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BIOENERGETIC AND CARDIOVASCULAR RESPONSES TO EXERCISE IN RESIDENTS AT 2.850 M, WITH ASYMPTOMATIC CHAGAS' DISEASE

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Abstract. Cardiovascular and energetic responses at rest, during 30 min of exercise (mechanical output: 125 watts) and for a subsequent recovery period of 5 min were compared in two groups, each comprising 21 residents at an altitude of 2.850 m. One group was in the asymptomatic phase of Chagas' disease with positive serological tests for *T. cruzi*, whereas the other was without Chagas' disease (negative serological tests). The two groups were similar as regards age, weight-for-height, blood parameters, nutritional status and heart and lung functions, including heart rate and frontal plane QRS axis determinations.

At rest, they differed in that maximal and minimal arterial blood pressures were slightly but significantly lower in the group with Chagas' positive serological tests than in the controls. During exercise and recovery, the only differences between them and the controls were that their minimal diastolic arterial blood pressure was significantly lower. In absolute values, the rises in arterial pressure due to exercise were exactly the same in the two groups. Maximal O_2 uptake was identical in both groups, as was exercise steady state VO2.

These findings indicate that the asymptomatic subjects with Chagas' disease had a normal work capacity and were not affected by high altitude.

Key words: bioenergetic studies; Chagas' disease; altitude, Bolivia

Introduction

Twenty four million people are estimated to be infested with *Trypanosoma cruzi* and sixty five million live in areas of South America to which Chagas' disease is endemic [1]. The impact of this disease on heart function explains why most authors, investigating muscular exercise in such patients, have focused their attention on the cardiovascular responses [2-6], whereas very few studies have been concerned with work capacity.

It is important to establish whether or not Chagas' disease reduces the capacity for physical work, since the possibility that this capacity would diminish during the asymptomatic phase could have a great social and economic impact, because it would lead to the elimination of workers on the basis of serological data only, as already practised in certain countries [7].

In addition, the influence of high altitude on Chagas' disease has never, as far as we know, been studied, even though infested subjects are encountered at altitudes up to

3.500m, and vectors, up to 4.500m [8, 9]. The effect of altitude on work performance could be of consequence in countries like Bolivia, where half the population lives at altitudes above 3.000m, and moves up and down from the Andean highlands to the lowlands, where Chagas' disease is endemic.

In the present study, the energetic and cardiovascular responses to exercise were compared in two groups of residents in a high-altitude region. One group was in the asymptomatic stage of Chagas' disease (with positive serological tests for *T. cruzi*), whereas the other group was without Chagas' disease; in all other respects, the groups were similar.

Materials and Methods

Subjects . The study included two groups of 21 male adults born and living permanently in Chivisivi, a village located at 2.850m in the Sapahaqui valley (district of La Paz in Bolivia). They were Quechua Indians working in agriculture. All the clinical examinations and experiments were carried out in Chivisivi.

One group was *T. cruzi* infested, since the results of their serological tests (see below) were positive. The other was the control group, since their serological test results were negative. The two groups will be respectively referred to below as 'Chagas positive' and 'Control' subjects.

All subjects exhibited normal physical activity and showed no evidence, either of disease on routine clinical examination of height, weight, skin colour, systemic arterial pressure, and pulmonary and cardiac auscultation, or of abnormal heart or lung conditions, assessed by functional tests, simplified on account of the technical limitations by local facilities. Accordingly, the infested subjects with positive serological data could be considered as asymptomatic in all respects.

Subjects were tested at rest for serology, heart and lung function, and nutritional status, and during exercise, by measurement of heart rate, O_2 uptake and blood pressure.

Measurements at rest . A blood sample was drawn from an antecubital vein for determination of the hematocrit and hemoglobin concentration, and for serological tests.

Hematocrit and hemoglobin. Hematocrit was measured in one portion of the sample by centrifugation at 3.000 rpm for 5 min and the hemoglobin concentration, by the cyanmethemoglobin technique of Drabkin, using a Jobin and Yvon Standard V spectrophotometer. The remainder of the sample was sent to La Paz for the serological tests.

Tests for T. cruzi infestation. Samples were screened for anti-*T. cruzi* antibodies using immunofluorescence (IF), complement fixation test (CFT), enzyme-linked immunosorbent assay (ELISA) and immunoelectrophoresis (IEP) and the same batch of *T. cruzi* antigenic extract. The tests were interpreted as indicated in previous studies [10]. The positive detection limits were 1/40 and 1/2 for IF and CFT respectively, and the limit extinction value for ELISA was 0.17. The IEP was considered positive when at least one precipitation band was present. The 21 sera of the infested group were positive for all the tests ($40 \leq$ IF titres ≤ 320; $0.17 \leq$ ELISA extinction value ≤ 0.48; $1/2 \leq$ CFT titres $\leq 1/64$; $1 \leq$ IEP precipitation bands ≤ 11) and the 21 control group sera were negative.

