Structural adaptations of the heart to physical exercises in the Chagas' disease

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Abstract

The objective of this investigation was to carry out a literature review on the structural adaptations of the heart to physical exercises in the Chagas' disease with search on *PubMed*, *Web of Science*, *LILACS* and *MEDLINE* databases using keywords in English without time restrictions. The Chagas' disease, caused by a protozoan *Trypanosoma cruzi*, is one of the most important endemics that involve the inhabitants of Latin America. Its prevalence is estimated in approximately 10 to 12 million contaminated individuals, of which close to 3 million in Brazil, causing cardiopathies in 25% to 30% of those affected. Alterations in the structure and physiology of the cardiomyocytes became evident during the intracellular development of the *T. cruzi*. This infection promoves changes in the manifestation of the surface carbohydrates and modulates the intracellular traffic in cardiomyocytes. Individuals with the Chagas' disease have myocardiac lesions with myocyte hypertrophy, chronic and fibrous myocarditis, influencing the appearance of arrythmias and the development of congestive cardiac insufficiency. There is a great accumulation of collagen in the interstice and perivascular space of the myocardium, promoving morphological, geometrical and functional alterations to the heart. During physical exercise the heart adjusts to the increases in the metabolic and mechanic physical activity, promoving biochemical, electrical, morphological and mechanical adaptations in the cardiac muscle that, altogether, provide improvement in the cardiac function.

Keyword: Chagas' disease, heart, exercise.

1 Introduction

The Chagas' disease, one of the most important endemics that involve the inhabitants of Latin America, was described by the physician of Minas Gerais State Carlos Justiniano Chagas Ribeiro in 1909, after 7 months of research at the Institute of Maguinhos, Rio de Janeiro. It was announced by the director of the Institute at the time, Dr. Oswaldo Cruz, and published under the title "New Human Trypanosomiasis" in the first volume of the magazine Memories of the Oswaldo Cruz Institute, in august of the same year.

Its prevalence is estimated in approximately 10 to 12 million contaminated individuals, of which close to 3 million in Brazil, causing cardiopathies in 25% to 30% of those affected. The most recent data show that the Chagas' disease affects individuals over 45 years old and continues as a problem for public health and psychosocial commitment in all those who are diagnosed with that disease (OMS, 2006)

Subsequently, the cardiac, digestive and neurological involvement was described, with the additional degeneration bundle of Hiss, the extrasistoles, the atrioventricular blockages, the bradicardia, the Stoke-Adams syndrome and cardiac insufficiency (DIAS, 1987).

2 Material and methods

PubMed, *Web of Science*, *LILACS* and *MEDLINE* databases were used as search reference performed using keywords in English and no time restrictions In this systematization, papers were searched, using the keywords "Chagas'disease", "heart" and "exercise" by randomized combination until these terms were included.

3 Results

The Chagas' disease is caused by a protozoan, the *Trypanosoma cruzi*, and affects mainly the heart and the colon. The Chagas cardiopathy can appear in several ways: severe phase, where the individual can present diffuse myocarditis, serous pericarditis and a certain degree of endocarditis; undetermined phase, asymptomatic and without evidences of cardiac involvement, but able to last throughout the entire life and chronic phase, where approximately 30% of those affected develop cardiac and/or digestive problems. In this phase the person with miocardiopathy presents cardiac insufficiency and several cardiac arrythmias (DIAS, 1989; FRAGATA FILHO, 2009).

Besides myocytes and conjunctive tissue in the myocardium, there is an intense network of sanguineous capillaries among the myocytes, following a longitudinal direction. The cardiac muscular fiber is similar to the skeletal fiber, but with more sarcoplasm, mitochondrions, glycogen and the "T" small tubes are well developed and associated to the sarcoplasmatic reticule (BAILLEY, 1973).

The striated muscular cardiac tissue, as well as the skeletal one, presents fairly long fibercells. They are mono or binucleated, with nuclei located more towards the center of the cell. They also have *intercalated discs*, which are junction lines between one cell and another that appear rosier than the transversal lines. In the cardiac tissue, *the Purkinje fibers* are fairly important, being cells responsible for the distribution of the electric impulse that generates the muscular contraction of the different cardiac fiber cells (HAM, 1983).

