

HEADACHE IN CHAGASIC WOMEN

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SUMMARY

The aim of this study was to compare the frequency of headache between Chagasic and Non-chagasic women. The cross-sectional study comprised 647 female ≥ 40 years old, Chagasic (n = 362) and Controls (n = 285) at a Brazilian University Hospital. Chagasic were classified as Cardiac (n = 179), Megas (n = 58) or Indeterminate (n = 125) clinical forms. Headache was ascertained according to Headache International Society diagnostic criteria. The age (57.0 ± 11.3 versus 57.3 ± 10.4 years), and the percentage of white women (75.8% versus 77.1%) were similar between Chagasic and Controls, respectively. Headache was more prevalent among Chagasic (32.9%) than Controls (16.1%), mainly in Cardiac form (odds ratio, 2.41; 95% confidence interval, 1.38-4.23), phenomenon possibly related to parasympathetic denervation and cerebral vessels changes.

KEYWORDS: Chagas' disease; Headache; Parasympathetic denervation.

INTRODUCTION

Chagas' disease or American trypanosomiasis, important public health problem in Latin American countries, is transmitted by Reduviidae bugs, transplacental via or contaminated blood transfusions. Generally, there is an non symptomatic acute phase followed by an indeterminate phase with persistent low level of parasitemia. The clinical chronic phase is associated with autonomic nervous system imbalance due to parasympathetic injury⁸, besides microvascular changes, focal mononuclear cell infiltrates and fibrosis, important factors in cardiomyopathy and mega syndromes pathogenesis²².

The presence of meningoencephalomyelitis during the acute phase, with variable intensity of the parasitism, is well documented^{14,17,26}. In the chronic phase, there is peripheral nervous system involvement⁶, while the characterization of an encephalopathic form is still controversial^{1, 10,14,17}.

However, it is well known that chronic Chagas' disease can reactivate in immunosuppressed, with multiple focuses of necrotic encephalitis and presence of *T. cruzi* amastigotes^{1,11,14}. Moreover, 52% of chronic chagasic adults have antineuron-glia antibodies,¹⁰ which supports the idea of non symptomatic CNS involvement. Despite these ill-characterized anatomopathological aspects, some clinical findings in chronic Chagas' disease are thought to be associated with

CNS diffuse or focal changes, including sensitive, motor, frontal lobe and convulsive syndromes, psychoneurotic-like disturbances²⁵ and low cognitive performance, besides speech and language disorders^{7,9,10}. Headache is one of the most common non specific complaints, reaching up to 40% of adults seeking for medical care in Brazil²³. This symptom also occurred in 22.7% of African trypanosomiasis patients studied in Congo, mainly in women (32.6%)⁵. Based on the presumed autonomic imbalance as etiology of certain types of headache³, and the reported 72.7% of headache among a small sample of chronic chagasic Argentinean⁷, we hypothesized that chagasic women, seeking for medical assistance, would have higher headache prevalence than controls. The aim of this study was to compare the headache frequency between Chagasic and Non-chagasic women, aged ≥ 40 years, who seek medical care at Triângulo Mineiro Medical School Hospital.

MATERIAL AND METHODS

This retrospective study was conducted at an University Hospital of The Medical School of Uberaba-MG, Brazil, between June 1993 and July 1995, after official approbation by Ethic Committee board. The patients' records were obtained from an electronic file of the Hospital Computer mainframe. The data were organized in a database, and included the three routine serologic tests for Chagas'

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disease (immunofluorescence, hemagglutination and complement fixation) and information such as age, color and the main signs and symptoms. The patients were classified as white and non-white, according to the registered color, being considered non-white those described as blacks, browns or mulattoes.

The sample's size was calculated by using an expected headache average prevalence of 18%²³, a variation range between 15 and 21% and a confidence interval of 99%¹². In order to assure a systematic randomized sampling, 3,854 patients' records were disposed in numerical order, and all the first 800 records of aged ≥ 40 years female were selected. This gender and age range were chosen because the higher headache complaints²³ frequency and positivity of Chagas' disease serology in middle-aged women¹⁷.

Owing to a presumed etiologic relationship with headache, all cases of alcoholism, stroke, infection, clinical or surgical trauma and pregnancy were excluded. The charts of the remaining 647 patients were perused to obtain relevant clinical details and diagnosis, on the occasion the results of Chagas' disease tests were registered. The data, obtained by a single observer from medical records, included the spontaneous or evoked complaints of headache and palpitation, and diagnoses of high blood pressure (HBP) and congestive heart failure (CHF).

