Physiology and Pharmacology 26 (2022) 239-247
Original Article

Effect of endurance and resistance training on adropin and insulin resistance among overweight men: a randomized clinical trial

Elaheh Akhavan Rasoolzadeh[1], Parvaneh Nazarali[1], Rostam Alizadeh[2*]

1. Department of Exercise Physiology, Faculty of Sports Sciences, Alzahra University, Tehran, Iran
2. Department of Sports Science, School of Literature and Humanities, Ilam University, Ilam, Iran

ABSTRACT

Introduction: Insulin resistance and low adropin level are two risk factors for comorbidity in overweight individuals. The aim of this study was to investigate whether eight weeks of endurance (ET) and resistance training (RT) could affect adropin and insulin resistance among overweight men.

Methods: In this clinical trial, 27 overweight university students (20-28 years of age; 25 <body mass index> 29.9) were recruited and randomly allocated into three groups: control (n=9), RT (n=9) and ET (n=9). The RT consisted of eight moves (3 sessions/ week) performed in two sets of 6 repetitions with 30% of 1 repetition maximum (RM) during week 1, and gradually increased to four sets of 6 repetitions with 70% of 1RM by the 8th week. The ET program included treadmill running (3 days/ week) performed during 15-40min for eight weeks with an intensity of 50-80% of the maximum heart rate.

Results: The results showed that the levels of adropin in the ET group significantly increased more than that of RT and control group. Moreover, fasting blood insulin and homeostasis model assessment of insulin resistance significantly decreased in both groups, while fasting blood glucose and quantitative insulin-sensitivity check index did not significantly change.

Conclusion: It is concluded from the results of this study that eight weeks of ET and RT could help improve the metabolic profile among overweight youngsters. It is also possible that ET is more beneficial in this matter than RT.

Keywords:
Resistance training
Endurance training
Insulin resistance
Adropin
Overweight

Introduction

The prevalence of obesity and overweight is alarmingly increasing (Mokdad et al., 2003). According to the report of World Health Organization, 39% of adults ≥18 years were overweight in 2016 (WHO, 2020). Plenty of adverse health outcomes have been reported to be associated with overweight, such as cardiovascular diseases, diabetes mellitus, etc. (Kopelman, 2007; Kuczmarski et al., 1994), which indicates the need for action to address this problem, especially among youngsters.

The correlation between obesity with glucose and lipid abnormal metabolism has been well established, yet the exact mechanisms linking obesity to metabolic disorders remain elusive (Chen et al., 2019). Peptide

* Corresponding author: Rostam Alizadeh, r.alizadeh@ilam.ac.ir
Received 7 April 2021; Revised from 29 May 2021; Accepted 20 June 2021

Citation: Akhavan Rasoolzadeh E, Nazarali P, Alizadeh R. Effect of endurance and resistance training on adropin and insulin resistance among overweight men: a randomized clinical trial. Physiology and Pharmacology 2022; 26: 239-247. http://dx.doi.org/10.52547/phypha.26.3.5

hormones are critical molecules involved in controlling energy homeostasis, and adropin is one of them. It is suggested that serum adropin level decreases in overweight and obese individuals (Yosaee et al., 2017). This small peptide is encoded by the energy homeostasis-associated gene (Jasaszwili et al., 2020). Adropin is known as a fat-burning hormone, due to activating the peroxisome proliferator-activated receptor-γ, which regulates the expression of genes associated with lipid metabolism (Gao et al., 2014). There is also evidence indicating that adropin modulates physical activity and motor coordination through various signaling pathways in the brain (Wong et al., 2014). Another complication of overweight and obesity is insulin resistance (Kahn and Flier, 2000). Insulin, being an important metabolic hormone, controls metabolism of glucose and other macronutrients (Hall, 2010). Excessive body fat and altered adipocyte-derived factors such as free fatty acids, impair insulin activity and cause insulin resistance in obese and overweight adults (Greenberg and McDaniel, 2002).

