

The Effect of Physical Activity and Responses of Leptin

Sh. Khoshemehry, M. J. Pourvaghar, M. E. Bahram

Abstract—In modern life, daily physical activity is relatively reduced, which is why the incidence of some diseases associated with overweight and obesity, such as hypertension, diabetes and other chronic illnesses, even in young people are observed. Obesity and overweight is one of the most common metabolic disorders in industrialized countries and in developing countries. One consequence of pathological obesity is cardiovascular disease and metabolic syndrome. In the past, it was believed that adipose tissue was ineffective and served only for storing triglycerides. In this review article, it was tried to refer to the esteemed scientific sources about physical activity and responses of leptin.

Keywords—Disease, leptin, obesity, physical activity.

I. INTRODUCTION

MODERN life has resulted in a relative decrease in daily physical activity; that is why some diseases associated with obesity, weight gain and inactivity including type 2 diabetes, hypertension, metabolic syndrome and other chronic diseases can be seen even in younger people [1]. Obesity is considered as a global pandemic in developed countries. More than one and a half million people in the world are suffering from overweight; and 400 million are suffering from obese disease [3], [2]. Surely, the problems with the change of lifestyle can be seen in the reduction of the amount of physical activity and increase in consumption of high-calorie foods in the past few decades [4]. Those, increased fat tissues that cause obesity, in addition to storing lipids, causes the secretion of several protein cytokines which has various biological effects [4]. Leptin is the most important peptide secreted from the adipose tissue [5]. Leptin is the product of the obesity gene and a secreted hormone transmitted to the brain. The amount of leptin in the blood stream depends on the body's fat tissue. In addition, several other factors also have some effects on serum leptin concentrations. Other factors such as weight loss, decreases leptin concentration; and weight gain increases it [6]. This protein hormone secreted from adipose tissue has molecular weight of 16 kDa (KDA) which play an important role in regulating body weight, appetite, satiety and hunger. In fact, leptin acts as a warning mechanism for adjusting body fat content. Despite numerous studies, pathophysiologic role of

leptin in human obesity has not been determined. This deficiency can be caused by factors such as the inability of leptin to pass which is resulted from blood-brain delay and inability to pair with neuropeptide Y; and thus, it is caused by change in the amount of food intake and a defect in signaling to the leptin receptor in the brain [7]. It has been shown that serum leptin levels are correlated with body fat percentage; and as a result of weight loss, leptin levels are reduced, too [3]. Leptin in normal conditions is an important regulator of energy homeostasis; but if the abnormal blood values appear, it will cause many health problems [8]. It is reported that the received energy regulates leptin gene expression in a negative and a positive way. Therefore, it is possible that changes in the received energy by physical activity depend on leptin levels [9]. Also, leptin by reducing food intake and stimulating energy expenditure affects the central nervous system, particularly the hypothalamus. Leptin increases fat oxidation and decreases triglyceride deposits in the skeletal muscle. The amount of stored body fat regulates leptin levels; the more number of fat cells in a person, the higher leptin levels will be in the blood. However, in obese and overweight, the leptin resistance in the hypothalamus receiver or reduction of these hormone receptors causes disruption of leptin and increases the levels of circulating leptin beyond the normal value [10], [8]. Also, serum leptin levels are directly connected to the body mass index, and high levels of it can increase fat mass and body weight. So, high levels of leptin should not only be seen as a consequence of adipose tissue, but also, this index should be considered as predictors and risk factors for weight gain and metabolic and cardiovascular diseases and diabetes. Leptin is basically produced in fat tissue. This protein is found in small quantities in other tissues, such as tissues of the abdominal, cardiac and epithelial tissue such as epithelium, breast and placenta. After having secreted by adipose tissue, leptin, like ghrelin, enter into the brain through adipose tissue. Leptin of the stomach reach the adipose tissue through the vagus nerve and the special nucleus. Leptin is a major peptide which is secreted from adipose tissue. Its serum concentration is an important environmental messenger in adjusting in the context of food and energy [9], [8]. The results of the study of the impact of exercise on serum leptin levels are quite contradictory. Moonikh and colleagues (2015) showed that plasma leptin and body composition did not change after six weeks of resistance training [10]. Burr and colleagues (2010) reported that insulin stimulated by the uptake and metabolism of glucose by fat cells was effective in lowering the concentration of plasma leptin after exercise [11]. Qin and colleagues (2010) reported that there was an increase in serum

Sh. Khoshemehry, is with the Ministry of Education, Tehran, I. R. Iran (phone: 0098 9122111134, fax: 0098315555333, sheydamehry@gmail.com).

