Short Communication

Adiponectin – Its role in metabolic and inflammatory disorders

Geetha Rani R

Department of Anatomy, Sree Balaji Medical College and Hospital, BIHER University, Chennai

Abstract

Adiponectin is a complex protein hormone that is produced by adipocytes and skeletal muscle, as recent studies have shown. The level of adiponectin is higher in healthy individuals and paradoxically, decreased in obesity and related metabolic disorders. Though it was discovered a decade ago, the physiological roles of the hormone have come to light only recently, with advances in biochemical methods to measure its plasma level. A relatively new hormone, adiponectin has been found play important regulatory roles in many metabolic pathways. Various studies have shown that an increase in adiponectin levels has a protective effect in insulin-resistance, type 2 diabetes mellitus, coronary heart disease (CHD) and cerebrovascular accidents (CVA). This short communication aims to highlight the physiological actions of adiponectin and its potential value in the management of these conditions.

Keywords: adipoytes, hormone, metabolism

Corresponding author
Dr. Geetha Rani R, Tutor, Department of Anatomy, Sree Balaji Medical College and and Hospital (BIHER University), No.7, Works Road, Chrompet, Chennai.
Telephone: + 91 8825838126, Email: geethanatesh2012@gmail.com

Introduction

Adiponectin, also known as Acrp30 (adipocyte complement-related protein of 30kDa) is a complex 244-amino acid protein hormone exclusively secreted by adipocytes and skeletal muscle, as recent studies have shown. Paradoxically, plasma levels of adiponectin are reduced in obesity, in contrast ot those of most adipokines.[1,2]

It is an abundant serum protein, structurally similar to complement factor C1q, accounting for up to 0.05% of total serum protein.[2,3] Circulating adiponectin levels range from 0.5 to 30 µg/ml in humans, which are a thousand-fold higher than circulating levels of insulin or leptin.[2] A plasma level lower than 0.5µg/ml is associated with obesity and risk of acquiring metabolic disorders.[1] Adiponectin levels are generally higher in women.[2] Human adiponectin is encoded by the ADIPOQ gene, involved in regulating glucose levels as well as fatty acid metabolism.[1] The actions of adiponectin on glucose uptake and fatty acid oxidation are mediated through its receptors, AdipoR1 and AdipoR2.[1] Both the receptors contain seven transmembrane domains but they are structurally and functionally completely distinct from G-protein-coupled receptors.[1]

Physiological Effects

Adiponectin has been found to play regulatory roles in a number of metabolic pathways. The insulin-sensitizing and anti-diabetic effects of adiponectin are well established. It is also reported to be cardio-protective and acts as an anti-inflammatory agent.

Role in Diabetes Mellitus and Obesity

Acting in an autocrine and endocrine manner, adiponectin exhibits two major mechanisms of action

by which it exerts its anti-diabetic effects: one is by increasing insulin sensitivity and the other way is by increasing fatty acid oxidation.[4]

Adiponectin acts via AdipoR1 receptors abundantly expressed in skeletal muscle to activate the AMP-activated protein kinase (AMPK) pathway which causes the translocation of GLUT-4 receptors to the cell surface, bringing about an increase in glucose uptake by the cell.[1]

Adiponectin induces fatty acid oxidation in muscle cells by sequential activation of AMPK, p38 MAPK (mitogen activated protein kinase) and peroxisome proliferator-activated receptor-α (PPARα). The AdipoR2 receptors that mediate the actions of adiponectin on fatty acid oxidation are mainly expressed in the liver. It is interesting that adiponectin levels are lower in obese individuals than their lean counterparts.[1] Decreased levels are implicated in the development of insulin resistance.[5] Adiponectin is emerging as a potentially significant biomarker in type 2 diabetes.[1]Studies reveal that serum adiponectin levels are inversely related with fasting insulin and C-reactive protein (CRP).[6]

Anti-atherogenic role of Adiponectin

Atherosclerosis is a pathologic phenomenon characterized by an increase in vessel wall thickness, which gradually leads to the development of coronary heart disease (CHD) and cerebrovascular accidents (CVA).[7] T-cadherin localizes adiponectin to the vascular endothelium.[1] The anti-atherogenic effects of adiponectin are exerted by reducing TNFα-induced monocyte attachment to endothelial cells and inhibiting platelet derived growth factor-BB to minimize vascular smooth muscle cell proliferation.[2] Exogenous adiponectin administration has been shown to protect against development of atherosclerosis in apolipoprotein E–deficient mice.[8] Another interesting finding is that supplementation with adiponectin causes revascularization in a limb that has completely lost its blood supply due to plaque formation.[9]

Role of Adiponectin in adipose tissue

Adiponectin supplies energy by increasing the mobilization of lipids in adipose tissue. Increased levels of adiponectin help in the release of cholesterol and lipids in serum and also bring about oxidization of free fatty acids.[5] The high level of adiponectin helps in insulin sensitization, in protecting arteries and keeping coronary functions under normal level, actions that are enhanced by an increase in the levels of nitric oxide.

