



Bioactive of Adiponectin in Metabolic Diseases a Review Article

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Abstract: The current study demonstrates adiponectin role in pathogenesis also as a biomarker diagnostic indicator with metabolic syndrome and insulin resistance (IR). Adiponectin is Lipoprotein secreted by adipocytes ,chemical structure of protein adiponectin contains 244 amino acids four domains, amino terminal peptide signal followed species_specific,, collagen-like The variable space region 22 Gly-X-Y repeat, globular carboxyb_ terminal domain binds to adiponectin receptor, which resembles complement factor C1q and a triangle-like topology for T.N.F levels of several adipokines (including adiponectin) leads to an increase in body weight and tends to act in a pro-inflammatory manner. On other hand, the concentration of adiponectin decreases in obese subjects. Adipokine works a suppress inflammation Processes,. Clinical research articles indicate low concentrations of adiponectin may be involved in the increase in obesity-related diseases, including cardiovascular disease, inflammation, and insulin resistance. current article concerned with influence of adiponectin protein at insulin resistance ,metabolic syndrome in patients with type 2 diabetes and comorbid disorders associated with obesity .

Keywords: Adiponectin Metabolic Syndrome Insulin Resistance, Diabetes Type 2

Introduction

There is a trend, ongoing scientific work, and great efforts to understand the mechanisms of obesity in causing metabolic syndrome diseases, and type 2 diabetes in particular. This scientific research has led to the concept that adipose tissue is more than just a simple energy storage compartment, but is also an important secretory organ for bioactive molecules referred to as a dipokines. Adipokines contribute to the pathophysiology of obesity-related disorders through their ability to modulate inflammation, and metabolic processes. Levels of several adipokines (including adiponectin) are increased in obesity and tend to act in a pro_inflammatory manner [1,2]., On the other hand the concentration of adiponectiin decreases with people who suffer from obesity, a dipokine works to stop of inflammation. Bio clinical research suggest lower adiponectin concentrations may support a higher body mass index [2]. Development of obesity_related including CVD disease, inflammation AND insulin resistance . Current review study focuses effect of

Citation: Jamal Harbi Hussein Alsaadi, Huda M.Younis. Bioactive of Adiponectin in Metabolic Diseases a Review Article. Central Asian Journal of Theoretical and Applied Science 2024, 5(3), 132-142.

Received: 17th June 2024
Revised: 19th June 2024
Accepted: 19th June 2024
Published: 26th June 2024



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adiponectin on ,metabolic syndrome ,type2 diabetes ,insulin resistance and obesity-related comorbid disorders. Metabolism disorder syndrome is known as a group of risk factors that promote the development of atherosclerosis, Type 2 diabetes, strokes in the brain, and other diseases. Metabolic syndrome is also called insulin resistance syndrome. [3]. Metabolic syndrome goes by several other names, including metabolic disorder syndrome. Vascular syndrome, cardiovascular disease, clinical obesity, insulin resistance, dyslipidemia, and hypertension are common to everyone. [4] Its central obesity and high blood sugar levels Dyslipidemia and high blood pressure characterize the so-called metabolic process Syndrome (MS). [5].

Materials and Methods

Adiponectin secreted from adipose tissue could be a blood-based bio-marker [9]. Decreased concentrations of lipid profile parameters in the blood occur due to changes in some inherited factors like S.N.Ps in a diponectin protein synthesis genes , some environmental, factors responsible for Obesity. It plays t has an important function in IR , diabetes mellitus and Mtabolism syndrome associated with obesity. The adiponectin receptor proteins, A-dipoR1 and A-dipoR2, that moderate the antidiuretic metabolic effects of adiponectin reproduced and upregulated in Obesity-associated Insulin Resistanc... [6] Adipokines are key regulators of glucose and fatty acid metabolism and infections.[7,8].