M. J. Pourvaghar, Associate prof., is with the Department of Physical Education University of Kashan, Kashan, Iran (phone: 0098 21 77897752, fax: 0098315555333, vaghar@kashanu.ac.ir).

M. E. Bahram, is with the Faculty of Physical Education, University of Isfahan (phone: 0098 9132627940, fax: 0098 3155912543, bahramsport2010@gmail.com).

leptin after 40 days of high intensity interval training (HIIT) [12]. Soori and colleagues (2012) found that 16-weeks of intensive - average interval training decrease plasma leptin, fat percentage and waist-to-hip ratio [13]. In this regard, Hakimi and colleagues (2014) showed that there was significant decline in plasma leptin and body composition in young men in response to exercise extreme [14]. Many studies have shown that overweight is one of the independent markers of diabetes and cardiovascular disease in humans. Many environmental effects of leptin indicate the involvement of leptin in glucose and lipid metabolism, production of clotting and blood pressure regulation, and it plays an important role in energy homeostasis in humans and is considered as a messenger to set long-term fat by the brain.

II. LEPTIN RESPONSES TO PHYSICAL ACTIVITY

The results of a study showed that 12 weeks of intense interval exercise caused a significant decrease in the levels of plasma leptin, insulin, glucose, insulin resistance and adiposity indicators such as body weight, BMI, body fat and overweight men (WHR) [23]. These results are consistent with many findings of the studies done by Haghighi, Soori, Daryanoosh, Burr et al. [13], [11], [8], [1]. Daryanoosh et al. showed that 8 weeks of intense aerobic activity decreased the levels of leptin and insulin [8]. Soori et al. also reported that intense interval training plays an important role in improving and controlling fat metabolism in overweight and obese men by adjusting the levels of the hormone leptin and improving body composition [13], which confirms the results of the present study. It is reported that the reduction in plasma leptin concentration and body fat percentage after an extreme interval training is associated with increase in testosterone; and testosterone is associated with the effect on fat breakdown and increase in the number of beta-adrenergic receptors, adenylate cyclase, protein kinase A and lipase. Thus, it can improve metabolic function and body composition [17], [16], [13]. Although testosterone levels were not measured in this study, but due to the effect of the exercise protocol, improvements in body composition and decrease in leptin levels could be caused by the increase in testosterone levels [18], [16], [13]. Also, this study showed a significant decrease in insulin, weight and body fat percentage in the experimental group. Burr et al., in a study, showed that insulin by stimulating the uptake and metabolism of glucose via fat cells is effective in lowering the concentration of the plasma leptin after exercise [11]. The studies have shown that by reducing insulin, leptin levels will decrease, too; it will result in the entry of glucose into fat cells through protein glucose transporter (GLUT4); then, glucose acts as intracellular signals which stimulate the secretion of leptin from fat cells. It is likely that one of the mechanisms of reduced levels of leptin to be resulted from decrease in insulin levels causes decrease in insulin resistance and glucose after exercise training [19], [18]. Several physiological mechanisms, such as the activity of the sympathetic nervous system, changes in weight and energy balance, glucocorticoids, not eating and some unknown factors can widely change the levels of leptin, which is associated with fat

mass [21], [20]. Observations show that Leptin has effects on the hypothalamic receptors, and it prevents weight gain; and increase of leptin sensitivity is effective in preventing obesity and overweight [23], [22], [19]. Shirazy concluded that intense interval training for 12 weeks significantly reduced insulin resistance and leptin in obese men as well [23]. It is reported that three factors of insulin resistance, body weight and negative energy balance in the regulation of leptin are interrelated with each other. In this regard, it has been found that by blocking 3-kinase inositol phosphatidylinositol, a key enzyme in insulin signaling, the ability of leptin in fatty acid redistribution is largely disappeared in the oxidation and away from the path of stored fat [22], [21].

