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The importance of adiponectin in the human body

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Abstract

Adipose tissue produces various types of proteins, including adipocytokines, which is why it should be treated as an endocrine organ. Adiponectin is one of the most important adipokines in the human body. We distinguish three factions of adiponectins: low molecular weight (LMW), middle molecular weight (MMW) and high molecular weight (HMW).

The purpose of this article is to attempt to summarize the current state of knowledge regarding adiponectin, in particular its role in the human body.

Adiponectin significantly influences the metabolism of carbohydrates by stimulating the activity of AMPK and PPAR-α through the AdiopoR1 receptors, which results in an increase in uptake and oxidation of glucose in cells. The literature has repeatedly demonstrated a negative correlation of serum adiponectin concentrations in relation to the BMI index, insulin and triglyceride levels, HOMA-IR and blood pressure. Decreased adiponectin levels have been demonstrated in such diseases as obesity, type 2 diabetes, hypertension, ischemic heart disease or in patients after a stroke. The significant effect of this adipocytokine on the

reduction of inflammation, lipid metabolism and effect on the vascular endothelium is of key importance in the process of atherosclerotic plaque formation.
In conclusion, the correct concentration of adiponectin is important for maintaining proper function of the whole organism. It affects numerous metabolic processes, mainly the metabolism of carbohydrates and lipids. It has antiatherogenic and anti-inflammatory properties. Due to the low concentrations of adiponectin found in patients with chronic diseases, including type 2 diabetes, there is a need for further research to determine the exact effect of adiponectin on these morbidities.

Keywords: adipose tissue, adipocytokines, adiponectin

Introduction:

In recent years, the perception of body fat has changed. Due to the discovery of adipocytokines, pleiotropic proteins produced by adipocytes, adipose tissue should be treated as an endocrine gland. One of the best-known and also produced in relatively large amounts adipokine is adiponectin. The purpose of this article is to review the scientific literature and attempt to summarize the current state of knowledge regarding adiponectin and its role in the human body.

Adiponectin- construction and mode of action

Adiponectin (other names: ADPN, apM1 Acrp30, Adipo9, GBP28) is a polypeptide hormone synthesized and secreted into the blood by mature cells of adipose tissue (adipocytes), which has a pleiotropic effect on a number of metabolic processes in the human body. The protein is encoded by the ACDC gene (APM1) located on the long arm of the third chromosome and is composed of 244 amino acids with a total mass of 30 kDa. The total serum adiponectin concentration ranges from 3-30 g / ml. ADPN makes 0.01% of all plasma proteins and is a substance with a long half-life, its blood concentration is stable and relatively high compared to other hormones. In women, serum ADPN is higher than in men [1,2]

Considering the molecular weight of adiponectin, we can distinguish 3 fractions that circulate in the body: low-molecular fraction with trimer structure - LMW (low molecular weight),

medium-size fraction of hexamer structure - MMW (middle molecular weight) and high molecular weight fraction with multimer structure - HMW (high molecular weight). [3]

It is believed that mutations in the coding gene (ACDC) resulting from various causes can lead to disturbances in the multimerization of adiponectin molecules, which may have a significant association with insulin resistance. [4]

The metabolic effect of adiponectin results from membrane receptor activation, mainly by phosphorylation of kinases: MAPK (mitogen-activated protein kinase), AMPK (AMP-dependent protein kinase) and by activation of the nuclear PPAR-α receptor. According to current scientific reports, we can distinguish 2 isoforms of membrane receptors for adiponectin, differing in the chromosome and organ localization: AdiopoR1 and AdipoR2. The AdiopoR1 receptor is found, inter alia, in skeletal muscles, in smaller amounts in the brain, heart, kidneys, liver, placenta, pancreatic β cells and macrophages. The AdipoR2 receptor, however, is located in the liver and skeletal muscles. In addition, adiponectin exerts its action via T-cadherins, acting as a receptor for ADPN in vascular smooth muscle cells and endothelial cells

The role of adiponectin

Adiponectin affects various metabolic processes in the human body. For many years it was postulated that it has an important role in the regulation of the carbohydrate metabolism, through the increase in glucose uptake and its oxidation induced by the stimulation of AMPK and PPAR-α activity via AdiopoR1 receptors located in skeletal muscles by low- and medium-molecular weight adiponectin fractions (LMW and MMW). In the liver, macromolecular adiponectin (HMW) multipliers through the type 2 receptors (Adipo R2), by increasing the activity of AMPK and PPAR-α, affect the reduction of hepatic gluconeogenesis. Adiponectin also plays an important role in regulating lipid metabolism. The reduction of acetyl-CoA (ACC) activity in the skeletal muscles and the liver via both AdiopoR1 and Adipo R2 receptors stimulates and intensifies the β-oxidation process of fatty acid, a direct consequence of which is the lowering of serum triglycerides and subsequent increase in insulin sensitivity of the tissue. [6, 7, 8]

