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Serum levels of irisin, adropin and preptin in obese and athletes

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Abstract: The aim of this study is to investigate the endocrine factors thought to play a role in the regulation of energy homeostasis of irisin, adropin and preptin. Our study consists of men between 30-40 years of age including individuals from overweight or obese (n = 25), practicing regular aerobic exercise (n = 25) and sedentary (control, n = 25) groups. Irisin, adropin and preptin levels were studied on blood serum samples prepared using commercially available ELISA kit. The serum irisin level in the obese group was significantly higher than the both exercising and control groups (p <0,05). The serum adropin level in the obese group were significantly lower than control and exercising groups (p <0,05). The serum preptin level in the exercising groups were significantly lower than control (p <0,05). In addition, negative correlation was found between serum adropin and irisin levels (p <0,05). When ROC curves are analyzed, it is seen that high irisin value and low adropin value in obese individuals distinguish obese individuals from other groups with high sensitivity. In this study, serum irisin levels may increase in the obese individuals is due to more muscle activity. In addition, low levels of serum adropin and no change in preptin levels in obese individuals were considered as risk factors in terms of metabolic diseases. As a result, an active lifestyle is suggested to take advantage of the physiological benefits of irisin

Keywords: irisin, adropin, preptin, exercise, obesity

1. Introduction

Obesity, which is defined as excessive accumulation of fat in the body, has been rapidly spreading all over the world and is one of the main factors underlying many diseases (Spiegelman and Korsmeyer 2012). Exercise has been recognized to be helpful to the health, however it is not fully understood yet that how this effect is realized performed (Aydin 2014). Energy homeostasis refers to the metabolic events that involve the storage of energy in the adipose tissue, nutritional behavior, and energy expenditure. It is known that peripheral tissues are involved in energy homeostasis. Therefore, researches have focused on molecules which are effective or considered effective in the endocrine functions of the peripheral tissues, and the energy balance (Aydin, 2014; Irving et al. 2014). Irisin is a thermogenic protein that is primarily muscle originated and providing energy consumption and weight loss by turning white adipose tissue into brown adipose tissue. Irisin has been associated with positive effects on metabolic diseases such as obesity and type 2 diabetes mellitus (T2DM) (Polyzos et al. 2018). Studies on these proteins showed that exercising changes the level of irisin (Kristin et al., 2013). For this reason, we think that it can provide clinical benefit by playing role in cellular communication against obesity.

Adropin is a peptide-structured hormone that is involved in the regulation of lipid metabolism, defined in the liver and brain. Its main functions are to improve glucose tolerance, preventing insulin resistance and dyslipidemia (Aydin, 2014). Adropin is a peptide with effective cardiovascular functions on lipid metabolism. It was shown to be elevated in mice that were fed with high fat diet and were genetically altered obese mice (Kumar et al. 2008). As the result of the study on mice that are lacking adropin, adipose tissues of mice have been increased in significant quantities. It was suggested that it protects endothelial cells by affecting nitric oxide and thus it might be effective in treating cardiovascular disorders (Lovren et al. 2010). Preptin is a peptide that is synthesized from the pancreas, which is effective on glucose metabolism. It has been reported that, preptin is secreted together with insulin from the β cells and increase insulin secretion and be involved in the regulation of glucose metabolism in this way, when blood glucose levels are high (Cheng et al. 2012).

The definition of some beneficial effects of exercise on metabolic diseases led to the hypothesis that myocines associated with exercise may be related to these effects. Despite the many researches on irisin, the facts that the findings are incompatible with each other, and there is a small number of studies on adropin and preptin are important factors in the design of this study. The aims of this study were 1: to investigated reveal how the new physiological factors, which are irisin, adropin and preptin, are involved in the regulation of energy homeostasis; change in obese, exercising and sedentary individuals, 2: to investigated the relationship between adropin, irisin and preptin levels and whether these parameters change with regularly exercise.

