RESEARCH ARTICLE

Correlation of Moderate-Intensity Physical Exercise on Irisin, Oxidized-Low-Density Lipoproteins and High-Density Lipoproteins Cholesterol Level in Over 50 Years Old Obese Men

Made Putra Semadhi[1,2,*] Melisa Intan Barliana[3], Dewi Muliaty[2], Andi Wijaya[2]

[1]Magister Program of Clinical Pharmacy, Faculty of Pharmacy, Universitas Padjajaran, Jl. Raya Bandung Sumedang Km 21, Jatinangor 45363, Indonesia
[2]Prodia Clinical Laboratory, Jl. Kramat Raya No.150, Jakarta 10430, Indonesia
[3]Department of Biological Pharmacy, Faculty of Pharmacy, Universitas Padjajaran, Jl. Raya Bandung Sumedang Km 21, Jatinangor 45363, Indonesia

*Corresponding author. E-mail: putra.semadhi@prodia.co.id

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Abstract

BACKGROUND: Irisin is secreted by our muscle during physical exercise, which has been recently studied to be linked with lipid metabolism. The aim of this study was to investigate the role of irisin that interact with the oxidized-low density lipoprotein (ox-LDL) and high density lipoprotein cholesterol (HDL-C) levels that are affected by moderate intensity exercise in obese men aged ≥50 years.

METHODS: This was a cross-sectional study with 70 obese men whose age ≥50 years old as participants. Participants were classified into two groups of men with and without physical exercised, based on American College of Sports Medicine (ACSM). Irisin and ox-LDL plasma levels were analyzed using enzyme-linked immunosorbent assay (ELISA), meanwhile the HDL-C serum level was analyzed using homogenous enzymatic methods.

RESULTS: The result showed an association between the duration of physical exercise per week and irisin level (R=0.584, $p<0.01$), also between the duration of physical excercise per week and ox-LDL level (R=-0.274, $p<0.05$). Meanwhile, there was a negative association between irisin levels and ox-LDL (R=-0.294, $p<0.05$). Irisin indicated to be correlated with HDL-C (R=0.215, $p>0.05$).

CONCLUSION: Based of the study result, moderate-intensity physical exercise is correlated with the decrease of ox-LDL and the increase of irisin level among obese men subjects aged ≥50 years old. In addition, it can be concluded that the higher the irisin level showed the lower levels of ox-LDL and higher level of HDL-C.

KEYWORDS: obesity, elderly, irisin, ox-LDL, HDL-C, physical exercise

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Introduction

Obesity in people whose age ≥50 years old causes more cardiovascular and cardiometabolic risk damage, and also linked to physical disability and various organ system problems.(1,2) The mechanism of obesity at the age ≥50 tends to be complex, with the increase of reactive oxygen species (ROS) (3), increase of inflammation (4), decrease of muscle function and mass characterized by mitochondrial dysfunction (5), increase of fat mass, significant increase in cardiovascular risk marked by the increasing circulation of oxidized-low density lipoprotein (ox-LDL), significant decrease of high density lipoprotein cholesterol (HDL-C) in the blood, and the presence of senescence mediator (6).

Ox-LDL is induced by oxidative stress that increases the concentration of p38 protein mitogen activated protein kinase (MAPK) which eventually activates nuclear factor kappa B (NF-κB) and will increase the regulation of proinflammatory processes that have an impact on endothelial dysfunction.(3) Many experts recommend

improving and maintaining the quality of life of ≥50 years old man with obesity by doing regular physical exercise. However, this could be difficult since the motor muscles ability and function of elderly people are decreasing. There's also a reduction in mobility to cognitive abilities caused by a significant imbalance of energy intake and expenditure.(1,5,7)

The elderly people are recommended to do moderate intensity exercise according to the criteria of the American College of Sport Medicine (ACSM). Moderate intensity exercise consist of several form of exercise, such as jogging, swimming, elderly gymnastic, and yoga, that are done consistently at least 30 minutes per day, 3 times per week, for 8 consecutive weeks. In the last few years, irisin has been found secreted by human bodies during physical exercise, including moderate intensity exercise which has been studied and found related to fat metabolism.(8)

