

The level of physical activity for hypertensive and diabetic patients and the damage caused by the physical exercise requirement

O nível de actividade física para doentes hipertensos e diabéticos e os danos causados pela necessidade de exercício físico

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ABSTRACT

Physical exercise has been identified as a major non-pharmacological agent, assuming a protective role in the treatment of chronic non-communicable diseases, especially in hypertension and diabetes mellitus. The levels of physical activity as well as its intensity are of great impact for the full benefits to come of this practice. We know that the level of physical activity is a relevant factor for maintaining good health, however, little attention has been paid to what is established in relation to high-intensity daily exercise adjusted to cardiac damage or adaptation. The objective was to reflect on the prescription of physical activity in the treatment of hypertensive and diabetic patients and how eccentric exercise is related to the cardiomyocyte tissue in the damage process. We observed that the highest level of physical activity was associated with better quality of life, and that active patients have an 80% chance of survival when compared to sedentary ones. Thus, despite the potential benefits from the metabolic point of view, public health efforts should also focus on maintaining and protocols of physical activity levels since our study showed that intense eccentric physical activity had harmful effects at the cardiac level.

Keywords: Hypertension, diabetes mellitus, damage, physical activity

RESUMO

O exercício físico foi identificado como um importante agente não-farmacológico, assumindo um papel protector no tratamento de doenças crónicas não transmissíveis, especialmente na hipertensão e diabetes mellitus. Os níveis de actividade física, bem como a sua intensidade, são de grande impacto para que esta prática possa trazer todos os benefícios. Sabemos que o nível de actividade física é um factor relevante para manter uma boa saúde, no entanto, pouca atenção foi dada ao que é estabelecido em relação ao exercício diário de alta intensidade ajustado a danos cardíacos ou adaptação. O objectivo era reflectir sobre a prescrição de actividade física no tratamento de doentes hipertensos e diabéticos e como o exercício excêntrico está relacionado com o tecido cardiomiocitário no processo de lesão. Observámos que o nível mais elevado de actividade física estava associado a uma melhor qualidade de vida, e que os doentes activos têm 80% de hipóteses de sobrevivência quando comparados com os sedentários. Assim, apesar dos potenciais benefícios do ponto de vista metabólico, os esforços de saúde pública devem também concentrar-se na manutenção e protocolos de níveis de actividade física, uma vez que o nosso estudo mostrou que a actividade física excêntrica intensa teve efeitos nocivos a nível cardíaco.

Palavras-chave: hipertensão, diabetes mellitus, danos, actividade física

1 INTRODUCTION

Physical exercise has been identified as a major non-pharmacological agent, assuming a beneficial and protective role in the treatment of chronic non-communicable diseases (NCDs).

The World Health Organization (WHO) defines CND as cerebrovascular and cardiovascular diseases, diabetes mellitus, obstructive respiratory diseases, asthma and neoplasms, which share several risk factors and which have long periods of latency and prolonged course, increasing a public health challenge (1).

In the Global Study of Burden of Illness, Injury and Risk Factors, researchers sought to identify all available data on the causes of death in 187 countries from 1990 to 2010 and deaths from noncommunicable diseases increased by just under 8 million between 1990 and 2010, representing two out of three deaths worldwide by 2010, totaling 34.5 million people (2).

Considering all this population demand affected mainly at the cardiovascular level and the beneficial and protective relationship of exercise in the treatment of chronic diseases, there is a search for the improvement of adequate guidance to the patient regarding the prescription of physical activity (PA).

The PA levels as well as their intensity are of great impact in order to achieve the full benefits of this practice. We know that the level of PA practice in the elderly is a relevant

factor for maintaining good health (3) and all of this benefit is largely achieved with the regular practice of PA (4). Such practice and regularity may require repetitive exposure to the muscle, especially in the cardiac.

This repetitive exposure of the exercise to which the muscle is submitted generates a stress that produces structural and ultrastructural changes that are affected by the different types of muscle contraction (5).

There are three types of muscle contraction that can be used during physical exercise, namely, concentric, isometric and eccentric activation. Eccentric exercise is characterized by the initial unfavorable effects, such as muscle damage, pain, reduced fiber excitability and muscle weakness, and when compared to concentric and isometric contraction exercises, it produces greater muscle microlesions and greater mechanical tension, but it is related to which can result in greater muscle adaptations (6) .

