Original Article

Effects of Interval Training on Irisin and Insulin Resistance in Overweight Men

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Abstract

Background: Irisin increases the calorie consumption and exothermicity, leading to the weight loss. The present study aimed to investigate the impact of high-intensity interval training (HIIT) and moderate-intensity continuous training (MICT) on levels of Irisin and Insulin resistance in overweight men. Methods: Therefore, 36 overweight men, who could regularly attend physical activity sessions, were selected and randomly divided into three groups, namely high-intensity interval training (n=12), moderate-intensity continuous training (n=12), and control (n=12). All three groups were similar in terms of weight and body mass index. The training programs of HIIT and MICT groups included 3 sessions per week for 8 weeks with different intensities. The control group did not attend any regular training program during the research. Blood samples were taken for measuring level of Irisin and determining the Insulin resistance index. The one-way analysis of variance (ANOVA) and paired t-test were utilized at a level of $P<0.05$ for comparing mean of parameters. Results: The results indicated that the HIIT and MICT changed levels of Irisin ($P=0.024$) and Insulin resistance index ($P=0.011$). The comparison of inter-group changes indicated no significant difference between HIIT and MICT groups. Conclusions: According to research results, the high-intensity interval training and moderate-intensity continuous training could be effective in preventing and treating overweight and obesity through increasing levels of Irisin and improving the Insulin resistance.

Keywords: High-intensity interval training (HIIT); Moderate-intensity continuous training (MICT); Irisin; Insulin resistance index; Overweight

Introduction

Overweight and obesity are great challenges of the world health [1] and their developing trends have involved health sectors of most countries with their issues and side effects. The challenges indicate that their frequency distributions depend on numerous components such as gender, age, physical activity, type of diet, and social factors in a great number of countries [2]. Despite the contribution of numerous factors in the development of obesity, the lack of balance between receiving and consuming energy is the most important factor of obesity. The fat tissue has two different functional componenets, namely white and brown fat. White fat stores energy, and brown fat has an exothermicity role and converts the chemical energy to thermal energy [3]. Reducing the white fat tissue and increasing the brown fat tissue are effective ways in preventing the incidence of metabolic diseases. Based on research results, a peptide, called Irisin, is a molecular mechanism for converting white fat tissue to brown fat tissue, and it is secreted from muscular tissues. During or immediately after physical activity, myocytes secrete molecules called Myokines that are mainly chimyokines and cytokines. Myokines regulate a variety of metabolic processes in different tissues and organs such as liver, skeletons, brain, or fat tissues through signaling paths of Endocrine and paracrine glands [4].

Irisin is a new Myokines and product of Fibronectin type 3 domain-containing protein 5 (FNDC5) gene and it mainly produced in muscles and regulated by peroxisome proliferator-activated receptor gamma coactivator1α (PGC-1α). Over-expression of PGC-1α browns the subcutaneous white fat tissue [5]. Irisin causes the UCP1 gene expression in the brown fat tissue. UCP1 converts the white fat tissue to

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brown fat that affects the blood glucose, insulin sensitivity, mitochondrial density, and fat metabolism. The researchers consider the PGC1-α-irisin-UCP1 mechanism, which may be expressed in response to insulin resistance or over-increase of fat, as a path towards controlling diabetes, obesity and its consequences. [6]

It seems that Irisin is a stimulated hormone by training, so that the white fat tissue is stimulated and converted into brown fat tissue, and thus increases the consumed calorie and exothermicity, and lead to the weight loss [5]. Therefore, Irisin causes the weight loss, increases oxygen consumption, improves glucose homeostasis, and insulin sensitivity. Based on the results, Irisin plays a mediating roles in metabolic disorders, including obesity and insulin resistance, which are improved by training, through controlling mitochondrial biogenesis and oxidative metabolism in most cells. [7]

A great number of researchers have mentioned the positive role of training on Irisin [5-8]. However, there are studies that reject the theory [9]. Given the research results, it seems that training is an effective factor in secretion of Irisin and its other actions on the energy metabolism [10]. Results of a research by Denis et al. (2015) indicated that short and intense training increased levels of Irisin in children and adults [11]. However, since the hormone is recently discovered, a few studies on it have had contradictory results [9]. There is no study on the impact of training on Irisin by the same method. On the other hand, an active lifestyle is significantly important in preventing and treating most diseases and it seems that attending a regular training program can play a significant role in treating and improving the patients. The research results indicate that high-intensity interval training has useful and even better effects on the BMI reduction than the moderate-intensity continuous training [12]. Therefore, the present study was conducted with an aim to investigate the effects of high-intensity interval training and moderate-intensity continuous training on levels of Irisin and Insulin resistance in overweight men.