III. BENEFITS OF PHYSICAL ACTIVITY

Physical activity, by creating metabolic changes and by disrupting the cellular energy charge, increases cell demand for supplying energy to survive. Indeed, exercise, can lead to negative energy balance; following that, it can change the plasma levels of leptin and increase sensitivity to insulin [22], [16], [15]. Several studies have reported that exercise can increase muscle mass and improve body composition, which is very helpful for obese patients [21], [23], and decrease fat mass by increasing the basal metabolic rate [24]. Also, some studies have shown that weight loss by exercise and the subsequent reduction in body mass index can alter the plasma levels of the leptin [25], [16]. Much of the fatty acids required for the working muscles are supplied by increasing triglyceride lipolysis in adipose tissue three to four times more. Sport increases blood flow to the active muscles of your body by creating the period of relaxation; and thereby, it increases oxidative metabolism and imbalances between energy intake and expenditure, and it creates a negative caloric balance that in the long run, can reduce fat and weight and improve body composition via changes in adiponectin and leptin [13], [15], [16]. Also, it has been reported that after regular exercise, the activity of lipoprotein lipase will be increased and cholesterol ester transferase will be decreased. These changes reduce the total plasma triglycerides and lipid profile values. It is likely that by increasing the activity of enzymes related to lipids, fat oxidation will increase which causes fat percentage and BMI [26]. Furthermore, reducing myostatin protein expression in skeletal muscle and myocardial has been observed after four weeks of interval exercise [28]. Likely, these changes can increase mitochondrial mass and skeletal muscle and improve the lipid profile and metabolic condition of individuals after intensive interval training [27], [29]. On the other hand, Qin et al. reported that levels of leptin are increased after extreme interval training [12]. Hosseini et al. also reported that an intense exhaustive exercise session has no significant acute effect on leptin [30]. Soheili et al. showed that insulin levels and insulin resistance has no significant decrease after a period of moderate-intensity aerobic exercise [16]. It seems that differences in exercise protocols, type of training, period, intensity, duration and differences in the population can be the causes of this disruption [29], [30], [16], [12], [10].

Another possible explanation in regard to the effect of high intensity interval exercise on the increase of serum plasma and decrease in body weight, BMI, body fat percent in this research is that fact that the large proportion of fatty acid needed for the muscular contractions during physical activity is provided by a three to four times increase in lipolysis of glycerides in fat tissue. High intensity exercise leads to a twofold increase in blood circulation to the fat tissue and leads to a 10-fold increase in circulation to the active muscles. Many researchers claim that the decrease in body fat, WHR, and body composition is due to the imbalance of input-expenditure of energy and production of negative electricity which may lead to the increase in the level of adiponectin and decrease of plasma leptin following participation in exercise [25]. It seems like all the needed factors were present in this high intensity exercise to increase the level of serum adiponectin.

Recent findings show that chemerin can play an important biological role in the formation of white adipose tissue during normal development and during pathological conditions such as obesity. Bad configuration of chemerin (dysregulation of chemerin) during maturation of fat cells results in the low expression of adiponectin, leptin and glucose transporter -4 (GLUT4) by mature fat cells. Leptin plays an important role in balancing the energy, and it has a key role in preventing receiving energy against ghrelin and body weight regulation and energy homeostasis. Leptin levels are very high in obese children. Furthermore, leptin levels reduce during weight loss. The studies done on children and adolescents who are overweight has shown that being female and having a high rate of BMI has an independent relationship with serum leptin levels [32], [31]. It is reported that there is relationship between the increases in the chemerin levels and coronary artery disease in patients with metabolic syndrome [32].

IV. CONCLUSION

There are several studies on the role of leptin and other endocrine hormones from adipose tissue, such as adipokine, chemerin called cytokines; however, the results of these studies are inconsistent. Leptin is secreted by fat cells; its role is to control body fat by influencing the center of satiety in the hypothalamus. In general, it can be concluded that with a decrease in leptin, insulin and glucose and an increase in insulin sensitivity, high intensity interval training might be used as an effective method in reducing weight, body fat and maintaining body composition, and it decreases the potential risk of developing some diseases associated with obesity and extra weight and metabolic syndrome. However, to achieve more conclusive results, other more detailed research is essential.

