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CHANGES OF RABBIT PULMONARY ELASTIC PROPERTIES AND BRONCHOMOTRICITY IN EXPERIMENTALLY INDUCED CHRONIC CHAGAS' DISEASE

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SUMMARY

In order to study the role of bronchial denervation in Chagas' disease, the mechanical properties and the bronchomotricity of 6 chronic chagasic and 4 control rabbits were investigated. The whole-body plethysmograph method was used and the measurements were performed before and after intravenous administration of histamine chlorhydrate (0.11 mg/kg body weight). A smaller increase of the functional residual capacity, an almost unchanged peak passive expiratory flow after the histamine administration and a shift to the right of the static transpulmonary pressure/volume curve observed in the chagasic animals indicate an alteration of the bronchial tree, mainly consisting of a decreased bronchoreactivity.

KEY WORDS: Experimental trypanosomiasis — Rabbit — Changes in pulmonary — Elastic properties.

INTRODUCTION

The clinical picture of Chagas' disease is dominated by cardiac and digestive (megaesophagus and megacolon) manifestation [1,9]. The respiratory system may be envolved by thromboembolism of cardiac origin or by aspiration of esophageal content [1], but clinically it is not considered as a primary or even significant target of the ilness. However, bromchiectasis [5] and pulmonary hemossiderosis [8] were observed at autopsy and described as primary morphological alterations. A destruction of the parassympathetic ganglion cells of the bronchial wall was described by KÖBERLE [5,6] and used to explain the genesis of the bronchiectasis. This led to clinical investigations in order to detect evidences of bronchial dilatation and autonomic disregulation in the lungs, with conflicting results [4,11,12,14,17]. A comprehensive review about this matter was written by MANÇO & TERRA FILHO [10].

The antagonic clinical findings and disputed anatomopathological observations, since some reports do not confirm neither bronchiectasis and nor pulmonary hemossiderosis [13,18] led us to study the bronchomotricity and pulmonary mechanics of chagasic rabbits.

MATERIAL AND METHODS

A) Animals

Six chronic chagasic and 4 control rabbits, weighing 3763 ± 200 g were used. The chagasic animal were inoculated with the age of 2

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months with 4500 to 5000 leishmanians of the São Felipe strain developing positive parasitemia after 10 days that lasted 4 to 14 days. Before the experiments, the animals were checked by hemaglutination and seraglutination reactions for Chagas' disease, which were positive. The experiment was performed at the age of 18 months.

B) Pulmonary function tests procedures

The pulmonary function measurements were performed in anesthetized animals (nembutal — 30 mg/kg of body weight). The tracheal cannulation was done by peroral insertion of a pediatric tracheal tube (4 mm of internal diameter) provided with a cuff, filled to prevent air reflux. A water polyetylene catheter (4.5 mm internal diameter) was inserted up to the point where esophageal pressure record the greatest intensity. The ear marginal vein was cannulated and attached to a slowly infused physiologic solution container. The animals were placed in a acrilic whole body plethysmograph. Special holes in the lid allowed the passage of the esophageal, tracheal and ear marginal vein catheters. The connection of the tracheal catheter was a T-shaped device to permit the animal breathing while the airway pressure was measured. The dead space of the tracheal system was 0.8 ml. The pressures inside the plethysmograph airways and esophagus were simultaneously recorded by means of transducers (Beckman 4-327-0129) and a polygraph (Beckman 511-A). The plethysmograph pressure changes were transduced to volumes by calibration of the system with repeated injections of known amounts of air, with the rabbit positioned inside the chamber. A schematic view of the experimental system is presented in Fig. 1.

The following parameters were measured:

1. Tidal Volume (TV). Measured during spontaneous respiratory movements.
2. Respiratory frequency (f).
3. Transpulmonary Basal Pressure (P_{t}). Obtained during spontaneous respiratory movements, assuming the esophageal pressure as similar to the pleural pressure.

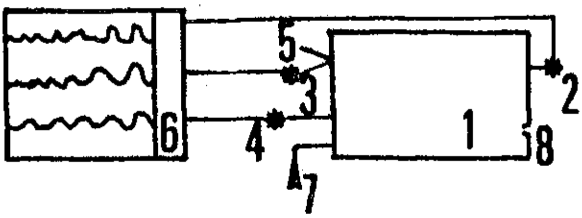

Fig. 1 — Schematic view of the experimental system.
1 — plethysmograph
2 — pressure transducer connected to the plethysmograph
3 — pressure transducer connected to the tracheal catheter
4 — pressure transducer connected to the esophageal catheter
5 — free exit of the tracheal catheter
6 — polygraph
7 — ear marginal vein cannula
8 — opening in the plethysmograph to equilibrate the thermal drift.