Previous publications declared that increasing physical activity and limiting sedentary time could improve insulin sensitivity on target tissues (Alizadeh et al., 2018; Rice et al., 1999; Ryan and Nicklas, 2004). A positive association between aerobic exercise training and serum adropin level has also been observed in obese elderly adults (Fujie et al., 2017). On the contrary, Sanchis-Gomar et al. (2015) did not observe any significant changes in the adropin level among professional football players. Such contradictory results led us to design this study to better understand the effect of exercise on adropin and insulin resistance, two hallmarks of overweight and obesity. Besides, previous studies have mainly focused on aerobic exercise (Dengel et al., 1996; Nishida et al., 2004) which may be different from resistance training (RT) due to lower intensity of the intervention. Endurance and resistance training result in specific, different and sometimes opposite physiological adaptations of the muscles. Here, we aim to compare endurance training (ET, also known as aerobic exercise) with RT, in which muscle groups are trained by repetitively lifting heavy weights (Beckers et al., 2008). To sum up, our hypothesis is that both ET and RT could significantly improve adropin and insulin sensitivity in overweight male students. We also aim to compare the effects of these two types of exercise as well.

Material and methods

Study design

This study was a randomized, three-armed clinical trial. Participant recruitment within male university students was conducted at the Ilam University, Ilam, Iran, from April 2018 to March 2019. This study had been approved by the Ethics Committee of Sports Sciences Research Institute of Iran (SSRII) (reference no: IR.SSRI.REC.1397.363). The authors ensure that the work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) and this paper is written according to the CONSORT checklist.

Participants

In this randomized controlled trial, 27 male university students were voluntarily recruited to the present study. Females were excluded from this study due to the effect of menstrual cycle on body composition and physical fitness. Sample size was calculated based on the primary outcome of this study, adropin. According to Fujie et al. (2017) study, with an effect size of 2.1 and a power of 80% (α=0.05), assuming approximately 10% dropout rate, the total sample size was calculated as 27 (9 participants in each group). The inclusion criteria included: (1) university dormitory students from 20 to 28 years of age, (2) with the body mass index (BMI) greater than 25 and less than 30, (3) those who were not professional athletes (with no history of regular exercise program within the past six months before the study and no other exercise program during the course of the study), (4) non-smokers, (5) those who only consumed meals provided by the university with no change in their diets, and (6) those with no history of using supplements within the last six months prior to, as well as during the course of the study. There were also two exclusion criteria: (1) those with problems restricting their exercise performance (i.e., neurological, muscular and skeletal problems) and (2) those who missed the exercise programs either more than three consecutive days or for a total of four sessions. Written informed consent was obtained from the participants before the beginning of the intervention.

Study protocol

Male students were informed about the study conditions and protocol through advertisements and flyers