Eccentric adaptations induced by exercise include muscle hypertrophy, increased cortical activity and changes in motor unit behavior, which contribute to improving muscle function and adaptation (7).

It is well established that to the adaptations of the skeletal muscle, cellular stress and the resulting metabolic signals for mitochondrial biogenesis largely depend on the intensity of the exercise (8), in which the muscle was submitted. Such adaptation makes the muscle more tolerant of an exercise in which it has already been submitted (5) (9).

On the other hand, little is known about the molecular aspects of muscle adaptation and remodeling. Muscle contractions associated with greater mechanical tension are likely to cause greater damage to contractile proteins, resulting in more severe exercise-induced muscle damage (10).

It is well documented that the eccentric contraction has a greater magnitude of harmful potential for the muscle, recruiting a smaller number of motor units for the same mechanical requirement, triggering an inflammatory response (6).

The adequate reparative tissue process is essential, as it is in this sequence that the adaptations that make the muscle more tolerant to an exercise in which it has already been submitted are established (9) (5). This whole system of adaptation has repercussions at the cardiovascular level.

It is well documented about the intensities of physical training in water and the protective factors in the myocardium (11) (12) , high and medium intensity training in elderly rats (13) , high intensity in the dynamic patterns of the macrophage phenotype in the

muscle skeletal through eccentric stimuli induced by exercise (14) , the role of exercise in the plasticity of damage (15) , however to what is established in relation to high-intensity daily exercise with modulation of eccentric contraction adjusted to damage or cardiac adaptation has been dedicated little attention.

Thus, it is in fact that most studies suggest that the benefits of physical activity increase progressively with increasing physical activity and exercise training benefits the population, but it is possible that prolonged exercise and exercise training may adversely affect cardiac function. in some individuals (16) (17) (18). However, few studies have examined the effects of extreme resistance exercise throughout life on cardiac risk.

This support goes beyond hypertensive and diabetic patients who benefit from the usual practice of physical activity, promoting quality of life, preventing comorbidities and increasing survival. This time, there is a reflection on the adequate protocol in the prescription of physical activity for hypertensive and diabetic patients.

To this end, the present study aimed to establish a reflection based on data obtained and the proper prescription protocol without causing harm to patients with hypertension and diabetes and thus assist in the identification of possible gaps in knowledge.

2 MATERIALS AND METHODS

This is a reflective theoretical study based on the publication of the results of articles conducted by the authors. The preparation of this article followed the assumptions of the level of physical activity for hypertensive and diabetic patients, the associated comorbidities, the benefits of physical activity and the damage that the exercise requirement can cause.

The reflective process was taken as the basis experience during the project that started in 2012, with articles from studying 200 patients with hypertension and diabetes approach and histology laboratory animal on muscle damage. The studies are entitled “ Association between different levels of physical activity, quality of life and comorbidities in hypertension in a city in the state of São Paulo ” (19) , “ Impact of Physical Activity on Survival in Hypertensive and Diabetic Patients in the Interior of São Paulo ” (20) and “ Cardiac Structural Repercussions Induced by Exhaustive Physical Training in the Animal Model (21) ” with an approach to the maintenance of physical activity, with emphasis on proposals for adherence to physical exercises on public health.

The animal study had a sample of 15 male WISTAR rats (Charles River Laboratories Barcelona) at 4 weeks of age. The animals were housed in collective cages (2 per cage) with

controlled temperature and humidity ($22 \pm 2^\circ\text{C}$ and $60 \pm 10\%$) and 12 hours inverted light / dark with access to food and water *ad libitum*.

After one week of acclimatization, the rats were randomly assigned to 02 groups: Sedentary (SED $n = 5$) and trained (TR $n = 10$) that were subdivided into 01 week (TR1 $n = 5$) and 03-week training (TR3 $n = 5$). The TR animals practiced running on a treadmill (-25° ; 30m/minute; 60 min whose intensity increased 1.25 meters/minute in each training session, reaching a maximum intensity at the end of the first and third weeks) 6x/week, during 01 and 03 weeks respectively with eccentric contraction exercise due to mechanical demand and inflammatory response from intense physical exercise (25).