2. Materials and Method

The study started with the approval of Gaziantep University clinical research ethics committee (date: 19.10.2015, protocol number: 2015/271). A total of 75 participants, 25 of whom were overweight or obese, 25 exercising and 25 controls (sedentary), have participated in our study. All of our study groups consisted of male subjects. BMI was used for identifying overweight or obese groups. The BMI can be easily calculated by dividing the body weight in kilograms to the square of the height in meters [body weight/height^2]. BMI should be >25.00 kg/m ^{2} in determining the overweight or obese people that would participate in the study. It was also noted that overweight or obese people included in the study had no health problems and were not implementing a regular exercise program.

The criteria for determining the athletic groups were identified as regular aerobic exercise practicing individuals. It was noted that the exercise protocol was regularly applied over 120 pulses for 3-4 days a week for at least 40 minutes a day. In addition, the exercising group's BMI were considered to be <25 kg/m^2. The criteria for determining the control group (sedentary) was selecting the individuals that do not practice a regular exercise program, that have the BMI <25 kg/m ^{2} and do not have any health problems (cardiovascular disease, renal disease, diabetes mellitus, hypertension, hyperlipidemia and autoimmune disorders).

Blood was taken from the brachial veins of all groups included in the study to 5 ml gelled tubes after an 8 hour overnight fasting. The blood was taken to the gelled flat tubes in order to study the proteins in the serum samples, and they were centrifuged at 4000 rpm for 10 minutes at 4°C. The serum part was separated into ependorfs and stored at -20°C until analysis. After completion of the blood collection procedure, serum samples were studied using commercially available ELISA kits for irisin, adropin and preptin (Catalog Number: CSB-EQ027943HU, CSB-EL007669HU, 201-12-1449 respectively).

SPSS for Windows version 22.0 package program was used for statistical analysis and p < .05 was considered as statistically significant. one way ANOVA and Kruskal–Wallis test was used to compare of the parameters among the control, athletic and obesity groups. Post hoc Tukey was conducted to compare the concentrations of the parameters between the groups. Receiver operator characteristic (ROC) curve analysis was performed to derive cut-off values for the study parameters in irisin and adropin.

3. Results

The mean age was 32.52 ± 4.53 years in the control group, 32.60 ± 3.77 years in the obese group and 31.84 ± 3.66 years in the athlete group. The mean height was 1.74 ± 0.06 m in the control group, 1.75 ± 0.06 m in the obese group and 1.77 ± 0.06 m in the athlete group. There is no statistically significant difference between the groups in terms of age and height (p> 0.05). The mean weight was 71.80 ± 6.45 kg in the control group, 93.50 ± 11.36 in the obese group and 76.14 ± 8.45 kg in the athlete group. The BMI was 23.46 ± 1.20 kg / m2 in the control group, 30.24 ± 2.48 kg / m2 in the obese group and 24.19 ± 2.21 kg / m2 in the athlete group. The weight and BMI data of the obese group were statistically significantly higher than that of both the control and athlete groups (p <0.01) (Table 1).

Table 1. The demographic characteristics of the volunteers participating in the study.

	Control (Mean ± Sd)	*Obese (Mean ± Sd)*	*Athletic (Mean ± Sd)*
Length (m)	1.74±0.06	1.75±0.06	1.77±0.06
Weight (kg)	71.80±6.45	93.50±11.36 #*	76.14±8.45
BMI (kg/m ^{2})	23.46±1.20	30.24±2.48 #*	24.19±2.21
Age	32.52±4.53	32.60±3.77	31.84±3.66

Obese group compared with the control group (*p* < 0,05)
* Obese group compared with the athletic (exercising) group (*p* < 0,05)

There was no statistically significant difference between control and athletic groups in terms of the amount of serum irisin. However, the amount of serum irisin of obese group was found to be statistically significantly higher than both the control and athletic (exercising) groups (*p* < 0,05). The serum adropin level was significantly lower in the obese group than in the control group and the exercising group. No statistically significant difference was found, when control and exercising groups were compared in terms of serum adropin amount (*p* > 0,05). As a result of statistical analysis, there was a significant difference between the control group and the exercising group in terms of serum preptin concentration (p <0.05) (Table 2).