Headache was ascertained according to the Headache International Society diagnostic criteria²⁰. Palpitation was defined by the report of the unpleasant perception of own heart beating. HBP was considered when resting blood pressure was higher than 150/90mmHg. CHF was defined by cardiac hypertrophy or dilatation, disclosed by physical and/or radiographic examination, or signs and symptoms of systemic or pulmonary congestion.

Patients with three positive serologic tests for Chagas' disease were designated Chagasic; cases with the three negative results were considered Non-chagasic. According to clinical data¹⁷, the Chagasic group was subdivided in the following forms: 1) Megas, including patients with megaesophagus (diagnosed by radioscopy or contrasted x-ray of the esophagus) or megacolon (confirmed by colon dilatation in the opaque enema and by the presence of chronic intestinal constipation, longer than 10 days); 2) Cardiac, defined by thorax x-rays evidence of cardiac hypertrophy or dilatation or electrocardiography abnormalities¹⁹, as ventricular premature complexes, second or third degrees atrioventricular block, complete right bundle branch block, divisional anterosuperior left bundle branch block or atrial fibrillation; 3) Indeterminate form, in cases of three positive Chagas' disease serologic tests, in the absence of signs and symptoms or radiographic and electrocardiography changes attributable to the other clinical forms. As Mixed clinical forms were scanty, Cardiac plus Megas forms were excluded.

The continuous numeric variables with normal distribution were expressed in the form of mean \pm standard deviation. Analysis of variance (ANOVA), with Bonferroni adjustment was used in the comparison among the Control group and the Chagasic subgroups. The proportions were compared by the Chi-square's or the Fisher's exact tests¹². The results were considered significant when $p < 0.05$.

RESULTS

The study included 647 patients distributed in the groups Chagasic ($n = 362$) and Non-chagasic ($n = 285$). There was white color predominance (76.8%) in patients of all the studied groups. The Controls age average was 57.0 ± 11.3 years; among Chagasic, the

TABLE 1
Characteristics of Indeterminate, Megas and Cardiac chagasic subgroups and Non-chagasic women aged ≥ 40 years, in Uberaba-MG, Brazil, between June 1993 and July 1995.

Parameters	Controls (n = 285)	Indeterminate (n = 125)	Megas (n = 58)	Cardiac (n = 179)
Age (years)*	57.0 \pm 11.3	55.4 \pm 10.5	60.0 \pm 10.1 ^(a)	57.8 \pm 10.5
White color (%)	75.8	80.0	75.9	75.4
Palpitation (%)*	6.0 ^(b)	12.0	19.0	19.5
HBP (%)*	38.9 ^(c)	26.4	25.9	49.7 ^(c)
CHF (%)	4.2	0.0	5.2	5.6
Headache (%)*	16.1 ^(d)	24.8	36.2	37.4

* $p < 0.05$. HBP: high blood pressure. CHF: congestive heart failure. (a): Patients of Megas group are statistically older; (b): Palpitation was statistically less frequent in Controls; (c): HBP was more frequent in Controls and in Cardiac form; (d): Headache was statistically less frequent in Controls.

Megas group age (60.0 ± 10.1 years) was statistically higher than the others (Table 1).

Specific diagnosis in Megas group were: megacolon ($n = 30$), megaesophagus ($n = 18$) and megacolon plus megaesophagus ($n = 10$). The palpitation frequency was lower in Non-chagasic (6.0%) than Chagasic (16.8%). HBP occurred in 248 cases (38.3%), with predominance in the Cardiac form (49.7%) when compared to Indeterminate (26.4%) or Megas (25.9%). CHF was absent or registered in low frequency among all patients of the study (Table 1).

Moderate to severe headache was the patients' main complaint in 20% of the 647 cases. Chagasics had higher (odds ratio = 2.41; 95% confidence interval, 1.38-4.23) headache frequency (32.9%) when compared to Controls (16.1%). There was no significant difference in the headache frequency in the Cardiac form (37.4%), comparatively to the Megas (36.2%) and to the Indeterminate (24.8%) forms (Table 1).

