ECG Manifestations of the Biggest Outbreak of Chagas Disease due to Oral Infection in Latin-America
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Abstract

Background: Chagas disease affects more than 15 million people worldwide. Although vector-borne transmission has decreased, oral transmission has become important. Recently, our group published the clinical and epidemiological characteristics of the largest outbreak of orally transmitted Chagas disease reported till date.

Objective: To describe electrocardiographic changes occurring in the study population during the outbreak caused by ingestion of contaminated guava juice.

Methods: We evaluated 103 positive cases, of which 76 (74%) were aged ≤ 18 years (average age: 9.1 ± 3.1 years) and 27 (26%) were aged > 18 years (average age: 46 ± 11.8 years). All patients underwent clinical evaluations and ECG. If the patients had palpitations or evident alterations of rhythm at baseline, ambulatory ECG monitoring was performed.

Results: A total of 68 cases (66%; 53 children and 15 adults) had ECG abnormalities. Further, 69.7% (53/76) of those aged ≤ 18 years and 56% (15/27) of those aged >18 years showed some ECG alteration (p = ns). ST-T abnormalities were observed in 37.86% cases (39/103) and arrhythmias were evident in 28.16% cases (29/103). ST alterations occurred in 72% of those aged ≤18 years compared with 19% of those aged >18 years (p < 0.0001).

Conclusion: This study reports the largest number of cases in the same outbreak of acute Chagas disease caused by oral contamination, with recorded ECGs. ECG changes suggestive of acute myocarditis and arrhythmias were the most frequent abnormalities found. (Arq Bras Cardiol. 2013;101(3):249-254)

Keywords: Chagas Disease / complications; Electrocardiography; Chagas Cardiomyopathy; Arrhythmias, Cardiac; Juices; Contamination.

Abbreviations:

T. cruzi - Trypanosoma cruzi
ECG - Electrocardiogram
NS - Non-significant
AHA - American Heart Association
ACC - American College of cardiology
HRS - Heart Rhythm Society
ST - ST segment
T - T wave
Right BBB - Right bundle branch block
Left BBB - Left bundle branch block

Introduction

Chagas disease is caused by Trypanosoma cruzi and transmitted by several types of triatomines1. It is endemic in Latin America, although migration flows have resulted in the spread of the disease in Europe and the United States as well2,3. It has been estimated that there are approximately 15 million diagnosed cases and approximately 109 million people at risk of contracting this illness1. Although these numbers have shown a decrease from 1990 to 20064, in recent years, the description of endemic outbreaks of orally transmitted disease have opened a new area of study and analysis4-8. From being an unknown route of contamination, the oral route has become one of the most active in cases reported in Venezuela, Brazil, and Colombia4,8.

Our group previously published epidemiological and clinical characteristics of the largest outbreak of orally transmitted Chagas disease reported till date9. Here we analyze ECG manifestations of this outbreak, considered unique for occurring in a closed environment (in a school) in a Latin American capital.

Methods

The epidemiology of the outbreak is shown in Figure 1ª. Of the total positive cases (n = 103), 76 were aged


Results

A total of 68 cases (66%: 53 children and 15 adults) had ECG alterations, whereas 42 (33.9%: 23 children and 12 adults) had normal ECGs. Some major ECG changes were identified in 69.7% patients (53/76) aged ≤18 years and 55.5% (15/27) of those aged >18 years (p = ns). ECG manifestations are described in Table 1. Because some patients had more than one ECG alteration, the total number of alterations identified is greater than the number of patients.

The most common finding was alteration of the ST segment and T wave that was present in 37.86% cases (39/103). QT prolongation analyzed by the method of Bazett was present in 2.91% cases (3/103).

Blockade of the right branch was present in 1.94% cases (2/103), whereas inhibition of the left branch of the anterior subdivision was present in 2.91% cases (3/103). Looking at age groups, it was clear that those aged ≤18 years had a higher incidence of ST abnormalities compared with those aged >18 years (72% vs. 19%) (p < 0.00001). There were no significant differences in other ECG alterations between both groups.

Echocardiograms were performed in 84% cases with ECG alterations (57/68). The echocardiograms of 68% cases were normal, whereas 32% showed mild to moderate pericardial effusion.

Arrhythmias were evident in 32 cases (33/103). The different types of arrhythmias observed are shown in Table 2. Supraventricular arrhythmias occurred in 22.3% cases (23/103), ventricular in 5.8% cases (6/103), and AV block in 2.91% cases (3/103).

Inappropriate sinus tachycardia was the most common arrhythmia occurring in 9.71% cases (10/193), followed by atrial ectopic arrhythmia that was present in 8.74% cases (9/103). Because of the reduced number of cases, statistical analysis in relation to arrhythmias was performed by comparison of proportions between age groups.

