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Review

Adipose Tissue As an Endocrine Organ: A Perspective From Adiponectine and Irisin

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ABSTRACT:
In recent years, adipose tissue has been defined as a new endocrine organ via its paracrine, autocrine and endocrine effects. With the secreted hormones and cytokines it plays a major role in the regulation and integration of metabolism. The metabolic pathways involving these hormones and cytokines including insulin sensitivity show a connection with the pathogenesis of obesity, type II diabetes mellitus, metabolic syndrome, inflammatory diseases, many chronic diseases and even cancer. Adipokines or adipocytokines are cytokines secreted by adipose tissue. In this mini-review, information about two of the most important adipokines, adiponectin and irisin, is given and their important effects are presented to the attention of the reader.

Keywords: Adiponectin, adipose tissue, endocrine, irisin

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1. INTRODUCTION

Adipose tissue is a tissue in which lipids are stored for use as an energy source. There are two types of adipose tissue in mammals and humans. White adipose tissue and brown adipose tissue. Fatty acids formed by lipogenesis in the presence of insulin are stored as triglycerides in the white adipose tissue, and triglycerides are broken down by lipolysis in the presence of glucagon and the released fatty acids are used as an energy source. The second type of adipose tissue, brown adipose tissue, is specialized for thermogenesis and appears brown due to the large number of mitochondria it contains. Thanks to the very high number of mitochondria they have, they provide more energy production, more calorie consumption and heat production [1]. The conversion of white adipose tissue to brown adipose tissue (browning) plays a key role in the prevention of metabolic diseases, especially obesity. The most important factor that provides browning is exercise [2].

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Adipose tissue acts as an endocrine organ in addition to its fat storage and metabolic functions. Adipose tissue is an endocrine organ that transmits soluble signals called locally and systemically acting adipokines. It also communicates with the cells of the immune system [3]. Many mediators (enzymes, cytokines, growth factors) secreted from adipose tissue play an active role in the regulation of appetite, insulin resistance, inflammation, and atherosclerosis processes. Some of these mediators are leptin, TNFα, adipsin, IL-6, plasminogen activator inhibitor, visfatin, adipsin, apelin, angiotensinogen, metallothionine, and resistin [4].

During the obesity-insulin resistance-metabolic syndrome connection process, the normal functions of adipocytes are impaired, and synthesis of proinflammatory cytokines secreted from adipocytes increases and synthesis of anti-inflammatory cytokines decreases. This increase in inflammation contributes to the formation of diabetes. Among the mediators secreted from adipose tissue, the most important hormone that increases insulin sensitivity is adiponectin. Adiponectin is a hormone that enhances fatty acid oxidation and insulin sensitivity [5]. Adiponectin reduces hepatic glucose production and potentiates the effects of insulin in the liver, thereby increasing insulin sensitivity [6]. Similarly, in animal models, adiponectin has been shown to increase hepatic insulin sensitivity [7]. It is known that adiponectin levels are decreased in obesity, type II diabetes and metabolic syndrome, and adiponectin may have a very important role in these diseases. Obese people have decreased adiponectin levels. As insulin resistance increases, adiponectin levels decrease [8]. It has been reported in the literature that the risk of developing type 2 diabetes in individuals with high adiponectin levels is lower than those with low adiponectin levels. The risk of developing type 2 diabetes in individuals with high adiponectin levels is lower than those with low adiponectin levels [9].

The relationship of TNFα and IL-6 with insulin resistance is thought to be mediated through adiponectin [10]. Adiponectin, which increases insulin sensitivity and fatty acid oxidation, also has a regulatory effect on inflammation by reducing TNFα and IL-6 levels [11]. Insufficient efficacy of adiponectin in obese individuals is one of the factors responsible for the increase in circulating TNF α and IL-6 levels. One mechanism of activating inflammatory pathways in diabetes is decreased adiponectin levels [12]. In conclusion, besides its anti-inflammatory effect, adiponectin shows antiobesity and antidiabetic effects by increasing insulin sensitivity in hepatocytes and skeletal muscle cells. Adiponectin also shows anti-atherogenic properties due to its role in preventing the formation of atherosclerotic plaques [8] and has anti-inflammatory effects on macrophages [13]. In a study conducted on 48 hypertensive and 32 normotensive individuals, it was reported that serum adiponectin levels were lower in hypertensive patients than in normotensive individuals, and low adiponectin levels were associated with risk factors for atherosclerosis, and low adiponectin levels may be a risk factor for atherosclerosis. [14]. Serum adiponectin levels have been found to be low in

ischemic heart disease [15]. One of the adiponectin gene mutations, I164T mutation has been shown to be associated with low adiponectin levels and coronary artery disease [16, 17]. This result shows that adiponectin mutations may be part of the genetic background of the metabolic syndrome. Considering all reports in the literature adiponectin can be defined as an anti-obesity, anti-diabetic and anti-atherosclerotic hormone.