Furthermore, it is believed that adiponectin may play an important role in the regulation of appetite. In studies conducted so far in mice it was shown that the stimulation of AdipoR1 receptors in the hypothalamus stimulates appetite, however, intraventricular injections of

adiponectin induced an increase in the process of thermogenesis resulting in a reduction of body weight in the test animals. [9]

Another positive metabolic effect of adiponectin is its protective effect on the vascular endothelium. The vasoprotective mechanism is extremely complex and consists, among other things, of the vasodilatation effect, inhibition of adhesion molecule expression, stimulation of nitric oxide (NO) production, angiogenesis stimulation, inhibition of proinflammatory cytokine-induced inflammation (TNFα) and retention of endothelial and smooth muscle cell proliferation and migration. Adiponectin and in particular its macromolecular fraction (HMW) play an important role through their anti-atherogenic mechanism. The mechanisms responsible for its protective effect in relation to all stages of the progressive process of atherosclerosis are primarily: prevention of endothelial dysfunction (by increasing nitric oxide synthesis, inhibiting endothelin cell apoptosis and inhibition of free radical production), inhibition of atherosclerotic plaque formation and development (by reducing VCAM synthesis -1, ICAM-1, E-selectin, NF, TNF α, IL-8 and oxidation of LDL cholesterol, inhibition of foam cell formation, reduction of proliferation and migration of endothelial cells and smooth muscle cells, increase in IL-10 concentrations), prophylactic effect by the stabilization of atherosclerotic plaque and an anticoagulant effect (reduction of platelet aggregation, inhibition of thrombus formation). [10, 11]

In previously published work it has repeatedly been demonstrated that a negative correlation exists between serum adiponectin concentrations and the BMI index (Body Mass Index) , serum insulin and triglyceride concentrations, insulin resistance calculated using the HOMA-IR index and arterial pressure. However, a positive correlation was observed in relation to HDL cholesterol concentrations and the age of the subjects. [12, 13, 14, 15, 16, 17]

Many authors have shown that reduced levels of adiponectin have been observed in such diseases as obesity, type 2 diabetes, hypertension, ischemic heart disease or in patients after a stroke. Additionally, it was found that low adiponectin concentrations may be a predictor of acute conditions such as sudden cardiovascular events or strokes. [18, 19, 20, 21, 22, 23, 24, 25, 26]

On the other hand, the increase in adiponectin levels was observed in conditions with a decrease in body weight, such as anorexia nervosa, after treatment with PPARγ - (thiazolinedione) agonists, in elderly patients, in patients with renal failure or circulatory insufficiency. [27, 28, 29, 30]

Considering the size of the adiponectin molecule, it was found that the multimer fraction (HMW) shows the strongest metabolic activity in the body among the others. In comparison to total adiponectin, the HMW fraction exerts a stronger cardioprotective and anti-atherosclerotic effect, which may be indicative of the metabolic state of the body. In turn, total adiponectin concentrations show a better correlation with the mortality rate in people with cardiological ailements. Its high serum values may indicate a significantly higher risk of cardiovascular events in the course of coronary disease and cardiovascular failure among the elderly. In addition, it was found that the ratio of high molecular weight adiponectin to total adiponectin (HMW / Total) may also be prognostic. In available publications, it has been demonstrated that the reduced values of this index are typical for people with metabolic syndrome and its components (type 2 diabetes, hypertension, lipid disorders, ischemic heart disease). Furthermore, it was found that the decreased concentrations of high molecular weight adiponectin (HMW) are observed in people with excess visceral adipose tissue, which may also have a predictive value regarding the onset of metabolic syndrome. Liang et al. demonstrated a correlation between the decrease in HMW adiponectin fraction and the stage of atherosclerosis of coronary arteries assessed by angiographic methods. [31, 32, 33, 34] Interesting conclusions were drawn in the study by Aguilar-Salinas et al. in which HMW adiponectin levels were evaluated in patients with gross obesity without metabolic syndrome (healthy metabolically). Normal HMW concentrations were demonstrated in only 20% of patients recruited for the study. [35]

Summary:

Taking into account the influence of adiponectin on a number of metabolic processes occurring in the body, including carbohydrate-lipid metabolism, antiatherosclerotic effect, anti-inflammatory and increasing insulin sensitivity, it should be considered as a potential biomarker of metabolic disorders and a prognostic factor of diseases related to obesity and insulin resistance such as type 2 diabetes or ischemic heart disease and complications accompanying them. Further research is necessary to determine the exact effect of adiponectin on tissues and organs, which may allow a future reduction of metabolic disorders leading to the development of many diseases and related complications.

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