4 Discussion

Alterations in the structure and physiology of the cardiomyocytes became evident during the intracellular development of the *T. cruzi*. Infection by the *T. cruzi* promoves changes in the manifestation of the surface carbohydrates and modulates the intracellular traffic in cardiomyocytes, revealed by the low regulation of Rabs and its effectors, including EEA1, Rab 7 and Rab 11, showing the commitment of the endocytic track in infected cardiomyocytes. Alterations in the cytoskeletal structure and cellular junctions also became evident during the infectious process. The breaking of miofibrils, the disorganization of costameres and guiding system can contribute to the anomalies seen in the Chagas' disease. The changes shown in the cytoskeleton components are not limited to the structural disorganization, showing that the infection alters the levels of the β RNAm and cardiac α-actine. Besides the evident changes in the cytoskeleton of cardiomyocytes, studies show that the infection by the *T. cruzi* provokes alterations in the appearance of the components of the extracellular matrix, presenting a considerable reduction of fibronectine on the surface of the infected cell. Further, induction of the cellular death during *T. cruzi*-cardiomyocyte interaction was proved, suggesting that the apoptose of cardiomyocytes infected by the *T. cruzi* can contribute to the silent but persistent infection in the chronic phase of the Chagas' disease (PEREIRA and MEIRELLES, 2000).

The collagen protein forms the collagen fibers. This is a scleroprotein made up of two tropocollagen molecules that are lined up to form the collagen fibril. Several joined fibrils form a collagen fiber and several fibers form a sheaf of collagen fibers. There are several kinds of collagens, of which four are the most important. These are: type I collagen, the most common one, appears in the tendons, in the fibrous cartilage, in the common flabby conjunctive tissue, in the dense conjunctive tissue (where it prevails over the other types), always forming fibers and sheaves; type II collagen, produced by condrocytes, appears in the hyaline cartilage and in the elastic cartilage, but does not produce sheaves; type III collagen constitutes the reticular fibers and type IV collagen appears in the basal sheet, one of the components of the basal membrane of the epitheliums (GENESER, 1987).

Individuals with the Chagas' disease have myocardiac lesions with myocyte hypertrophy, chronic and fibrous myocarditis, influencing the appearance of arrythmias and the development of congestive cardiac insufficiency (HIGUCHI, 2003). According to Nunes, Ramires, Pimentel et al. (2006), there is a great accumulation of collagen in the interstice and perivascular space of the myocardium, provoking morphological, geometrical and functional alterations to the heart.

Some authors explain that the progressive accumulation of interstitial collagen interfere in the normal conformation of the myocardium, leading to the loss in the synchronicity of the ventricular contractions during the systole, and contributing to a range of ventricular malfunctions that involve both the systolic and diastolic phase of the cardiac cycle. The fibrosis of the myocardium is probably involved in the genesis of tachyarrhythmia (ventricular tachycardium or fibrillation), main causes for spontaneous death in patients with chronic Chagas. The increase of collagen fibers also interferes in the electrical properties of the myocardium. Fibrosis blocks the cardiac impulse that circulates along an alternate way, reducing the speed of the circulation. Furthermore, the thick collagen septums between the muscular sheaves could interfere in the lateral circulation of the electrical impulse, as shown in senescent hearts compared to young individuals. Besides fibrosis, alterations in the circulation system of the electrical impulse represent another important manifestation of Chagas myocardiopathy (WAGHABI, 2002; HIGUCHI, 2003).

Independently of the etiology, the accumulation of collagen in the interstice and in the myocardium perivascular space is present. The myocardium collagen is known to perform important functions that directly affect the morphology, geometry and functional performance of the heart. Studying cardiomyopathy patients, for the first time showed that the increase of myocardium fibrosis was found in patients with more mortality (SHIREY, PROUDFIT, HAWK, 1980). Considering patients with dilated cardiomyopathy, did not show a record of the morphological data, such as hypertrophy of the cardiomyocytes and increase in quantity of interstitial collagen, with prognostic information (SCHWARZ, 1984).

The cardiac muscle requires a blood supplement of its own (coronary circulation), in order to provide it with oxygen and remove the worn-out products. When the cardiac work increases during a contaminated individual's exercise, the demand for a bigger quantity of oxygen is not satisfied by corresponding increases in the extraction of oxygen. On the contrary, there is an increase in the coronary blood flow (FOSS and KETEYAN, 2000).

The physiopathological base of the formation of the Chagas ventricular aneurism is related both to the inflammation and the chronic fibrosis and diffuse loss of myocardiac myocytes. The consequence is a depression predominantly of the ventricular systolic function, reflected by a fraction of low ejection, with maintenance of the cardiac intensity at the cost of tachycardia and increase in the volume of diastolic filling, thus increasing the tension on the wall and the consumption of oxygen by the myocardium and later, the complacency and diastolic pressure (COOLEY, COLLINS, MORRIS Jr. et al., 1958).