Adiponectin protein secreted by lipids tissues , presents insulin sensitivity, anti-inflammatory, anti-hormonal, proapoptotic, and anti-proliferative, properties. Adiponectin protein concentrations are inversely-related to increased diabetes, CVD, poor blood vessels and many types of cancer in life. [12]. The chemical structure of the protein adiponectin contains 244 amino acids 4 –domains , the amino-terminal peptide signal a species-specific, collagen-like domain Region 22 –Gly.X-Y repeats , carboxylated Spherical terminal . The bind to a adiponectin receptor proteins, which Similar with complement factor C1q & triangle-like of T-N-F- [13, 14].

The collagen-like zone of adiponectin allow” s Protein oligomerization cross-disulfide linkage and through the hydroxylation & glycosylation of 4 reserved , lysine active site residues, which are important to formation [16].

Changes in adiponectin levels caused by environmental or genetic factors have direct impact on many pathological conditions Influencing factors like obesity and dietary regime a play a role causing (IR) insulin [metabolic syndrome, type 2 diabetes [17,18 ,19]

Diabetes resulting from pregnancy [20], high blood pressure ,

(CVD) cardiovascular disease and many cancers [21, 22]. Hypoadiponectinemia is usual denominator for risk factors groups that make up metabolic diseases is hypertension pressure, high lipid levels & body obesity.

Hyperglycemia, (IR) insulin resistance Recent researches including a 14,598 patients & 2,623 subjects of diabetes showed increase of adiponectin concentrations were connected with lower danger of developing diabetic typ-2 [23]. Levels of adiponectin highest and were connected with a modest decrease in the danger of heart disease and arterial disease in male with diabetes. [24]. Adiponectin is produced by adipose tissue and binds with surface adiponectin receptors (AdipoR1 & AdipoR2) and activates A.M.P-activated-protein-kinase (A.M.P.K) & peroxisome proliferator-activated protein (PPAR) α at hepatocytes & skeletal muscle. It also activates the production of endothelial (NO), which leads to improving vascular dysfunction and has anti-atherosclerosis effects by inhibiting inflammation in various blood vessels. [25; 26; 27; 28].

Adiponectin circulates in the bloodstream in the form of three polymeric complexes such as trimer, hexamer and a high molecular weight (12-18) [29]. It has also been observed that adiponectin regeneration reduces insulin resistance, improves vascular function, glucose intolerance and vascular function in Laboratory animal. [30; 27; 28]

1.2. Obesity

Obesity is an abnormal increase in body weight and characterized by excess weight. Visceral mass, which is considered a risk factor for many diseases, including cardiovascular diseases and metabolic syndromes such as diabetes and other diseases.

[31] Accumulation of fat in abdomen and appearance (apple shape) in men is factor effect that rise risk developing cardiovascular diseases, while pear-shaped obesity of the female because fat accumulation is considered normal or even protective for cardiovascular. In abdominal obesity, concentrations dipokinases in the blood plasma are dysregulated, leading to insulin resistance in the body, and shift towards a pro-inflammatory phenotype, gluteal obesity, dipokine balance shifts at anti-inflammatory profile. [32].

The protein adiponectin is produced individually from A.T, Blood levels of adiponectin decrease in patients with obesity and insulin resistance. It has multiple Good effects on the heart and blood vessels in body and also antioxidant, anti-apoptotic, anti-inflammatory, and vasorelaxant properties. [33]. Reduced adiponectin levels may contribute to high risk of various cardio diseases in patients with obesity and diabetic. However, Previous studies found a significant increase in adiponectin levels in heart failure (HF) patients [32]. Studies demonstrated direct and indirect role of adiponectin in cardiovascular diseases, adiponectin as

well as a clinical biomarker in cardiovascular diseases remains controversial. Recent research provides evolving perspectives on the future clinical effects of adiponectin. In current article review, discuss the bioactivity of adiponectin & relationship to obesity its associated diseases, we then test Explain the use of plasma adiponectin levels as a biomarker for the development of cardiovascular disease [33,34].

1.3. Diabetes-Type_2

Adiponectin Serum levels decrease at obesity in a study a animal model (monkey) that frequently develops type 2 diabetes [35].