4. Dynamic Compliance (Cdyn). Calculated by dividing TV/TBP.
5. Increase of Volume to Functional Residual Capacity (VFRC). Measure of the respiratory baseline shift in the course of histamine induced bronchospasm (Fig. 2).

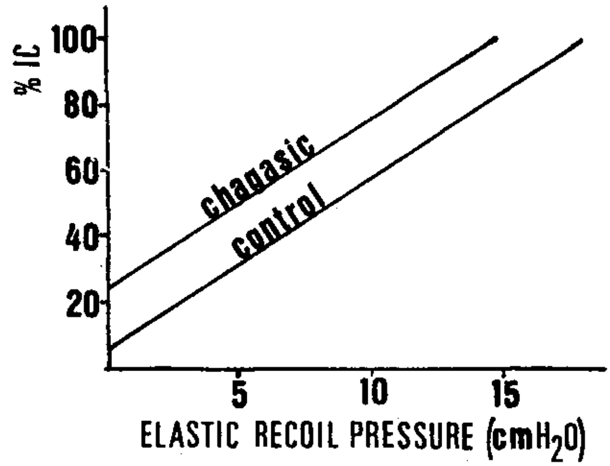

Fig. 2 — Elastic recoil pressure x inspiratory capacity curve (P_{L}/V) of control and chagasic rabbits.

6. Transpulmonary Pressure/Volume curve (P_{L}/V). This curve was obtained by injecting increasing amounts of air in the lungs and letting them to return to normal respiratory movements between each injection. This maneuver allowed to establish the maximal insuflation volume (MIV),

defined as the volume of the lung that caused a transpulmonary pressure of 15 cm of H_2O. This was considered a safe limit to avoid barometric traumas to the pulmonary parenchima.

7. Passive Expiratory Maneuvers (PEM) These were performed by insufflating the lung to MIV and letting them to return passively to the Functional Residual Capacity. The Volume/Time curve obtained by this procedure was analysed by a microcomputer system, provided with an analog-digital interface, connected to a digityzer. The Volume/Time curve was derivated to obtain the Flow/Time curve and, using the microcomputer, Flow was plotted against Volume at 10 ms intervals.

   The Flow/Volume curve permitted to measure the Peak Flow of Passive Expiration (PPF).

The pulmonary volumes were expressed in ml/kg of body weight. All the measurements were done before and immediately after the airway challenge procedures.

C) **Airway Challenge Procedure** (SCP)

Histamine chlorydrate (0.11 mg/kg of body weight) was injected in the marginal ear vein. This dose elicited a transient bronchospasm, that lasted about 40 seconds.

D) **Statistical Analysis**

The parameters were compared using the t test of Student or Mann-Witney test, according to the observed variance. The TP/V curves were compared using a single linear regression model [2].

RESULTS

The results of pulmonary mechanics before and after ACP are expressed in Table I. The PPF, which decreases in normal rabbits, remained almost unchanged in the chagasic animals.

The VRFC in the normal group was 4.22 ± 1.23 and 2.48 ± 0.46 **ml/kg in the** chagasic group (statistically significant at 5% level). This more pronounced increase of VRFC in control animals points to a lesser bronchoreactivity in the chagasic rabbits.

The P_L/V mean curves of both groups are presented in figure 2. For the control group the regression equation obtained was $y_1 = 3.78 + 5.38\ x_1$ and for the chagasic group it was $y_2 = 24.13 + 5.19\ x_2$. The statistical analysis showed that the curves were parallel, had the same slope and were non-coincident. A shift to the right is observed in the chagasic group, meaning that for the same volume the chagasic animals have a lower transpulmonary pressure.

TABLE I
Parameters of respiratory function before and after airway challenge procedure (ACP)

Parameter	Normal			Chagasic		
	Before ACP	After ACP	Δ **	Before ACP	After ACP	Δ **
TV (ml/kg)	7.85 ± 0.74	6.76 ± 1.15	— 1.09 ± 0.90	6.85 ± 0.86	5.51 ± 0.46	—1.36 ± 0.47
f (min⁻¹)	34.50 ± 7.09	61.41 ± 6.29	28.00 ± 1.64	38.20 ± 1.88	55.67 ± 2.32	17.33 ± 2.31 *
P_L (cm H_2O)	6.63 ± 0.75	7.95 ± 0.71	1.33 ± 0.89	7.20 ± 1.01	7.97 ± 1.14	0.77 ± 0.74
Cdyn (ml/cm H_2O)	4.33 ± 0.72	3.15 ± 0.85	— 1.18 ± 0.44	4.13 ± 0.79	3.30 ± 0.90	—0.53 ± 0.35
PPF (ml/s)	232.46 ± 20.52	182.88 ± 14.03	—49.59 ± 21.47	176.22 ± 16.99	191.85 ± 20.69	15.64 ± 4.47 ***