Irisin is an adipomyokine, a muscle cell cytokine and adipose cell produced by proteolytic domain-containing protein 5 (FNDC5) fibronectin type III membrane protein. (9) FNDC5 is the main transmembrane protein present in muscle cells.(10) Excretions of irisin are thought to be cyclic and autocrine, in response to physical exercise activities, both acute and chronic.(11) The main function of irisin is activating thermogenesis which causes white adipose tissue (WAT) to be beige adipose tissue (BAT), by inducing uncoupling protein 1 (UCP1) through the p38 MAPK pathway and extracellular signal-regulated kinase (ERK)/MAPK.(12-14) Therefore, author is intrigued to investigate the role of irisin in a mechanism which is associated with obesity, ox-LDL, HDL-C levels that are affected by moderate intensity physical exercise in men aged ≥ 50 years old.

Methods

This research had been approved by the Ethics Commission of The Faculty of Medicine, Universitas Padjadjaran (No. 1208 / UN6.C.10 / PN / 2017). The method of present study was cross-sectional study. Seventy people had been selected using the inclusion criteria as follows: men ≥50 years old, body mass index (BMI) >25 kg/m^2, abdominal circumference >90 cm. While the exclusion criteria were: obese men using assisted transportation/mobility (wheelchairs, stick tetra pods, *etc.*), genetically abnormal muscles and cancer, acute infections, suffering from asthma, kidney disorders, severe aortic stenosis, taking anti-inflammatory drugs for the past 3 months, smoking and consuming alcohol or febrile. The subjects were consists of men aged ≥50 years old who had and had not been done moderate intensity physical exercise routinely and consistently at least 30 minutes per day, 3 times per week for 8 consecutive weeks (according to the ACSM definition), such as jogging, swimming, elderly gymnastic and yoga. Field observations, interviews and data check had been conducted to ensure the subject was appropriate with the criteria.

Samples and data for questionnaire had been collected in September 2017 to January 2018. The duration of physical exercise per week, BMI, abdominal circumference, blood pressure, ox-LDL levels, irisin levels and HDL-C level had been analyzed. Irisin plasma assay was prepared without Aprotinin. Preparation process was done at 2-8^{o}C, starting from the sample storation in ethylenediaminetetraacetic acid (EDTA) tubes, until the process of centrifugation and aliquoting. Irisin level had been analyzed with irisin enzyme-linked immunosorbent assay (ELISA) kit reagent (Phoenix Pharmaceuticals, Inc., California, USA). The preparation of sample for ox-LDL plasma level analysis had been done at room temperature of 18-25^{o}C. The sample were analyzed with ox-LDL ELISA reagent (Mercodia, Uppsala, Sweden). Meanwhile, HDL-C plasma had been analyzed with Roche Enzymatic based photometry (Roche, Basel, Switzerland).

All samples had been stored at -70^{o}C before work. Data had been analyzed using SPSS version 20 (IBM Corporation, New York, USA). Normality test, different test using Saphiro-Wilk test, and correlation test using Spearman-Rho test were done.

Results

The duration of physical exercise per week showed a significant correlation to the increase of irisin levels, with R=0.584, p<0.01 (Figure 1A). However, it was different for ox-LDL(Figure 1B), the length of physical exercise per week was correlated negatively with ox-LDL levels (R=-0.274, p<0.05). Longer of physical exercise duration was followed by significant increased levels of irisin and decreased levels of ox-LDL. Analysis between irisin and ox-LDL showed that irisin was correlated negatively with ox-LDL (R=-0.294, p<0.05). The higher the irisin level, the lower the ox-LDL level had been indicated (Figure 2). Besides, higher irisin level also indicated higher HDL-C level (R=0.215, p> 0.05) (Figure 3).

