

Some Adipocytokines (Leptin, Resistin, Vesfatin) Relationships with Obesity

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Abstract

Adipose tissue is widely concerned as an active endocrine organ, and have a crucial role in the innate immune system . Adipocytokines perform a role in the pathogenesis of insulin resistance and related metabolic complications, and also they cause both beneficial and detrimental immune and inflammatory effects. And most of these adipocytokines are physiologically important for metabolism, such as leptin, resistin, and visfatin which may serve as a missing connection between obesity and diabetes in the causal relation. Also it may have myriad anti-inflammatory effect. It should be considered the functional balance of the adipokines and obesity.

Keywords: Adipokines , Obesity, Diabetes, Immunity.

Introduction

Obesity remains a global public health concern. The prevalence is rising in both the developed and developing countries, Improved food patterns and activity levels [1-2]. There is a higher risk of overweight obese for a wide range of chronic and life-threatening impairments and early death [3-4]. Visceral obesity can be seen as a risk factor with too many aspects of hazard and mortality [5]. It also leads not just in health consequences but also in a clear inverse correlation to social status, as stated by many advantaged communities [6-7]. Over weight is primarily related to an imbalance in energy between calorie intake and consumption, and several complex underlying physiological, environmental and behavioral factors influence the outcome [7]. Given that people eat meals consisting of complex association from nutrients and non-nutrients, total meals should be viewed in relation to dietary intakes, rather than single nutrients. Scientists are becoming more and more involved in studying dietary patterns to understand the growing problem of obesity [8]. Not only is obesity regarded a disease on its own, so it causes and exacerbates several diseases and has

been assumed to provide a major risk to many chronic disorders, particularly diseases such as diabetes, heart disease, osteoporosis and other cancers, high mortality and morbidity pathologies in Europe and the rest of Europe[9].

Characteristics of personality such as psychological influences, social and economic status, educational rates and lifestyles may determine eating habits that contribute to increased risk of excess weight. Therefore, physicians and nutritionists could not ignore these features that alter the normal diet not only of their patients, but also of the general population[10,11].

Visceral fat is a complex endocrine gland network, classified into white adipose tissue (WAT) and brown adipose tissue (BAT). In addition to the body's energy storage function, WAT is primarily responsible for insulation and structural support, while BAT is specialized in thermogenesis and lipid metabolism [11]. BAT activation also controls channel capacity for clearing triglyceride-rich lipoprotein (TRL) and preventing excessive aggregation of lipids in the blood [12].

Visceral and subcutaneous adipose tissues are the most abundant depots which produce unique adipokine profiles [13]. Such molecules were also arranged via a multi-functional network of different functional categories such as immunity (complementary factors, haptoglobin), endocrine function (leptin, adiponectin, visfatin, resistin, apelin, omentin, sex steroids, various growth factors), metabolic function (fatty acids, resistin, vaspin, adiponectin), angiotensinogenic cardiovascular function, prostaglandin, adiponectin and fatty acid [14-15].

Fat tissue secretes numerous bioactive adipokines with various functions [13]. Adipokines, were proteins with low molecular weight which use several biochemical activities to exercise pleiotropic processes [16]. Several molecular pathways shed light on the role of the adipokines within the human body at the early 20th century. More than 20 specific hormones have been reported to date (both orexygenic and anorexygenic). Adiponectin's biological functions range from anti-diabetic, anti-atherogenic, anti-inflammatory and anti-cancer, and are manifold. Low amounts of adiponectin were related with metabolic disease, diabetes mellitus, heart disease and high blood pressure[16,17].

Effect of hormones on obesity

Hormones are chemical messengers that regulate processes within our bodies. Leptin and insulin hormones, sex hormones, and growth hormones have an effect on our appetite, metabolism (the pace our body consumes kilo joules for energy), and body fat distribution. Due to their important role as mediators and their involvement in metabolic pathways, adipokines have levels of these hormones that promote irregular metabolism and aggregation [19]. These hormones often reach the key target located in the hypothalamic region efficiently via the blood-brain barrier, exercise their actions and mediate satiety and hunger balance.

