Visfatin: A protein with insulin mimetic properties

Visfatin is a novel adipocytokine enriched in visceral fat. It has been discovered in 2005 by Fukuhara et al.[1] The molecular weight of visfatin is 52 KDa, which is active as a diamer form. It has 491 amino acids with 13 α-helices and 19 β-sheets in each monomer.[1,2] Visfatin corresponds to a protein recognized formerly as pre-β cell colony-enhancing factor (PBEF), secreted by lymphocytes. A short time ago, it was found that visfatin is also identical with Nampt (Nicotinamide phosphoribosyltransferase) gene that codes for NAD biosynthetic enzyme.[1,3]

Recent research has shown that Nampt/visfatin mediated systemic NAD^+ biosynthesis is important for β cell function of insulin secretion, signifying that visfatin helps in regulation of glucose homeostasis.[2,3] Amino acid sequence of visfatin is the same as PBEF/Nampt. A unique protein with three dissimilar names and three divergent functions have made it distinctive and crucial biologically.[2]

Besides being produced in white blood cells and adipocytes, visfatin's mRNA expression was also found in heart, liver, kidneys, muscle, brain, spleen, bone marrow and liver.[3,5] Visfatin acts as endocrine, paracrine and autocrine mediator. Autocrine and paracrine functions assist adipocyte differentiation and fat deposition. Endocrine role alter insulin sensitivity in peripheral organs.[3,6,7]

Visfatin shares properties with insulin that are manifested from animal experimental studies both in vivo and in vitro. It facilitates glucose uptake in adipocytes and myocytes, causes inhibition of hepatic glucose release, stimulation of triglyceride buildup and its synthesis from glucose in pre-adipocytes.[1] Autocrine effects of visfatin may play an important role in regulation of insulin sensitivity in liver.[3]

Visfatin exhibits insulin like activity synergistic to the effects carried out by insulin, though physiologically its plasma concentration is at least 10 times less in contrast to insulin. It activates insulin signaling through insulin receptor with similar affinity and does not compete for binding site as the binding sites are different for both proteins. The mechanism of action involved is tyrosin phosphorylation and downstream protein kinase β activation alike that of insulin.[1,8]

Blood glucose lowering effect of visfatin administration was observed in insulin resistant and insulin deficient mice.[1,8] Thiazolidinediones enhance insulin sensitivity in subjects with insulin resistance and type 2 diabetes mellitus (T2DM). It has been observed in a study that treatment of high fat diet rats with rosiglitazone considerably reduced the levels of serum visfatin, glucose and insulin which may be a consequent effect for the improvement of insulin resistance.[7] Heterozygous mutations in the visfatin gene exhibit glucose intolerance primarily because of insulin secretion deficiency and it can be corrected by the administration of nicotinamide mononucleotide (NMN), the visfatin product in NAD biosynthesis. As there is very little concentration of visfatin in pancreas, it has been proposed that the maintenance of high levels of circulating NMN by extracellular visfatin are decisive for normal β-cell function[9]. Raised serum visfatin levels have been reported in obesity and T2DM in many studies. This may be explained as a compensatory mean to improve insulin resistance in these metabolic conditions.[10-14]

Increased serum visfatin concentration in T2DM might be helpful in synergizing the effects of insulin and intends to ameliorate the functional consequences of insulin deficiency or it may be a component of pathophysiology of DM. Although, it has insulin like effects, still there is a dispute for its role regarding insulin resistance. More studies are required to establish a true picture. On account of insulin like activity, visfatin might emerge as potential anti-diabetic drug, which could be helpful in stalling or slackening the global epidemic of DM and its subsequent complications.

As the worldwide prevalence of T2DM is growing rapidly and our means to avert or cure the disorder are limited regardless of enormous research efforts, hence new trials like visfatin are most welcome, even if they are to be proven false.

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