THE EFFECT OF HIGH-INTENSITY INTERVAL TRAINING ON TELOMERASE ACTIVITY OF LEUKOCYTES IN SEDENTARY YOUNG WOMEN

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ABSTRACT: Telomere is at the end of chromosome and is shortened through every cell division until the cell grows old. The major cause of an increase in telomere sequence length in most eukaryotes, and especially in humans, is the telomerase. This purpose of study was to examine the effect of an 8-week high-intensity interval training (HIIT) on telomerase activity of leukocytes in sedentary young women. For this reason, 21 students voluntarily participated in this study and were randomly divided into two groups, Experimental group (n=11, age=23.25±2.01 years, height=163.32±5.44 cm, & weight=62.2±7.56 kg) and control group (n=10, age=24.42±1.32 years, height=165.00±4.88 cm, & weight=66.6±6.80 kg). The Experimental group performed the HIIT, 3 sessions a week for 8 weeks. Every session included 3-6 times of running with maximum speed in a 20-m area with 30 s rest from each other. The fasting blood samples were collected immediately before and after the exercise protocol. The telomerase activity was measured using PCR-ELISA method. The data were analyzed using independent and paired t-tests. The results showed that the level of telomerase activity in the Experimental group increased significantly (P=0.045). Moreover, the body fat percentage, BMI, and weight in the Experimental group decreased significantly. The results of this study showed that a HIIT-as an efficient and appropriate method of exercising-increased the telomerase activity, and consequently, improved the telomere length in sedentary young women.

Keywords: HIIT, Telomerase Enzyme, Sedentary Young Women.

INTRODUCTION

Aging is defined as the accumulation of cellular damages resulting in incompatibilities of the organism (Nazem et al., 2012). Aging a physiological process in which the telomere length is shortened, and the ability of cell growth and division is reduced as well (Nazem et al., 2012). Telomeres are repetitive DNA-protein complexes that protect the ends of linear chromosomes and maintain genomic stability. The predominant mechanism of increased telomere sequence length in most eukaryotes, and especially in human, is telomerase. Telomerase is a ribonucleoprotein that consists of two central components: a protein reverse transcriptase component (TERT) and an RNA template (TERC). From a functional standpoint, telomerase is thought to be preferentially recruited to short telomeres (NasehGhafoori et al., 2008; Zhang et al., 2011). At each cellular division, telomeric DNA terminal regions are not fully replicated, which, if not counteracted by elongation by telomerase, can lead to telomere shortening (Andrew et al., 2010). Epidemiologic studies have shown links between shortened leukocyte telomere length (LTL), telomerase activity and increased risk of age-related outcomes, such as cancer incidence and mortality, type 2 diabetes, and cardiovascular disease (Cherkas et al., 2008; Andrew et al., 2010). Many of these same diseases and risk factors have also been associated with an inactive lifestyle. Physical activity and exercise training have been associated not only with prevention and improvement of disease symptoms but also with telomere length, indicating a possible role for PA influencing telomere biology as a potential mechanism for
prevention or delay of age-related disease (Andrew et al., 2008; Andrew et al., 2011). Traditionally, high volume of aerobic exercise reduces the risk of cardiovascular and metabolic diseases though it is time consuming (Hemmatinafar et al., 2013). Furthermore, the nature of some exercises including endurance exercises, which require continuous exercising and regular presence, poses some limitations. In this respect, the study of an alternative exercising program with similar metabolic adaptations and without time commitment seems necessary. Furthermore, one of the exercising protocols that have recently been attended to by researchers of exercise physiology is high-intensity interval training (HIIT). The HIIT involves intervals of maximum-intensity exercise and resting intervals of low-intensity exercise (Smith, 2008). The intervals of low-intensity exercise between intervals of repeated exercise in interval training cause to perform more exercises and receive higher effectiveness (Smith, 2008). Therefore, regarding the diversity, very low time consumption, metabolic effects similar to endurance activities, and efficacy of these exercises, this study was conducted to examine the effect of HIIT on telomerase activity in sedentary young women.