The animals of the TR subgroup were sacrificed at the end of the first week (TR1 $n = 5$) and at the end of the third week (TR3 $n = 5$). The SED animals remained limited to the space of the cage throughout the study and were sacrificed one day after the first week of the protocol. For sacrifice, the animals were weighed and anesthetized with ketamine (90 mg/kg, Merial, France), xylazine (10 mg/kg, Bayer, German) and sacrificed by exsanguination and the cardiac tissue collected and processed for structural analysis by optical microscopy and immunohistochemistry.

The processing of the tissues took place from the histological routines of the research laboratory and after the processing of the tissues, they were cut to $5\mu\text{m}$ thick and stained with haematoxylin-eosin (26) for analysis of muscle damage through the signs of cell degeneration necrosis, the presence of an inflammatory reaction and the degree of tissue disorganization (27) and also for the quantification of the cross-sectional area through analysis of round cells with nucleus in the center. Picrosirius Red staining (28) was used to analyse the collagen content and preparations for immunohistochemistry in the study of macrophage polarization (M1 and M2 activation), expression of kappa B nuclear factor (NF-kB) p65 and cell proliferation (KI 67).

The sections were analysed with an optical microscope (Axio Imager A1, Carl Zeiss; Germany) and the images recorded with a coupled digital camera (Leica DM4000B, Nussloch, Germany). A total of 150 photos were analyzed, 50 for each group, 10 for each animal in each subscript technique.

The data were tabulated using EXCEL for WINDOWS® and the data analysis was performed using the GraphPad Prisma® version 8 program. The normality of the data was verified using the test and Kolmogorov-Smirnov and Shapiro- Wilk. The variables studied with normal distribution (NF-kB p65, M1, M2, KI67) were presented using means and

standard deviations (SD). For the inferential analysis, One-way ANOVA was used followed by the Bonferroni post hoc comparison test. The data with non-normal distribution were then analysed with Kruskal- Wallis followed by Dunn's post hoc comparison test. The abnormal variables (degeneration, necrosis, infiltration and organization, collagen levels and cross-sectional area) were presented as medians and interquartile ranges (first and third). The level of significance was set at 5%.

A longitudinal study was conducted with 200 patients aged over 18 yrs , both sexes, who enrolled in the Hiperdia Program of the city of Agudos. They had already participated in a previous study in 2009, where the number of patients was determined using the Hiperdia population average sample formula reaching 200 patients.

From May to August 2018 the same patients were evaluated and data were collected in a standardized assessment by questionnaires, anthropometric, biometric parameters and blood pressure measured according to the recommendations of the VI Hypertension Guidelines (11) .

Laboratory tests were obtained from a specific patients database registered in Hiperdia, that has been considered the last examination requested by the physician.

Regarding the patients who died, an investigative research was conducted to verify the cause of death through the death certificate. The inclusion criteria comprised participants aged over 18 yrs , aware and able to answer the questionnaires and the exclusion criteria encompassed intellectual disabilities and patients aged under 18 yrs .

All the involved have read and gave written informed consent and all the procedures were in accordance with the Botucatu Protocol 1.642.169. The instruments used for evaluation were the Kidney Disease and Quality of Life Short-Form (KDQOL-SFTM) (12) and the International Physical Activity Questionnaire (IPAQ) (13), both in their translated version, adapted and validated for the brazilian culture.

3 RESULTS

Previous cross-sectional study carried out by our group and called “ Characterization of patients with hypertension and diabetes seen at basic health units in the city of Agudos and evaluation of the association between level of physical activity and cardiovascular risk factors, quality of life and comorbidities (19) ”Concluded that sedentary people had higher rates of stroke, infarction, hospitalization for heart failure, kidney disease, dialysis and a higher frequency of family history of arterial hypertension. On the other hand, the highest

level of physical activity was associated with a better quality of life, even after excluding patients incapacitated by stroke, dialysis or heart failure.

