRS duration results

No obvious alterations were seen with use of different dosages of amiodarone on R amplitude and QRS duration ($P > 0.05$, Figures 3 and 4).

3.4 PR intervals results

In the assessment of amiodarone effects on PR intervals, significant differences were seen between 15 and 25 mg/kg doses with control ECGs ($P < 0.05$). No obvious differences were seen among 10, 15, and 25 mg/kg of amiodarone (Figure 5).

3.5 QT intervals results

In the evaluation of QT intervals, significant differences were seen between all doses and controls ($P < 0.05$, Figure 6).

3.6 Heart rate results

Obvious differences were seen between the heart rates of control cats and different doses and even between the first and the second dose of amiodarone ($P < 0.05$, Figure 7).

4. Discussion

Amiodarone acts as a sodium and calcium channel blocker (4,18), but it is principally categorized as third-class antiarrhythmic agent (4–8). In comparison to many human medicine studies that have proven amiodarone's beneficial effects (3), there are only a few studies on veterinary medicine, especially in cats. Therefore, there is a need for more investigations about amiodarone's effects (3,4) in veterinary medicine. This study was performed

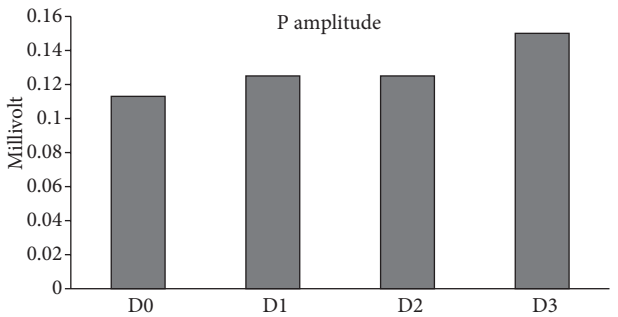

Figure 1. The average P amplitude (s): D0 = control group, D1 = 10 mg/kg, D2 = 15 mg/kg, and D3 = 25 mg/kg.

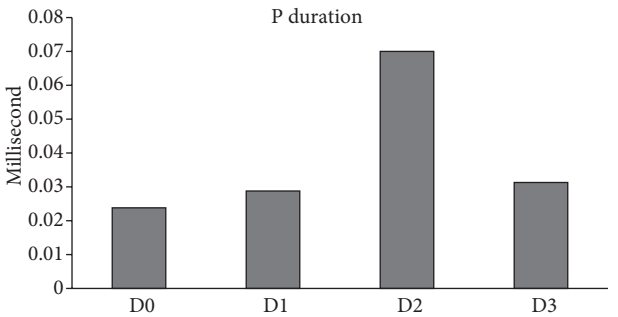

Figure 2. The average P duration (s): D0 = control group, D1 = 10 mg/kg, D2 = 15 mg/kg, and D3 = 25 mg/kg.

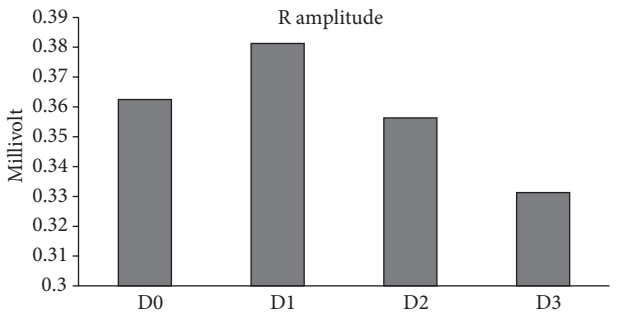

Figure 3. The average R amplitude (s): D0 = control group, D1 = 10 mg/kg, D2 = 15 mg/kg, and D3 = 25 mg/kg.

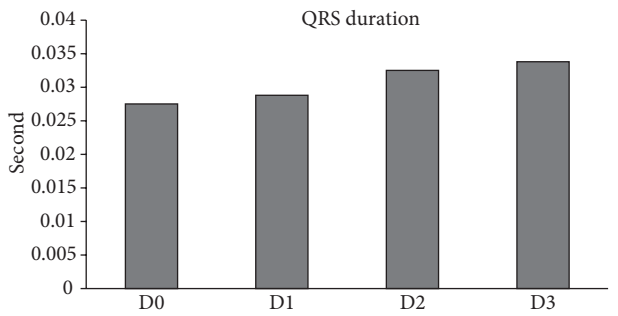

Figure 4. The average QRS (s): D0 = control group, D1 = 10 mg/kg, D2 = 15 mg/kg, and D3 = 25 mg/kg.