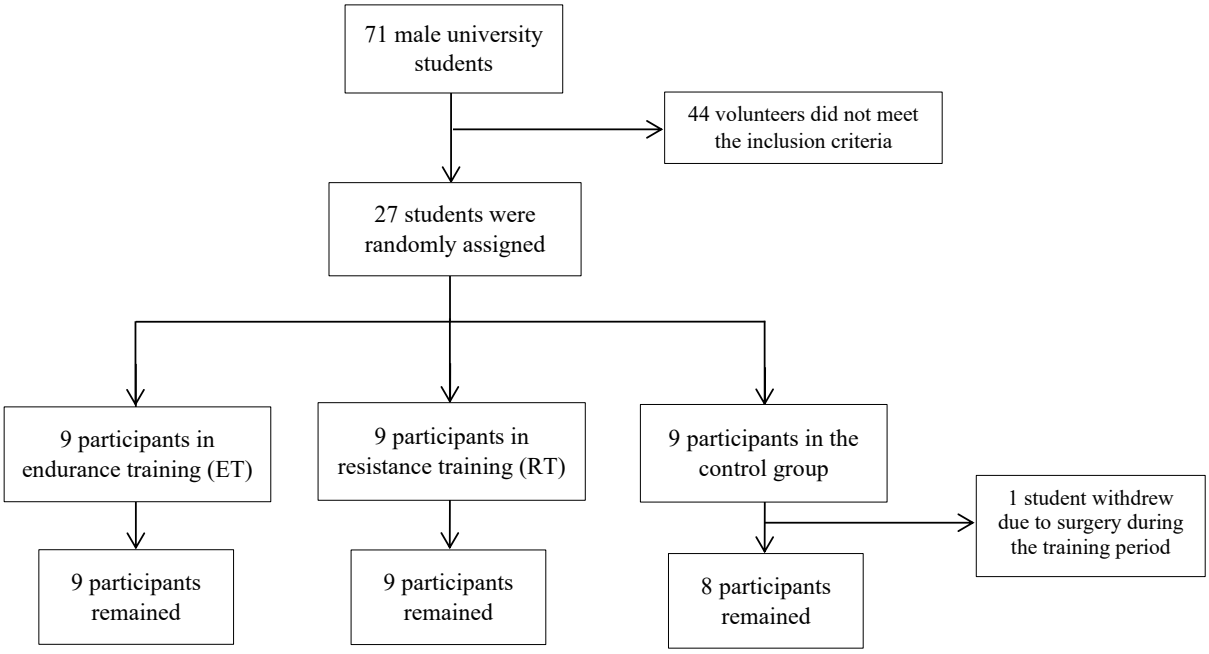

FIGURE 1. flowchart of participant recruitment

posted on the walls throughout the university. Volunteers were then checked for the eligibility and if proven eligible, would sign the written informed consent and be recruited to the study. We used the permuted block randomization with quadruple blocks. Twenty blocks were produced and in order to apply the concealment in the randomization process, unique codes were written on a piece of paper and were put in similar envelopes. Concealed envelopes were then used to randomly allocate the patients to either RT (n=9), ET (n=9) or the control group (n=9) (Figure 1). Technicians taking blood samples, lab technicians performing biochemical assessment and the statistical analysist were blinded to the randomization.

Participants completed a questionnaire on general information and then assessed for the anthropometric indices. Body weight was measured with minimal clothing using the Seka scale (Hamburg, Germany). Height was measured standing up without shoes using a tape measure. BMI was calculated by dividing weight (kg) by squared height (m). Two samples of 10ml blood were collected from the participants after a 12h overnight fast, 48h before beginning the first training session and 48h after the last session. These samples were centrifuged at 4000rpm for 10min, after that serum samples were separated and stored at -80°C. Biochemical analysis of the fasting blood glucose (FBG) level were determined through enzymatic colorimetric method by commercial kits (Pars Azmoon, Tehran, Iran). Plasma insulin level was measured using an ELISA kit (Mercodia, Sweden) with a sensitivity of less than 1 micro-units/l and within a range of 1-200 micro-units/l. Serum adropin level was measured using ELIZA kit (Zellbio, Germany). Homeostasis model assessment of insulin resistance (HOMA-IR) was assessed using FBG and fasting blood insulin (FBI) according to this equation (Matthews et al., 1985):

$$HOMA - IR = \frac{\text{FBG} \times \text{FBI}}{22.5}$$

Quantitative insulin-sensitivity check index (QUICKI) was measured based on the following equation (Katz et al., 2000):

$$QUICKI = \frac{1}{\log FBI + \log FBG}$$

Exercise training programs

All participants were briefed on how to work with fitness machines at the gym and were involved in the exercise program 3 nonconsecutive sessions per week, for 8 consecutive weeks. A 10min warm-up consisting of stretching of the major muscle groups and slow walking was carried out preceding the main exercise.

The RT exercise included 10 stationary movements

TABLE 1: Protocol of resistance and endurance training

		Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8
ET	Exercise Duration (minute)	15	15	20	25	30	35	35	40
	Intensity (percent/maximum HR)	50	50	60	60	70	70	80	80
RT	Set/ Repetition	2×10	3×10	3×10	3×10	3×10	3×10	4×8	4×6
	Resistance (1RM percent)	30	30	40	40	50	60	60	70

HR: heart rate, RT: resistance training, ET: endurance training, RM: repetition maximum.

in a circular motion and there were 12 repetitions per station, 30s between each station and 2min rest between rounds. Movements included warm-up, chest press, half-squat, sit-ups, arm bends, launch, torso opening and cooling (1 to 2min rest between the sets, and 3-5min rest between the stations). To calculate the maximum strength of the subjects, a certain weight was selected and exercise using that weight was performed to the point of exhaustion. Then, by placing the amount of weight and the number of repetitions in the relevant formula, the maximum strength was estimated. Relative maximum strength was calculated from the maximum power distribution per body movement:

1 repetition maximum (RM) = (weight) / ((repetition × 0.0278)- 1.0278)

During week 1, two sets of 6 repetitions with 30% of 1RM were performed. For weeks 2 to 6, three sets of 10 repetitions were performed (week 2 with 30% of 1RM, week 3 with 40% of 1RM, week 4 with 40% of 1RM, week 5 with 50% of 1RM, and week 6 with 60% of 1RM). During week 7, four sets of 8 repetitions with 60% of 1RM were performed and finally, during week 8, four sets of 6 repetitions with 70% of 1RM were performed (Table 1).