Resistance to insulin and type 2 diabetes mellitus may also be caused by excessive adipose mass. This term is associated with tissue-secreted adipose signaling molecules which have effectiveness on the glucose balance, including leptin, fatty acids, resistin, adiponectin, Leptin, and resistin that play a vital role in the regulation of weight and in the metabolism of glucose between all these hormones [20].

In a study conducted by Zieba and Barć [21], leptin and resistin have been shown to act in a same and oppositely directed, and are related. In obesity models, circulating leptin and resistin levels are improved in rodents when fed on a diet with a high-fat. Both leptin and resistin are equally controlled by dietary intake: they are limited by fasting, and decreased by feeding.

Adipokines have several mediators such as resistin, visfatin, retinol-binding protein-4, and leptin, includes adiponectin, pre-B cell colony enhancing factor (PBEF). Adiponectin is an exciting adipokine that has an inverse relationship associated serum concentrations with fatness. It is concerned with improving anti-atherogenic actions, anti-inflammatory effects, insulin sensitivity, and metabolic homeostatic control regulation. It is also recognized that NF- κ B stimulates overexpression of the transcription system, which triggers inflammation and progression of tumours. The inhibition of NF- κ B pathway could have been a powerful therapeutic strategy for cancer treatment and for inflammation [22].

Many other researches have been revealed that lipid deposition in the liver contributes in hepatic inflammation through NF- κ B activation and production of downstream of cytokine, contributing to insulin resistance both hepatically and systemically [21,22]. Some of the hormones of adipokines such as resistin, leptin, ghrelin, and adiponectin, have a role in controlling the metabolism of glucose, and are engaged in development of inflammation, obesity, diabetes, metabolic syndromes, and autoimmunity.

Level of leptin that circulates is appropriate relative to body fat. Such concentrations range from 5 -10 ng/ml in healthy subjects to 40 -100 ng/ml in obese subjects [24]. A temporary increase happens during a diet, while levels of leptin reduce with fasting, evoke dramatic alterations in hormone levels the energy balance [25-26]. Leptin plays a crucial role in controlling appetite and the regulation of energy expenditure [27]. Leptin exerts pleiotropic impacts in the hypothalamus and other tissues, by binding and activating specific leptin receptors (obR). It has direct and indirect effects in metabolically active tissues, and regulates many other neurohormonal axes [28-29].

Resistin

Resistin is another distinctive cysteine-rich signaling molecule obtained from adipocytes, which mainly consists of 114 amino acids and is initially recognized in obese mice. The molecule resistin-like gene family (RELM) is a peptide with the N-terminal signal. In humans the resistin pre-peptide length is 108 amino acid residues and 114 aa residues in mouse and rat; molecular weight is ~12.5 kDa. [30-31].

Resistin expression in white adipose tissue was greater from brown adipose tissue[32] Resistin in mice is expressed in higher adipose tissue while resistin in humans is expressed in lower adipose tissue [33]. Yet resistin is primarily expressed in human macrophages. Resistin is thus known as insulin resistant. Resistin was also reported to increase circulating rates in humans who are overweight. It is considered to be a molecule of proinflammatory cytokines that also have a critical role in the diabetes and its complications of pathogens. Resistin is a recurring release [34].It was seen as evoking 'high' bad cholesterol (low lipoprotein density) and contributing to heart disease [30-32].

Resistin promotes the development of LDL in human liver cells, as well as adversely affects liver LDL receptors. The liver may be less capable of removing 'poor' cholesterol from the body [34].

Visfatin

Visfatin, considered the pre-B colony designed to improve the factor (PBEF), is a highly conserved, 52-kDa protein present in living species from bacteria to humans [35].

Owing to its important sequence and functional homology with nicotinamidephosphoribosyltransferase (NAM-PRTase), an enzyme involved in nicotinamideadeninedinucleotide biosynthesis (NAD), visfatin is also referred to as NAMPT [36] The visceral adipose tissue is created from that. In subjects with abdominal obesity and type 2 diabetes, visfatin is induced [33].

Conflict of Interests.

There are non-conflicts of interest .