Tablo 2: The amounts of serum irisin, adropin and preptin in the groups.

	Control (Mean ± Sd) (n=25)	*Obese (Mean ± Sd) (n=25)*	*Athletic (Mean ± Sd) (n=25)*
İrisin (ng/ml)	34,87±26,23	60,85±25,30*#	38,60±14,50
Adropin (pg/ml)	2387,54±694,38	1911,06±386,73*#	2296,88±610,55
Preptin (ng/ml)	294,13±240,21	169,70±151,65	152,52±80,45◊

Obese group compared with the control group (*p* < 0.05).
* Obese group compared with the athletic (exercising) group (*p* < 0.05).
◊ Control group compared with the athletic (exercising) group (*p* < 0.05).

We also examined the demographic characteristic and correlation between serum adropine, irisin and preptin levels. Accordingly, when the parameters were analyzed by Weight (kg) and BMI (kg/m^2), a negative correlation between serum adropin and preptin levels, and positive correlation with irisin were detected. There was also a positive relationship between age and serum irisin level. İn addition to negative correlation between serum adropine and serum irisin was detected (Table 3 and 4).

Table 3: The demographic characteristic and correlation between serum adropine, irisin and preptin levels.

	Adropin (pg/ml)		*İrisin (ng/ml)*		*Preptin (ng/ml)*
	r	p	r	p	r
Age	0,047	0,663	0,267*	0,035	0,035
Weight (kg)	-0,372**	0,002	0,522**	0,000	-0,286*
BMI (kg/m^2)	-0,381**	0,002	0,671**	0,000	-0,271*

** Correlation is significant at the 0.01 level (2-tailed).
* Correlation is significant at the 0.05 level (2-tailed).

Table 4: the correlation between serum adropine and irisin levels.

	İrisin (ng/ml)	
	r	**p**
Adropin (pg/ml)	**-0,309***	**0,012**

* Correlation is significant at the 0.05 level (2-tailed).

The values obtained as a result of ROC analysis for serum irisin and adropin are shown in figure 1 and 2. When ROC curves are analyzed, it is seen that high irisin value and low adropin value in obese individuals distinguish obese individuals from other groups with high sensitivity.

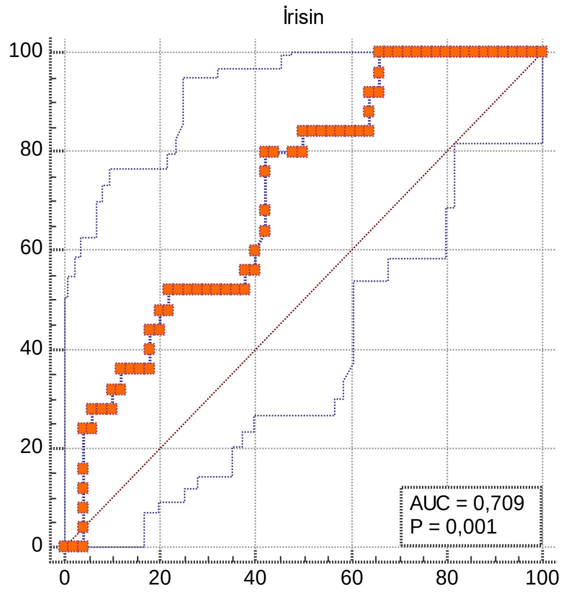

Fig 1. ROC curve belongs irisin values in obesity group is depicted. Area under the curve (AUC):0.709, Sensitivity: 0.80, Specificity:0.58, 95% CI lower border:0.593, 95% CI upper border:0.808.