Irisin, another important mediator secreted from adipose tissue, is defined as myokine or adipo-myokine. Irisin, secreted mainly from skeletal muscle and adipose tissue, is a thermogenic protein that provides energy expenditure by converting white adipose tissue to brown adipose tissue. In 2012, Boström et al. discovered a protein that is released from skeletal muscle after exercise and protects the person from metabolic diseases when systematic exercise is performed [1]. This is a membrane protein named fibronectin type III domain 5 (FNDC5) and it was understood that irisin protein is released into the circulation by proteolysis of FNDC5. FNDC5 is also referred to as protein 2 (FRCP2) and Pep containing fibronectin type III repeats. Irisin released from skeletal muscle is a hormone with autocrine, paracrine and endocrine effects [18].

Investigation of serum irisin levels in obesity, obesity-related diabetes mellitus (DM) and other obesity-related diseases is a current issue. In one of these studies, serum irisin levels of a total of 135 Type II Diabetes patients (with and without cardiovascular disease) were found to be significantly lower than the healthy control group of 70 individuals. When a comparison is made among Type II Diabetes patients, it has been reported that serum irisin levels were lower in people with cardiovascular disease than in people without cardiovascular disease. Researchers concluded that circulating irisin may be a new potential independent cardiovascular disease risk biomarker in Type II DM patients [19]. In another study that included 96 patients with Type I DM and 34 healthy individuals, the researchers concluded that higher irisin levels were associated with better glycemic control and bone health in children with Type I DM [20]. In a study investigating the relationship between single point genome mutations (SNPs) of the FNDC5 protein and obesity, it was stated that rs16835198 and rs726344 SNPs were associated with obesity [21]. Among the maternal and neonetal FNDC5 polymorphisms, rs726344 polymorphism has been reported to be associated with preterm birth [22].

According to the results of many studies revealing the relationship between irisin and glucose metabolism, it has been stated that irisin breaks insulin resistance in obese and Type II DM, and irisin can be considered as an alternative for the treatment of diseases such as obesity and Type II diabetes [23]. Although some studies with different methodologies after applying different exercise types in special patient groups have reported a few inconsistent results with the relationship of irisin to glucose metabolism, it is known that irisin stimulates thermogenesis by reducing ATP production via UCP protein by converting white

adipose tissue to brown adipose tissue [24]. Irisin expression and secretion increase in response to exercise and the mRNA expression level of UCP-1 protein, which is involved in the conversion of irisin from white adipose tissue to brown adipose tissue, increases 7-500-fold by exercise [25].

2. CONCLUSION

Since irisin and adiponectin have similar effects in terms of their antiobesity and antidiabetic effects, maintaining high adiponectin and irisin levels in diabetic patients is the basis for treating diabetes with diet/exercise. Discussions regarding the metabolic effects of irisin and adiponectin and their role in obesity still continue. The roles of these two mediators in the pathogenesis of many diseases, including diabetes-related cancer, are under investigation. Although there are very important findings about both myokines, their functions are still not fully elucidated. More studies are needed in large patient groups to use irisin and adiponectin, which are promising compounds, in the treatment of many diseases, especially cancer.

Conflict of Interest

Author has no personal financial or non-financial interests.

REFERENCES

1. Boström PJ, Wu MP, Jedrychowski A, Korde L, Ye JC, Lo, et al. A PGC1-α-dependent myokine that drives brown-fat-like development of white fat and thermogenesis. Nature 2012;481(7382):463-8.

2. Lehnig AC, Stanford KI. Exercise-induced adaptations to white and brown adipose tissue. J Exp Biol 2018;221(Pt Suppl 1).

3. DiSpirito JR, Mathis D. Immunological contributions to adipose tissue homeostasis. Semin Immunol 2015;27(5):315-21.

4. Luo L, Liu M. Adipose tissue in control of metabolism. J Endocrinol 2016;231(3):R77-r99.

5. Yamauchi TJ, Kamon H, Waki Y, Terauchi N, Kubota K, Hara, et al. The fat-derived hormone adiponectin reverses insulin resistance associated with both lipoatrophy and obesity. Nat Med 2001;7(8):941-6.

6. Berg AH, Combs TP, Du X, Brownlee M, Scherer PE. The adipocyte-secreted protein Acrp30 enhances hepatic insulin action. Nat Med 2001;7(8):947-53.

