

The effect of eight weeks of continuous aerobic exercise (CT) on BCL-2 and BAX gene expression of Wistar male rats

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ABSTRACT

Introduction and necessity: The role of sports activities to reduce the risk factors associated with heart disease, including obesity, high blood pressure, hyperglycemia and hyperinsulinism, are well known, but there is still little information about the potential mechanisms of high intensity periodic interval exercises (HIIT) And aerobic continuity (CT), in the development of adaptations that prevent and even treat cardiovascular disease. **Objective:** The aim of this study was to investigate the effect of 8 weeks of continuous and periodic aerobic exercises on the expression of BCL-2 and BAX genes in the left ventricle (left ventricular) heart tissue of male Wistar rats. **Method and tools:** 12 male Wistar rats from the Razi Institute were purchased and all natural conditions (temperature, sleep cycle and awakening, food, etc.) were provided to them. The rats were randomly divided into two groups, the continuous aerobic group (N = 6) and the control group (N = 6). The aerobic continuous aerobic group performed 5 days a week with an intensity of 70% of maximum speed and scheduled time. The following groups were described after each anesthesia, to measure the expression of BCL-2 and BAX genes from the Real Time technique PCR was used. **Analysis:** SPSS 16 software and the KRUSKAL-WALIS test were used with the MANN-WHITNEY post hoc test (P <0.05). **Results:** Results showed that BCL-2 gene expression increased significantly after exercise compared to control group. BAX gene expression decreased in training group compared to control group. **Results:** Since these two factors are one of the most important factors involved in the process of apoptosis, today research indicates that apoptosis is one of the causes of diseases and cardiac arrest. The results show the positive and influential role of continuous aerobic exercise in preventing cardiovascular disease and treatment of heart failure is.

Keywords: Continuous Aerobic Exercise (CT), BCL-2, BAX.

Introduction

Regular exercise has a great influence on cardiovascular risk factors and chronic diseases such as obesity, hypertension, diabetes, and cardiovascular disease. In this context, researchers' information about the importance of genes is being completed. There are certain genes that Cardiovascular disease, atherosclerosis, Alzheimer's, and other irregularities^[1]. Cardiac muscle hypertrophy is a kind of physiological adaptation

by which the heart compensates for increased workload. In some places, this process can be defined as an athlete's heart (physiological) in healthy people or as a patient's heart (pathologic) in cardiac patients^[2].

Exercise with the release of cortisol stimulates lymphocytes and, as a result, free TNF inflammatory factor. By attaching cell death receptors, this factor triggers inflammatory pathways. This factor leads to positive atrophic pathway regulation and, by creating atherogenic responses, causes muscle protein breakdown. This factor activates NFκB, which also stimulates protein breakdown through the pathway of iubicotin. Consequently, it inhibits the synthesis of myogenic proteins and inflammatory pathways. TNF activates BCL by increasing free radicals, resulting in atrophy^[3].

Apoptosis plays an important role in heart disease such as infarction, heart failure. In fact, cardiac apoptosis inhibition has a significant effect on the treatment of cardiovascular disease. Many studies on cardiac insufficiency of human and animal models suggest that apoptosis may be one of the most important

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factors in heart failure. Apoptosis inhibition can play an important role in the treatment of heart disease, including heart failure [4].

In a 2016 study, Zhao et al. Showed that swimming practice affects the factor associated with apoptosis of MICRO RNAS and reduces apoptosis in the heart of mice. Group 1 was practiced 8 times a day with increasing load 5.

Group 2 was practiced with the same training method as group 1, except that they were practiced at the end of the fifth week twice a day. The study showed that the apoptosis-related factor of miRs and its underlying proteins can be influenced by the practice of swimming.^[5]

Afshar Jafari et al. In a study entitled "The effect of three-month aerobic training on some of the myocardial apoptosis indices on 5 Rats received this evidence in 2015: The exercise was conducted in a two-group experimental animal model for three months on 16 male male rats. The results show that three months of aerobic exercise has a significant effect on reducing the mitochondrial apoptosis inducing proteins. However, according to the results of the 2bcl- definitive opinion is subject to further research.

conducted a study on the effect of 3 weeks of exercise reduction in hypoxia on apoptotic index of Bax / Bcl2 ratio and epithelial cell population of lung ganglia. The findings indicate that a period of intense periodic training and subsequent hypoxia may possibly increase apoptosis of the lung tissue and threaten their physiological health [6].