METHODS
The study was performed as quasi-experimental and subjects were inactive normal young women studying in Shiraz University and aged 20-26 years. Of the population, 21 students voluntarily participated in this study and were randomly divided in two groups, the exercise group (n=11) and the control group (n=10). The information on the level of physical activity and health of participants was acquired using a questionnaire. Participants had no any of cardiovascular diseases, diabetes, hereditary blood disorders, and respiratory problems, nor used medications, nor had regular exercises at least 6 months before the study. Anthropometric measures, including height, weight, body fat, body mass index (BMI) were collected using standard procedures. VO2max was measured before and after eight weeks exercise by treadmill. The participants in the Experimental group executed the exercise protocol in a 20-meter distance marked with three cones three times a week for eight weeks as described below (Figure 1). Upon the start of exercise protocol, the participants began to run at maximum speed from the starting point (Cone 1) toward Cone 2 (Pathway A), then returned and ran 20 meters at maximum speed and in the opposite direction toward Cone 3 (Pathway B), and eventually returned and ran at maximum speed toward the starting point (Cone 1) (Pathway C) in order to complete the distance of 40 meters. The participants continued the above process at maximum speed until the 30-second period of the exercise protocol ended, and then, they repeated the process after 30 seconds recovery. The three repetitions of 30-second exercise in the first and second weeks increased to four repetitions in the third and fourth weeks, five repetitions in the fifth and sixth weeks, and six repetitions in the seventh and eighth weeks. In each session, the participants warmed themselves up for five minutes (stretching and flexibility exercises along with slow running) before beginning the exercise protocol and cooled themselves down for 5 minutes at the end of the session. The exercise protocol consisted of a 40-meter round at maximum speed that was a valid test of anaerobic performance (Glaister et al., 2009). During the eight weeks of exercise protocol, the participants in the control group did not have any regular exercising program. The fasting blood samples of 10 cc were drawn from brachial vein (antecubital vein) 24 hours before the first session of exercise and 24 hours after the last session (8:30 am) in the laboratory. The blood samples were immediately poured into the tubes containing anticoagulant (EDTA). The tubes were centrifuged with 3000 rpm for 10 minutes at 4°C.

Fig.1. The exercise protocol of HIIT
To measure telomerase activity, the blood mononuclear cells were removed using concentration gradient method (through ficoll). Then, the telomeric repeat amplification protocol (TRAP) method based on the two techniques of polymerase chain reaction (PCR) and ELISA (kit of German Roche Company) was used through Holt’s method (Holt et al., 1996). The relative activity of participants’ telomerase was calculated through putting the obtained values for absorption in the standard curve. The collected statistical data were analyzed using SPSS18 software. The Kolmogorov-Smirnov test was used to determine the normal distribution of data. Considering that the result of Kolmogorov-Smirnov test showed the normal distribution of data, the parametric statistical tests were used. In this respect, the dependent t test and independent t-test were respectively used to examine the intragroup changes and intergroup changes. All the statistical tests were performed at significance level of \( \alpha=0.05 \).

RESULTS
Subject characteristics are shown in Table 1.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Control group</th>
<th>Case group</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pretest</td>
<td>Posttest</td>
<td>Pretest</td>
<td>Posttest</td>
</tr>
<tr>
<td>Age (year)</td>
<td>24.42±1.32</td>
<td>-</td>
<td>23.25±2.01</td>
<td>-</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>165.22±4.88</td>
<td>163.32±5.44</td>
<td>62.20±7.56</td>
<td>60.41±6.80*</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>66.67±6.30</td>
<td>67.10±6.94</td>
<td>62.20±7.56</td>
<td>60.41±6.80*</td>
</tr>
<tr>
<td>Body mass index</td>
<td>23.72±4.36</td>
<td>23.95±4.14</td>
<td>24.42±4.38</td>
<td>23.18±4.83*</td>
</tr>
<tr>
<td>(kg/m²)</td>
<td></td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>20.52±0.95</td>
<td>20.42±0.78</td>
<td>19.96±2.21</td>
<td>17.87±1.13*</td>
</tr>
</tbody>
</table>

* Significant changes

Table 2: Mean telomerase activity in the two blood samplings in both groups

<table>
<thead>
<tr>
<th>Variables</th>
<th>Groups</th>
<th>Pretest</th>
<th>Posttest</th>
<th>Significance level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Telomerase activity</td>
<td>Control</td>
<td>0.102</td>
<td>0.094</td>
<td>0.18</td>
</tr>
<tr>
<td>(Optical absorption rate)</td>
<td>Case</td>
<td>0.082</td>
<td>0.098</td>
<td>0.04*</td>
</tr>
</tbody>
</table>