Decreased blood adiponectin concentrations were found to coincide with diabetes appears in these animals with observation Insulin sensitivity, decreases at same time [35]. Decreased plasma adiponectin levels in obese people, especially those with visceral obesity, Inverse relation to insulin resistance [36-37]. It also significantly associated with the development of type 2 diabetes in the Pima Indian race [38]. Decreased conc. of adiponectin in the plasma, also Usually noted at a variety of conditions Often linked with (IR), CVD. [39,40], (high blood pressure) hypertension [41, 42].

The action of adiponectin has been found to cause insulin resistance.

For the first time by 3 independent groups in 2001 (43,44). It was evaluated adiponectin is able to improve (IR) insulin resistance in K.K.A. mice, K.K Laboratory animals (mice) expressing agouti protein, as a model of metabolism diseases and diabetic associated with obesity. A significant decrease in adiponectin levels was observed in the blood of K.K.A. y animal laboratory- mice with a high lipids diet..

Regeneration a protein adiponectin ameliorate the elevated. Diet causing insulin resistance and hyperlipidemia led to the suggestion adiponectin is an, insulin sensitive adipokines. [43] These results also These results strongly suggest that a high percentage of fat leads to diet_induced low adiponectin associated with obesity is a cause It is involved in obesity_related insulin resistance & metabolism diseases. Scherer et al., reported a significant increasing in conc. Of adiponectin leads to a decline in blood sugar concentration by inhibiting both hepatic expression, . Gluconeogenic enzymes and glucose rate production in diabetic -1 & 2 lab. Animals, thus suggested Adiponectin improves insulin sensitivity [45].

Results and Discussion

3.1. obesity

Insulin resistance has an incomprehensible genetic cause Quite to date, which is often conveyed across generations. Moreover, obesity has an important genetic link This exacerbates insulin resistance.

Thus, obesity and insulin resistance usually are present for many years before the other appeared. Other changes such as hypertension, dyslipidemia and T2DM and cardiovascular disease [46,47]

It is often associated with insulin resistance. With increased body weight and impaired cardiovascular function. In addition, many adipokines such as adiponectin, TNF- α , resistin and interleukins are associated with this pathological condition [48].

Some previous studies showed that high levels of adiponectin increased insulin sensitivity, resulting in decreased blood glucose levels and glucose production of hepatic by inhibition of hepatic glucose expression enzymes and rate production of endogenous glucose [49; 50].

3.2. Insulin Resistance

Insulin resistance has an important and prominent role in disorders of glucose metabolism. Understanding the role, synthesis and Insulin secretion, through a wide range of physiological activity & its effect on cell metabolism, along with its influence from molecular level to whole-body, a significant implications to the diseases that appear in the population [51]. Main causes of IR in diabetes TYPE2 is the damage & influence of β -cells, and in some cases also long-term stress causes an increase in the hormone cortisol, as the high level of this hormone leads to damage to β -cells, by way, which reduces production of insulin and high of Insulin resistance [52].

2.4- Adiponectin with Insulin Resistance

Adipo. Rs It a major role in activating AMPK protein kinase enzyme & a peroxisome proliferator-activated receptor- α (P.P.A.R- α) ligand activities [47]. Adiponectin had been influenced on glucose absorption & Beta-type Oxidation by AMPK [48]. AMPK activation of skeletal muscle, It is stimulated by globular, all-length adiponectin. Also in liver it is present in its complete form [48,49]. Cause of low glucose Adiponectin may be responsible for The process of adding a phosphate group by enzyme acetyl coxylase, and an increase in fatty acids catabolism, Glucose sugar absorption, production of lactate at muscle cells. All activities led to, adiponectin limits gluconeogenesis in liver through PPAR- α .