In the ET group, to determine the intensity of endurance activity, the 10-point Borg scale was used along with the maximum heart rate (HR). The maximum HR was calculated using the following formula: age-220 = maximum heart rate. On weeks 1 and 2, the duration of activities was 15min with the intensity of 50% of the maximum HR (score 3-4 of the pressure perception scale). For weeks 3 and 4, the duration increased to 20-25min with the intensity of 60% of the maximum HR (score 5-6 of the pressure perception scale). For weeks 5 and 6, the duration was between 30 and 35min with the intensity of 70% of the maximum HR (score 7-8 of the pressure perception scale). And finally, for weeks 7 and 8, the duration was between 35 and 40min with the intensity of 80% of the maximum HR (score 9-10 of the pressure perception scale). Obviously, the overload principle increased according to the program and the improvement of endurance from 15min of exercise with the intensity of 40% the maximum HR, to 40min of exercise with the intensity of 80% the maximum HR (Table 1).

Statistical analysis

To assess the normality of the variables, the Shapiro-Wilk test was used. Continuous variables were represented as mean and standard deviations (mean±SE). To compare the data between the three groups at the baseline, one-way ANOVA was used (to increase the comparability of the data and reduce type I error). To compare the outcomes between the three groups after the intervention with adjustment for baseline amounts, ANOVA and Banferroni post hoc test were used was used. $P<0.05$ was considered statistically significant. All statistical analyses were performed using the SPSS. VERSION 22 (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.).

Results

Of the 27 overweight participants, 1 student from the control group (due to surgery during the training period) withdrew the study and finally, the study was completed with 26 participants (9 in RT, 9 in ET and 8 in the control group; Figure 1). Table 2 summarizes the demographic and anthropometric characteristics of the participants. Students in the RT, ET and control group had a mean age of 22.40, 22.62 and 23.12 years respectively, with no significant difference between the

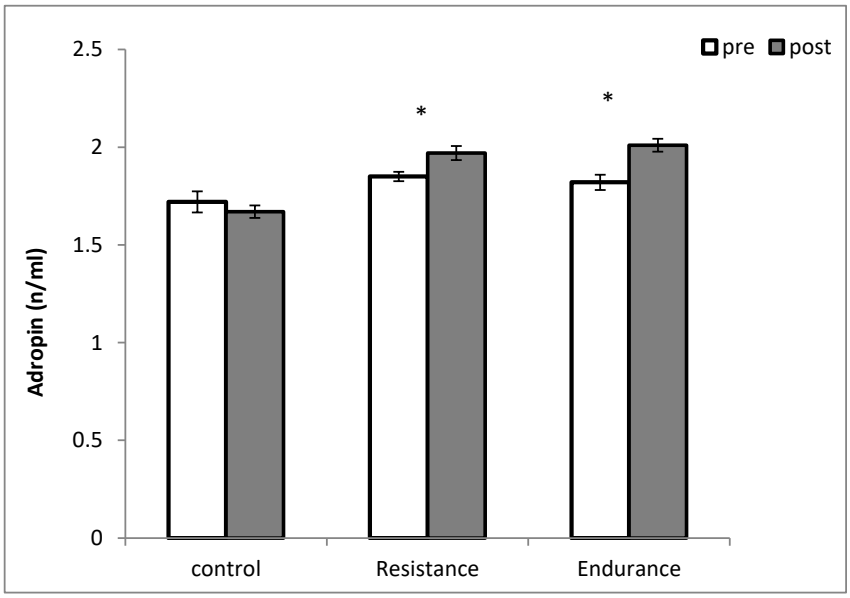

FIGURE 2. Changes in adropin within and between the three groups. Data are mean ± SE.

TABLE 2: Baseline characteristics of the participants.

Variable	RT (n=9)		ET (n=9)		Control (n=8)	
	Mean	SE	Mean	SE	Mean	SE
Age (year)	22.40	0.65	22.62	0.73	23.12	0.55
Height (cm)	175.50	1.64	170.88	1.46	172.38	1.40
Weight (kg)	83.80	2.17	80.62	0.94	81.75	1.97
BMI (kg/m^2)	27.15	0.27	27.63	0.40	27.49	0.43
Fat mass (%)	23.70	4.40	24.10	4.74	24.2	3.92
WHR	0.89	0.3	0.89	0.03	0.88	0.03

RT: Resistance Training, ET: Endurance Training, BMI: Body Mass Index, WHR: waist-to-hip ratio. No significant differences were found between the groups (P> 0.05, one-way analysis of variance)

three groups (P>0.05). ANOVA test also showed no remarkable difference between the three groups regarding height, weight, BMI, waist to hip ratio or body fat mass at baseline (P>0.05, P-values are not reported according to CONSORT 2011).

