## JOURNAL OF CONTEMPORARY MEDICINE

DOI:10.16899/jcm.1223872 J Contemp Med 2023;13(1):82-85

Original Article / Orijinal Araştırma



# The Effect of Exercise on Serum Resistin and Leptin Values in Rats Fed with a High Fat Diet

## Yüksek Yağlı Diyetle Beslenen Ratlarda Egzersizin Serum Resistin ve Leptin Değerlerine Etkisi

### Bahattin Bulduk<sup>1</sup>, DNizamettin Günbatar<sup>2</sup>

<sup>1</sup>Van Yüzüncü Yıl University, Van Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Van, Turkey <sup>2</sup>Van Yüzüncü Yıl University, Van Facuty of Health Sciences, Department of Nursing, Van, Turkey

### Abstract

**Aim**: This study was performed to investigate the effect of exercise on serum resistin and leptin values in rats fed with a high-fat diet.

**Material and Method**: 24 Wistar albino male rats were used in the study. They were randomly divided into 4 groups, with 6 rats in each group. The groups were determined as the control group (C), exercise group (E), high-fat diet (HFD) group, and high-fat diet + exercise (HFDE) group.

**Results**: In this study, resistin values were found to be similar in the C, E, and HFDE groups, but different in the HFD group. It was determined that the resistin value in the HFD group was higher than the other groups. It was observed that exercise decreased the value of rising resistin. When evaluated in terms of leptin levels, the C and E groups showed similarity, while the HFD and HFDE groups showed similarity with each other. Although exercise slightly decreased the leptin level, which was highly increased with a high-fat diet, it was not statistically significant.

**Conclusion**: It has been determined that feeding with a high-fat diet causes an increase in serum resistin and leptin levels, and exercise provides a significant decrease in resistin values, but is not effective in leptin levels.

## Öz

**Amaç**: Bu çalışma, yüksek yağlı diyetle beslenen ratlarda egzersizin serum resistin ve leptin değerlerine nasıl bir etkisinin olacağını araştırmak için yapıldı.

**Gereç ve Yöntem**: Çalışmada 24 adet Wistar albino ırkı erkek rat kullanıldı. Her grupta 6 adet rat olacak şekilde rastgele 4 gruba ayrıldı. Gruplar kontrol grubu (C), egzersiz grubu (E), yüksek yağlı diyet (HFD) grubu ve yüksek yağlı diyet + egzersiz (HFDE) grubu olarak belirlendi.

**Bulgular**: Bu araştırmada resistin değerleri C, E, ve HFDE gruplarında benzer, HFD grubunda ise farklı bulunmuştur. HFD grubunda resistin değerinin, diğer gruplara göre yüksek olduğu tespit edilmiştir. Egzersizin yükselen resistin değerini düşürdüğü görülmüştür.

Leptin seviyeleri açısından değerlendirildiğinde C ve E grubu benzerlik gösterirken, HFD ve HFDE grupları da birbiri ile benzerlik göstermektedir. Yüksek yağlı diyet ile oldukça artan leptin seviyesini egzersiz bir miktar düşürse de, istatistiksel açıdan anlamlı bulunmamıştır.

**Sonuç**: Yüksek yağlı diyet ile beslenmenin serum resistin ve leptin düzeylerinde artışa sebep olduğu, egzersizin resistin değerlerinde anlamlı bir düşüş sağladığı fakat leptin düzeylerinde etkili olmadığı tespit edilmiştir.

Keywords: Resistin, Leptin, Exercise, High-fat diet

Anahtar Kelimeler: Resistin, Leptin, Egzersiz, Yüksek yağlı diyet



The phenomenon of high-fat dietary nutrition and related obesity observed in Western societies has become a worldwide recognized problem. It is a well-known fact that high-fat dietary nutrition and obesity are the triggers and causes of many diseases.<sup>[1]</sup> High-fat diets cause disruption of energy balance and increase in adipose tissue mass. Regular exercise reduces the amount of fat in the body. It is known that exercise reduces deaths due to heart diseases, prevents osteoporosis and hypertension, as well as plays an important role in protecting against diseases such as diabetes and obesity.<sup>[2-4]</sup>

Resistin has been defined as a special hormone belonging to adipose tissue and has been reported to be associated with obesity, metabolic syndrome and diabetes. It is known that the release of resistin increases in obesity caused by diet. Resistin both prevents glucose from entering the cell and causes insulin resistance.<sup>[5,6]</sup> Leptin is a peptide hormone that has protein structure. Its rate in the body is directly proportional to the amount of adipose tissue. Leptin is known to be effective on growth and development, determining the metabolic rate and activating the sympathetic nervous system.<sup>[7,8]</sup> Leptin levels decrease with weight loss and increase with weight gain. As the number and size of fat cells in the body increase, leptin production increases and begins to be released into the circulation. When increased leptin reaches the hypothalamus, it reduces food intake.<sup>[9]</sup>

#### MATERIAL AND METHOD

This study was carried out with the permission dated 31/03/2022 and numbered 2022/03-05 given by Van Yüzüncü Yıl University Animal Experiments Local Ethics Committee. 24 Wistar albino male rats were used in the study. All conditions were met according to laboratory animal care standards. Rats were randomly divided into 4 groups, with 6 rats in each group.