Materials and Methods

Participants

The research method had experimental type with pretest-posttest design and control group. Therefore, overweight people aged 25-35 years were used as participants. The sample size was calculated according to a research by Bakhshi et al. [13] by considering a confidence level of 95%, test power of 80%, and two- sequence test, based on about 20% of change in target variables according to the following formula:

$$n=[(Z_{1-\alpha/2}+Z_{1-\beta})^2\times(SD_1^2+SD_2^2)]/(Mean_1-Mean_2)^2$$

The purposive and convenience sampling was performed using a public citation. After primary screening from 53 volunteers, 36 ones with inclusion criteria were selected as the samples. The inclusion criteria were as follows: body mass index (25-30 kg/m^2), being healthy and no history of consumption of drugs with effects on lipid profile, no smoking, no history of sleep disorders, cardiovascular diseases, liver, kidney, and psychological diseases. The samples received the permission of attending the training activity from a specialist. Furthermore, their lack of regular training was identified by a lifestyle questionnaire with reliability coefficients of 0.84 to 0.94, and Cronbach's alpha coefficients of 0.76 to 0.89. [14]

The participants were homogenized based on weights, BMI, and body fat percentage, and classified into three groups, namely high-intensity interval training (HIIT), moderate-intensity continuous training (MICT), and control by a simple random method. The HIIT and MICT groups implemented the training protocols for eight weeks (3 sessions per week). The control group had no regular training during the research period.

Implementation method

The participants were first invited to attend a briefing for research stages. In this briefing, the participants received explanations of research implementation methods and completed the consent forms. Thereafter, their heights, weights, BMIs, and body fat percentages were measured by a height measuring instrument (VG200) made in Japan, and Body Composition Analyzer (inbody), Model 720 made in South Korea, by a biological electrical resistance method. All participants were invited to attend the laboratory a day before the training protocol. In the laboratory, 10 cc of blood was taken from the brachial vein of participants by a laboratory specialist after they stayed in sitting state for 20 minutes in order to determine basic levels of Irisin, fasting blood glucose and Insulin. The participants of experimental groups then attended the HIIT and MICT for eight weeks. Finally, 48 hours after the last training session, 10 cc of blood was taken from participants of experimental and control groups who did not received any regular training during this period. Both blood sampling stages were implemented from 8 to 9 am after 12 hours of fasting.

Training protocol

High-intensity interval training (HIIT)

After a week of preparation and familiarity with the protocol implementation method, the participants performed their training programs, including Shuttle Run Test for a distance of 20 m, shown by 3 cones, for 8 weeks in training hall at a temperature of 26 °C during fall according to the following procedure. After warming up, including 10 min of jogging and 5 min of active stretching exercise, the participants ran from the starting point (cone 1) towards the cone 2 (path 1) with a maximum speed, and then returned and ran in the inverse direction towards the cone 3 (path B) with a maximum speed of 20 m. Finally, they re-returned, and ran towards the starting point (cone 1) with a maximum speed (path C) to complete the 40-m distance. The participants continued the trend with a maximum speed and completed a

30-second period of training protocol, and repeated the training protocol after 30 seconds of rest. The training was progressed by increasing frequency of 30-second repetition from 4 times in the first and second weeks to five times in the third to fourth weeks, six times in fifth and sixth weeks, and eight times in the seventh and eighth weeks. The training intensity was measured for all participants at all protocol stages, over a Heart Rate Maximum (HRmax) of 90% using a formula of HRmax= 220-age, and it was controlled by a heart rate monitor, made in Finland. The training program was derived from a 40-m Shuttle Run Test with a maximum speed as it was a valid test for evaluating the anaerobic performance [15]. At the end of each training session, the participants walked and did stretching training and exercise for cooling down during 10 minutes.