REFERENCES

- [1] A. H. Haghighi, H. Yarahmadi, A. DarAbadi, A. Rafiepour. "The effect of aerobic training on serum levels of ghrelin and leptin in middle-aged men," *Daneshvar med*, 19(97):84-95, 2012.
- [2] H. Mohebbi, F. Fatahi, H. Faraji, M. Mohammad-Mohseni. "The effect of upper and lower limb resistance training on leptin in overweight men" *Int J Sport Studies*, 3 (12):1318-24, 2013.
- [3] C. Martins, L. M. Morgan, S. R. Bloom, M. D. Robertson. "Effects of exercise on gut peptides, energy intake and appetite" *J Endocrinol*, 193(2): 251-8, 2007.
- [4] M. Hakimi, M. Ali-Mohammadi, "Comparison between the effects of a resistance training combined with massage, PNF and static stretching on performance in non-athlete male students" *Int J Sport Studies*, 4(1): 37-44, 2014.
- [5] M. Fasshauer, J. Klein, U. Lossner, R. Paschke. "Interleukin (IL)-6 mRNA Expression Is Stimulated by Insulin, Isoproterenol, Tumour Necrosis Factor Alpha, Growth Hormone, and IL-6 in 3T3-L1 Adipocytes," *HormMetab Res*, 35(3):147-52, 2003.
- [6] Y. Zhang, P. J. Scarpace, "The Role of Leptin in Leptin Resistance and Obesity," *PhysiolBehav*, 88(3):249-56, 2006.
- [7] M. Eizadi, M. Karimi, M. Kohandel, H. Duali. "Effect of aerobic exercise on serum leptin response and insulin resistance of patients with type 2 diabetes," *JQUMS*, 16(4): 33-39, 2013.
- [8] F. Daryanoosh, M. Mehboodi, M. Mortazavi, E. Motesharee. "The Effect of 8 weeks of intense aerobic exercise on plasma levels of obestatin, leptin, insulin and growth hormones in male obese Sprague," *AMUJ*, 17(90): 37-45, 2014.
- [9] F. Thong, R. Hudson, R. Ross, I. Janssen, T. Graham, "Plasma leptin in moderately obese men: independent effects of weight loss and aerobic exercise," *AJP- Endo*, 279(2):307-13, 2000.
- [10] Kh. Moonikh, M. Kashef, A. Azad, A. Ghasemian. "Effects of 6 weeks resistance training on Body Composition, serum Leptin and muscle strength in non-athletic men," *QHMS*, 21(2):135-140, 2015.
- [11] JF. Burr, CP. Rown, VK. Jamink, MC. Riddle. "The role of physical activity in type 2 diabetes prevention: physiological and practical perspectives," *Phys Sports Med*, 38 (1):72-82, 2010.
- [12] L. Qin, Y. Xiang, Z. Song, R. Jing, C. Hu, ST. Howard. "Erythropoietins a possible mechanism for the effects of intermittent hypoxia on bodyweight, serum glucose and leptin," *RegulPept*, 165 (2-3):168-73, 2010.
- [13] R. Soori, N. Rezaeian, O. Salehian. "Effects of Interval Training on Leptin and Hormone levels Affecting Lipid Metabolism in Young Obese/Overweight Men," *Iranian Journal of Endocrinology and Metabolism*, 14(3):248-305, 2012.
- [14] M. Hakimi, D. Sheikh Vatani, M. Ali-Mohammadi. "Effect of eight weeks with a combination of resistance training (resistance-massage) on serum leptin, lipid profile and body composition in overweight 139 young men," *Sport physiology*, 2(3):2-15, 2014.
- [15] S. Khalili, R. Nuri, M. Moghadassi, M. Mogharnasi. "Leptin and Insulin Resistance in Young Adult Obese Females: Effect of Eight Weeks Resistance Training," *Research in Endocrinology*, Vol. 2014, Article ID 665365, 8 pages, 2014.
- [16] Sh. Sohaily, R. Soori, N. Rezaeian. "Hormonal adaptations to moderate-intensity endurance training in sedentary obese men," *Koomesh*, 14(2):181-191, 2013.
- [17] Z. Hojjati, F. Rahmaninia, B. Soltani, N. Rahnama. "Acute effect of aerobic and resistance exercise on serum leptin and some of heart coronary dangers factors in obese girls," *Olympic J*, 16(2):7-17, 2008.
- [18] M. Glaister, H. Hauck, CS. Abraham, KL. Merry, D. Beaver, B. Woods, G. McInnes. "Familiarization, reliability, and comparability of a 40-m maximal shuttle run test," *J Sports Sci Med*, 8(1):77-82, 2009.
- [19] A. Esteghamati, O. Khalilzadeh, H. Ashraf, et al. "Physical activity is correlated with serum leptin independent of obesity: results of the national surveillance of risk factors of noncommunicable diseases in Iran (SuRFNCD-2007)," *Metabolism*, 59(12):1730-5, 2010.
- [20] T. Fuentes, I. Ara, A. Guadalupe-Grau, S. Larsen, B. Stallknecht, H. Olmedillas, et al. "Leptin Receptor 170 kDa(OB-R170) Protein Expression Is Reduced in Obese Human Skeletal Muscle: A Potential Mechanism of Leptin Resistance. *ExpPhysiol*, 95(1):160-71, 2010.
- [21] R. Otsuka, H. Yatsuya, K. Takakoshi, K. Matsushita, K. Wada, H. Toyoshima, "Perceived psychological stress and serum leptin concentrations in Japanese men, *Obesity*, 14(10):1832-8, 2006.
- [22] RL. Leibel, M. Resenbaum, J. Hirsch. "Changes in energy expenditure resulting from altered body weight," *N Engl J Med*, 332(10):621-28, 1995.
- [23] R. Rezaee Shirazi, "Effects of 12 weeks high intensity interval training on plasma Adiponectin, Leptin and insulin resistance in obese males with non-alcoholic fatty liver," *Metabolism and Exercise, A bioannual journal*, 5(1):25-37, 2015.
- [24] R. Pratley, B. Nicklas, M. Rubin, J. Miller, A. Smith, M. Smith, A. Goldberg. "Strength training increases resting metabolic rate and