**1. Control (C) Group:** Standard nutrition program was applied to this group. During the experiment, normal pellet rat food and tap water were given.<sup>[10]</sup>

**2. Exercise (E) Group:** Along with the standard nutrition program, an exercise program was applied 3 days a week.

**3. High-Fat Diet (HFD) Group:** In the high-fat diet group, 300 g/kg margarine was melted and added to the standard pellet meal. The prepared mixture was applied daily for 8 weeks.<sup>[11]</sup>

**4. High Fat Diet + Exercise (HFDE) Group:** In this group, 300 g/kg margarine was melted and added to standard pellet feed. The prepared mixture was applied daily for 8 weeks. At the same time, an exercise program was applied 3 days a week.<sup>[10,11]</sup>

Exercise testing was performed on a Rat-specific treadmill. In order for the rats in the exercise group to adapt to the treadmill, after running at the lowest speed of the protocol for a period of 2 weeks (15 min/day), the treadmill protocol was adapted for 17 cm/sec speed to be 40 cm/sec at medium intensity (30 mins/day), 3 days a week.<sup>[10]</sup>

Test animals were anesthetized with Ketamine HCL (50 mg/kg) at the end of the 8th week. The blood taken from the hearts of the animals with the help of syringes were transferred to biochemistry tubes. After the tubes were centrifuged, serums were obtained. Commercial kits used in the study were determined by ELISA in accordance with the kit procedure.

Statistical Analysis: One-way Anova test was used for the analysis because the groups for resistin were normally distributed, and the group variances were homogeneous. Since the groups for leptin were not normally distributed and the group variances were not homogeneous, the Kruskal wallis test, one of the non-parametric tests, was used for analysis. Tukey test, one of the Post-Hoc tests, was used to determine the significant groups. The statistical significance level was taken as 5% in the calculations and the SPSS (ver.21) statistical package program was used for the calculations.

#### RESULTS

The effect of exercise on serum resistin and leptin values and statistical data in rats fed with a high-fat diet are given in **Table 1**.

Table 1. Resistin and leptin levels of the groups used in the study.			
Groups	Ν	Resistin	Leptin
Control (C) Group	6	4.34±0.20 <sup>b</sup>	613.76±18.97 <sup>b</sup>
Exercise (E) Group	6	4.26±0.22 <sup>b</sup>	607.24±12.95 <sup>b</sup>
High-Fat Diet (HFD) Group	6	4.87±0.24ª	1690.76±201.81ª
High Fat Diet + Exercise (HFDE) Group	6	4.42±0.18 <sup>b</sup>	1584.16±140.55ª
* Different letters in the same column indicate statistical significance at p< 0.05. a,b: Shows the difference between groups (Tukey)			

When the findings obtained in this study were evaluated statistically, it was determined that the resistin values were similar in the C, E and HFDE groups, and higher in the HFD group compared to the other groups. It was observed that resistin value increased with high-fat diet and decreased with exercise. When evaluated in terms of leptin levels, the K and E groups show similarity, while the HFD and HFDE groups show similarity with each other. Although exercise slightly decreased the leptin level, which was highly increased with a high-fat diet, it was not found to be statistically significant.

#### DISCUSSION

In this study conducted to examine the effects of high-fat diet and exercise on serum resistin and leptin values in rats, it was determined that feeding a high-fat diet increased the level of resistin in rats. Pagano et al. (2005) found in their study that serum resistin level was directly related to obesity.<sup>[12]</sup> It is known that serum resistin levels increase in rats set up with an experimental diet.<sup>[13]</sup> Steppan et al. showed in their study in 2001 that resistin is a hormone belonging to adipose tissue and its amount in the body is directly proportional to the amount of fat.<sup>[5]</sup> In another study, they reported that obesity and resistin were related, and body fat mass and serum resistin level were related.<sup>[14]</sup> Koerner et al. (2005) stated in their study that the nutritional character had an effect on the level of resistin, the amount decreased with hunger, and increased again with food intake.<sup>[15]</sup> In a study, they found that 12 weeks of exercise and a low-calorie diet decreased the level of resistin.<sup>[16]</sup> The reason for this decrease in resistin level was also reported as weight loss. It has been found that exercise performed 4 times a week for 4 months causes a decrease in the level of serum resistin.<sup>[17]</sup> In studies on test animals, it has been reported that resistin causes changes in insulin metabolism in cells and increases glucose production in the liver, resulting in insulin resistance.<sup>[18]</sup> It was determined that in mice fed a high-fat diet, insulin resistance developed, and with the subsequent resistin oligonucleotide treatment, insulin resistance decreased.<sup>[19]</sup> In another study, it was shown that resistin is effective in liver cells and causes insulin resistance.<sup>[20]</sup> It can be considered that in this study, serum resistin level increased in rats fed a high-fat diet, and this was due to the weight gain in rats. As in the literature, it has been determined that the diet that causes weight gain increases the serum resistin level, and there is no increase in rats that are not fed with a high-fat diet. Resistin values were similar in the C, E and HFDE groups, but higher in the HFD group. When HFDE and HFD groups were compared, the difference between the resistin values was found to be statistically significant. Resistin values did not increase in the HFDE group, in which both high-fat diet and exercise were applied, and showed parallelism with the control group. When the studies conducted in recent years are examined, it has been reported that regular exercise is beneficial in diseases such as diabetes, high blood pressure and cardiovascular diseases, and reduces the risks.<sup>[21]</sup> In this study, it was determined that the increase in serum resistin levels caused by high-fat diet decreased with exercise.