Discussion

The presence of blood trypomastigotes in orally inoculated animals who later developed Chagas disease was shown as early as 1921; however, it was not until 1991 that 26 acute cases of the disease caused by ingestion of infected cane juice in the state of Paríba in Brazil were described. Although the description of ECG changes associated with vector-borne Chagas disease has been extensive and detailed, the same cannot be said for cases caused by oral transmission.

The fact that the cases we investigated occurred in a city in a closed environment (school) allowed us to analyze both non-contaminated and contaminated populations and administer rapid medical intervention in the entire population. Thus, this investigation is unique and can be a point of reference. Moreover, it is important to highlight that ours is the only investigation that can compare ECG manifestations in children and adults, because of the number of patients studied. We have compared our results with those reported by other studies of vector-borne and orally transmitted disease.

Table 3 shows a comparison of our results with those reported in different studies of oral infection. It is worth noting that some reports represent recollection of cases and not an outbreak of the disease itself. In addition, the time between the onset of symptoms and realization of ECG is variable. As shown, abnormal ECG was observed in 50%–100% cases (66% in our study). The most frequent ECG alteration was the change of the T wave and ST segment, ranging between 16.6% and 100% (37.86% in our study). The presence of right branch blockage, characteristic of chronic disease, was present only in 5%–25% cases (1.94% in our study). The presence of atrial fibrillation varies between 0% and 8% (2.9% in our study).

In Table 4 we compare our findings on ECG changes in acute Chagas disease transmitted via vector with those reported by Parada et al in Venezuela and Shikanai-Yasuda et al in Brazil. In our study, we observed a higher incidence of ST-T changes (37.86%) compared with that reported by Parada et al (4.4%) and Shikanai-Yasuda et al (6.9%). Right branch blockage occurred in 1.94% of our cases, compared with 5.1% in the study of Parada et al and 1.1% in the study of Shikanai-Yasuda et al.

Anselmi et al used an experimental model of intraperitoneal inoculation and observed signs of acute myocarditis in 54% of cases (17/31), underscoring the importance of the transmission route and parasite load in clinical manifestations and ECGs.

As we can see, there are differences when comparing vector-borne and oral routes of transmission, as well as among studies of oral transmission. Possible explanations for these differences may be as follows:

1. Differences in pathogenicity of strains of T. cruzi. Camandaroba et al showed differences in pathogenicity between different strains administered to mice orally as well as intraperitoneally. Comparing Peruvian and Colombian strains, they found that Peruvian strains had high infectivity and pathogenicity when administered intraperitoneally, but low infectivity and pathogenicity when administered orally; in contrast, Colombian strains (biodeme type III) had high pathogenicity following oral administration.
Figure 1 - Epidemiological description of an acute Chagas disease outbreak in Caracas in 2007.

Table 1 - ECG alterations detected in confirmed cases (n = 103)

| Alteration                          | < 18 a n = 53 | > 18 a n = 15 | Total n = 68 | % of the total of cases (n = 103) |
|-------------------------------------|---------------|---------------|--------------|-----------------------------------|
| ST T changes (ST elevation and T inversion) | 38            | 1             | 39           | 37.86                             |
| QT prolongation                     | 3             | 0             | 3            | 2.91                              |
| Microvoltaje                        | 2             | 2             | 4            | 3.88                              |
| Right BBB                           | 2             | 0             | 2            | 1.94                              |
| First degree AV block               | 2             | 0             | 2            | 1.94                              |
| Left BBB                            | 1             | 2             | 3            | 2.91                              |

2. - Differences in oral pathogenicity. Covarrubias et al. used a strain of *T. cruzi* related to an outbreak of orally transmitted disease in Santa Catarina, Brazil, to analyze the expression of surface molecules and infectivity when administered to mice orally. They found that metacyclic trypomastigotes, that in vitro have high concentrations of gp90, a surface molecule that acts as a negative regulator of the invasion of host cells, when administered orally have low levels of themselves, because they are destroyed by gastric acid. [Remark 2] In contrast, gp89, a surface molecule that promotes cellular invasion, is resistant to gastric fluid. Thus, surface molecules that promote cell invasion persist, whereas the inhibitors are destroyed by gastric fluid, which causes the same strain to become much more aggressive when administered orally than when studied in vivo or administered parenterally.