Adiponectin increases the processes of fatty acid metabolism and bioenergy burning, leading to their decrease Triglycerides and increased insulin sensitivity in skeletal muscle and liver cells. [50]

Studies, confirmed in lab. Animals importance of AdipoRs in the regulation of physiological metabolism via adiponectin, highlight functional differences [51,52], and also report different results. Adiponectin-induced AMPK activation in lab. Animals by deletion of AdipoR1, resulting in decline adiponectin-stimulated (P.P.A.R- α) signal; Simultaneous ablation of AdipoR1 & AdipoR2 Forbidden adiponectin binding, action, resulting in insulin resistance and glucose intolerance

[51]. AdipoR-1- mice noted elevated obesity, glucose_intolerance, while AdipoR-2- lab. mice appear were lean and renitent to diet_induced glucose intolerance, suggesting . AdipoR-1 & AdipoR-2 may opposite effects [52]. also , deletion, of Adipo-R2 reduced diet_ induced I R , a increased sensitivity Type2 –Diabetic[53]. .

3.3. Diabetes type2

More of 284 million people in worldwide, which is approx. 2010 world's population. In addition, forecasts for the year (2030%) 6.4. The number of people with diabetes may be as high as(439) million, or 7.7% of the world's population. Which leads to an increase in expenses million US dollars in 2010, the total economy in the past decade, million US dollars in 2010, the total is expected to (376.000) reach 490. thousand million dollars in 2030 expected to (376.000) reach 490.

Generally, inactive lifestyle leads to excessive gain in body weight (obesity) [53]. Approximately 1.4 billion people are high weight , 500 million or more suffer from obesity. Obesity is one of the most important risk factors of many diseases, especially type 2 diabetes, and thus increases mortality among Older people [54]. Diabetes is high blood levels glucose which leads to dangerous complications affecting important organs in the body, such as the eyes, blood vessels, kidneys, and nerves. Type 2 diabetes constitutes about 90% of all diabetics [55]. Obesity is a major factor in occurrence of insulin resistance(IR) in body, IR is one of causes of type 2 diabetes, which is associated with a defect insulinsecretion, carbohydrate and fat metabolism [56]. Insulin resistance is a pathological condition defined as a defect functioning of insulin hormone in metabolism of target tissues [57]. Globally, there is a significant increase in number of people with type 2 diabetes, reaching approximately 6.5% (285 million people) in 2010, expected to rise to 7% (439 million people) in 2030 [53]. . Explaining reason for increase is the most important step towards treating the disease. The main reason for increase in infections is a change in inactive lifestyle, eating large amounts of unhealthy food, and no exercise, but there is also an emerging body of evidence. Suggesting the influences of genetic factor [56]. Adiponectin is one of proteins secreted from adipose tissue and plays an important roles in increasing lipids metabolism, regulating glucose tolerance and controlling insulin sensitivity to save person with diabetic [58]. Also , a diponectin is one a biochemical parameter of most important biomarkers of diabetic multues [59]. Studies have confirmed influence of adiponectin on insulin sensitivity were conducted on laboratory mice. [60]. Studies confirmed a negative correlation between plasma adiponectin levels with high insulin resistance with type 2 diabetes [61]. Main reference of certificate for ability of adiponectin to increase glucose sugar tolerance in rat _ diabetic , a single conc. administration of adiponectin resulted in significant decrease in nutrient and blood glucose concentrations . [62].

Conclusion

Adiponectin is a key mediator of glucose homeostasis and insulin sensitivity. This effect is achieved through a variety of actions. It targets several important tissues such as pancreas, liver, cardiac muscle cells, and immune system, as well as adipose tissue. On the other hand, Adiponectin protein works to inhibit glucose production from liver and reducing inflammatory in various body cells, as well as macrophages. Adiponectin has a significant effect on sphingolipid metabolic pathways and antiapoptotic activities. It has been specifically documented for β -cells and cardiomyocytes. In spite of very great interest in adiponectin and a significant increase in number of publishing on adiponectin. In addition to being a risk factor for a number of diseases, which include obesity, metabolic syndrome, and diabetes. Depletion of adiponectin or attenuation of its activity may provide a new therapeutic option for the treatment of diabetic multiuse and obese.

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