When this study was examined in terms of leptin levels, the C and E groups were found to be statistically similar to each other, but different when compared with the HFD and HFDE groups. When HFD and HFDE groups were compared with each other, the difference between leptin levels was not found to be significant. In other words, it was observed that feeding with a high-fat diet increased the leptin level, and although exercise slightly decreased the increased leptin level, it was not statistically significant. As it is known, the most important task of leptin in the organism is to reduce the risk of obesity by regulating food intake and energy metabolism.[22] Severe obesity has been reported in leptindeficient mice.<sup>[23]</sup> In another study, it was shown that leptin levels were quite high in obese mice, and this ratio did not change with exercise.<sup>[24]</sup> Although prolonged and heavy exercise reduces leptin level by approximately 1/3, it was observed that leptin level increased to the level before the exercise 18-24 hours after the exercise.[25] It is considered that this is not related with weight loss and rather the longterm fasting or exercise reduces leptin secretion by affecting fatty acids in the blood. In the study by Olive et al., it was

reported that the leptin level did not decrease immediately after the exercise, but decreased after a day or two. Another study found that leptin levels did not decrease even one day after exercise, but a decrease of approximately 30% was found after two days of exercise.<sup>[26]</sup> When the literature was searched, quite different opinions were found about the relationship between leptin and exercise. Generally, studies have reported that short-term exercise does not reduce leptin levels, and decreased leptin levels are also associated with circadian rhythm.<sup>[27,28]</sup> It has been determined that long-term exercises significantly reduce leptin levels, and the duration and form of exercise are important.[25,29,30] In this study, it was observed that feeding a high-fat diet significantly increased leptin levels, but exercise was not very effective in reducing leptin levels. It is considered that longer and more intense exercises can reduce leptin levels by affecting body fat ratio and free fatty acids in the blood.

#### CONCLUSION

As a result, significant increases were observed in both resistin and leptin levels in rats fed with a high-fat diet. It was observed that a 12-week exercise was effective in reducing the serum resistin level, but the duration and form of this exercise was not effective in reducing the leptin level. It is considered that longer and more vigorous exercises may produce different results.

#### ETHICAL DECLARATIONS

**Ethics Committee Approval:** The study was approved by the Van Yüzüncü Yıl University Animal Experiments Local Ethics Committee (Dater: 31/03/2022, Decision No: 2022/03-05).

**Informed Consent:** Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

**Financial Disclosure:** This study was supported by Van Yüzüncü Yıl University, Coordination Unit of Scientific Research Projects (P:VSYO-B256)

**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

#### REFERENCES

- 1. Mosby TT, Cosgrove M, Sarkardei S, et al. Nutrition in adult and childhood cancer:role of carcinogens and anti-carcinogens. Anticancer Res 2012;32(10):4171-92.
- 2. Toumilehto J, Lindström J, Eriksson JG, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med 2001;344:1343-50.
- Swinburn BA, Caterson I, Seidell JC, et al. Diet, nutrition and the prevention of excess weight gain and obesity. Public Health Nutr 2004;7(1a):123-46.

