ELECTROCARDIOGRAPHY IN ADULT DOGS INFECTED WITH
Trypanosoma cruzi DURING ACUTE AND CHRONIC PHASES

(AVALIAÇÃO ELETROCARDIOGRÁFICA DE CÃES ADULTOS INFECTADOS
EXPERIMENTALMENTE COM Trypanosoma cruzi DURANTE
FASE AGUDA E CRÔNICA INDETERMINADA)

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SUMMARY

Chagas’ disease or South American tripanosomiasis is caused by Trypanosoma cruzi, a hemoflagelated protozoan. It was described by CHAGAS (1909) and affects approximately 16 millions of persons in the American continent (WHO, 1997), being 5 millions in Brazil. Since many adult dogs can be contaminated with this protozoan and also for not knowing the clinical characteristics of the myocardiopathy to be developed, the present study aims to characterize the electrocardiographic alterations in experimental infected dogs, during the acute and indetermined chronic phases. For such a purpose, a group of ten adult female dogs without defined race were experimentally infected with T. cruzi (1000 tripomastigotas/kg body weight, Colombian Strain) and submitted to electrocardiographic evaluations during the acute phase (5 weeks) and the indetermined chronic phase (7 months), a group of 4 dogs was considered as control group. The most frequent alterations observed in the acute phase were an increase in the heart rate, a low-voltage in the QRS and a PR interval increase. In the indetermined chronic phase, the persistence of the low-voltage of the QRS complex was the most observed alteration. This electrocardiographic alterations allowed to conclude that the infected adult dogs developed chagasic myocarditis, but with less evident clinic signs, denoting a less expressive presentation.

KEY-WORDS: electrocardiography, dogs, Chagas’ disease.

RESUMO

A doença de Chagas ou tripanosomiasi sul-americana causada pelo protozoário hemoflagelado Trypanosoma cruzi, descrita por CHAGAS (1909), afeta aproximadamente 16 milhões de pessoas no continente Americano (WHO, 1997), sendo 5 milhões no Brasil. Tendo em vista, que muitos cães adultos podem se contaminar com o referido protozoário e desconhecendo as características clínicas da provável miocardiopatia a ser desenvolvida, o estudo em tela visa caracterizar as alterações eletrocardiográficas em cães adultos, experimentalmente infectados, durante as fases aguda e crônica indeterminada. Para tanto, um grupo de 10 cães adultos, fêmeas, sem raça definida, foram infectados experimentalmente com T. cruzi (1000 tripomastigotas/kg de peso corpóreo, cepa Colombiana) e submetidos a avaliação eletrocardiográfica durante a fase aguda (5 semanas) e durante a fase crônica indeterminada (7 meses), tendo 4 cães como grupo controle. As alterações observadas mais frequentemente na fase aguda da infecção foram: aumento da frequência cardíaca; supressão da milivoltagem do QRS; aumento do intervalo PR. Na fase crônica indeterminada, a variação mais observada foi a persistência da supressão...
da milivoltagem do complexo QRS. Estas modificações eletrocardiográficas retomencionadas, permitiram concluir, que os cães adultos inoculados desenvolvem miocardite chagásica, porém com sinais clínicos menos evidentes, denotando uma apresentação clínica menos expressiva.

PALAVRAS-CHAVE: eletrocardiograma, cães, doenças de Chagas

INTRODUCTION

Chagas’ disease or South American tripanosomiasis caused by the hemoflagelated protozoan Trypanosoma cruzi (CHAGAS, 1909), affects approximately 16 millions of people in the American continent (WHO, 1997) being 5 millions in Brazil (DIAS, 1987).

