

BIOENERGETIC STUDIES IN RESIDENTS AT HIGH ALTITUDE (2,850 m) WITH ASYMPTOMATIC CHAGAS' DISEASE

by

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Summary — Cardiovascular response and working capacity were studied at rest and during a 125 W exercise in residents at high altitude (2,850 m), comparing 21 asymptomatic (normal EKG) but *T. cruzi* infected subjects (positive serology) to 21 healthy controls (negative serology). Ages, anthropometric, nutritional, and hematological data were similar in the two groups ($P > 0.05$), indicating the homogeneity of the studied population. Cardiac axis, heart rates, and oxygen uptakes, were not different between the two groups, at rest and/or during exercise ($P > 0.05$). At rest, diastolic and systolic pressures were significantly lower in the infected group than in the control group ($P < 0.05$). During exercise and recovery at the 1st and 5th min, diastolic pressure was also significantly lower in infected patients than in control group whereas systolic pressure was significantly lower only during recovery at 5th min. The calculated $\dot{V}O_2$ max were similar in the two groups, indicating a normal working capacity for the studied asymptomatic infected patients. The altitude does not seem to affect the responses to exercise, since the results obtained at high altitude were similar to those obtained at sea level (Macedo *et al.*, 1973).

KEYWORDS : Chagas' Disease, Asymptomatic; *Trypanosoma cruzi*; Altitude; Bioenergetics.

Introduction

Twenty-four million people are estimated to be infected by *Trypanosoma cruzi* and 65 millions are living at risk in areas endemic for Chagas' disease, which involves long term cardiac and digestive pathologies (WHO, 1982). Indeed the demonstration of a decrease in the physical ability of infected patients could have important economic consequences in developing countries where this parasitosis is endemic. Therefore attention was mainly focused on the cardiovascular response of infected patients to exercise at the cardiac chronic phase of Chagas' disease (Gallo *et al.*, 1975; Marin Neto *et al.*, 1975; Marins *et al.*, 1976; Silva *et al.*, 1976; Siqueira *et al.*, 1976; Faria *et al.*, 1978; Hirschhaut & Aparicio, 1978; Palmero *et al.*, 1980; Molina *et al.*, 1981; Wajngarten *et al.*, 1982). On the contrary, the demonstration of a normal working capacity, at least in patients with asymptomatic form of Chagas' disease, would prove unjustified the elimination of workers based only on serological data as observed in some countries. However, if cardiovascular responses to exercise of infected but asymptomatic patients have been studied (Pereira *et al.*, 1976; Siqueira *et al.*, 1976; Faria *et al.*, 1978; Palmero *et al.*, 1980; Almeida *et al.*, 1982), the working capacity of such patients was scarcely studied and only at sea level (Macedo *et al.*, 1973).

As far we know, the influence of altitude on Chagas' disease has never been studied, though infected patients are found up to 3,500 m and vectors beyond 4,500 m (Usinger *et al.*, 1966; Flores *et al.*, 1979; personal data). This could be important in some countries, such as Bolivia, where one half of the population lives above 3,000 m and travels often from endemic lowlands to the Andean highlands and conversely.

Therefore the aim of this work was to study the cardiovascular and bioenergetic responses, at rest and during exercise, of residents at high altitude (2,850 m), by comparing an asymptomatic, *T. cruzi*-infected group to an uninfected healthy control group.

Subjects and Methods

Subjects

According to clinical examinations, electrocardiogram leads (EKG), and hematological data (see below), 42 adult male farmers were selected as asymptomatic. They live permanently in Chivisivi, a village located at 2,850 m above sea level, in the valley of Sapahaqui (department of La Paz, Bolivia) where Chagas' disease is known to be endemic.

According to the *T. cruzi* serology (see below), they can be divided in 21 *T. cruzi*-infected subjects (positive serology) and 21 controls (negative serology).

Serological tests for T. cruzi infection

The *T. cruzi* serology was performed using immunofluorescence (IF), complement fixation test (CFT), enzyme-linked immunosorbent assay (ELISA), immunoelectrophoresis (IEP) and the same batch of *T. cruzi* antigenic extract. The tests were performed and interpreted according to previous studies (Brenière *et al.*, 1985).

The 21 men of the infected group were positive and the 21 men of the control group were negative in all the serological tests.

Basic clinical examinations and tests

Routine clinical examinations showed neither disease nor abnormal cardiopulmonary conditions.

Skin folds were measured in four sites with a Lange Caliper apparatus, previously calibrated, allowing calculation of the lean body mass value (LBM), according to the equation of Durin & Rahaman (1967).

EKG was recorded in frontal plane (L1, L2, L3) and in horizontal plane (AV1 to AV6) with a Hewlett Packard model (type 1504 A). The mean QRS (\bar{A}_{QRS}) axis in the frontal plane was calculated with frontal leads, according to the graphical technique, assuming that the population was normally distributed. Axis, expressed in angle units, located in the two inferior quadrants were considered as positive, and those in the right superior quadrants as negative.