Role of Adiponectin in inflammation

Adiponectin plays a protective role in inflammatory diseases.[10] It is found to decrease inflammation in endothelial, epithelial and muscle tissues by activating cyclic AMP and protein kinase pathways. Via ADIPOR1, adiponectin increases the expressions of a number of genes, including those that code for NF-kβ, TNFα, IL1 and IL4. Further, NF-kβ decreases the expression of VCAM1, ICAM1 and IL18, which are important mediators of inflammation.[1] Studies have shown that low level of adiponectin is an indicator of CVA and CHD.

Does an increase in the level of adiponectin help in the control of uncontrolled diabetes mellitus, CHD and CVA?

In cultured muscle cells, treatment with rosigiltazone has been shown to increase the secretion of adiponectin and enhance insulin sensitivity.[6] Some support for the idea that adiponectin levels are strongly related to type 2 diabetes is suggested by observations that newer drugs with beneficial effects on insulin resistance and glucose intolerance (such as the peroxisome proliferator-activated receptor-γ agonists and the selective cannabinoid-1 receptor blocker rimonabant) increase adiponectin concentrations.[11] As blood adiponectin concentration is a modifiable risk factor, it can be efficiently targeted by lifestyle modifications, mainly weight loss and dietary changes. The role of recombinant adiponectin holds promise. If pharmacological preparations of adiponectin can be rendered economically viable and achieve an increase in half-life, they could be of potential value in the management of metabolic disorders.

Conclusion

Adiponectin is a new hormone that has emerged as a crucial regulatory adipocytokine as well as myokine.[12] Despite its low half-life, its value in the management of many metabolic and inflammatory disorders is of interest. Decreased adiponectin is implicated in the development of insulin resistance and progressive inflammation, which indicates that the replenishment of adiponectin might provide a novel treatment modality for insulin resistance, type 2 diabetes, coronary heart disease and cerebrovascular accidents.

Acknowledgment: Nil

Conflicts of interest: Nil

References

1. Ghoshal, K.; Bhattacharyya, M. Adiponectin: Probe of the molecular paradigm associating diabetes and obesity. World J. Diabetes 2015, 6, 151–166. [CrossRef] [PubMed]
2. Park KG, Park KS, Kim MJ, Kim HS, Suh YS, Ahn JD, Park KK, Chang YC, Lee IK. Relationship between serum adiponectin and leptin concentrations and body fat distribution. Diabetes Res Clin Pract. 2004; 63:135–142.
3. Maeda, K.; Okubo, K.; Shimomura, I.; Funahashi, T.; Matsuzawa, Y.; Matsubara, K. cDNA cloning and expression of a novel adipose specific collagen-like factor, apm1 (adiposemost abundant gene transcript 1). Biochem. Biophys. Res. Commun. 1996, 221, 286–289.
4. Yamauchi T, Kamon J, Waki H, Imai Y, Shimozawa N, Hioki K, et al. Globular adiponectin protected ob/ob mice from diabetes and ApoE-deficient mice from atherosclerosis. J Biol Chem. 2003; 278: 2461–2468.
5. Scherer, P.E.; Williams, S.; Fogliano, M.; Baldini, G.; Lodish, H.F. A novel serum protein similar to c1q, produced exclusively in adipocytes. J. Biol. Chem. 1995, 270:26746–26749.
6. Yang WS, Jeng CY, Wu TJ, Tanaka S, Funahashi T, Matsuzawa Y, et al. Synthetic peroxisome proliferator-activated receptor-gamma agonist, rosiglitazone, increases plasma levels of adiponectin in type 2 diabetic patients. Diabetes Care. 2002; 25: 376–380.
7. Matsuda, M.; Shimomura, I.; Sata, M.; Arita, Y.; Nishida, M.; Maeda, N.; Kumada, M.; Okamoto, Y.; Nagaretani, H.; Nishizawa, H. Role of adiponectin in preventing vascular stenosis the missing link of adipo-vascular axis. J. Biol. Chem. 2002; 277:37487–37491.
8. Yamauchi, T.; Kamon, J.; Waki, H.; Terauchi, Y.; Kubota, N.; Hara, K.; Mori, Y.; Ide, T.; Murakami, K.; Tsuboyama-Kasaoka, N. The fat-derived hormone adiponectin reverses insulin resistance associated with both lipoatrophy and obesity. Nat. Med. 2001; 7: 941–946.
9. Nakano, Y.; Tobe, T.; Choi-Miura, N.-H.; Mazda, T.; Tomita, M. Isolation and characterization of gbp28, a novel gelatin-binding protein purified from human plasma. J. Biochem. 1996; 120:803–812.
10. Díez JJ, Iglesias, P. The role of the novel adipocyte-derived hormone adiponectin in human disease. Eur. J. Endocrinol. 2003; 148:293–300.
11. Ahima RS, Flier J.S. Adipose tissue as an endocrine organ. Trends Endocrinol. Metab.2000; 1:327–332.
12. Liu Y, Sweeney G. Adiponectin action in skeletal muscle. Best Pract Res Clin Endocrinol Metab. 2014; 28(1):33-41.