Nutritional evaluation. Skinfold was measured at the bicipital, tricipital, sub-scapular and supra-iliac sites with a precalibrated Lange Caliper appartus (Lange Skinfold Industry), thus allowing determination of lean body mass (LBM), according to the equation of Durnin and Rahaman [11]. Body surface area was calculated according to Dubois' table.

Heart and lung tests. For recording of electrocardiograms (ECG), only leads I, II, III and VI to V6, were used with a Hewlett Packard apparatus, (model 1504 A). The value of the QRS axis in the frontal plane was calculated with the frontal leads according to the graphic technique of Bailey and Cabrera. The axes located in the two lower quadrants were taken as positive, and those in the right upper quadrant, as negative. It was assumed that the population was normally distributed, thus allowing calculation of the arithmetical mean. This was justified by the fact that the axes are expressed in angle units.

Blood arterial pressure. These were measured with a Vaquez-Laubry sphygmotensiometer in identical conditions for all patients.

Pulmonary function tests. These, including measurement of pulmonary volumes, forced expiratory flow and maximal breathing capacity were conducted with a Warren and Collins type spirometer, after subjects had become familiar with the necessary procedures.

Measurements during exercise As the subjects had never either cycled or worn a mouth piece, they became accustomed to both in preliminary bouts of exercise during the days before the experiment. In the course of that period, various intensities of exercise were tested in order to find a reasonable level, i.e. an exercise power sufficiently high to elicit clear responses but not severe enough to risk causing heart disorders. A mechanical output of 125 watts was chosen. The final experiment was conducted in the morning. On that day, the subject was given the usual breakfast; he then rested in the sitting position for 30 min, during which the ECG electrodes were attached and the sphygmotensiometer was adjusted.

The subject then mounted the cycle, a Funbec model, equipped with a mechanically braked ergometer. The resting values of the different parameters were measured, and the exercise began at 125 watts and lasted 30 minutes.

O_2 uptake (VO_2) was calculated by the open circuit method: the subject breathed through a mouthpiece and valves connected with a 120-liter light-weight Douglas bag of low carbon dioxide permeability. The bag was flushed with expired gas for a preliminary period before the actual collection, and the gas was then collected over a 5 min period at rest, and for 2 min during exercise. The gas thus collected was promptly sampled with a tight syringe and stored over mercury. O_2 and CO_2 concentrations were determined in duplicate according to the Scholander technique. The volume of the bag was measured with a flowmeter (American meter, Cy model). VO_2 was determined twice at rest and twice during the period between the 10th to 25th minutes of exercise.

Maximal systolic and minimal diastolic blood pressure (Pmax and Pmin) were measured just before gas sampling, so as not to disturb O_2 uptake measurement. Two more measurements were made during the first and fifth minutes of recovery.

ECG was continuously monitored on a Thomson Medical scope and recorded simultaneously together with blood pressure.

Maximal O_2 uptake (VO_2 max) was estimated from the heart rate and VO_2, according to Astrand's technique [12].

Statistical comparisons between the group with Chagas' disease and the controls were made by the Student t-test; the level of $p < 0.05$ was taken as the threshold of statistical significance. Means are given ± SD.

Results

Table 1 shows that the Chag. pos. and control groups were comparable for age, weight, heigth, body surface area, nutritional status (LBM), and hematocrit and hemoglobin levels, as well as for all the ventilatory parameters recorded in *table 2.*

The mean values for QRS in the frontal plane were not significantly different (+37° in the Chag. pos. subjects vs + 47° in the controls).

The ECG leads remained normal during exercise in both groups and in particular, no premature ventricular beats were observed. The heart rate, both at rest and during exercise steady state and recovery, was not significantly different in the two groups of subjects (*table 3*).

Figure 1 demonstrates that under all the conditions measured, minimal arterial pressure (Pmin) was significantly lower in the Chag. pos. group than in the controls. Maximal arterial pressure (Pmax) was only lower in resting conditions, i.e. before the exercise test, and at the 5th min of recovery; during exercise, this trend was not statistically significant. The increment in arterial pressure due to exercise was similar in both groups: Pmax increased by + 31.6 mmHg in the Chag. pos. vs 30.5 in the controls whereas P min rose by + 2.5 mmHg in both groups).