With aging, together with inactivity, the arteries suffer alterations that vary in kind and degree in different blood vessels of one same individual. The elastic arteries, especially the aorta, show more alterations than the arteries of the extremities, such as the femoral or brachial (BAILEY, 1973).

The cardiac is the most serious form of involvement in 30-40% of the individuals infected with the Chagas' disease. Approximately 70% of these do not develop a clinical disease and remain in the so-called undetermined stage of the disease and have a good forecast in the long run. Chronic myocardiopathy is one of the main manifestations associated to the morbidity of the Chagas' disease, possibly developed by the inherent parasite interaction that takes place during the intense phase. It is clinically evident and can include tachycardia, severe by-ventricular malfunction, progressive cardiac insufficiency, serious disturbances of the atrioventricular and intraventricular circulation, complex ventricular arrhythmias, tromboembolic and cardiomegalia phenomena with high indexes of morbidity and mortality, be it for myocardium or sudden death. Diffuse lymphocytary myocardium, scarce parasite nests, diffuse interstitial fibrosis and atrophy of the

myocytes are histologically verified. After an undetermined period of the disease, the Chagas patient can present symptoms of cardiac insufficiency, electrocardiographic and contractibility alterations of varied degrees and with evolutive potential. The first appearance of Chagas myocardiopathy can often be sudden death or pulmonary or systemic tromboembolic phenomena. Fibrosis is one of the most significant manifestations of chronic Chagas cardiopathy and is associated to inflammatory infilters and cardiomyocytes in degeneration (WAGHABI, 2004).

It is well known that physical exercise is a stimulus for the development of the left ventricular hypertrophy. Studies in athletes have shown that there is an increase of the left ventricular cavity and thickening of the myocardium as a result of prolonged repetitive training. This is manifested by the increase of the ejection volume and of the ventricular cavity, as well as a reduction in cardiac frequency in inactivity (MARON, 1997).

Another effect of the increase of muscular strength is to avoid excessive increases in cardiac frequency and of blood pressure in daily efforts, protecting the heart. Weak muscles demand great effort in physical activities, whereas strong muscles allow tasks with little effort. This happens because weak muscles exercise the necessary tensions, recruiting a larger numbers of fibers, which activates the muscular ergoceptors more intensely. These stimulated nervous terminations produce reflexes that increase the cardiac frequency, blood pressure and breathing frequency, characterizing acute cardiovascular risk situations or simply discomfort (McCARTNEY, McKELVIE, MARTINTIN, 1993).

During intense physical training, the sympathetic nervous system is activated; however, in longer daily periods of inactivity, there is a vagal preponderance that probably counterbalances the deleterious effects of the catecholamines in the myocardium, as well as the activation of other neuro-hormonal systems by the sympathetic nervous system. Increase in the number of mitochondrions, the capillary neoformation, and the normal activity of the ATPase of the myosin observed in the hypertrophied myocardium by the physical training, prevent the disproportion between the oxygen offer and consumption and the occurrence of ischemia, contrary to that observed in pathological hypertrophies (BARROS NETO, 1994).

Besides the type and intensity of the exercise, other important determinants of the athlete's heart structural adaptations are age, gender, race and genetic component. There is a consensus in the literature that genetic factors play an important role in the development of the ventricular hypertrophy in athletes, to justify the great differences in the cardiac alterations and in the athletic performance, observed in individuals with the same anthropometrical characteristics and submitted to the same level of training (DOUGLAS, O'TOOLE and KATZ, 1997).

The structural alterations resulting from physical training depend on the nature, duration and intensity of the exercise. The different kinds of sports have been basically divided into two large groups: resistance sports, in which the isotonic forms or dynamics of the exercise predominate and sports of strength, in which the isometric or static forms of the exercise predominate. However, athletic conditioning is rarely only isotonic or isometric; most of the physical activities involve a dynamic or static component, with one of them prevailing (GHORAYEB and BATLOUNI, 1998).

During physical exercise the heart adjusts to the increases in the metabolic and mechanic physical activity. Physical training provokes biochemical, electrical, morphological and mechanical adaptations in the cardiac muscle that, altogether, provide improvement in the cardiac function (BLOMQVIST and SALTIN, 1983). These adaptations take place reducing the stress on the ventricular walls (GROSSMAN, JONES, MCLARIN, 1975) and, at the same time, meet the greater demand of the blood supply of the muscles in exercises.