7. Combs, TP, UB, Pajvani AH, Berg Y, Lin LA, Jelicks M, Laplante, et al. A transgenic mouse with a deletion in the collagenous domain of adiponectin displays elevated circulating adiponectin and improved insulin sensitivity. Endocrinology 2004;145(1):367-83.

8. Higashiura KN, Ura J, Ohata N, Togashi S, Takagi S, Saitoh, et al. Correlations of adiponectin level with insulin resistance and atherosclerosis in Japanese male populations. Clin Endocrinol (Oxf) 2004;61(6):753-9.
9. Spranger JA, Kroke M, Möhlig MM, Bergmann M, Ristow H, Boeing, et al. Adiponectin and protection against type 2 diabetes mellitus. Lancet 2003;361(9353):226-8.
10. Guerre-Millo M. Adipose tissue and adipokines: for better or worse. Diabetes Metab 2004;30(1):13-9.
11. Wang ZV, Scherer PE. Adiponectin, the past two decades. J Mol Cell Biol 2016;8(2):93-100.
12. Bastard JP, Maachi M, Lagathu C, Kim MJ, Caron M, Vidal H, et al. Recent advances in the relationship between obesity, inflammation, and insulin resistance. Eur Cytokine Netw 2006;17(1):4-12.
1**3.** Yokota T, Oritani K, Takahashi I, Ishikawa J, Matsuyama A, Ouchi N, et al. Adiponectin, a new member of the family of soluble defense collagens, negatively regulates the growth of myelomonocytic progenitors and the functions of macrophages. Blood 2000;96(5):1723-32.
14. Uygungelen B, İçağasıoğlu S, Acıbucu F, Kılıçlı F, Uslu A, Gül İ. Serum adiponectin level in hypertensive patients and its association with atherosclerotic risk factors. Cumhuriyet Medical Journal 2013;35(2):206-14.
15. Kumada M, Kihara S, Sumitsuji S, Kawamoto T, Matsumoto S, Ouchi N, et al. Association of hypoadiponectinemia with coronary artery disease in men. Arteriosclerosis, thrombosis, and vascular biology 2003;23(1):85-9.
16. Kondo H, Shimomura I, Matsukawa Y, Kumada M, Takahashi M, Matsuda M, et al. Association of adiponectin mutation with type 2 diabetes: a candidate gene for the insulin resistance syndrome. Diabetes 2002;51(7):2325-8.
17. Takahashi M, Arita Y, Yamagata K, Matsukawa Y, Okutomi K, Horie M, et al. Genomic structure and mutations in adipose-specific gene, adiponectin. International journal of obesity 2000;24(7):861-8.
18. Panati K, Suneetha Y, Narala VR. Irisin/FNDC5--An updated review. Eur Rev Med Pharmacol Sci 2016;20(4):689-97.
19. El-Lebedy DH, Ibrahim AA, Ashmawy IO. Novel adipokines vaspin and irisin as risk biomarkers for cardiovascular diseases in type 2 diabetes mellitus. Diabetes Metab Syndr 2018;12(5):643-8.
20. Faienza MF, Brunetti G, Sanesi L, Colaianni G, Celi M, Piacente L, et al. High irisin levels are associated with better glycemic control and bone health in children with Type 1 diabetes. Diabetes Res Clin Pract 2018;141:10-7.
21. Abdu Allah AM, Hammoudah SA, Abd El Gayed EM, El-Attar LM, Shehab-Eldin WA. Obesity and its Association with Irisin Level Among Individuals with FNDC5/Irisin Gene Variants RS16835198 and RS726344. Protein Pept Lett 2018;25(6):560-9.

22. Salem H, Yatchenko Y, Anosov M, Rosenfeld T, Altarescu T, Grisaru-Granovsky S, et al. Maternal and neonatal irisin precursor gene FNDC5 polymorphism is associated with preterm birth. Gene 2018;649:58-62.
23. Moreno-Navarrete JM, Ortega F, Serrano M, Guerra E, Pardo G, Tinahones F, et al. Irisin is expressed and produced by human muscle and adipose tissue in association with obesity and insulin resistance. J Clin Endocrinol Metab 2013;98(4):E769-78.
2**4.** Crujeiras AB, Pardo M, Casanueva FF. Irisin: 'fat' or artefact. Clin Endocrinol (Oxf) 2015;82(4):467-74.
25. Huh JY, Panagiotou G, Mougios V, Brinkoetter M, Vamvini MT, Schneider BE, et al. FNDC5 and irisin in humans: I. Predictors of circulating concentrations in serum and plasma and II. mRNA expression and circulating concentrations in response to weight loss and exercise. Metabolism 2012;61(12):1725-38.