A blood sample was collected for the serological tests and to measure hematocrit and hemoglobin concentration (cyanmethaemoglobin technique).

Bioenergetical studies

As the subjects were not familiar with either cycling or wearing a mouth piece, they were accustomed via preliminary bouts of exercise the days before the experiments. For the final experiment, the subject rested in the sitting position for 30 min, during which the EKG electrodes were attached and the sphyngotensimeter (type Vaquez-Lauby) was fixed.

Then, the subject mounted the cycle (mechanically braked ergometer, type Funbec): the values at rest of the different parameters were measured, and the exercise began at 125 W and lasted 30 minutes. The technical limitations of the locally available facilities imposed a limit to the effort and to the heart rates to reach, particularly in order to avoid occurrence of cardiac fibrillation.

The O_2 uptake (VO_2) was calculated according to the open circuit method: the subject breathed through a mouth piece and the valves were connected with a 120 liters light weight Douglas bag of low permeability to carbon dioxide. Expired gas was collected over a 5 min period at rest and 2 min during exercise, following a preliminary period during which the bag was flushed with expired gas. The expired gas was promptly sampled with a tight syringe and stored over mercury. The O_2 and CO_2 content were determined in duplicate, according to the Scholander technique. The volume of the bag was measured with a flowmeter (type American Meter Cy.). Determination of VO_2 was made twice at rest and twice from the 10th to 25th min of exercise.

Arterial systolic and diastolic pressures were measured, in identical conditions for all patients, just before gas sampling not to disturb O_2 uptake measurement. Two additional measures were made during the first and fifth min of recovery. Heart rate was recorded at the same time as arterial pressures but was continuously monitored on a scope (type Thomson Medical).

The maximal O_2 uptake (VO_2 max) was estimated from heart rate and VO_2 according to the technique of Astrand (1960).

Results

Homogeneity of the studied population

As shown in table 1, the ages, anthropometric (weights, height, body surfaces), nutritional (LBM) and hematological data (hemoglobin concentration and hematocrit) were comparable in the selected two groups ($P > 0.05$).

TABLE 1
Ages, anthropometric, hematological and nutritional data of the two groups of subjects

Subjects		Age years	Weight kg	Size cm	A_0 m^2	Hb g %	Ht	LBM kg	LBM/weight %
Infected	m	33,0	59,1	163,5	1,64	16,8	46,3	49,5	84,4
	sd	8,6	4,9	4,8	0,08	1,2	4,3	3,9	3,9
Control	m	28,9	60,0	162,1	1,64	16,3	45,6	49,0	81,4
	sd	9,7	7,5	4,3	0,11	1,0	3,3	4,5	5,4
	P	> 0,05	> 0,05	> 0,05	> 0,05	> 0,05	> 0,05	> 0,05	> 0,05

A_0 = body surface area; Ht = hematocrit; Hb = hemoglobin concentration; LBM = lean body mass.

Cardiac and energetic exploration at rest

The mean values of \dot{A}_{QRS} in the frontal plane was $+37^\circ$ in the infected group and $+47^\circ$ in the control group and without significant difference ($P > 0.05$), as the mean heart rates and the oxygen uptakes of the two groups.

As shown in table 2, diastolic and systolic arterial pressures were demonstrated significantly lower in the infected group than in the control group ($P < 0.05$).

TABLE 2
Systolic (Pmax) and diastolic (Pmin) pressures (mm Hg) at rest, during the steady state of exercise and recovery, of the two groups of subjects

Subjects		Rest		Exercise		Recovery 1st min.		Recovery 5th min.	
		P max	P min	P max	P min	P max	P min	P max	P min
Infected	m	112,5	66,3	144,1	68,8	130,3	69,4	113,4	68,1
	sd	8.0	5.0	16.3	9.8	16.4	7.9	9.8	7.0
Control	m	120,3	74,2	150,8	76,7	137,2	75,0	121,9	74,4
	sd	11.2	6.0	14.5	8.4	14.9	9.9	16.1	9.2
	P	< 0.05	< 0.05	< 0.05	< 0.05	< 0.05	< 0.05	< 0.05	< 0.05

Cardiac and energetic studies at exercise (125 W)

The EKG leads remained normal during exercise in both groups, particularly ventricular beats were not observed. Heart rates of both groups were without statistical difference during the steady state of exercise ($P > 0.05$) and infected subjects recovered normal rate as well as control ones ($P > 0.05$).

As shown in table 2, mean diastolic pressure was significantly lower ($P < 0.05$) in the infected group than in control group both during the steady state of exercise and recovery at the 1st min and 5th min. However the tendency to a lower value of systolic pressure, observed in the infected group at rest, was statistically confirmed, only for the recovery at the 5th min ($P < 0.05$).