Table 1. Ages and anthropometric, hematological and nutritional data for the subjects with Chagas' positive serological tests and Controls (AD: body surface area estimated according to Dubois: Ht: hematocrit; Hb: hemoglobin concentration; LBM: lean body mass)

Subjects		*Age* Yrs	*Weight* kg	*Height* cm	*AD* m^2	*Hb* g%	*Ht*	*LBM* kg	*LBM/weight* %
Chag. pos.	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
Controls	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	NS	NS	NS	NS	NS	NS	NS	NS

Table 2. Ventilatory data for subjects with Chagas' positive serological tests and Controls (RR: respiratory rate; VT: tidal volume; VC: vital capacity; ERV: expiratory reserve volume; IRV: inspiratory reserve volume; MBC: maximal breathing capacity; FEV1: forced expiratory volume in the 1st sec)

Subjects		*RR* min^{-1}	*VT* l_{BTPS}	*VC* l_{BTPS}	*ERV* l_{BTPS}	*IRV* l_{BTPS}	*MBC* $l_{BTPS} \cdot min^{-1}$	*FEV1* $l_{BTPS} \cdot s^{-1}$	*FEV1/VC* %
Chag. pos.	m	14.47	0.48	5.25	2.06	2.31	168.7	4.25	81.6
	SD	4.47	0.18	0.61	0.52	0.71	17.7	0.45	10.0
Controls	m	15.69	0.57	4.92	1.72	2.22	161.4	4.04	82.5
	SD	4.27	0.22	0.61	0.52	0.51	20.6	0.52	7.0
	P	NS	NS	NS	NS	NS	NS	NS	NS

Table 3. Heart rates (beats.min-1) at rest, during exercise steady state and during recovery in subjects with Chagas' positive serological tests and controls

Subjects		*Rest*	*Exercise*	*Recovery* 1st min	5th min
Chag. pos.	m	65.2	130.7	88.6	77.8
	SD	12.7	21.8	19.8	14.6
Controls	m	69.4	132.2	89.4	82.4
	SD	8.1	18.7	15.4	11.9
	P	NS	NS	NS	NS

Table 4, shows that the energetic data, for the two groups were similar. As their VO_2 max and O_2 uptake during the steady state were not significantly different, their energy production, expressed as the percentage of VO_2 max, was obviously identical.

Table 4. Resting O_2 uptake (VO_2), calculated VO_2 max obtained by Asdtrand's method, and exercise steady state (VO_2), in absolute values and in percentages of VO_2 max, in subjects with Chagas' positive serological tests and controls

Subjects		*Rest* $l._{STPDS}.min^{-1}$	VO_2 *max* $l.min^{-1}$	VO_2 *max.kg*$^{-1}$ $l.min^{-1}.kg^{-1}$	VO_2 *exercise* $l._{STPD}.min^{-1}$	*%* VO_2 *max*
Chag. pos.	m	0.377	2.57	0.044	1.78	0.69
	SD	0.144	0.63	0.012	0.44	0.28
Controls	m	0.356	2.75	0.046	1.88	0.68
	SD	0.095	0.53	0.009	0.30	0.16
	P	NS	NS	NS	NS	NS

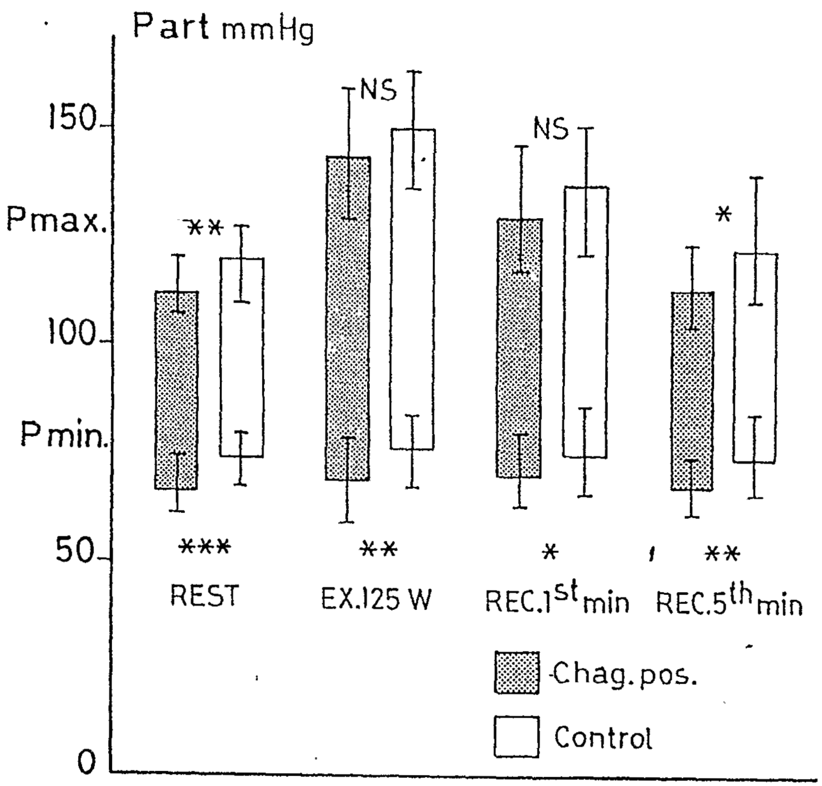

Figure 1. Maximal (systolic) and minimal (diastolic) arterial blood pressure at rest, during exercise steady state and during recovery. Asterisks indicate the level of statistical significance (*: $P < 0.05$; **: $P < 0.01$; ***: $P < 0.001$).