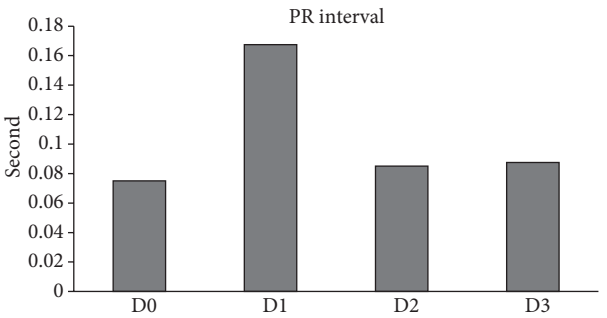

Figure 5. The average PR interval (s): D0 = control group, D1 = 10 mg/kg, D2 = 15 mg/kg, and D3 = 25 mg/kg.

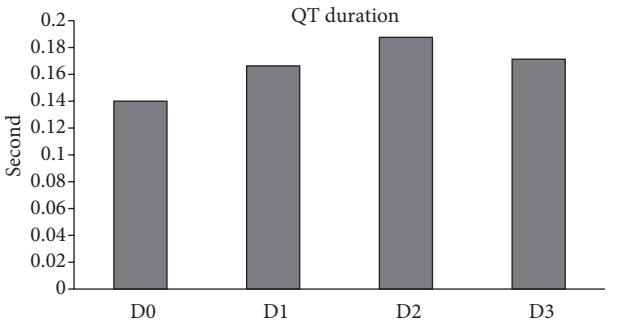

Figure 6. The average QT (s): D0 = control group, D1 = 10 mg/kg, D2 = 15 mg/kg, and D3 = 25 mg/kg.

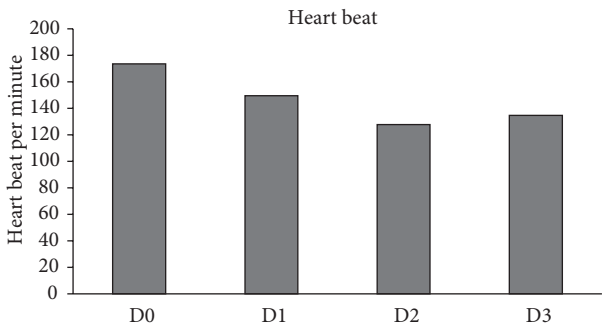

Figure 7. The average heart rate (s): D0 = control group, D1 = 10 mg/kg, D2 = 15 mg/kg, and D3 = 25 mg/kg.

to evaluate the effects of different amiodarone dosages on intact feline hearts.

Based on our results, there were no significant effects on P amplitude, but in P duration obvious changes were seen with the use of high doses of amiodarone (25 mg/kg). Similar to P duration, increases in PR intervals were seen (Figures 8 and 9). The inductions of delay in P duration and PR intervals were predictable because of amiodarone's direct effects on Na^+, Ca^{2+}, and potassium (K^+) channels and heart automaticity (9,19,20). Furthermore, these alterations can be induced by amiodarone blocking effects on cardiac β-receptors because of its β-blocker properties (18,20–22).

Bradycardia is a major reported side effect in human beings and it seems that the same complication could be observed in veterinary medicine. In addition to the direct effects of amiodarone on the sinoatrial (SA) node (9), some reports showed the obvious effects of amiodarone on the atrioventricular (AV) node (4,9). Furthermore, Webster showed that amiodarone's effects on ventricular and Purkinje fibers are more obvious than its effects on the atrium and AV node (23). Although SA arrest was not

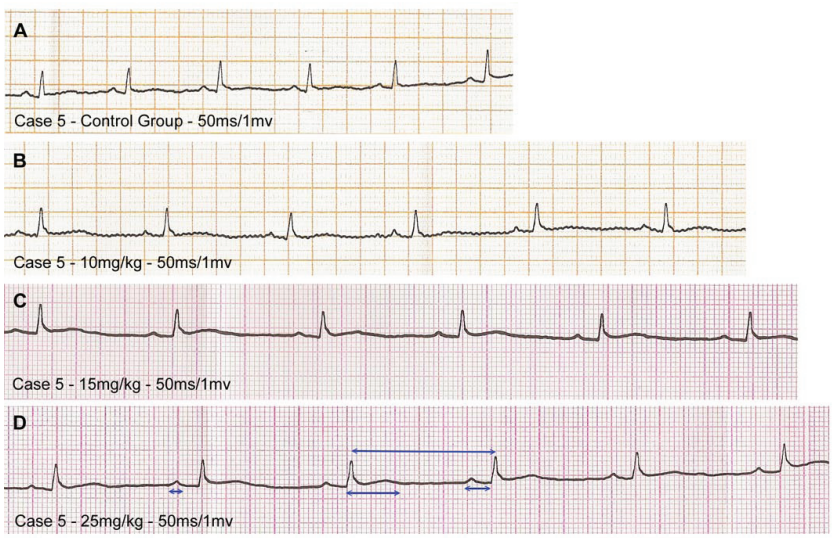

Figure 8. Example of amiodarone's effects on electrocardiograms of a normal cat (ECG: 50 ms/1 mv).