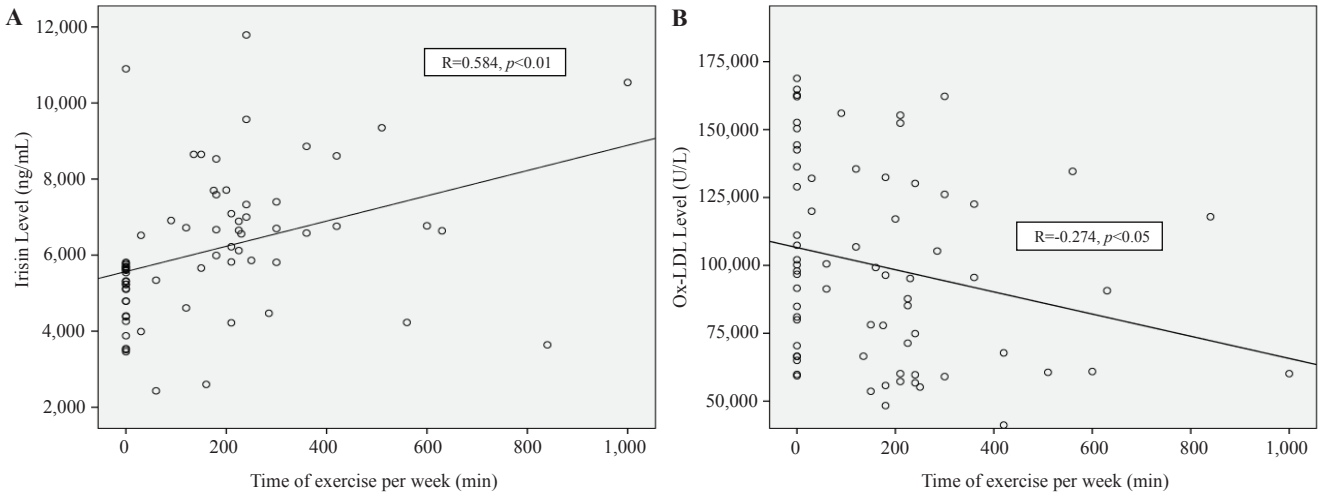

Figure 1. Correlation between time of exercise per week (minute) with concentration of irisin and ox-LDL (95% CI).

Discussion

Subjects aged ≥50 years tend to have an altered body composition, which decreases the muscle strength and mass which affects the expression and circulation of irisin levels in the blood, despite doing routine physical exercise. (5,15,16) However, the results of this study indicate significant difference in irisin levels were measured in both groups. This indicates a decrease in muscle strength and mass due to an increase in age does not necessarily affect the secretion of irisin levels.(17,18) However, this has not been completely eliminated, because this study did not measure the level of irisin groups at younger age, and not carried out mass measurements muscle in both groups of subjects.

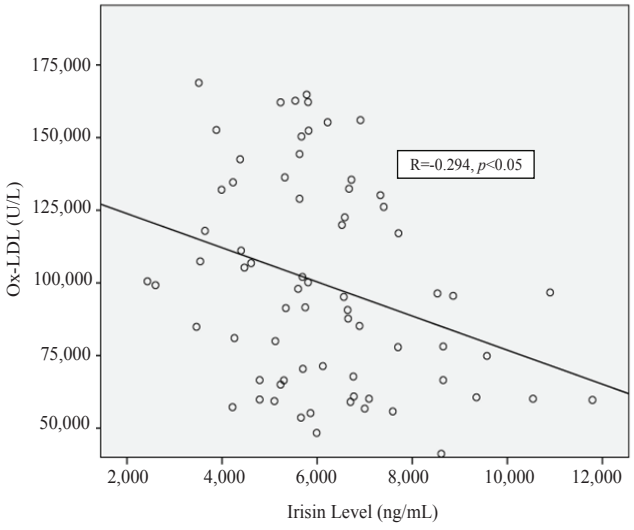

Figure 2. The correlation between the level of irisin and ox-LDL (95% CI).

