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Review

Type II DM Candidate Biomarkers in the Framework of Obesity, Exercise, and Diet

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ABSTRACT:
Biomarkers used in the early diagnosis and treatment of prediabetes and diabetes, which are based on obesity and metabolic syndrome, are inadequate due to the complexity of the etiology of diabetes, and studies for developing new biomarkers for diabetes and/or determining an early diagnosis biomarker are ongoing in the scientific world. Since obesity can be prevented to a certain extent by long-term diet and exercise, it can be considered that the long-term and periodic investigation of a group of cytokines related to exercise and body fat mass may be meaningful. For example, the cytokines irisin (a myokine released from the muscle by exercise) and adiponectin (adipokine, an indicator of decreased body fat mass have similar effects in terms of antiobesity and antidiabetic effects. Therefore, high levels of adiponectin and irisin can be considered in diabetic patients, and delayed micro and macrovascular complications of diabetes due to obesity and metabolic syndrome can be considered. On the other hand, adiponectin levels are low in diabetes and obesity, and these patients generally have low irisin levels due to being sedentary. It is a common belief that for overweight individuals, other than morbid obese people, and prediabetic and diabetic individuals, candidate biomarker (s) from cytokines to monitor the effectiveness of diet and exercise can generally be detected. It is known that adipokines are involved in the pathogenesis of obesity and Type 2 diabetes mellitus together with pro-inflammatory cytokines and can be used as prognostic markers and may be involved in the therapeutic approaches to obesity-related Type 2 DM. During the long-term latent course of diabetes at the prediabetic stage, it is important to identify an early diagnostic biomarker.

Keywords : Adiponectin, biomarker, diet, exercise, irisin, obesity, type II DM.

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1.INTRODUCTION

Overweight status and obesity are defined using body mass index (BMI). A BMI of 25 to 29.9 is considered overweight, and a BMI ≥ 30 is considered obese [1] . Obesity is an important risk factor for the development of Type II DM, hypertension, obstructive sleep apnea and heart disease. It is known that Type II DM develops in approximately

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80% of all obese people. In adults, elevated BMI due to increased adiposity is known to lead to adiposity (ectopic adiposity in liver and muscle), which leads to various health risks such as diabetes and cardiovascular diseases [2] .

Diabetes is a current health problem in developed and developing countries. The World Health Organization (WHO) report on diabetes states that the number of adults living with diabetes has almost quadrupled since 1980, reaching more than 400 million people. The prevalence of diabetes has reached epidemic proportions and is expected to reach approximately 629 million by 2045 [3]. In 2012 alone, 1.5 million people died worldwide due to diabetes, which can lead to complications such as heart attack, stroke, blindness, kidney failure and lower extremity amputation. WHO estimated that the number of diabetics in Turkey, which was approximately 3 million in 2000, will reach 6.5 million in 2030, but this value estimated for 2030 was reached in 2013 in our country [4]. Today, this figure is over 7 million. According to the data of the Ministry of Health in 2017, the prevalence of diabetes in our country is 9.1%. It is noteworthy that this rate is considerably higher than the 5.1% prevalence of European Union countries. Diabetes-related death rate in our country increased by 11% from 2002 to 2017 and ranked 9th among the causes of death in our country [5]. Years of life lost due to diabetes increased by 29.2% between 2002 and 2017 in our country, ranking 10th among diseases.

During the obesity-insulin resistance-metabolic syndrome connection process, normal functions of adipocytes are impaired, and an increase in the synthesis of proinflammatory cytokines secreted from adipocytes and a decrease in the synthesis of anti-inflammatory cytokines occur. This increase in inflammation contributes to the formation of diabetes. Studies on metabolic changes in diabetes, understanding the mechanisms by which various hormones and neurotransmitters affect energy balance, and studies on developing new biomarkers and new treatment approaches for diabetes are carried out with interest by researchers all over the World [6]. As a result of these studies, a number of biomarkers that can be an indicator for the estimation of DM risk have been proposed to date. In addition to blood glucose and glucose tolerance test, the most prominent ones are; hemoglobin A1c (HbA1c), parameters showing blood lipid profile, inflammatory markers, adiponectin, liver enzymes and fetuin-A [7]. However, most biomarkers fall short in the face of the complexity of Type 2 DM etiology [8]. The results of some promising studies on the use of adipokines as an early biomarker in the diagnosis of Type II DM can be summarized as follows:

- Serum adiponectin levels can be used as a strong risk marker of new-onset prediabetes in healthy Caucasians and blacks (parents with a history of Type II DM) (a cohort study) [9].

- Adiponectin levels are lower in prediabetic patients than in healthy individuals; shows that circulating adiponectin levels begins to decline before diabetes occurs (a meta-analysis) [10]
- High serum adiponectin levels appear to be associated with a reduced risk of Type II DM in different populations (a meta-analysis) [11]
- Elevated plasma adiponectin levels are associated with a reduced risk of Type II DM and a subsequent reduction in cardiovascular risk [12]

Irisin is secreted mainly from skeletal muscle with the effect of exercise and is a thermogenic protein that converts white adipose tissue to brown adipose tissue and releases energy in the form of heat. Irisin makes significant changes in subcutaneous WAT. As a result, it stimulates the expression of UCP1, provides WAT-BAT conversion and performs thermogenesis in the formed BAT cells. This results in a significant increase in total body energy expenditure and the breakdown of obesity-related insulin resistance. 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 molecule for the treatment of diseases such as obesity and Type II diabetes with exercise [13].

Breaking the cycle between obesity, metabolic syndrome and Type II DM is mainly through diet and exercise. Dietary restriction (and accompanying weight loss), one of the two most important factors, reduces total fatty acids. The lipid composition of the diet stimulates the gene expression of proteins involved in fatty acid oxidation and fat burning via PPARs and other transcription factors [14].

The second important factor, exercise, activates AMPK like adiponectin; AMPK inhibits the synthesis of fatty acids and activates fatty acid degradation. It increases AMP by increasing the use of ATP. This, like adiponectin, provides energy homeostasis [14]. Irisin increases gene expression of the UCP1 protein in white adipose tissue. Irisin also stimulates the conversion of white adipose tissue to brown adipose tissue [13].

The biochemical mediator AMP-activated protein kinase (AMPK) plays a central role in energy metabolism. Although the body's main energy sources are glucose and triacylglycerols, the energy metabolism management of AMPK is based on TAG storage and burning [15]. Adiponectin, an adipokine, is secreted from adipose tissue in response to decreased body fat mass. Adiponectin causes the activation of the AMPK molecule with a mechanism similar to the effect of exercise and is effective in many metabolic events through the AMPK molecule. These metabolic events; It can be summarized as increasing insulin sensitivity, increasing fatty acid oxidation, increasing glucose uptake in muscle, decreasing gluconeogenesis in the liver, increasing cardiac glycolysis and suppressing synthesis reactions in general. It is

known that the level of adiponectin is low in obese and Type 2 DM individuals, and high in patients with anorexia nervosa [16].
Understanding biochemical pathways and connections in the framework of obesity, exercise, diet will enable the development of new biomarkers for Type II diabetes.

Conflict of Interes
Author has no personal financial or non-financial interests.

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