References

- [1] National Task Force on the Prevention and Treatment of Obesity. Overweight, obesity, and health risk. Arch Intern Med. 2000; 160: 898 – 904.
- [2] Azizi F, Azadbakht L, &Mirmiran P. (2005)Trends in overweight, obesity, and central fat accumulation among Tehranian adults between 1998 – 1999 and 2001 – 2002: Tehran Lipid and Glucose Study. Ann.NutrMetab.; 49: 3 – 8.
- [3] Fontaine KR, Redden DT, Wang C, Westfall AO, & Allison DB. (2003).Years of life lost due to obesity. JAMA.; 289: 187 – 193.
- [4] Jee SH, SulJWI, Park J, Lee SY, Ohrr H, Guallar E, et al. (2006).Body mass index and mortality in Korean men and women. New Engl J Med. 355: 779 – 787.
- [5] National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). (2002)Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and



- Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *circulation*; 106: 3143 – 3421.
- [6] Wardle J, Waller J, Jarvis MJ. (2002) Sex differences in the association of socioeconomic status with obesity. *Am Public Health.*; 92: 1299 – 1304
- [7] Sarlio-Lahteenkorva S, & Lahelma E. The association of body mass index 1999; 28: 445 – 449.
- [8] Togo P, Osler M, & Sorensen T. (2001) Food intake patterns and body mass index in observational studies. *Int J Obes.*; 25:1741-51.
- [9] Szapary PO, Bloedon LT, & Foster GD. (2003) Physical activity and its effects on lipids. *CurrCardiol Rep* 5: 488-92.
- [10] Belliste F. (2003) Why should we study human food intake behaviour? *NutrMetabCardiovasc Dis*; 13: 189-93.
- [11] Hahn P, Novak M (1975). Development of brown and white adipose tissue. *J Lipid Res*, 16:79–91.
- [12] Koh-Banerjee P, Chu NF, Spiegelman D, Rosner B, Colditz G, Willett W, & Imm E. (2003) Prospective study of the association of changes in dietary intake, physical activity, alcohol consumption, and smoking with 9- y gain in waist circumference among 16587 US men. *Am J Clin Nutr*; 78: 719-27.
- [13] Kershaw EE, Flier JS: Adipose tissue as an endocrine organ. *J Clin Endocrinol Metab* (2004). 89:2548–2556.
- [14] Wiecek A, Kokot F, Chudek J, Adamczak M. (2002) The adipose tissue—a novel endocrine organ of interest to the nephrologist. *Nephrol Dial Transplant* 17:191–195.
- [15] Yamawaki H, Kuramoto J, Kameshima S, Usui T, Okada M, Hara Y. (2011) Omentin, a novel adipocytokine inhibits TNF-induced vascular inflammation in human endothelial cells. *Biochem Biophys Res Commun*, 408:339–343.
- [16] Brochu-Gaudreau K., Rehfeldt C., Blouin R., Bordignon V., Murphy B.D., Palin M.-F. (2010) Adiponectin action from head to toe. *Endocrine.* ;37:11–32.
- [17] Xia J.Y., Holland W.L., Kusminski C.M., Sun K., Sharma A.X., Pearson M.J., Sifuentes A.J., McDonald J.G., Gordillo R., Scherer P.E. (2015) Targeted Induction of Ceramide Degradation Leads to Improved Systemic Metabolism and Reduced Hepatic Steatosis. *Cell Metab.* ;22:266–278.
- [18] Gualillo O, Gonzalez-Juanatey JR, Lago F (2007) The emerging role of adipokines as mediators of cardiovascular function: physiologic and clinical perspectives. *Trends Cardiovasc Med*, 17:275–283.
- [19] Galic S, Oakhill JS, Steinberg GR (2010) Adipose tissue as an endocrine organ. *Mol Cell Endocrinol*, 316:129–139.
- [20] Zieba, D.; Barć, B. (2020). Roles of leptin and resistin in metabolism, reproduction and leptin resistance. *Domestic Animal Endocrinology*. DOI: 10.1016/j.domaniend..106472.
- [21] Deepa SS, Dong LQ: (2009) APPL1: role in adiponectin signaling and beyond. *Am J Physiol Endocrinol Metab* 296:E22–36.
- [21] Tilg H, Moschen AR (2006). Adipocytokines: mediators linking adipose tissue, inflammation and immunity. *Nat Rev Immunol* 6:772–783.