In a paper titled "The effect of an interval training on the expression of P53 and Bax gene expression in tumors of breast cancer mice," Ala'alinezhad et al. (2017) found that the performance of endurance exercise in the long term led to an increase in apoptosis in the tissue A tumor that can be considered as a positive mechanism in the treatment and prevention of tumor growth.^[7]

The effect of pre-treatment of aerobic exercise on the expression of the left ventricular apoptosis gene following induction of doxorubicin in rats in the model of aging showed that with a significant decrease in the Bax / Bcl-2 ratio in the heart of rats The practice group treated with doxorubicin can conclude that aerobic exercise training before and during treatment with doxorubicin may possibly be a non-pharmacological strategy that protects the heart cells from apoptosis induced by doxorubicin^[8].

Guy Yu-Kou et al., In an article titled: Treadmill training, reduces induction of apoptosis aging in the heart of mice (The effect of exercise on treadmill on bcl-2 / bax gene expression on the heart muscle of the rats) resulted in the following results: Expression of bcl-2 was higher in the elderly exercised group than the younger ones ($p < 0.05$). On the treadmill, it definitely stops the expression of bax in the elderly trained group ($p < 0.05$)⁸. In the young trained group, the expression of bax is inhibited. Although the bcl-2 / bax ratio increased in the elderly group, this proportion was lower than the younger group^[9].

With regard to the fact that the positive effect of exercise on anyone is unnecessary, it seems that research on cellular and molecular performance of exercise can in the future lead to the use of exercise as a targeted treatment without complications. Also, due to the lack of studies on the effect of exercise on the expression of the BCL2 and BAX2 gene, and according to the searches conducted in this study, no research has ever conducted on the effects of exercise activity on the amount of changes in the expression of factors affecting apoptosis. has not done. On the one hand, given that sport activity is an important factor in suppressing inflammatory factors such as NF-kb and TNF, and since these factors trigger internal and external pathways for apoptosis and caserole activation^[10].

Materials and Method

The present research is experimental and fundamental. In this research, simple random sampling was performed. Data analysis method was used quantitatively to prove or reject the hypothesis or to answer the research questions.

The present study was conducted on 18 male Wistar 8 week old male rats with an average body weight of 263 ± 12 grams as a research sample (Institute of Razi Institute). The mice were kept in a chewed group and in an environment with a mean temperature of ± 22.1 ° C, humidity of 55 ± 4 and a dark-light cycle of 12:12 hours in specific cages of polycarbonate. All animals had free access to water and special diet of the mouse. The subjects of this study were the production of the Pars Animal Feed Company. At all stages of the research, the water needed for the animal was freely available to them. All stages of mice storage and slaughter were performed based on the Animal Ethics Committee of Shahid Beheshti University. The mice were randomly divided into two groups of 6: Continuous Endurance (CT), Control (CO). At the same time, the mice were introduced to two CT groups with treadmill, and control group mice were exposed to treadmill. First, the BCL-2 BAX mRNA sequence was extracted using the NCBI site. The primers were made by AllelID software, and then each primer was evaluated by BLAST software to ensure the primacy of the placement of primers was unique. Primers were made by Sinagan Company. In this research, the GAPDH gene was used as an internal control.

Each PCR reaction was performed using PCR master mix (Applied Biosystems) and SYBR Green in the ABI Step One (Applied Biosystems, Sequence Detection Systems, Foster City, CA) device according to the manufacturer's protocol.

In order to determine the maximum oxygen consumption, the standardized Bydford et al. (1979) standard test, standardized by Carroll Gouis Rindleau et al. (2007), was standardized for Wistar rats. The test consists of 10 steps of three minutes. The speed of the first stage is 0.3 km / h and will be rapidly increased by 0.3 km / h in the next steps

- **Hypothesis 1:** Ho-Assumption: 8 weeks of continuous aerobic exercise and severe periodic exercises do not have a significant effect on BCL2

expression of the heart tissue of male rats. The results of Kruskal-Wallis statistical test showed that there is a significant difference in the expression of BCL2 gene between the groups.

The results of Mann-Whitney test showed that there was a significant difference between the control group and the HIIT group ($P = 0.002$) and the control group and the aerobic training group ($P = 0.002$) in expression values of BCL2 gene. Also, in the post hoc test, there was a significant difference between the two groups of aerobic training and HIT training in BCL2 values ($P = 0.026$). Second hypothesis: Ho: 8 weeks of aerobic training and severe periodic exercises have no significant effect on BAX gene expression in the heart tissue of male rats. Kruskal Wallis statistical test showed that there is a significant difference in BAX gene expression between the groups.

Discussion and Conclusion

Today it has been widely accepted that intense physical activity induces major homeostathetic changes in the internal environment of our bodies, which means challenging cells to survive under stress conditions [11]. The mechanical and metabolic needs increased by exercise in several organs. And tissues, especially skeletal and cardiac muscles, may break their homeostasis capacity, thereby increasing the expression of cellular damage / death factors, inflammation, and immunological changes in the blood. In the meantime, acute exercise has been specially induced, or eccentric, in addition to necrosis, is known to cause cell apoptosis, and apoptosis has attracted particular attention among sports science researchers [12].