The duration of physical exercise in one week is proved to have an important role in the secretion process and circulation of irisin level in the blood (16,19,20), this was shown in the presence of a significant positive correlation between the duration of physical exercise in one week to the measured irisin levels (Figure 1A). The higher duration of physical exercise is followed by the higher measured of irisin levels. This is in line with the results of the analysis conducted by multiple studies which showed that physical exercise both strenous accute and long term would result in increased irisin levels despite using different amounts of samples, subject groups and different types of physical exercise.(20-23)

Negative correlation between ox-LDL levels and duration of physical exercise in one week can be explained using the reported meta-analysis which obtained several effects of aerobic exercise (representation of moderate intensity physical exercise) on lipid profiles, one of which is LDL-C.(24,25) It is suspected that long-term aerobic exercise works in inhibiting the regulatory element-binding protein factor 2 (SREBP2) sterol signaling pathway which will increase cholesterol ester protein transfer (CETP) inhibitors and reverse cholesterol transport (RCT) pathways and increase lipoprotein lipase (LPL) activity. This process will suppress cholesterol differentiation into a smaller size, so it will inhibit the possibility of the formation of LDL modification in this case ox-LDL.(26,27)

A significant correlation between levels of irisin and ox-LDL (Figure 2) can be attributed to the correlation between physical exercise and irisin and ox-LDL levels. The results of this study indicate that physical exercise can affect the secretion process of irisin which in turn can affect ox-LDL levels. This result also shown in mice that that

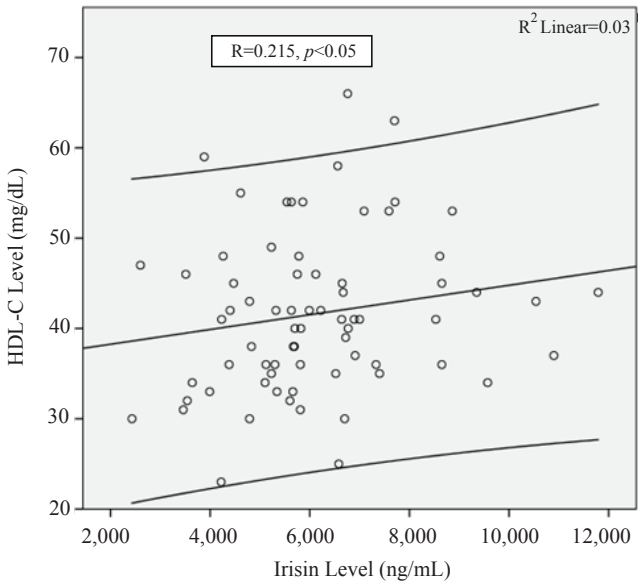

Figure 3. The correlation between level of irisin and HDL-C (95% CI).

irisin works to activate the 5'AMP activated protein kinase (AMPK) signal which will inhibit SREBP2.(28) Another research in mice showed that irisin works to inhibit ox-LDL in the oxidative stress pathway of ROS/p38 and MAPK/NF-κB.(29)

In addition, based on data we found that irisin level may have correlation with HDL-C level. It is suspected that moderate intensity exercise that secreted irisin works in increasing the activity of the SREBP2 signal pathway which increases CETP inhibitor mechanism and RCT pathway and increases LPL activity.(24,25) Irisin secreted in physical exercise such as aerobics is allegedly working on SREBP2 pathway to inhibit the synthesis of cholesterol in the liver. This process will increase HDL-C levels and suppress the levels of triglycerides, LDL-C and Apo-B.(28) Based on this result, we can analyze that higher secretion of irisin level may indicate increasing level of HDL-C in ≥50 years old obese men.

Conclusion

Based on this research, higher duration of physical exercise is correlated with the decrease ox-LDL level and increase of irisin level in man aged ≥50 years old with obesity. In addition, strong levels of irisin is alleged to increase the level of HDL-C and affect ox-LDL levels triggered by physical exercise.

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