* significant at 5% level
** = after — before ACP
*** n = 4

COMMENTS

The bronchoconstrictive response of rabbits to intravenous histamine is very poor. When establishing the correct histamine dose in normal animals, we noted that the those needed for measurable responses was very close to the lethal one and several animals died, as well as 2 chagasic rabbits, during the experiment due to the systemic effects of the histamine. The weak response of rabbits to bronchial challenge may be explained by the thin bronchial muscular layer and the elusive distribution of the parasympathetic intramural neurons: in normal rabbits the sequential histological examination of 1 cm length left main bronchus failed to spot one single ganglionar cell. These facts could explain another characteristics of the rabbit airways: the very high compliance expressed by the pulmonary air trapping when negative pressure was applied to the trachea, during the simulation of the forced expiratory maneuvers. That was the reason that led us to prefer the passive expiratory maneuvers rather than the forced one (Fig. 4).

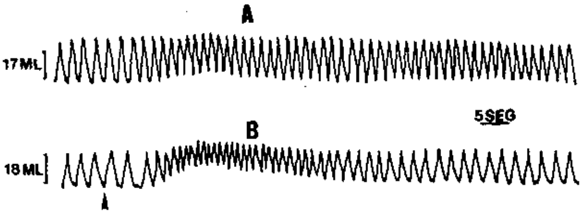

Fig. 3 — Register of the TV during the airway challenge procedure (ACP) in a chagasic rabbit (A) and in a normal rabbit (B). The arrow indicates the begining of the histamine injection.

The lower FRC increase and the almost unchanged PPF after histamine administration point to a lesses bronchoreactivity of the chagasic rabbits. Thus, our results are in contradiction with previous reports. TERRA FILHO [17] failed to show any difference between normal and chagasic patients stimulated with metacholine aerosol. Using the same trigger, GODOY [4] and MANÇO [11] reported a higher bronchoreactivity in patients with chronic Chagas' disease, as it is expected in the case of autonomic denervation according to Cannon's law [3]. The lack of broncoconstrictor response in acute chagasic dogs, found by TAVARES [15], also supports the denervation hypothesis.

The destruction of the parasympathetic intravisceral neurons in the acute phase of Chagas' disease is well documented in the heart, esophagus and colon [6,7], but in the respiratory system should be better investigated; the human casuistics is small and the lack of information in other species is almost total.

Another alteration observed in the chagasic animals was the shift to the right of the static transpulmonary pressure/volume curve, that may be explained by two possibilities. The first one could be an increase of airway volume, which may be estimated as 15% of the IC (Fig. 3). Previous radiologic findings support this affirmative, showing cylindric bronchiectasis in 42% [14] to 28.6% [12] in chagasic patients. Unpublished data of our laboratory showed an increase of the anatomic dead space in chagasic patients, not confirmed by TERRA FILHO [16].

The second possibility could be due to alterations of the elastic components of pulmonary parenchyma. This possibility is less probable, since the curves presented the same slope (Fig. 3).

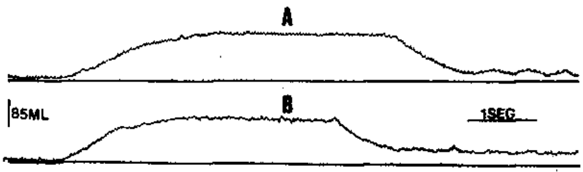

Fig. 4 — Passive expiratory maneuver (A) compared with a forced one (B) in a normal rabbit.

In conclusion, the 2 alterations observed in the chagasic rabbits — decreased bronchomotricity and shift of the elastic recoil curve — could be determined by an impairment of the parasympathetic ganglionar cells of the bronchial wall, and this fact stimulates further investigations to clarify the morphologicy of the autonomic nervous system in the lungs, the extent and nature of its destruction caused by Chagas' disease and finally, to settle down the doubts whether chagasic patients do or not suffer from primary pulmonary lesions.

RESUMO

Alterações das propriedades elásticas dos pulmões e broncomotricidade em coelhos, na doença de Chagas crônica induzida experimentalmente.

Com o intuito de estudar a denervação brônquica na fase crônica da doença de Chagas investigaram-se as propriedades mecânicas e a motricidade brônquica de 6 coelhos chagásicos crônicos e 4 controles. Utilizou se o método da pletismografia de corpo inteiro e todas as medidas foram feitas antes e depois da administração endovenosa de cloridrato de histamina (0,11 mg/kg).

No grupo chagásico crônico obteve-se um menor acréscimo da capacidade residual funcional e uma quase inalteração do pico de fluxo na expiração passiva após a administração de histamina. Este grupo apresentou também um desvio para a direita na curva estática de pressão transpulmonar/volume. Estes resultados sugerem uma alteração na árvore brônquica, que consiste principalmente numa broncoreatividade diminuída.

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