Clinically, Chagas’ disease presents three characteristic phases: acute, indetermined chronic and symptomatic chronic (cardiac and/or digestive). The acute phase is easily developed in young dogs (GOBLE, 1952; MARSDEN & HAGSTRON, 1968; ANDRADE & ANDRADE, 1980). Lesions are disseminated and they can reach several organs, however, the most important physiopathologic consequences are related to the heart and the central nervous system (RAMOS, 1987). The presence of countless protozoa in the blood during this phase constitutes the period of an evident parasitemia, which can be used as a direct method of diagnosis under normal optic microscopy during the first six weeks of the disease (FERREIRA & ÁVILA, 1994).

The acute phase can last 40 days and it is followed by the indetermined chronic phase characterized by the disappearance of the clinic signs. During the initial phase, the laboratory diagnostic can be done by xenodiagnosis and indirect immunofluorescence (FERREIRA & ÁVILA, 1994). In the initial stages of the symptomatic chronic phase, the infected dog can be symptomless or can present clinic signs related to heart rate disturbance, cardiomegaly, and congestive heart failure during a period that can vary from 3 to 35 months (LARANJA, 1985; LANA et al., 1988).

The alterations detected by the electrocardiogram (ECG) in the acute phase of the disease can reflect the advance and distribution of the inflammatory process in the atria and in the right portion of the ventricular septum (ANDRADE et al., 1980).

According to ANSELMI et al. (1965), CÂMARA et al. (1979), LIMA et al. (1979), ANDRADE & ANDRADE (1980), ANDRADE et al. (1980), ANDRADE et al. (1984), LARANJA (1985), ANDRADE et al. (1987), LANA et al. (1992), BARR et al. (1992), BRENER et al. (2000), the first alterations of ECG in Chagas’ disease during the acute phase can occur between 7 and 45 days, among them: sinusal tachycardia; atrium silence; atrium fibrillation; junctional rythm; larger and low voltage P waves; decrease in the QRS complex voltage; S-T segment elevation; heart axis deviation; indetermined supraventricular rhythm; first degree atrium-ventricular blockage (BAV); complete blockage of the right branch (BRD) with or without left anterior hemi blockage (HBAE), can be pointed out.

Thus, during the indetermined chronic phase, approximately 3 months after infection, ECG tends to normalize, fact that characterizes this period as symptomless or indetermined (ANDRADE et al., 1987, ANDRADE et al., 1984, LANA et al., 1992, ANDRADE et al., 2000). In the other hand, authors such as ANSELMI et al. (1965), ANDRADE et al. (1980), ANDRADE et al. (1981), BARR et al. (1992), mention that between 8 and 36 months after inoculation with Trypanosoma cruzi, changes like increa of the QRS complex, decrease of the voltage of the waves P and R, occurrence of BRD and BAV of 1º and 2º degrees, occurrence of ventricular premature complexes, and alterations in the heart electric axis, can occur.

Since many adult dogs can be naturally contaminated with Trypanosoma cruzi and for not knowing the clinic characteristics of a provable myocardiopathy to be developed, the present study has as objective to identify the electrocardiographic alterations in adult dogs experimentally infected, during the acute and indetermined chronic phases.

MATERIAL AND METHODS

The present study was performed at the Laboratory of Cardiology of the Veterinary Medicine Hospital of the School of Agricultural and Veterinary Sciences, São Paulo State University, Jaboticabal Campus, SP.

Fourteen adult female dogs, without defined race were kept in individual cages, receiving ration and water “ad libitum” daily. Animals were dewormed and vaccinated against distemper, hepatite, leptospirose, parvovirus and coronavirus, according to the standard rules for these operations.

Two experimental groups were constituted, a control with four animals, and an infected group composed of 10 inoculated animals with T. cruzi. Animals, were studied during the period of 5 weeks (acute phase) and for 7 months after inoculation (indetermined chronic phase).

The Colombian Strain of the protozoan was used for inoculation (FEDERICI et al., 1964, ANDRADE & ANDRADE, 1966). The inoculum was obtained from the
blood of *T. cruzi* infected mice, and the concentration was 1000 trypomastigotes per kg of body weight. Inoculation was made via intraperitoneal. Studies on parasitemia were performed during the period of 4 to 34 days after inoculation, according to BRENER (1962).