Intensive and prolonged physical training induces cardiovascular adaptations that allow the exceptional physical performance of the athlete's heart (BEVERGARD, HOLMGREN, JOHNSON, 1963). However, these adaptations include functional and anatomical alterations that can be beyond the normal limits and whose clinical significance and forecast have been intensely discussed and led to controversies (ROST, 1986).

In recent revisions in scientific literature on physical activity and health, the National Institutes of Health and the Centers for Disease Control and Prevention, North American governmental agencies, concluded that all the types of exercises seem to have the same beneficial effects for health in general and for the heart specifically. These conclusions are solidly based on classical epidemiological criteria such as consistency, strength, temporary sequence, dosis-response and coherence. The beneficial action of the exercises for cardiovascular health does not seem to be related with major cardiac vascularization, as had already been believed. (SANTAREM, 2004).

A recent study showed that old people that aged practicing running or swimming presented the same levels of muscular hypotrophy found in sedentary old people. On the contrary old people who aged practicing exercises with weights maintained the muscular mass. A current concept in geriatric rehabilitation is not to recommend walks to weakened old people before a program of muscular strengthening with weights, so as to avoid falls and serious fractures (KLITGAARD and MANTONI, 1990).

The limited capacity to do exercises, characterized by premature tiredness, presented by cardiopathic individuals can also be explained by muscular metabolic alterations developed by these patients. The activity of enzymes in the supply of aerobic energy in the skeletal musculature is inversely related to the accumulation of the sanguine lactate during sub-maximum exercises. The reduced activity of these enzymes in the skeletal musculature plays an important role in the precocious tiredness presented by patients with chronic cardiac insufficiency submitted to physical exercise (HEITKEMP and HIPP, 2001). Besides this, a damaged endothelium-dependant dilation of the resistance vessels is observed in situations of cardiac insufficiency, which also contributes to intolerance of exercise presented in this disease. This inefficient vessel-dilation can be simply due to the reduction of the nitric oxide (NO), as well as the interaction of other factors such as that of reactive species of oxygen (ERO) or liberation of prostanoids (SULLIVAN, 1991).

The prediction of the Chagas' disease in athletes cannot yet be precisely determined since no prospective long-term follow-up study with an adequate number of individuals in these conditions has been performed so far. Therefore,

there is no reason to believe in significant differences in the evolution of athletes with the Chagas' disease compared to non-athletes. On the contrary, the overload imposed to the cardiovascular system during the performance of very intense exercises and long duration can be an aggravating factor for damages in the heart of these athletes. The incidence of thromboembolic phenomena in those individuals with a chronic condition of the disease is high, being described as the cause for death in 4% of the patients in some series with a long-term follow-up (GARZON, 1998).

Overall, physical activity has physiological effects contrary to those of sedentariness. The body make-up tends to worsen with sedentariness due to the increase in fatty tissue and reduction of the bony and muscular mass. The levels of all physical aptitude qualities are reduced in sedentary people, making daily life difficult and reducing psychological and social welfare. The fact that the effects of sedentariness are slowly set in, explains why young sedentary people are not usually aware of their misdemeanor. On the other hand, elderly people feel the effects of sedentariness in the limitations they find in daily life and in the appearance of chronic diseases. In spite of all this research, there is not even a conclusive result of the influence of physical exercises in the chronic phase of the Chagas' disease in athletes (EVANS, 1999).

Treatment of the clinical forms must follow the same guidelines for non-athletes; however, the decision to remove the athlete or not from competitive activities and when to do so is still a controversial matter. While some authors who studied the undetermined form, do not justify removing any activity from those simply with positive serology or even with initial myocardium damage (BARRETO and IANNI, 1995), others alert for the possibility of a worse prognosis represented by even discreet alterations in more sophisticated complementary exams and recently available (MARIN NETO, SIMÕES and SARABANDA, 1997)

In a recent publication sponsored by the World Heart Federation, by the International Federation of Sports Medicine and by the Committee in Exercise, Cardiac Rehabilitation and Prevention of the American Heart Association, the authors propose total liberation for those athletes that present only positive serology, as long as the ECG, the Ergometric Test and the Echocardiogram are normal. On the other hand, any evidence of cardiac involvement would counter indicate all the intense competitive sports activities (MARON, 2001).

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