* Significant changes

DISCUSSIONS
The results showed that the level of telomerase activity in the exercise group increased significantly (P=0.045) after eight weeks of HIIT. However, there were no significant changes in the control group. Moreover, the body fat percentage, BMI, and weight in the exercise group decreased significantly. Most of the results of previous studies on the correlation between exercising and telomerase changes are contradictory. Ludlow et al. (2008) reported that the telomerase activity did not change in three groups with low, medium, and high exercise energy expenditure (EEE) and aged 50-70 years. Furthermore, Radak et al. (2001) also indicated that high-intensity exercises did not make any significant changes in telomerase activity of mice. This study implied the point that high-intensity exercises might not be enough for induction of telomerase. In this regard, some studies showed an inverted ‘u’ theory in relation to the level of activity and changes of telomere (Matsubara et al., 2006; Nieman, 1997), which showed that a moderate level of energy expenditure, unlike the low and high levels, was accompanied with increased telomere length and telomerase activity. This result referred to the point that moderate-intensity training can protect the telomere through reducing the oxidative stress, increasing the antioxidant defense, and consequently, increasing telomerase activity. The result of this study, in terms of the significant increase in telomerase activity, conformed to that of Zhu et al. (2010) and Cherkas et al. (2008). Zhu et al. (2010) reported that girls with high-intensity training (MET<6) had telomerase activity higher than girls with low- and moderate-intensity training. Cherkas et al. (2008) pointed out the positive significant correlation between exercising and biological changes in telomere in women. The exercise protocol in present study had a high intensity too. According to several studies (Zhu et al., 2011; Cherkas et al., 2008), adolescents, especially girls, should do more vigorous physical activity (VPA) for more anti-aging effects of exercises. There is a
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possibility that estrogen has a direct role in the transcriptional up-regulation of telomerase in human (Kyo et al., 1999; Misiti et al., 2000). Regular exercise increases the endothelial nitric oxide (NO) bioavailability and increases circulating endothelial progenitor cells. Both estrogen and NO are important signaling mediators in various tissues. Existence of a molecular circuitry of intracellular control of telomerase regulation, mediated by the association between estrogen receptor α (ERα) and the endothelial nitric oxide synthase (eNOS). eNOS is the essential cofactor for ERα, and the ERα and eNOS groups can activate telomerase transcription. This model also has made telomerase play an important role in cardiovascular diseases. Moreover, maximum effects of high-intensity training occur in sedentary people with minimum physical fitness. Therefore, even very little high-intensity training in inactive adolescent girls can affect telomerase activity significantly (Werner et al., 2008; Leon et al., 1998). Werner’s studies (2008 & 2009) referred to the role of IGF-1 in activation of telomerase. Recent evidence shows that aged people with low IGF1 have shorter leukocyte telomere length (Barbieri et al., 2008). As the high-intensity exercise stimulates expression of IGF1 in the skeletal muscle and liver, IGF1 can play an important role in increased expression of telomerase and biology of telomere (Berg et al., 2004). Furthermore, Exercise of all types can activate AMP-activated protein kinase (AMPK) and mammalian target of rapamycin (mTOR). Both of these pathways regulate gene expression are sensitive to energy and involved in aging process of cell (Hardie et al., 2011; Haendeler et al., 2009). Interestingly, these pathways are involved in insulin signaling, protein synthesis (mRNA translation), and cell growth and survival. All these pathways become very important when studying telomere. For instance, it has been shown that telomerase was associated with changes in AMPK (Narala et al., 2008). High-intensity training acts as a proliferative stress for immune cells (Cawthon et al., 2003). Mitogen stimulation of immune cells increases telomerase activity in T cells (Wright & Shay, 2009), suggesting that telomerase activity in response to repeated proliferative stress and pressures resulting from high-intensity training maintains telomere length. The contradictions observed in various studies may root in different races of people, activity measurements, and duration and different intensities of exercise.

CONCLUSION

Given the results of this study, it appears that 8-week HIIT is an efficient and appropriate method of exercising in increased telomerase activity in sedentary young women with normal range of weight.

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REFERENCES