The indirect immunofluorescence reaction in the dilution of 1:40 was performed in both experimental groups, before the inoculation and after a period of 7 months. In the infected group due to the reactions, dilutions up to 1:2560 were also used.

The electrocardiographic studies in both groups were registered before and after inoculation, during 5 weeks and after it, for 7 months.

Registers were obtained in the frontal plane in the I, II and III bipolar derivations; augmented unipolar limb leads aVR, aVL and aVF. The electrocardiograph used was ECG-6 (ECAFIX) at the speed of 50 mm/seconds and adjusted to 1 mv equal to 1 cm (TILLEY, 1992).

The electrocardiographic parameters were statistically analyzed by F test and means were compared by the Tukey’s test at the level of 5% of probability (SNEDECOR & COHRAN, 1967).

**RESULTS**

**Sorology and Parasitemia**

Before the inoculation, the indirect immunofluorescence tests (1:40) were negative for all animals, and also after 7 months for the control group. All inoculated animals of the infected group reacted positively in the 1:40 up to 1:2,560 dilutions.

After inoculation and for a period of 34 days, the investigation of parasitemia was done and no parasites were detected, indicating that parasitemia was sub patent.

**Electrocardiographic findings**

**Acute phase**

**Heart frequency and rhythms:**

During this phase, heart frequency values (b.p.m.) of the infected group appeared increased and they were significantly different during the 3rd week, in comparison to those of the control group. However heart rhythms found in the infected group were respiratory sinusural arrhythmia (RSA); sinusural rhythm (SR) and sinusual tachycardia (TS) (Table 1).

**Waves, Intervals and Segments**

The voltage of the QRS complex was significantly decreased during the 4th week in the infected group (Table 2). However no differences were found for P waves (seconds and milivolts).

**PR (Sec) and QT (Sec) Interval:**

PR interval from infected dogs presented a significant increase in or during the 1st and 3rd weeks, but with values inside normality for the species. No statically differences were observed among groups, regarding the QT interval (Table 3).

**ST Segments, T waves and Heart Axis**

With relation to these parameters no differences were observed between the two groups.

**Indetermined chronic phase**

**Table 1 -** Weekly values (X ± EPM) for heart rates and individual characterizations of heart rhythms registered by the ECG (DII) in dogs of Control (C) and Infected group (I) inoculated with 1000 tripomastigotias of *T. cruzi* (Colombian Strain) per kg of body weight.

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<th>Time (weeks)</th>
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<td>C (4)</td>
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<td>125 Aa</td>
<td>110 Aa</td>
<td>120 Aa</td>
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<td>±11</td>
<td>±23</td>
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<td>I (10)</td>
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<td>136 Aac</td>
<td>122 Abc</td>
<td>152 Ba</td>
<td>108 Ab</td>
<td>128 Babc</td>
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<td></td>
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<td>±20</td>
<td>±14</td>
<td>±23</td>
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**Heart rhythms**

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<td>TS 1</td>
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<td>TS 1</td>
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Different capital letters in the columns and small letters in the lines indicate statistical differences (p<0.05; Tukey test), between groups and weeks, respectively.

ASR – Respiratory Sinusural Arrhythmia; S - Sinusal; TS – Sinusal Tachycardia
Table 2 - Weekly values (X ± EPM) for QRS (sec. and mv) registered by the ECG (DII) in dogs of Control (C) and Infected group (I) inoculated with 1000 tripomastigotas of T. cruzi (Colombian Strain) per kg of body weight.