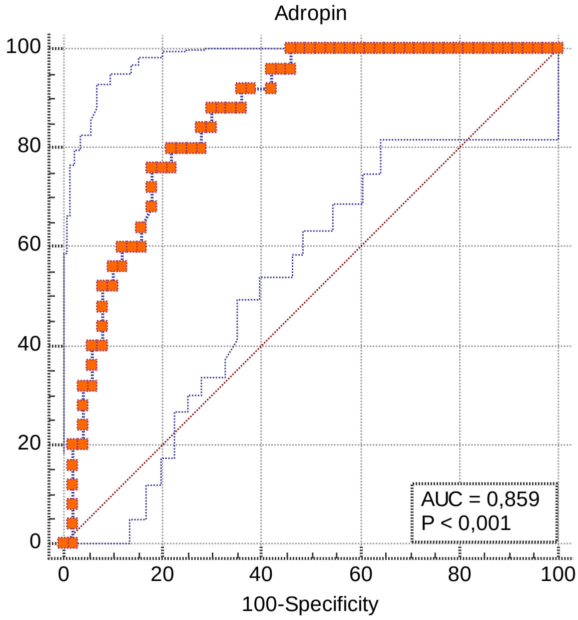

Fig 2 : ROC curve belongs adropin values in obesity group is depicted. Area under the curve (AUC):0.859, Sensitivity: 0.88, Specificity:0.70, 95% CI lower border:0.759, 95% CI upper border:0.928.

4. Discussion

The main findings from this study are as follows. 1: serum irisin levels were significantly higher in the obesity groups than in the control group. 2: serum adropin levels were significantly lower in the obesity groups than in the others. 3: The serum preptin amount decreased significantly with exercise.

Irisin, adropin and preptin are peptides secreted from peripheral tissues involved in regulation of energy homeostasis. The fact that there are uncertainties in the studies on these energy regulators and the lack of sufficient work has laid the ground for investigating this issue. To combat obesity, regular exercise is considered to be one of the most effective methods (Spiegelman and Korsmeyer 2012). Exercise also contributes to individual's continuing a more effective mental and physical life. It also may prevents many chronic illnesses from developing. Furthermore, it is an excellent therapeutic intervention for some types of cancer and control of many diseases such as obesity, type 2 diabetes, dementia, osteoporosis, depression (Aydin 2014; Irving et al. 2014). However, the biological intermediates and the mechanisms by which these therapeutic effects occur are important study areas of today's science.

In this study, consistent with the literature, serum adropine levels were significantly lower in obese individuals than in sedentary and athletic ones. Additionally, there is also only one study evaluating serum adropin level after the exercise. And in that study, the results were similar to our results and it was noted that there was no difference with the control group in terms of the serum adropin level after the exercise. Like other researchers we also think that exercise is not a useful strategy for determining serum adropin levels. Serum adropin level's being equal with the sedentary after the exercise gives rise to the thought that the amount of adropin increases acutely and drops to normal level after the resting period. The fact that there is no difference in sedentaries in the blood samples taken after exercise program in this study showed that this exercise program did not change the tendency to raise the serum adropin level. Previous studies have revealed a negative association between serum adropin level and BMI. In our study, the data obtained were compatible with the literature and correlation is significant at the 0.01 level (r value -0,381**, p value 0.002). Low serum adropin level has been shown as a marker for various diseases such as; obesity-related dyslipidemia (Butler et al. 2012), nonalcoholic fatty liver disease (Sayin et al. 2014), coronary artery disease (Zhao et al. 2015), acute myocardial infarction (Yu et al. 2014).