- 4. Kodama S, Tanaka S, Heianza Y, et al. Association between physical activity and risk of all-cause mortality and cardiovascular disease in patients with diabetes:a meta-analysis. Diabetes Care 2013;36(2):471-9.
- 5. Steppan CM, Bailey ST, Bhat S, et al. The hormone resistin links obesity to diabetes. Nature 2001;409(6818):307-12.
- 6. Ukkola O. Resistin-a mediator of obesity-associated insulin resistance or an innocent bystander?. Eur J Endocrinol 2002;147(5):571-4.
- 7. Lee GH, Proenca R, Montez JM, et al. Abnormal splicing of the leptin receptor in diabetic mice. Nature 1996;379(6566):632-5.
- 8. Fantuzzi G, Faggioni R. Leptin in the regulation of immunity, inflammation, and hematopoiesis. J Leukocyte Biol 2000;68(4):437-46.
- Keleş V, Büyükgüzel K, Büyükgüzel E. Leptin ve Metabolik Düzenlenmedeki Rolü. Türkiye Diyabet ve Obezite Derg 2018;2(1):17-22.
- 10. Yaşar S, Günbatar N, Yüksek S, et al. Effect of exercise on erythrocyte osmotic fragility in high fat diet fed rats during intermittent fasting. Eastern J Med 2017;22(4):176.
- 11. Günbatar, N, Bayıroğlu, F. The Effect of a Highly Saturated Fat Diet and Intermittent Fasting Diet on Experimental Colon Cancer Development and Some Serum Inflammation Markers in Rats, 1 Adiponectin and Lipid Metabolism . Van Veterinary J 2015;26 (3):123-7.
- 12. Pagano C, Marin O, Calcagno A, et al. Increased serum resistin in adults with prader-willi syndrome is related to obesity and not to insulin resistance. J Clin Endocrinol Metab 2005;90(7):4335-40.
- 13. Steppan CM, Lazar MA. Resistin and obesity-associated insulin resistance. Trends Endocrinol Metab 2002;13(1):18-23.
- 14. Eminler AT, Aygun C, Konduk T, et al. The relationship between resistin and ghrelin levels with fibrosis in nonalcoholic fatty liver disease. J Res Med Sci 2014;19 (11):1058.
- 15. Koerner A, Kratzsch J, Kiess W. Adipocytokines:leptin the classical, resistin the controversical, adiponectin—the promising, and more to come. Best Pract Res Clin Endocrinol Metab 2005;19(4):525-46.
- Jung SH, Park HS, Kim KS, et al. Effect of weight loss on some serum cytokines in human obesity:increase in IL-10 after weight loss. J Nutrition Biochem 2008;19(6):371-5.
- 17. Kadoglou NP, Perrea D, Iliadis F, et al. Exercise reduces resistin and inflammatory cytokines in patients with type 2 diabetes. Diabetes Care 2007;30(3):719-21.
- 18. Rajala MW, Obici S, Scherer PE, et al. Adipose-derived resistin and gutderived resistin-like molecule- $\beta$  selectively impair insulin action on glucose production. J Clin Invest 2003;111(2):225-30.
- 19. Muse ED, Obici S, Bhanot S, et al. Role of resistin in diet-induced hepatic insulin resistance. J Clin Invest 2004;114(2):232-9.
- 20. Palanivel R, Sweeney G. Regulation of fatty acid uptake and metabolism in L6 skeletal muscle cells by resistin. FEBS letters 2005;579(22):5049-54.
- 21. Kraemer RR, Castracane VD. Exercise and humoral mediators of peripheral energy balance:ghrelin and adiponectin. Experiment Biol Med 2007;232(2):184-94.
- 22. Lin TC, Huang KW, Liu CW, et al. Leptin signaling axis specifically associates with clinical prognosis and is multifunctional in regulating cancer progression. Oncotarget 2018;9(24):17210.
- Correia ML, Haynes WG. Obesity-related hypertension: is there a role for selective leptin resistance?. Curr Hypertens Rep 2004;6(3):230-5.
- 24. Pagano C, Marzolo M, Granzotto M, et al. Acute Effects of Exercise on Circulating Leptin in Lean and Genetically Obesefa/faRats. Biochem Biophysic Res Communicat 1999;255(3):698-702.
- 25. Landt M, Lawson GM, Helgeson JM, et al. Prolonged exercise decreases serum leptin concentrations. Metabolism 1997;46(10):1109-12.
- 26. Essig DA, Alderson NL, Ferguson MA, et al. Delayed effects of exercise on the plasma leptin concentration. Metabolism 2000;49(3):395-9.
- 27. Weltman A, Pritzlaff CJ, Wideman L, et al. Intensity of acute exercise does not affect serum leptin concentrations in young men. Med Sci Sports Exercise 2000;32(9):1556-61.
- 28. Kraemer R., Acevedo E, Synovitz L, et al. Leptin and steroid hormone responses to exercise in adolescent female runners over a 7-week season. Eur J Applied Physiol 2001;86(1):85-91.

- 29. Olive JL, Miller GD. Differential effects of maximal-and moderateintensity runs on plasma leptin in healthy trained subjects. Nutrition 2001;17(5):365-9.
- Gökbel H., et al. "Ratlarda zorlu egzersizde serum leptin düzeylerindeki değişme ve çinko eksikliği/takviyesiyle ilişkisi. I." Leptin Sempozyumu 2003;20-2.