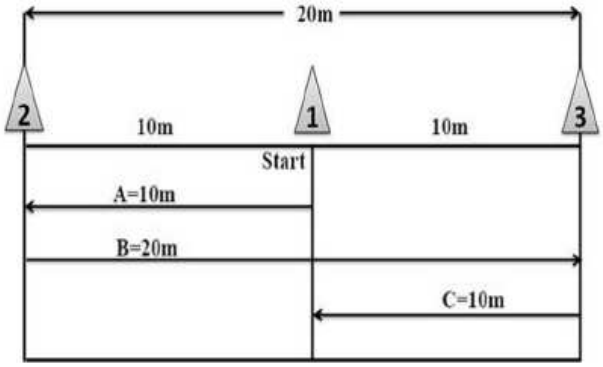

Figure 1. Schematic diagram of HIIT protocol

Moderate-intensity continuous training (MICT)

The MICT protocol was held after a week of training and preparation for 8 weeks in similar conditions to high-intensity interval training. Each session of training lasted for 40-50 minutes and included 15 minutes of warming up, 20-30 minutes of main training with an intensity of 60%-80% HRmax, and 5 min of cooling down. The continuous training intensity gradually increased from 60% to 80% HRmax. The training intensity with gradual increase in HRmax was in a way that the intensity was 60% in the first week, 65% in the second and third weeks, 70% in the fourth and fifth weeks, 75% in the sixth and seventh weeks, and 80% in the eighth week. The heart rate was controlled by a heart rate monitor, Polar Model, made in Finland [16].

Biochemical analysis

10 cc of blood was taken with all three groups with observation of health principles a day before the attendance at training and 48 hours after the last training session. The blood samples were frozen after the centrifuge and serum separation, and used for measuring the research variables. The measurement of serum Irisin was done by the Enzyme-linked immunosorbent assay (ELISA) using the EASTBIOPHARM kit, made in the US with a sensitivity of 0.023 µg/ml and the precision of CV< 10%. The fasting glucose was measured using the Hitachi 902 device, made in Japan, and a Pars Azmoon's Glucose kit, made in Iran; and Insulin was also measured by the Enzyme-linked immunosorbent assay (ELISA), and a special kit of Monobind Inc., made in the US, with a sensitivity of 0.75 micro unit/ ml and the intra-group coefficient of variation of 6.3%. The insulin resistance was measured by the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) and calculating the fasting glucose and insulin according to the following formula:

HOMA IR =[Fasting insulin (µU/ml) ×Fasting glucose (m mol/ l)] ÷22.5

Statistical analysis

The Shapiro-Wilk test was used to determine the data distribution normality. The Levene's Test was used for equality of variances; and descriptive statistics were utilized to measure central and dispersion indices. After confirming the data normality, the one-way ANOVA and paired t-test were utilized for the mean comparison of parameters. The significance level was considered to be P<0.05 for all statistical analyses. Data analysis was performed by SPSS 23.

Results

Based on results of Shapiro-Wilk test, the data distribution was normal in all variables of three groups. The statistical analysis of data in Table (1) indicated statistical significant inter-group changes in Irisin, blood glucose, Insulin resistance, Body mass index (BMI), and fat mass after training protocols.

Table 1. Investigation of inter- and intra-group changes in variables in three groups, HIIT, MICT, and Control groups

Variables	Group	Pre-test Mean and SD	Post-test Mean and SD	In-group P t		Intergroup P F	
Weight (kg)	(HIIT)	83.4±5.4	78.4±4.1	6.8	0.001*	**2.9**	**0.069**
	(MICT)	83.7±4.9	78.5±3.4	6.4	0.001*		
	control	82.4±5.6	82.2±5.6	1.7	0.104		
BMI (kg/m2)	(HIIT)	26.7±1.2	25.1±0.84	6.7	0.001*	**4.8**	**0.014¥**
	(MICT)	26.7±0.97	25.1±0.97	6.6	0.001*		
	control	26.2±1.2	26.1±1.19	1.7	0.107		
body fat percentage (BFP)	(HIIT)	29.1±3.4	25.8±3.1	4.3	0.002*	**7.6**	**0.002¥**
	(MICT)	29.2±3.3	25.8±2.6	4.1	0.003*		
	control	29.9±3.6	29.7±3	1.3	0.191		
Irisin (µg/ml)	(HIIT)	4.05±0.82	5.78±1.75	3.4	0.006*	**4.1**	**0.024¥**
	(MICT)	4.14±0.79	5.1±1.43	2.4	0.035*		