Irisin causes increase in total energy expenditure, improvement in glucose tolerance, decrease in fasting insulin, and protection against diet-induced obesity and diabetes in mouse models (Bostrom et al. 2012; Norheim et al. 2014). In studies related to the irisin there has been a mismatch, which is; some researchers have reported an increase in serum irisin level after exercise (Bostrom et al. 2012), while others have shown that there is no increase after chronic exercise, and there is increase only after acute exercise (Huh et al. 2012; Timmons et al. 2012; Pekkala et al. 2013; Norheim et al. 2014). Similarly; our study has also matched with the previous studies (Huh et al. 2012; Timmons et al. 2012; Pekkala et al. 2013; Norheim et al. 2014) and there was no increase in serum irisin level after exercise. Our findings suggest that there is only an increase in muscle activity at the level of irisin, and thus falls back to the sedentary level when the activity decreases in the athletes, i.e. after 8 hours rest period. Previous studies that have examined the association between BMI and serum irisin level have demonstrated a positive correlation. Our results were similar and correlation is significant at the 0.01 level (r value 0,671 **, p value 0,000). This relationship may be due to an induced mechanism to compensate the obesity. (Huh et al. 2012; Stengel et al., 2013). In most, but not all studies in humans, a positive correlation was found between serum irisin with body mass index (BMI) and different anthropometric parameters but has been reported in different results. (Huh et al. 2012; Stengel et al. 2013; Perakakis et al. 2017). In obese people, the circulating irisin concentration was found higher than individuals with normal body mass index (Pardo et al. 2014). The significantly high level of serum irisin found in obese individuals in our study suggests that acute ATP requirement and acute muscle activity to carry body weights of these individuals may be due to much greater activity than sedentaries and athletes. As a result, our study also supports that the level of serum irisin increases after the period when muscle tissue is active, and also supports an active lifestyle to benefit from the physiological benefits of irisin (such as the use of adipose tissue as energy).

Preptin is a peptide structured hormone that is secreted with insulin from β cells, consisting of 34 amino acids, is a derivative of IGF 2 and that increases the insulin secretion (Cheng et al. 2012). Yang et al. compared serum preptin levels in 50 (type 2 diabetes mellitus) T2DM patients, 56 impaired glucose tolerance (IGT) patients, and healthy control group of 54 individuals. Serum preptin level was significantly higher in patients with T2DM compared with IGT and control group. It has been stated that increased levels of preptin in T2DM patients may be due to an increase in preptin secretion or a decrease in preptin metabolism. Moreover, researchers have stated that there is no relationship between BMI and serum preptin level and this result might be linked to preptin and glucose-lipid metabolism and insulin resistance, but it is not linked to the insulin secretion (Yang et al. 2009). Mervat El-Eshmawy et al. compared the serum preptin levels between 100 obese and overweight individuals and healthy control group of 50 individuals. Serum preptin levels were significantly higher in obese and overweighed group than the control group. Researchers have expressed that elevated serum preptin level might be related to the obesity together with the insulin resistance (El-Eshmawy and Abdel Aal 2015). Insulin resistance in obesity leads to an excessive increase of insulin from pancreatic β cells. And in our study, the reason for obese individuals' not having insulin resistance yet is considered as a reason of the fact that serum preptin levels were not changed according to the control group. In our study, serum preptin level in exercise group was significantly more than control group. These data are compatible with the literature (Mohammad et al. 2020).

5. Conclusion

As the result; obese individuals have more acute ATP needs because they have to constantly carry their own body weights. The high level of irisin in obese individuals might be due to the need for this acute ATP. In the exercising group, the level of serum irisin is the same as that of the sedentary group, which might be due to the decrease to the sedentary level as a result of the rest period after meeting the same requirement for ATP. The facts that the level of serum adropin is low in obese individuals and the level of preptin is the same as the control groups, suggest that obese individuals have the suitable background for metabolic diseases such as impaired insulin metabolism in later life if they do not perform BMI control or lose weight. However, further studies are needed for certain reasons, such as; this study has been performed as the first time for some parameters or some of the literature information has been presenting incompatible results.

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