The O_2 uptakes, during the steady state of exercise, were similar in the two groups ($P > 0.05$), as the calculated VO_2 max and, obviously, the energetic production expressed in percentage of VO_2 max.

Discussion

Bioenergetical and cardiovascular responses at rest and during exercise were compared in two groups of residents at high altitude, one with *T. cruzi* infection (asymptomatic chronic form of Chagas' disease) and another without *T. cruzi* infection, as a control group. It is important to point out that the studied population was highly homogeneous, since it was composed only of male farmers, living in the same village, with similar ages and anthropometric data. Moreover, the percentage of LBM compared to the body weight was normal in both groups suggesting a good nutritional state.

The physiological effects of altitude were observed from the means of hemoglobin concentration and hematocrit which were higher in the studied groups than in patients living at sea level, in relation to the hyperglobulic response to the chronic hypoxia of altitude (Brendel & Zink, 1982). Likewise, the observed right deviation of the cardiac axis values can be related to an increase in the pulmonary arterial pressure, as demonstrated in another study with Nepalian patients, for which 3.000 m was a critical altitude to show such modifications (Raynaud *et al.*, 1981).

The absence of difference in the heart rates between the groups, confirmed previous works on infected asymptomatic patients (Macedo *et al.*, 1973; Faria *et al.*, 1978; Palmero *et al.*, 1980, 1981). However in the cardiac form of Chagas' disease, slow heart rates were generally found at rest (Palmero *et al.*, 1981) and during exercise (Gallo *et al.*, 1975).

The blood pressures (minimal and/or maximal) were significantly lower in our infected but asymptomatic subjects than in control group, at rest, during exercise and at recovery. This agrees with the results of Palmero *et al.* who observed such a difference for both pressures at rest (1979), but only for the diastolic one during exercise (1980), whereas Macedo *et al.* (1973) and Faria *et al.* (1978) showed no difference between normal and chagasic patients. Though weak, and only detected by statistical analysis and not increased by exercise, those differences between blood pressures of infected and control subjects could be interpreted as a possible indication of heart functional alteration in relation to Chagas' disease, since, in infected patients with evident cardiopathy, the decrease of blood pressures is a classical observation at rest (Laranga *et al.*, 1956; Anselmi & Moleiro, 1971; Palmero *et al.*, 1979) or during exercise (Marins *et al.*, 1976; Silva *et al.*, 1976).

No difference was evident between the two groups of residents at altitude, neither in O₂ uptakes at rest or during exercise at 125 W, nor in VO₂ max. This, clearly, shows that the physical ability of asymptomatic patients, infected by *T. cruzi*, is not altered, and is similar to that of other Bolivian farmers (Paz Zamora *et al.*, 1982) and agrees with the previous work of Macedo *et al.* (1973), carried out at sea level, on Brazilian patients.

The present results allow the following conclusions, for the asymptomatic (normal EKG), but *T. cruzi*-infected subjects: 1) altitude does not seem to affect the response to exercise, since the results obtained at high altitude are similar to those obtained at sea level; 2) the exercise test, for a 125 W charge, does not sensitize any particular cardiac or bioenergetic response; 3) their physical ability is not altered. Consequently the elimination of asymptomatic workers, based only on serological data, is arbitrary and not justified. However, as the Chagas' disease evolution is unforeseeable, regular clinical examinations could be recommended for such patients (particularly EKG and blood pressures) to detect eventual development of chagasic cardiopathy.

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Etudes bioénergétiques chez des habitants de haute altitude (2.850 m) avec maladie de Chagas asymptomatique.

Résumé — Les réponses cardiovasculaires et la capacité de travail étaient étudiées au repos et durant un exercice de 125 W chez des habitants de haute altitude (2.850 m) en comparant 21 sujets asymptomatiques (ECG normal) mais infectés par *Trypanosoma cruzi* à 21 sujets témoins non infectés (sérologie négative). Les âges et les données anthropométriques, nutritionnelles et hématologiques étaient similaires dans les deux groupes ($P > 0,05$), indiquant l'homogénéité de la population étudiée. Les axes cardiaques, les pouls et consommations d'oxygène ne montraient pas de différence entre les deux groupes, au repos ou durant l'exercice. Au repos, les tensions diastoliques et systoliques étaient significativement plus basses dans le groupe infecté que dans le groupe témoin ($P < 0,05$). Pendant l'exercice et la récupération à la première et la cinquième minute, la tension diastolique était aussi significativement plus basse chez les patients infectés que dans le groupe témoin, tandis que les tensions systoliques étaient significativement plus basses seulement pendant la récupération à 5 minutes. Les VO_2 max calculées étaient similaires dans les deux groupes, indiquant une capacité normale de travail pour les patients étudiés, asymptomatiques et infectés. L'altitude ne semble pas affecter les réponses à l'exercice, car les résultats obtenus en haute altitude sont similaires à ceux obtenus au niveau de la mer.

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