<table>
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<th>Time (weeks)</th>
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<th>I (10)</th>
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<tbody>
<tr>
<td></td>
<td>0,04 Aa ±0,01</td>
<td>0,04 Aa ±0,00002</td>
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<tr>
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<td>0,04 Aa ±0,008</td>
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<tr>
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<td>0,04 Aa ±0,01</td>
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<td>3</td>
<td>0,04 Aa ±0,01</td>
<td>0,04 Aa ±0,01</td>
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<td>0,04 Aa ±0,01</td>
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<tr>
<td>5</td>
<td>0,04 Aa ±0,01</td>
<td>0,04 Aa ±0,01</td>
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Different capital letters in the columns and small letters in the lines indicate statistical differences (p<0,05; Tukey test), between groups and weeks, respectively.

Table 3 - Weekly values (X ± EPM) for PR and QT. Intervals registered by the ECG (DII) in dogs of Control (C) and Infected group (I) inoculated with 1000 tripomastigotas of T. cruzi (Colombian Strain) per kg of body weight.

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<th>Time (weeks)</th>
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<td>1,7 Aa ±0,5</td>
<td>1,3 Aa ±0,6</td>
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<tr>
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<td>1,7 Aa ±0,5</td>
<td>1,3 Aa ±0,6</td>
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<td>2</td>
<td>1,5 Aa ±0,2</td>
<td>1,5 Aa ±0,6</td>
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<tr>
<td>3</td>
<td>1,4 Aa ±0,1</td>
<td>1,0 Aa ±0,4</td>
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<td>4</td>
<td>1,9 Aa ±0,3</td>
<td>1,0 Aa ±0,4</td>
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<tr>
<td>5</td>
<td>1,5 Aa ±0,3</td>
<td>1,1 Aa ±0,5</td>
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</table>

Different capital letters in the columns and small letters in the lines indicate statistical differences (p<0,05; Tukey test), between groups and weeks, respectively.

When the results of both groups were compared, no differences were found for heart frequency and rhythm. With relation to QRS complex, only the milivoltage showed a significant decrease during the 2nd month in the infected group (Table 4). However, during the II derivation, the P (sec. mV) waves, QT interval, ST segment and heart axis of the infected group remained inaltered.

Other alterations

Other electrocardiographic alterations found during the acute phase were first degree blockage, ventricular conduction disturbance, right atrium enlargement, left ventricle enlargement, sinusal tachycardia, ST segment elevation, ST segment depression and left bundle branch block.

In the indetermined chronic fase were found ventricular conduction disturbance, left atrium enlargement and sinusal tachycardia.

DISCUSSION

The present experiment demonstrates that reproduction of the acute phase in a symptomatic way is more difficult in adult dogs than it was demonstrated by LARANJA (1953), but the indetermined chronic phase can be reproduced in a similar way as in humans (JOHNSON, 1938, ANDRADE & ANDRADE, 1980).

The observed electrocardiographic findings during the acute phase varied from the absence of alterations to
those that can reflect the progression and distribution of the inflammatory process in the right side of the heart, mainly along the conduction system, which was also cited by ANDRADE et al. (1980), ANDRADE et al. (1981), ANDRADE et al. (1984), LARANJA (1985), LAURICELLA et al. (1986), LANA et al. (1992), SILVEIRA (1994), KLEIN (1995). As a general rule, it has been noted that electrocardiographic alterations depend on the amount of inoculum administered, since there is a correlation between the number of inoculating forms and clinic signs (FEDERICI et al., 1964, MARSDEN, 1967, MARSDEN & HAGSTRON, 1968, CAMACHO et al., 1994).

Highly concentrated inoculum is often used in research works that aim to obtain lesions in the conduction system that will reflect in serious electrocardiographic alterations. The use of 1000 trypomastigotes/kg of body weight as source of inoculum in the present work, did not evidence a blockage in the right side, which is the most frequent alteration observed in humans (LARANJA, 1985) and it can occur in young dogs during the acute phase when inoculum with high concentration are used, as it was observed by ANDRADE et al. (1980), ANDRADE et al. (1981), ANDRADE et al. (1984), LARANJA (1985), LAURICELLA et al. (1986), LANA et al. (1992), SILVEIRA (1994), CAMACHO et al. (1994).