- [22] PandzicJaksic V: Adipocytokines as mediators of metabolic role of adipose tissue. *Acta Med Croatica*, 64:253–262.
- [23] Tilg H, Moschen AR: (2010). Role of adiponectin and PBEF/visfatin as regulators of inflammation: involvement in obesity-associated diseases. *ClinSci*
- [24] Howard JM, Pidgeon GP, Reynolds JV(2010) Leptin and gastro-intestinal malignancies. *Obes Rev* 11:863–874.
- [25] Ahima RS, Prabakaran D, Mantzoros C, Qu D, Lowell B, Maratos-Flier E, Flier - JS: (1996) Role of leptin in the neuroendocrine response to fasting. *Nature*, 382:250–252.
- [26] Koerner A, Kratzsch J, Kiess W: (2005) Adipocytokines: leptin—the classical, resistin—the controversial, adiponectin—the promising, and more to come. *Best Pract Res ClinEndocrinolMetab*, 19:525–546.
- [27] Flier JS(1998) Clinical review 94: What's in a name? In search of leptin's physiologic role. *J ClinEndocrinolMetab*, 83:1407–1413.
- [28] Konturek PC, Konturek JW, Czesnikiewicz-Guzik M, Brzozowski T, Sito E, Konturek SJ(2005) Neuro-hormonal control of food intake: basic mechanisms and clinical implications. *J PhysiolPharmacol* 56(Suppl 6):5–25.
- [29] Hegyi K, Fulop K, Kovacs K, Toth S, Falus A(2004) .Leptin-induced signal transduction pathways. *Cell BiolInt*, 28:159–169.
- [30] Rajala MW, Lin Y, Ranalletta M, Yang XM, Qian H, Gingerich R, Barzilai N, Scherer PE: (2002) Cell type-specific expression and coregulation of murine resistin and resistin-like molecule- α in adipose tissue. *MolEndocrinol*, 16:1920–1930.
- [31] Chumakov AM, Kubota T, Walter S, Koeffler HP(2004) Identification of murine and human XCP1 genes as C/EBP- ϵ -dependent members of FIZZ/Resistin gene family. *Oncogene*, 23:3414–3425.
- [32] Nohira T, Nagao K, Kameyama K, Nakai H, Fukumine N, Okabe K, Kitano S, Hisatomi H(2004) Identification of an alternative splicing transcript for the resistin gene and distribution of its mRNA in human tissue. *Eur J Endocrinol*, 151:151–154.
- [33] Kusminski CM, McTernan PG, Kumar S(2005) Role of resistin in obesity, insulin resistance and Type II diabetes. *ClinSci (Lond)*, 109:243–256.
- [34] Chaurasia B., Summers S.A.(2015). Ceramides—Lipotoxic Inducers of Metabolic Disorders. *Trends Endocrinol. Metab.* ;26:538–550.
- [35] Rongvaux A, Shea RJ, Mulks MH, Gigot D, Urbain J, Leo O, Andris F(2002,) Pre-B-cell colony-enhancing factor, whose expression is up-regulated in activated lymphocytes, is a nicotinamidephosphoribosyltransferase, a cytosolic enzyme involved in NAD biosynthesis. *Eur J Immunol* 32:3225–3234.
- [36] Ray A(2012). Adipokine leptin in obesity-related pathology of breast cancer. *J Biosci*, 37:289–294.

الخلاصة

تعتبر الأنسجة الدهنية غدد صم ذات كفاءة كبيرة في الجسم، إذ ان لافرازات بعض العوامل الكيميائية والتي تعرف بالسيتوكينات الدهنية (Adipocytokines) من الأنسجة الدهنية دورا مهما في الاستجابة المناعية الفطرية و مقاومة الأنسولين و دورها لدى حالات الاعتلال الايضي في الجسم ، فضلا عن تأثيراتها المناعية المفيدة مرة والضارة تارة اخرى. ويعد الليبتين والريسيتين والفيزفانتين من اهم الاديبوكينات المفردة من النسيج الدهني التي تؤدي دورا منظما لعملية التمثيل الغذائي وللسمنة علاقة وثيقة بمستويات السيتوكينات في الجسم. ومازالت العلاقة بين تراكيز السيتوكينات الدهنية ومرض السمنة والسكري غير واضحة بصورة دقيقة.

الكلمات الدالة: السيتوكينات الدهنية، السمنة، السكري ، المناعة.