The result of ANOVA analysis is represented in Table 3. This test showed no significant differences among the three groups in terms of FBG (P=0.32) or QUICKI (P=0.91). In contrast, a significant difference was detected regarding adropin (P=0.001, and HOMA-IR (P=0.015) between the three studied groups. There was a significant reduction in FBI level (P=0.001) and a significant increase in serum adropin level in the RT and ET groups after the intervention (P<0.05), while such change was not observed for the mentioned variables in the control group (P>0.05). Plus, adropin changes in the ET group was slightly greater than that of RT group (mean change: 0.19 vs 0.12 ng/ml). However, Bonferroni post-hoc test showed that ET and RT were significantly higher compared to the control group (P=0.001), but no significant difference was observed between ET and RT (P=0.18). Highest reduction in terms of HOMA-IR was observed in the ET group (mean change: -0.68).

Discussion

The results of this clinical trial demonstrated that 8 weeks of RT and ET could significantly improve adropin, and reduce HOMA-IR and FBI in overweight young men, while such changes did not occur in the control group. FBG although was not significantly reduced following the intervention. Also, the effect of ET in improving metabolic health was slightly greater than RT.

Adropin is a secretory protein expressed in liver,

TABLE 3: Changes in adropin and markers of glucose metabolism before and after training.

variable	group	Before	After	Change	*p*- value
HOMA-IR	Control	3.07 ± 0.86	2.83 ± 0.13	-0.24 ± 0.73	0.015
	RT	2.95 ± 0.07	2.48 ± 0.05	-0.47 ± 0.02	
	ET *	3.12 ± 0.07	2.44 ± 0.10	-0.68 ± 0.03	
FBG (mg/dl)	Control	98.62 ± 2.52	94.52 ± 2.62	-4.10 ± 0.10	0.32
	RT	97.70 ± 1.68	96.72 ± 1.92	-0.98 ± 0.24	
	ET	99.25 ± 1.50	91.52 ± 3.14	-7.73 ± 1.64	
FBI (IU/ml)	Control	12.43 ± 0.30	11.92 ± 0.25	-0.51 ± 0.05	0.0001
	RT *	12.20 ± 0.13	10.41 ± 0.10	-1.79 ± -0.03	
	ET *	12.69 ± 0.29	10.80 ± 0.22	-1.89 ± 0.07	
QUICKI	Control	0.32 ± 0.05	0.32 ± 0.07	0.00 ± 0.02	0.91
	RT	0.33 ± 0.05	0.32 ± 0.08	0.01 ± 0.03	
	ET	0.33 ± 0.04	0.32 ± 0.07	0.01 ± 0.07	

RT: Resistance Training, ET: Endurance Training, FBG: Fasting Blood Glucose, FBI: Fasting Blood Insulin, HOMA-IR: Homeostasis model assessment of insulin resistance, QUICKI: Quantitative insulin-sensitivity check index. *significant change after the intervention (P<0.05). Results are presented as mean±SE.

brain, umbilical vein and coronary artery endothelial cells (Kumar et al., 2008). As reported by previous studies, serum adropin levels are significantly lower in overweight and obese individuals, which turns it into a risk factor for coronary heart disease, hypertension and metabolic syndrome (Gu et al., 2015; Yosaee et al., 2017; Yosaee et al., 2016). This research found that 8 weeks of ET and RT could increase serum adropin level in overweight men. Our result is in accordance with that of Kumar et al. (2008) who conducted an animal study, in which adropin was administered to diet-induced obese mice, and resulted in markedly attenuated insulin resistance and glucose intolerance. Fuji et al. (2017) also found that aerobic exercise could significantly enhance serum adropin level in older adults. Unfavorably, Sanchis-Gomar et al. (2015) reported that serum adropin level did not change significantly in football players after one season of training. This does not challenge the findings of the present study, as those participants were professional soccer players, while our participants were 20-28-year-old youngsters with no professional exercise background.