Three weeks after the inoculation with Trypanosoma cruzi, it was observed, during the acute phase, a significant increase of 38,1% in heart rate, with the alteration of heart rhythms like sinus arrhythmia, sinusual rhythm and sinusual tachycardia. These rhythms alterations can be considered as normal and also frequent in dogs (TILLEY, 1992).

P wave wideness evaluated in seconds presented by the inoculated group was significant different with the control group at the 5th week, but the obtained mean values remained inside the normal variation for the species, however many of these alterations have been identified in chagasic dogs by other researchers as ANSELMI et al. (1965), e LARANJA (1985). On the other hand, the voltage of the R wave was repressed during all the acute phase in the infected group, as it was mentioned by ANSELMI et al. (1965), LIMA et al. (1979), ANDRADE et al. (1980), ANDRADE & ANDRADE (1980), LARANJA (1985), LANÀ et al. (1992), SILVEIRA (1994), KLEIN (1995). They correlated this register to the diffuse damage of the myocardium, or areas with serious inflammatory alterations that became electrically inactivated. With relation to the mean values for PR intervals, there were significant differences between groups, but without the presence of atrium-ventricular of first degree, which is a frequent finding in the acute phase, according to ANSELMI et al. (1965), LIMA et al. (1979), ANDRADE et al. (1980), ANDRADE & ANDRADE (1980), LANA et al. (1992), SILVEIRA (1994). No significant differences were found for QT and ST intervals and heart axis for the studied groups, however alterations for them were cited by ANSELMI et al. (1965), LIMA et al. (1979), ANDRADE et al. (1980), ANDRADE & ANDRADE (1980).

No significant differences were found for QT and ST intervals and heart axis for the studied groups, however alterations for them were cited by ANSELMI et al. (1965), LIMA et al. (1979), ANDRADE et al. (1980), ANDRADE & ANDRADE (1980). During the indetermined chronic phase, mean values for heart rate and the determination of heart rhythms remained inside the normal variation for the species in both experimental groups, mentioned by MAGALHÃES & FREIRE (1945), PELLEGRINO (1946). In the same way, the evaluation of P waves (seconds and voltage) in the infected group did not presented significant differences in this phase, as it was demonstrated by ANDRADE et al. (1981). Otherwise, the low-voltage of the R wave remained present during this phase. This result is different from those presented by ANDRADE et al. (1981), however the lasting of the PR and QT intervals did not show significant differences in relation to the control group.

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<th>Groups</th>
<th>Time (weeks)</th>
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<td>0.04 Aa</td>
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<td>10</td>
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Table 4 - Weekly values (X ± EPM) for QRS complexes (sec. and mV) registered by the ECG (DII) in the period of 2 to 7 months, in dogs of Control (C) and Infected chronic group (IC) inoculated with 1000 trypomastigotes of T. cruzi (Colombian Strain) per kg of body weight.
Other electrocardiographic alterations infrequently recorded in the infected group during the acute phase and indeterminate chronic phase (AV blockage of 1st degree, ventricular conduction disturbance and increase of the left ventricle) showed variability in affected heart areas of the left atrium and ventricle, taking into consideration that adult dogs can develop a certain degree of chagasic cardiopathy, in spite of the higher resistance to experimental infection.

CONCLUSIONS

The results allowed to drawn the following conclusions:
1. The inoculum rate (1000 trypomastigotes of T. cruzi per kg of body weight, Colombian strain) was efficient to reproduce in infected adult dogs, the acute and indetermined phases that were presented in a discrete form.
2. Infected dogs developed sub patent parasitemia, even with a positive indirect immunofluorescence reaction.
3. The electrocardiographic alterations in the acute phase consisted in an increase of the heart rate, low-voltage and PR interval increase.
4. Observed electrocardiographic alterations as AV blockage of 1st degree, ventricular conduction disturbance and increase of the left ventricle, evidenced the presence of chagasic cardiomyopathy, mainly in the indetermined chronic phase.

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