	control	4.17±0.76	4.1±0.94	0.2	0.83	
glucose)mg/dl(	(HIIT)	93.7±21.8	80.5±10.6	2.9	0.014*	**4.3 0.021¥**
	(MICT)	95.6±20.3	81.1±9.27	2.9	0.013*	
	control	96±16	94.7±18.2	0.65	0.54	
Insulin)µg/ml(	(HIIT)	10.2±2.93	8.8±2.2	4	0.002*	**2.1 0.148**
	(MICT)	10.4±2.96	8.6±1.64	3	0.01*	
	control	10.4±2.87	10.4±3.1	1	0	
Insulin resistance)HOMA(	(HIIT)	2.33±0.79	1.75±0.49	4.1	0.002*	**5.1 0.011¥**
	(MICT)	2.46±0.94	1.71±0.32	3.8	0.003*	
	control	2.46±0.8	2.44±0.92	0.73	0.35	

*In-group Statistical significance; ¥ intergroup Statistical significance

The Bonferroni post hoc test indicated significant changes between HIIT and control groups in Irisin (P= 0.021), (Fig.2), Glucose (P= 0.041), insulin resistance (P= 0.033), (Fig.3), body fat percentage (P= 0.005), BMI (P= 0.034); and between MICT and Control groups in insulin resistance (P= 0.021), (Fig.3), body fat percentage (P= 0.006), and BMI (P= 0.032).

Intra-group mean changes in variables of Table (1) indicated that there was a significant difference between pre-test and post-test in the HIIT and MICT groups in terms of Irisin in Fig (2), and Insulin resistance in Fig (3).

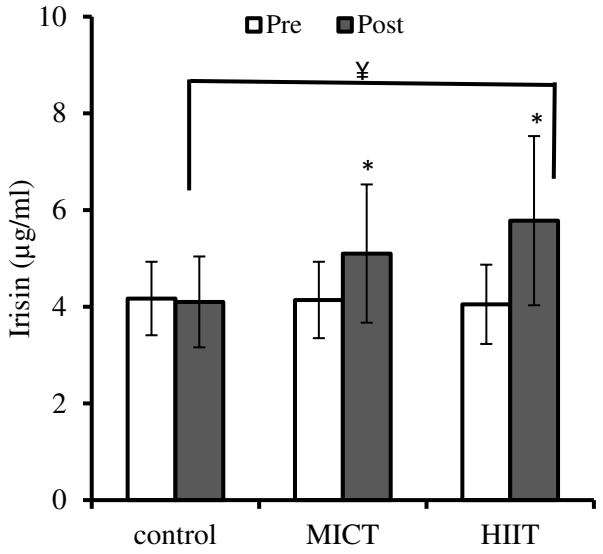

Figure 2. Mean (±Standard error) of Irisin before and after training in control, HIIT and MICT groups. *In-group Statistical significance; ¥ intergroup Statistical significance.

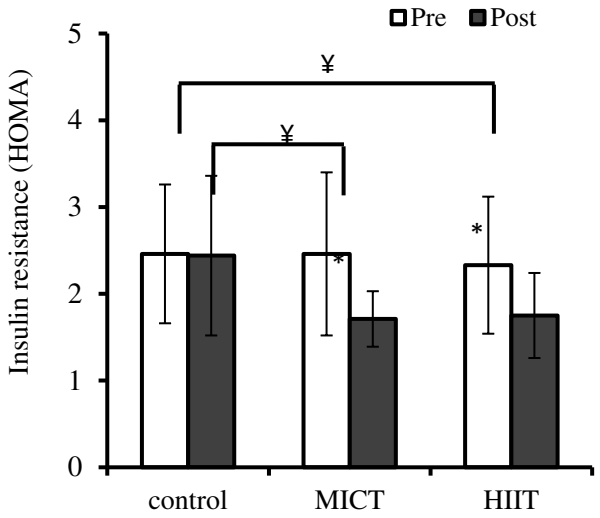

Figure 3. Mean (±Standard error) of Insulin resistance before and after training in control, HIIT and MICT groups. *In-group Statistical significance; ¥ intergroup Statistical significance.