The mechanism of the exercise-induced growth in serum adropin level is still not clear. Since the result of this study indicated that ET might more effectively improve adropin than RT, changes in VO_2max may be involved in increased adropin secretion. It is suggested that adropin suppresses glucose production in hepatocytes (Gao et al., 2019) and controls the metabolism of glucose and lipids in skeletal muscles (Gao et al., 2014). *In vivo* studies also showed that adropin could modestly increase whole-body insulin sensitivity (Thapa et al., 2019). Therefore, both ET and RT could be suggested to overweight young adults, in order to improve their glucolipid metabolism. We also found that ET could significantly reduce HOMA-IR, and ET and RT could remarkably increase FBI after 8 weeks in overweight students. Similarly, Hansen et al. (2012) found that endurance resistance training caused a significant reduction in the FBI level, and a positive change in insulin sensitivity in people at risk of type 2 diabetes. Poehlman et al. (2000) designed a similar study as ours, and compared the effect of ET and RT on metabolic outcomes in nonobese, young women. Although the duration of intervention in that study was longer (6 months), they too found that ET had a significantly greater effect on improving insulin sensitivity than that of RT.

In this study, HOMA-IR reduced significantly while QUICKI did not change. However, this was not contrary to our expectations, as assessment of correlation between HOMA-IR and QUICKI showed an average Pearson correlation coefficient of -0.55 (Rudvik and Månsson 2018). This shows that a reduction in HOMA-IR is not always accompanied by an increase in QUICKI.

Besides, a revised version of QUICKI was developed (which could not be calculated and reported in the present study, because we did not collect the information on non-esterified fatty acids in our participants) as the original QUICKI could not predict insulin sensitivity very well (Otten et al., 2014). Also, it has been reported that HOMA-IR is a better index in Iranian non-diabetic individuals (Esteghamati et al., 2010). Hence, it could be assumed that in this trial, insulin resistance has been significantly reduced.

The reduction of serum insulin and insulin resistance following ET and RT could be explained by reduction in total and visceral body fat caused by exercise (Despres et al., 1991; Kirwan et al., 1993). On the other hand, increased serum adropin level improves insulin sensitivity in obese adults (Jasaszwili et al., 2020). Adropin administration could reduce blood glucose level, improve insulin sensitivity and suppress inflammatory markers in a rat model of type 2 diabetes (Akcilar et al., 2016). Therefore, reduction of HOMA-IR in this clinical trial may have occurred following the increase in adropin level.

The present study had a number of limitations including the inability to control all confounding factors affecting the result of our intervention, such as genetic and congenital characteristics of the participants, and their psychological and spiritual conditions (such as fatigue and sleep quality) during the course of the study. We also could not report the influence of ET and RT on body fat mass and free fat mass, due to our limited facilities and budget. This study had plenty of strengths too. We compared the effect of ET and RT in the presence of a control group, which assures the reliability of our findings. We chose the university campus as our sampling site, so that our participants would all dine in the university and have the same dietary intakes, and we could control the effect of an important confounder, diet, on our results. Furthermore, using validated and reliable tools to measure the outcomes was another strength of the present research.

Conclusion

The results of this randomized clinical trial showed that 8 weeks of RT and ET had beneficial impacts on adropin and markers of glucose metabolism in overweight young men, with a favorable effect observed for ET. Therefore, adding RT and/or ET to the routine treatment of overweight youngsters could be suggested to improve their metabolic profile and prevent from adverse complications. Further studies on the mechanism of serum adropin enhancement following exercise are needed. We also suggest that other researchers conduct the same trial with different intensity and duration of RT and ET, and with a post-hoc Tukey test to further clarify the possible benefits of such exercises on metabolic profile following each exercise.

Acknowledgment

We should thank the students who cooperated and volunteered to participate in this study.

Conflict of interest

None to be declared.

References

Akcilar R, Kocak F, Simsek H, Akcilar A, Bayat Z, Ece E, et al. Antidiabetic and hypolipidemic effects of adropinin streoptozotocin-induced type 2 diabetic rats. Bratisl Lek Listy 2016; 117: 100. https://doi.org/10.4149/BLL_2016_020

Alizadeh R, Golestani N, Moradi L, Rezaeinejad N. Effect of aerobic exercise with maximal fat oxidation intensity, on adropin and insulin resistance among overweight women. Iranian J Endocrin Metab 2018; 20: 81-88.