DISCUSSION

Carlos Chagas repeatedly referred to a special chronic nervous form of the disease, which included a wide range of unexplained CNS abnormalities including cerebellar ataxia and involuntary movements¹³. Subsequent studies failed to characterize a chronic nervous form, although pathological changes ascribed to a reliquat of the acute phase may occur in up to 8% of necropsied chagasic^{14,15}. A few clinical studies have suggested spinal alpha motor neurons, dorsal root ganglia and sensory fibers involvement², besides pupil shape abnormalities¹⁸.

The present study documented that Chagasic women had higher headache frequency than Non-chagasic, matched by age and color. Headache pathogenesis include distension, traction, or dilation of intracranial or extracranial arteries and veins, inflammation of cranial nerves and muscles, and perturbation of intracerebral serotonergic projections²¹. This higher headache frequency among the Chagasic women could be secondary to cerebral vascular tonus changes, or a neurotic-like symptom due to organic hypersensitivity²⁵, associated with autonomous nervous system dysfunction.

In Chagas' disease, denervation is characterized by the preponderance of the sympathetic over the parasympathetic activity, a phenomenon that is thought to be involved in cardiomyopathy, megaesophagus and megacolon pathogenesis, and even functional abnormalities of pupils and gallbladder^{17,18}. Another possibility, would be microcirculatory abnormalities, including capillary basal membrane thickening and increased platelet aggregation, as have been described in chronic chagasic with atypical precordial pain and normal coronary arteries^{22,24}. Despite including patients with high blood pressure, none of them had conditions often associated with headache, including diastolic pressures above 120mmHg, pheochromocytoma, stroke, or malignant hypertension²¹. Moreover, mild to moderate HBP is an

uncommon cause of headache²¹ and probably do not explain all our findings.

Chagasic women had higher palpitation frequency than Non-chagasic, which is in agreement with the findings of POGACNIK et al.¹⁶, who documented higher incidence of cardiac arrhythmias in patients with vascular headache. Despite occurring in high proportion of healthy persons, palpitation is often secondary to myocardial lesions, including chagasic myocarditis. Nonetheless, palpitation may be a manifestation of autonomic dysfunction with sympathetic overactivity²⁴, a condition sometimes detected in patients previously classified in the indeterminate form of Chagas' disease.

Limitations of this retrospective study comprise eventual inclusion of patients with headache of psychogenic or metabolic origin, or related to a cerebral vascular disease. Other possible concern, is the inclusion of cases where headache would be a clinical expression of cardiovascular adaptation to hypertension, despite of evenly distribution of HBP among Chagasic and Non-chagasic patients. Even though it may be inadequate to extrapolate these findings to the whole chagasic population, the use of random sampling method, which homogeneously distributes eventual errors among groups, validate the present findings.

A better clinical characterization of chronic Chagas' disease encephalopathic form is still lacking, but the results of our study suggest that headache may be one of its symptoms. Moreover, headache frequency seems to have a direct relationship with the degree of autonomic dysfunction^{3,4}. In conclusion, these preliminary results suggest that chagasic adults have higher headache prevalence, a phenomenon possibly related to parasympathetic denervation or inflammatory responses to *T. cruzi*. These findings should be confirmed through more detailed prospective studies including subgroups with well-documented autonomic dysfunction.

RESUMO

Cefaléia em mulheres chagásicas

O propósito do estudo foi comparar a frequência de cefaléia entre mulheres Chagásicas e Não-chagásicas. O estudo retrospectivo compreendeu 647 mulheres com idade ≥ 40 anos, Chagásicas ($n = 362$) e Controles ($n = 285$) atendidas em um Hospital Universitário brasileiro. As Chagásicas foram classificadas nas formas clínicas: Cardíacas ($n = 179$), Megas ($n = 58$) e Indeterminada ($n = 125$). Cefaléia foi definida de acordo com os critérios da Headache International Society. A idade ($57,0 \pm 11,3$ versus $57,3 \pm 10,4$ anos) e a percentagem de mulheres de cor branca (75,8% versus 77,1%) foram semelhantes entre Chagásicas e Controles, respectivamente. Cefaléia foi mais freqüente entre Chagásicas (32,9%) que nas Controles (16,1%), principalmente na forma Cardíaca (odds ratio, 2,41; intervalo de confiança 1,38-4,23), fenômeno possivelmente relacionado com desnervação parassimpática e alterações vasculares cerebrais.

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