Discussion and Conclusion

The research results indicated that physical activity, especially high-intensity interval training (HIIT) and moderate-intensity continuous training (MICT) increased Irisin, decreased blood glucose, Insulin resistance, and glycemic indices such as BMI and body fat percentage. Furthermore, the Irisin expression was under the influence of training intensity, and thus the high-intensity interval training caused a higher increase in level of Irisin hormone than the moderate-intensity continuous training. The results were consistent with some studies [1, 6, 11, 17-19]. Löffler et al. compared six weeks of short HIIT and a year of MICT and acknowledged that the HIIT increased Irisin more than the MICT [11], while the results were not consistent with some studies [20, 21]. Huh et al. found no significant changes in levels of Irisin after eight weeks of running with high intensity [21]. The training model was a reason for inconsistency of results. Some researchers believe that the Irisin expression is affected by diet and training intensity [6]. Tsuchiya et al. investigated serum levels of Irisin in two different intensities of $VO2_{max}$= 40% and 80% and concluded that the serum Irisin response to intense training was higher [6] and its amount was also higher immediately after training [20]. Furthermore, Hakimi et al. found no significant changes in serum Irisin after eight weeks of low-intensity training instead of a significant reduction in weight, BMI, and body fat percentage (consistent with results of the present study). Long training and low intensity were reasons for non-change in Irisin levels [19]. The regular physical activity contributes to metabolism regulation through increasing the energy cost and indirectly by stimulating the secretion of some hormones such as Irisin. Irisin is a main factor of connecting the skeleton muscle and fat tissue and can affect the glucose homeostasis and insulin resistance by converting the white fat tissue, as a source of

energy storage, to brown fat as an energy consumer [5, 22]. Some intervening factors, such as type, intensity, and duration of training, participants' gender and age, acute and chronic effects, and interval of blood sampling from the last training session should be considered in the expression of physiological mechanism for the impact of a regular training on levels of Irisin. According to results of the present study, the selection of suitable duration and intensity and observing the gradual load increase as well as the appropriate and accurate control of training intensity led to the compatibility of increase in Irisin. It seems that the long-term moderate-intensity continuous training (MICT) and high-intensity interval training (HIIT), especially in inactive and overweight people can facilitate and increase amount of Myokines such as Irisin by changing the body composition and increasing the muscular-fat tissue ratio.

Reducing the fasting blood glucose and improving the insulin resistance are other important effects of regular training on the glucose homeostasis and glycemic blood factors. In the present study, both variable decreased after implementing the high-intensity interval training and moderate-intensity continuous training. The physical activity increases the insulin sensitivity and glucose tolerance and decreases the blood glucose [23, 24]. Furthermore, it increases the glucose uptake by active muscles. The mechanism is done through stimulating and transferring GLUT-4 to cell membrane and rapid uptake of glucose by active muscles through protein carriers [25]. According to findings of the present study, the implementation of training protocols improved the Insulin resistance index. The reduction of Insulin resistance in the present study was consistent with studies by [26, 27], but inconsistent with a study by Jeon et al. [28]. Several mechanisms have been proposed for reducing the Insulin resistance after training. They include increasing the available receptors and Insulin signaling [29], increasing the Glycogen synthase and hexokinase [30], reducing the release of free fatty acids, and increasing their cleaning rates [29], and increasing the delivery of glucose to muscles and changing its composition. The Insulin resistance is an insufficient response of insulin-sensitive tissues such as liver, fat tissue, and muscles to insulin levels. The higher production of cytokines and fatty acids activates the inflammatory paths in immunity and metabolic cells. The activation of inflammatory paths intervenes in the Insulin signaling path and leads to the Insulin resistance [8]. The physical activity affects the glucose homeostasis and decreases the Insulin resistance by increasing the Insulin signaling performance, transmitters of glucose from inside to membrane of cells, speed of glucose uptake speed, the capillary density, the gene expression of activity of proteins involved in Insulin signaling, the Glycogen synthase activity, and finally increasing the Glycogen storage [31]. It is worth noting that these types of training decrease the body mass index (BMI) as an important index in promoting the health level.

In general, the control of obesity and overweight and its risk factors can be achieved by several methods. The experts believe that being on a diet is not sufficient in controlling these diseases. Therefore, physical training should be also added to their daily routine. A regular physical activity with appropriate intensity can greatly contribute to reduction of adverse effects of overweight and obesity and increase in Insulin sensitivity in a target tissue by the Irisin expression.

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