Beckers PJ, Denollet J, Possemiers NM, Wuyts FL, Vrints CJ, Conraads VM. Combined endurance-resistance training vs. endurance training in patients with chronic heart failure: a prospective randomized study. Eur Heart J 2008; 29: 1858-1866. https://doi.org/10.1093/eurheartj/ehn222

Chen R M, Yuan X, Ouyang Q, Lin X Q, Ai Z Z, Zhang Y, et al. Adropin and glucagon-like peptide-2 are associated with glucose metabolism in obese children. World J Pediatr 2019; 15: 565-571. https://doi.org/10.1007/s12519-019-00296-6

Dengel DR, Pratley RE, Hagberg JM, Rogus EM, Goldberg AP. Distinct effects of aerobic exercise training and weight loss on glucose homeostasis in obese sedentary men. J Appl Physiol 1996; 81: 318-325. https://doi.org/10.1152/jappl.1996.81.1.318

Despres JP, Pouliot MC, Moorjani S, Nadeau A, Tremblay A, Lupien P, et al. Loss of abdominal fat and metabolic response to exercise training in obese women. Am J Physiol Endocrinol Metab 1991; 261: 159-167. https://doi.org/10.1152/ajpendo.1991.261.2.E159

Esteghamati A, Ashraf H, Khalilzadeh O, Zandieh A, Nakh-

javani M, Rashidi A, et al. Optimal cut-off of homeostasis model assessment of insulin resistance (HOMA-IR) for the diagnosis of metabolic syndrome: third national surveillance of risk factors of non-communicable diseases in Iran (SuRFNCD-2007). Nutr Metab 2010; 7: 26-26. https://doi.org/10.1186/1743-7075-7-26

Fujie S, Hasegawa N, Kurihara T, Sanada K, Hamaoka T, Iemitsu M. Association between aerobic exercise training effects of serum adropin level, arterial stiffness, and adiposity in obese elderly adults. Appl Physiol Nutr Metab 2017; 42: 8-14. https://doi.org/10.1139/apnm-2016-0310

Gao S, Ghoshal S, Zhang L, Stevens JR, McCommis KS, Finck BN, et al. The peptide hormone adropin regulates signal transduction pathways controlling hepatic glucose metabolism in a mouse model of diet-induced obesity. J Biol Chem 2019; 294: 13366-13377. https://doi.org/10.1074/jbc.RA119.008967

Gao S, McMillan RP, Jacas J, Zhu Q, Li X, Kumar GK, et al. Regulation of substrate oxidation preferences in muscle by the peptide hormone adropin. Diabetes 2014; 63: 3242-3252. https://doi.org/10.2337/db14-0388

Greenberg A, McDaniel M. Identifying the links between obesity, insulin resistance and β-cell function: potential role of adipocyte-derived cytokines in the pathogenesis of type 2 diabetes. Eur J Clin Invest 2002; 32: 24-34. https://doi.org/10.1046/j.1365-2362.32.s3.4.x

Gu X, Li H, Zhu X, Gu H, Chen J, Wang L, et al. Inverse correlation between plasma adropin and ET-1 levels in essential hypertension: a cross-sectional study. Medicine 2015; 94. https://doi.org/10.1097/MD.0000000000001712

Hall J E. 2010. Guyton and Hall textbook of medical physiology e-Book (Elsevier Health Sciences).

Hansen E, Landstad BJ, Gundersen KT, Torjesen PA, Svebak S. Insulin sensitivity after maximal and endurance resistance training. J Strength Cond Res 2012; 26: 327-334. https://doi.org/10.1519/JSC.0b013e318220e70f

Jasaszwili M, Billert M, Strowski MZ, Nowak KW, Skrzypski M. Adropin as a fat-burning hormone with multiple functions-review of a decade of research. Molecules 2020; 25: 549. https://doi.org/10.3390/molecules25030549

Kahn BB, Flier JS. Obesity and insulin resistance. J Clin Invest 2000; 106: 473-481. https://doi.org/10.1172/JCI10842

Katz A, Nambi SS, Mather K, Baron AD, Follmann DA, Sullivan G, et al. Quantitative insulin sensitivity check index: a simple, accurate method for assessing insulin sensitivity in humans. J Clin Endocrinol Metab 2000; 85: 2402-2410. https://doi.org/10.1210/jcem.85.7.6661

Kirwan JP, Kohrt WM, Wojta DM, Bourey RE, Holloszy JO. Endurance exercise training reduces glucose-stimulated insulin levels in 60-to 70-year-old men and women. J. Gerontol 1993; 48: 84-90. https://doi.org/10.1093/geronj/48.3.M84