The purpose of this study was to investigate the effect of eight weeks of continuous and periodic aerobic exercise on BCL-2 gene expression and BAX in heart tissue of male Wistar rats. For this purpose, the present study was conducted on 18 male Wistar male rats (8 weeks) with an average body weight of 263 ± 12 grams as a research sample (Institute of Razi Institute). Mice were kept in groups of six and in a medium with a mean temperature of $+2.1 \pm 22^\circ \text{C}$, humidity of 55 ± 4 and dark cycle of 12:12 hours in special cages of polycarbonate, then the rats The simple randomized design was divided into two groups: Continuous Aerobic (CT), And control (CO). The control group mice did not participate in any exercise program, but they were immobilized to create a completely identical situation 5 times a week for 10 to 15 minutes per session, and then exposed to the treadmill sound Were placed. The results of the research showed that:

1. Results of Kruskal-Wallis statistical test showed that there is a significant difference in the expression of BCL2 gene between the groups. The results of Mann-Whitney post hoc test showed that there was a significant difference between the control group and

the control group and the aerobic training group ($P = 0.002$) in expression values of BCL2 gene.

2. Results of Kruskal Wallis statistical test showed that there is a significant difference in BAX gene expression between the groups10.

The results of the Mann-Whitney post hoc test showed that there was a significant difference between the control group and the aerobic training group ($P = 0.002$) in expression values of the BAX gene. However, no significant difference was found between the two groups of aerobic training and HIIT exercises in BAX values in the post hoc test ($P = 0.180$).

Regarding the results of the present study, the 8-week continuous aerobic exercise has a significant effect on BCL2 expression on the heart tissue of male rats, and there is a significant difference in the expression of this gene among the groups. The results of Mann-Whitney post hoc test showed that there was a significant difference between control group and control group and aerobic training group ($P = 0.002$) in expression values of BCL2 gene expression.11. This research was consistent with the results of the research by Afshar Jafari et al. 2015^[6]. In this study, the effect of three months of aerobic exercise on some of the indicators of myocardial apoptosis in rats in 2015 was to achieve the following: A group (animal model) was performed on the 16 male male rats for three months. Subjects were randomly assigned into two groups of homogeneous training and control (8 groups each). The subjects in the training group participated in the aerobic training program (intensity 75-80% of maximal oxygen consumption) for 12 weeks (10-60 m, min-1.24-30 min d-1, 15%) for 14 days for 10 -15 minutes to get acquainted with treadmill. Rarely, an electric shock was used to run the mice on the treadmill. A control group was once a week familiarized with the surrounding area in the treadmill. All rats were anesthetized with ketamine (90 mg / kg body weight) and zyalapine (10 g / kg body weight) 48 hours after the last training session (also in control mice) and their heart (ventricle) Left extraction and extraction of RNA and Cdna synthesis. BCL2-BAX genes were evaluated using the REAI TIME -rt method. Data were analyzed by independent t-test and Kolmogrovo Smirnov at a significance level of 0.05. Results: Body mass decreased by 11%. BAX gene and BAX / BCL-2 ratio of myocardium group Exercise significantly was 81% and 89% less than control group, respectively12. While expression of Bcl2 in the training group was not significantly different ($p > 0.05$), although the expression of bcl-2 in the training group was more than control (11%). Overall, it seems that three-month aerobic training on reduction The proteins that induce mitochondrial apoptosis have a significant effect on the heart. However, according to the results of bcl-2, a definitive opinion is subject to further research. Also, 8 weeks of aerobic training of BAX gene expression in the heart tissue of male rats showed that the results of Mann-Whitney post hoc test showed a significant difference between control group and HIIT group ($P = 0.002$) and control group and aerobic training group ($P = 0.002$) in

expression values of BAX gene. However, no significant difference was found between the two groups in BAX in post hoc test ($P = 0.180$). The results of this study were similar to those of Sharifi et al., 2016. This study titled the effect of pre-treatment of aerobic exercise on the expression of the left ventricular apoptosis gene following the induction of doxorubicin in mice P.^[13]

Based on the findings of the present study, this exercise model is the implementation of 8-week continuous training with an increase in BCL, which is an anti-apoptotic gene, and a decrease in the BAX gene inducing apoptosis. Considering that apoptosis is one of the main causes of cardiovascular disease, it is recommended that this exercise be recommended by sports physiologists to cardiopulmonary patients, and since sport exercises as an agent for prevention of cardiovascular disease^[13].

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