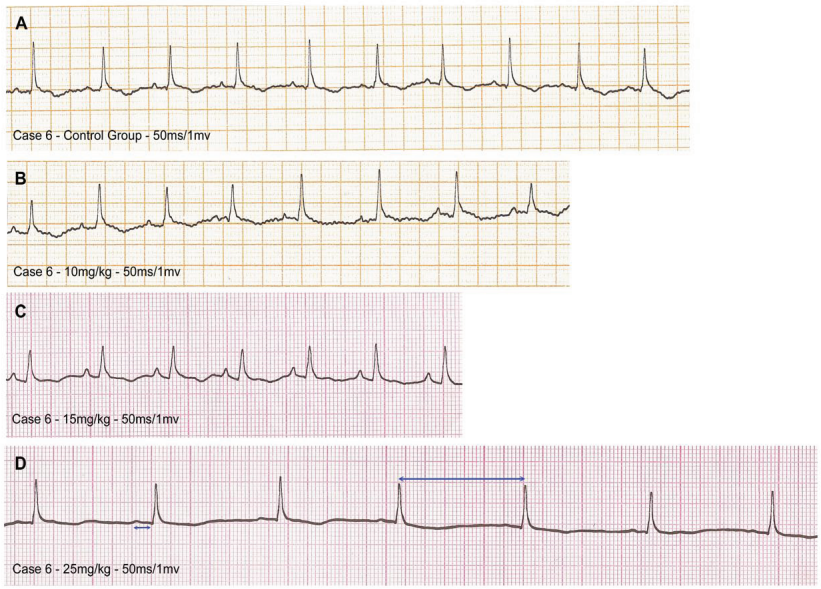

Figure 9. Example of amiodarone's effects on electrocardiograms of a normal cat (ECG: 50 ms/1 mv).

seen in this study, induction of bradycardia, especially at high doses, was pronounced. This showed amiodarone's potential effects on SA and AV nodes or ventricular functions (9,19,20).

This study confirmed amiodarone's significant effect on PR intervals, especially at 15 and 25 mg/kg, but no severe delaying and induction of second or third degree blocks were seen. This variation may be produced by amiodarone's effects on the cardiac channels functions because sodium, calcium, and potassium can affect heart functions directly. Furthermore, amiodarone has a great effect on ventricular function and it can induce delays in QT time and prolongation of the refractory period by blocking potassium channels (4). Because of amiodarone's effects on the prolongation of the refractory period, it is a choice drug for the treatment of human ventricular and supraventricular tachyarrhythmias (1,4,10,11,14,24). In this study, there was no variation in QRS time, but like in other reports, obvious changes and apparent delays were seen in QT intervals (2). Thus, it seems that amiodarone cannot change ventricular contraction time; it can affect only the refractory period. Therefore, amiodarone has the same effects in intact feline hearts, as well as in human medicine and some other veterinary reports (7,8,20,25).

Based on our results, amiodarone has potential effects on SA and AV nodes (especially in high doses); therefore, it seems that amiodarone's bradycardic effects can be produced by modulating different mechanisms on both atrium and ventricular functions. These results show the importance of careful monitoring at the time of amiodarone prescription, especially in patients with heart impulse impairments, as the most common published side effect in humans is the slowing of the heart conduction system (15,23,26), and our study proved these effects on intact cats' hearts.

It seems that reported different side effects in human beings are the main cause of amiodarone disadvantages in veterinary medicine (4,15). Different side effects such as central nervous system problems, liver damage, lack of appetite, GI dysfunctions, cardiac toxemia, and hypo- or hyperthyroidism were described (14,15). In some studies, GI disturbances occurred with use of high amiodarone doses in canines (14,15), but in our study, amiodarone could not induce the mentioned problems even in high doses. This may be due to the short time use of amiodarone.

Based on our results, all obvious changes in cats' ECGs were produced with high doses. Therefore, it seems that amiodarone is a safe drug and can be used for treatment of feline resistance ventricular and supraventricular tachyarrhythmia (2,4,9–14) if proper oral doses are recommended. Our results showed that amiodarone has good effects on heart slowing; therefore, the use of amiodarone in tachyarrhythmia and in slowing the heart rates in patients without cardiac conduction system impairments could be appropriate. However, there is a need for careful monitoring of the use of amiodarone in patients with conduction system impairments (14) and there is a need for further investigation on chronic use of amiodarone.

Owing to the lack of appropriate dosages in cats, we used the same doses recommended in canine medicine (4,16,17). This study showed that 10 mg/kg of amiodarone caused no visible changes in the cats' ECGs, but toxic doses (25 mg/kg), and even the dose of 15 mg/kg, produced some obvious changes in feline ECGs. Therefore, more studies are needed to find proper amiodarone doses in cats.

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