Kopelman P. Health risks associated with overweight and obesity. Obes Rev 2007; 8: 13-17. https://doi.org/10.1111/j.1467-789X.2007.00311.x

Kuczmarski RJ, Flegal KM, Campbell SM, Johnson CL. Increasing prevalence of overweight among US adults: the National Health and Nutrition Examination Surveys, 1960 to 1991. Jama 1994; 272: 205-211. https://doi.org/10.1001/jama.1994.03520030047027

Kumar KG, Trevaskis JL, Lam DD, Sutton GM, Koza RA, Chouljenko VN, et al. Identification of adropin as a secreted factor linking dietary macronutrient intake with energy homeostasis and lipid metabolism. Cell Metab 2008; 8: 468-481. https://doi.org/10.1016/j.cmet.2008.10.011

Matthews D, Hosker J, Rudenski A, Naylor B, Treacher D, Turner R. Homeostasis model assessment: insulin resistance and β-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 1985; 28: 412-419. https://doi.org/10.1007/BF00280883

Mokdad AH, Ford ES, Bowman BA, Dietz WH, Vinicor F, Bales VS, et al. Prevalence of obesity, diabetes, and obesity-related health risk factors, 2001. Jama 2003; 289: 76-79. https://doi.org/10.1001/jama.289.1.76

Nishida Y, Tokuyama K, Nagasaka S, Higaki Y, Shirai Y, Kiyonaga A, et al. Effect of moderate exercise training on peripheral glucose effectiveness, insulin sensitivity, and endogenous glucose production in healthy humans estimated by a two-compartment-labeled minimal model. Diabetes 2004; 53: 315-320. https://doi.org/10.2337/diabetes.53.2.315

Otten J, Ahrén B, Olsson T. Surrogate measures of insulin sensitivity vs the hyperinsulinaemic-euglycaemic clamp: a meta-analysis. Diabetologia 2014. https://doi.org/10.1007/s00125-014-3285-x

Poehlman ET, Dvorak RV, DeNino WF, Brochu M, Ades PA. Effects of resistance training and endurance training on insulin sensitivity in nonobese, young women: a controlled randomized trial. J Clin Endocrinol Metab 2000; 85: 2463-2468. https://doi.org/10.1210/jcem.85.7.6692

Rice B, Janssen I, Hudson R, Ross R. Effects of aerobic or resistance exercise and/or diet on glucose tolerance and plasma insulin levels in obese men. Diabetes Care 1999; 22: 684-691. https://doi.org/10.2337/diacare.22.5.684

Rudvik A, Månsson M. Evaluation of surrogate measures of insulin sensitivity - correlation with gold standard is not enough. BMC Med Res Methodol 2018; 18: 64-64. https://doi.org/10.1186/s12874-018-0521-y

Ryan AS, Nicklas BJ. Reductions in plasma cytokine levels with weight loss improve insulin sensitivity in overweight and obese postmenopausal women. Diabetes Care 2004; 27: 1699-1705. https://doi.org/10.2337/diacare.27.7.1699

Sanchis-Gomar F, Alis R, Rampinini E, Bosio A, Ferioli D, La Torre A, et al. Adropin and apelin fluctuations throughout a season in professional soccer players: are they related with performance? Peptides 2015; 70: 32-36. https://doi.org/10.1016/j.peptides.2015.05.001

Thapa D, Xie B, Manning JR, Zhang M, Stoner MW, Huckestein BR, et al. Adropin reduces blood glucose levels in mice by limiting hepatic glucose production. Physiol Rep 2019; 7. https://doi.org/10.14814/phy2.14043

WHO. 2020. 'Obesity and overweight', Accessed 10/22/2020. https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight.

Wong C-M, Wang Y, Lee JTH, Huang Z, Wu D, Xu A, et al. Adropin is a brain membrane-bound protein regulating physical activity via the NB-3/Notch signaling pathway in mice. J Biol Chem 2014; 289: 25976-25986. https://doi.org/10.1074/jbc.M114.576058

Yosaee S, Khodadost M, Esteghamati A, Speakman J R, Shidfar F, Nazari M N, et al. Metabolic syndrome patients have lower levels of adropin when compared with healthy overweight/obese and lean subjects. Am J Mens Health 2017; 11: 426-434. https://doi.org/10.1177/1557988316664074

Yosaee S, Soltani S, Sekhavati E, Jazayeri S. Adropin-a novel biomarker of heart disease: a systematic review article. Iran J Public Health 2016; 45: 1568.