In relation to the article *Impact of Physical Activity on Survival in Hypertensive and Diabetic Patients in the Interior of São Paulo* (20), the main findings in the present study were the 80% chance of active patients in survival when compared to sedentary ones. The data were maintained throughout the analysis process. The PA was associated with survival, though irregularly, with 65% survival chances of the patient does not maintain this practice.

Regarding the study, " *Cardiac Structural Repercussions Induced by Exhaustive Physical Training in the Model Animals* (21) " The results showed that different levels of eccentric exercise high intensity caused damage in cardiomyocytes, even with evidence of tissue remodeling during the physical activity process. We found data where muscle damage was induced by the requirement of eccentric exercise as it increased the exposure time of the activity.

4 DISCUSSION

The results obtained demonstrated that the different levels of high intensity eccentric exercise caused damage to the cardiomyocytes, even with the evidence of tissue remodeling during the entire process of physical activity.

Muscle damage was induced by the requirement for eccentric exercise as the exposure time of the activity increased. In the literature, we found studies that state that muscle contractions associated with greater mechanical tension are likely to cause greater damage to contractile proteins (10).

After the muscle injury induced by the most severe exercise, recovery, that is, the entire recurrent inflammatory process will depend on the extent of the initial muscle damage, which is influenced by the intensity and duration of the exercise (22). In our study, we observed tissue repair denoted in the reference to M2 immunohistochemistry among the sedentary group of activity for one week, but after the following weeks, despite the increase in regeneration cells, no significant differences were found between such regenerating cells.

The entire process of inflammatory response was evidenced in our study, and currently, the process of inflammatory response is generally accepted that, if well regulated, they are essential for muscle repair and regeneration, although inflammation has historically been seen as harmful to recovery from exercise (8). The metabolic stress and the

mechanical alterations contemplated to the muscular damage, stimulate several types of cells that comprise the skeletal muscle to initiate the process of the inflammatory responses (10).

In our study, the damage to the cardiomyocyte tissue may be related to the intensity of physical activity managed by the imposed protocol. In a study with a similar one that studied the soleus and tibial muscle, they reported that muscle damage shows different behaviors according to the type of work that each muscle does (23).

Currently, many studies seek the appropriate protocol for the level and intensity of physical exercise that is beneficial for different groups in society.

The search for the ideal protocol was attributed in the German study (24), where it is established that physical activity below 150 minutes per week is associated with significant health gains and can be accumulated in sessions of at least 10 minutes. The authors state that adults and the elderly should perform at least 150 minutes per week of moderate intensity or 75 minutes per week of high intensity aerobic activity for a beneficial adaptation of the muscle to exercise.

It is also documented in other studies for the elderly that maintaining moderate activity, with a pattern already established such as walking, and other protocols up to 45 minutes 3 times a week (25) can be efficient, but does not mention the damage according to the present study. Another study analyzing the effects of intensity between age showed that vigorous activity brought greater satisfaction, while moderate activity had a negative effect with a combination of both reporting significantly higher levels of well-being compared to those who do not attend guidelines (26).

Refferent to the level of physical activity we noted that our study found that the continuous process of high intensity eccentric exercise in the third week, may have characterized a given tissue by the requirement of the exercise or non-burst in physical activity. It is documented that the highest levels of physical activity at baseline and the increasing trajectories over time were protective against mortality (27), that the highest levels of leisure-time physical activity were associated with reduced risk of events of vascular diseases and all-cause mortality from vascular disease (28), which the low level of physical activity of patients with hypertension, is generally associated with a level that can decrease their chances of survival.

Another study, one of the first longitudinal studies with a prospective cohort that was conducted in London, relating physical activity and coronary artery disease, compared postal service workers and postal workers, as well as drivers and collectors of double-decker buses

in London. These researchers observed that occupational activities with higher energy expenditure were associated with lower rates of death from coronary heart disease (29).

5 CONCLUSIONS

Thus, despite the potential benefits from the metabolic point of view, public health efforts should also focus on maintaining and protocols of physical activity levels since our study showed that intense eccentric physical activity had harmful effects at the cardiac level. The eccentric exercise practiced during the first three weeks induced cellular responses to stress stimuli in the cardiac tissue, maintaining apoptosis and phagocytosis throughout the pro-inflammatory process through the interaction of adaptive immunity.

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