Discussion

Physiological characteristics

Comparison of the values for age, weight and size shows that the Chag. pos. and control subjects were anthropometrically similar. The ratio of lean body mass to body weight was normal in both groups and was not suggestive of malnutrition.

The finding that average hemoglobin and hematocrit values were higher than at sea level was in accordance with the expected polycythemia at high altitude. Thus, the range of the rises in Ht and Hb was comparable to that reported in natives of Leadville, located at almost the same altitude as Chivisi [13-15].

The ventilatory data for the Chag. pos. group were similar to those for the controls. This was only to be expected, as the spirometric exploration had been chosen to allow more reliable elimination of subjects of ventilatory insufficiency.

The average QRS axis value in the population we examined agreed with that reported by Raynaud [16] in Bolivians living in the highlands. This finding was not surprising, as 3.000m is known to be the critical altitude at which pulmonary arterial pressure begins to rise and the QRS axis migrates to the right. The mean value of this axis was the same in the two groups of subjects.

There was no difference, either, in their heart rate at rest. This agreed with the results of other authors [4, 17, 18] who found no alteration in heart rate as long as Chagas' disease remained asymptomatic, whereas slow heart rate was reported in forms affecting the heart [18].

Maximal and minimal blood pressures were significantly lower in the infested asymptomatic subjects than in the control group. Palmero [19] also reported lower resting arterial pressure values, although other studies failed to confirm this finding [17]. In this connection it is worth noting that although the decrease in maximal and minimal arterial pressures found here was small, the direction of the alteration was the same as in patients with evident cardiopathy displaying low arterial pressure [19-21].

Energetic and cardiovascular data at the exercise steady state

Table 4 shows that from the energetic point of view, there was no difference between the Chag. pos. and control subjects, and that their VO_2 max values were very close to those found for other Bolivian farmers [22]. Furthermore, the points obtained for both groups when heart rate values during exercise were plotted against those of corresponding VO_2 were located on the slope obtained by Grover [14] when plotting the same parameters, a finding which confirms that the energetic and cardiac responses of our subjects were similar to those of normal natives of Leadville residing at 3.100m. This clearly demonstrates that the physical capacity of asymptomatic patients infested by *T. cruzi* did not alter and that high altitude did not affect their responses, since they not only responded similarly to the control group but also in the same way as the normal subjects studied by other authors in different regions but at similar altitudes. To our knowledge, only Macedo [17] have studied working ability in asymptomatic subjects with Chagas' disease at sea level; like us, he reported no difference between subjects with the chronic form of this disease and healthy subjects.

The fact that the heart rate rose during exercise in the pathological group to the same level as in the control group agrees with results of most of the studies published [4, 17], which did not report lower heart rates in subjects with Chagas' disease. Only Gallo [2] recorded a smaller acceleration of heart rate during exercise, but this finding only concerned three asymptomatic subjects of the seven with Chagas' disease studied.

As clearly demonstrated in *figure 1*, arterial pressures during exercise were lower in the asymptomatic Chag. pos. group. This result agrees with those of Palmero [4] who reported variations in minimal arterial pressure. In the present study the fact that absolute increase during exercise was the same in the Chag. pos. group as in control subjects, meant that their response to exercise was normal. It should be emphasized that these moderate reductions in arterial pressure only had statistical significance in relation to a control group studied under the same conditions. In the absence of a reference group, isolated low pressure values should be interpreted with caution and at most be considered as no more than an alarm signal.

The present study results allow the following conclusions to be drawn about the asymptomatic subjects with positive *T. cruzi* serological tests: 1) the altitude did not affect their responses to exercise, since they resembled those of normal subjects living at the same altitude; 2) exercise did not sensitize any particuliar cardiac or energetic response, so that a difficult costly exercise test does not seem to be of interest; and 3) their work capacity did not alter. Consequently, any elimination of asymptomatic workers based on serological data only is arbitrary and unjustified. However, as the evolution of Chagas' disease is unpredictable, regular clinical examinations may be recommended for such patients, particularly ECG and arterial pressure measurement, for detection of possible Chagas' disease cardiopathy.

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