3. - Differences in host–parasite interaction. Although an increase in infectivity has been demonstrated when the parasite is administered orally, because of the destruction of gp90 by gastric juice, there have been no studies that assess how aging-related variations in pH of the stomach could be associated with greater or lesser infectivity according to the capacity to destroy gp90.
Table 2 - Arrhythmias detected in ECG or 24-h Holter monitoring

|                      | < 18 a | > 18 a | Total | % of total number of cases (n = 103) |
|----------------------|--------|--------|-------|--------------------------------------|
| Ectopic atrial tachycardia | 7      | 2      | 9     | 8.74                                 |
| Inapropriate sinus tachycardia | 3      | 7      | 10    | 9.71                                 |
| Supraventricular extrasystols | 1      | 0      | 1     | 0.97                                 |
| Atrial fibrilation    | 2      | 1      | 3     | 2.91                                 |
| First degree AV block | 2      | 0      | 2     | 1.94                                 |
| Second degree AV block | 1      | 0      | 1     | 0.97                                 |
| Ventricular extrasystols | 1      | 0      | 1     | 0.97                                 |
| Non sustained ventricular tachycardia | 0      | 1      | 1     | 0.97                                 |
| Sustained ventricular tachycardia | 1      | 0      | 1     | 0.97                                 |

Table 3 - Comparison of ECG changes in acute Chagas disease induced by oral contamination

|                      | Shikanai et al \cite{11} | Pinto et al \cite{17} | Pinto \cite{4} | Bastos \cite{21} | Marques et al |
|----------------------|--------------------------|----------------------|----------------|------------------|---------------|
| N                    | 24                       | 188 (multiple outbreaks analysis) | 11              | 13               | 103           |
| Age range            | 11-75                    | Not described        | 17-70          | 9-61             | 5-65          |
| Cases with ECG alterations | 12/24 (50%)              | 96/188 (51.1%)       | 6/11 (55%)     | 12/12 (100%) 1 ECG not performed | 68/103 (66%) |
| ST T changes         | 4/24 (16.6%)             | 40/188 (21.27%)      | 4/11 (36%)     | 12/12 (100%)     | 39/103 (37.86%) |
| Right BBB            | 2/24 (8.3%)              | 5/188 (5%)           | Não            | 3/12 (25%)       | 2/103 (1.94%) |
| Atrial fibrilation   | 0/12 (0%)                | 5/96 (2.6%)          | Não            | 1/12 (8%)        | 3/103 (2.9%) |
| Days between symptoms and ECG register | 33-35                  | Not described        | Not described  | 7-37 dias        | 32 dias |

Table 4 - Comparison of ECG changes in acute cases of Chagas disease induced by oral vs. vector-borne contamination

|                      | Parada et al \cite{11} | Shikanai-Yasuda et al \cite{11} | Marques et al |
|----------------------|------------------------|----------------------------------|---------------|
| N                    | 58                     | 180                              | 103           |
| Age range            | 17-50                  | 1-50                             | 5-65          |
| Cases with ECG alterations | 24/58 (41%)            | 78/180 (43.4%)                  | 68/103 (66%)  |
| ST T Change          | 4/58 (6.9%)            | 8/180 (4.4%)                    | 39/103 (37.86%) |
| Right BBB            | 3/58 (5.1%)            | 2/180 (1.1%)                    | 2/103 (1.94%) |
| Atrial fibrillation  | 1/58 (1.72%)           | Not described                    | 3/103 (2.9%)  |
| Microvoltages        | 10/58 (17.2%)          | 15/180 (8.3%)                   | 4/103 (3.88%) |
| Days between symptoms and ECG register | Not described | Not described | 32 dias |

4. - A more controlled study group. Our study is the largest investigation of cases occurring in a “closed” environment, in this case a school. Thus, we could study all the people exposed, which does not occur in other investigations.

5. - An earlier stage of the disease. In our study, the time between ingestion of the contaminated guava juice (October 28, 2007), the onset of symptoms, (first patient: November 9, 2007), diagnosis of the index case (December 6, 2007), and ECG recording of the population (December 11–14, 2007) was extremely accurate. This preciseness of records is not common in other studies, and could result in differences when analyzing other moments of the clinical profile.

It is important to mention that ECG alterations were not related to the presence of pericardial effusion. A full description of echocardiographic alterations will be discussed in a different paper. Analysis of ECG evolution in these patients,
which would more clearly define the different phases of the disease after oral infection, is the next step.

**Conclusion**

This is the largest study of clinical cases from a single outbreak of orally transmitted Chagas disease, with recorded ECGs. We found ECG changes suggestive of acute myocarditis and arrhythmias to be the most frequent abnormalities.

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**Author contributions**

Conception and design of the research and Analysis and interpretation of the data: Marques J, Mendoza I, Noya B; Acquisition of data: Marques J, Mendoza I, Noya B, Acquatella H; Statistical analysis: Marques J; Writing of the manuscript: Marques J, Mendoza I, Marques-Mejas M; Critical revision of the manuscript for intellectual content: Palácios I.

**Potential Conflict of Interest**

No potential conflict of interest relevant to this article was reported.

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**Study Association**

This study is not associated with any post-graduation program.

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