- norepinephrine levels in healthy 50- to 65-year-old men," *J ApplPhysiol*, 76(1):133-37, 1994.
- [25] F. Yamaner, T. Bayraktaroglu, H. Atmaca, MA. Ziyagil, K. Tamer. "Serum leptin, lipoprotein levels, and glucose homeostasis between nationalwrestlers and sedentary males," *Turk J MedSci*, 40(3): 471-7, 2010.
- [26] SD. Weise, PW. Grandjean, JJ. Rohack, JW. Womack, SF. Crouse. "Acute changes in blood lipids and enzymes in postmenopausal women after exercise," *J ApplPhysiol*, 99(2): 609-15, 2005.
- [27] U. Wisloff, A. Stoylen, JP. Loennechen, M. Bruvold, O. Rognmo, PM. Haram, et al. "Superior cardiovascular effect of aerobic interval training versus moderate continuous training in heart failure patients: A randomized study," *Circulation*, 115(24):3086-94, 2007.
- [28] K. Lenk, R. Schur, A. Linke, S. Erbs, Y. Matsumoto, V. Adams, G. Schuler, "Impact of exercise training on myostatin expression in the myocardium and skeletal muscle in a chronic heart failure model," *Eur J Heart Fail*, 11(4): 342-8, 2009.
- [29] K. Salehzadeh, AA. Gaeini. "Effects of selected long-term aerobic exercises on serum leptin level of non-athlete young men and women," *JQUMS*; 16 (4): 26-32, 2013.
- [30] M. Hosseini, M. Nikbakht, A. Habibi, A. Ahangarpour, H. Fathi Moghaddam, "Acute Effects of an Aerobic Exhaustive Incremental Exercise Session on Serum Leptin and Plasma Lipids," *Sci Med J*, 10(4):363-371, 2011.
- [31] D. Stejskal, M. Karpisek, Hanulova Z, et al. "Chemerin is an independent marker of the metabolic syndrome in a Caucasian population--a pilot study". *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub*, 152: 217-21, 2008.
- [32] B. Dong, W. Ji, Y. Zhang, "Elevated serum chemerin levels are associated with the presence of coronary artery disease in patients with metabolic syndrome," *Inter Med*, 50 (10): 1093-97, 2011.