

Possible interaction between visfatin, periodontal infection, and other systemic diseases: A brief review of literature

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ABSTRACT

Gingivitis and periodontitis are common bacterial infections caused by a variety of microorganisms. Despite the microorganisms' roles as etiologic agents, inflammation-induced substances also have crucial parts in the loss of connective tissue and the supporting alveolar bone. Visfatin is a pleiotropic mediator, which acts as growth factor, cytokine, and pre-B-cell colony-enhancing factor. A positive correlation was detected between the serum/plasma levels of visfatin and inflammatory disorders such as diabetes mellitus and cardiovascular disease. In addition, the visfatin level was higher in saliva and the gingival crevicular fluid (GCF) of subjects with periodontal disease. This review defined current, predictable patterns of possible interaction of visfatin with periodontal infection and other systemic diseases, using PubMed and Medline databases searching for articles written in English. Peer-reviewed articles were targeted using the following keywords: "visfatin," "periodontal disease," "inflammatory mediator," and "biomarker." Available full-text articles were read, and related articles were also scrutinized, while a hand search was also performed. Search was confined to human studies, and articles written in English and published between 1985 and 2016 were selected. It was concluded that periodontal infection and other systemic diseases could be related to the levels of visfatin in GCF, saliva, and serum as a biomarker of these diseases.

Key words: Biomarker, inflammatory mediator, periodontal disease, visfatin

INTRODUCTION

Periodontitis is a known oral inflammatory disease initiated through chronic bacterial infection. Based on the literature, Gram-negative anaerobic and aerophilic bacteria contained in the mouth's biofilm are responsible for disease initiation and progression.^[1] In its acute form, chronic periodontitis destroys periodontal tissue fibers and the supporting bone which leads to apical

migration of junctional epithelium and formation of deep periodontal pockets around the teeth. The untreated periodontal pockets host a variety of highly virulent microorganisms, and they lead to inflammatory-immune response and tissue destruction.^[2] To decrease periodontal disease and its damage, there is a growing demand to locate the most specific and sensitive biomarker in saliva

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and gingival crevicular fluid (GCF). Biomarkers are defined as an indicator of normal biological or pathogenic processes, or as a pharmacologic response to a therapeutic intervention.^[3]

In 2005, a new adipokine was identified and named visfatin (visceral fat adipokine).^[4] It is identified as pre-B-cell colony-enhancing factor, which is involved in the early development of B-cell growth factor and cytokine-like effects, and it also has a role in energy metabolism. Visfatin is a 52-KDa protein, increasing pre-B-cell colony release from lymphocytes and improving maturation of B-lymphocytes.^[5] Furthermore, production of interleukin-1 beta (IL-1 β), tumor necrosis factor alpha (TNF- α), and IL-6-induced by visfatin have also been reported during infection and inflammation.^[6] Visfatin is also known as nicotinamide phosphoribosyltransferase, an enzyme inhibiting the biosynthesis of nicotinamide adenine dinucleotide.^[7] Visfatin is secreted by visceral adipose tissue and macrophages. In addition, it is isolated from several tissues, such as white blood cells, lymphocytes, muscle, dendritic cells, and bone marrow.^[8] Therefore, it is considered an inflammatory adipokine that is available in inflammatory cells and inflammatory conditions. For example, the expression of visfatin increases in acute and chronic inflammatory conditions.^[9] This review defined current, predictable patterns of possible interaction of visfatin with periodontal infection and other systemic diseases, using PubMed and Medline databases searching for articles written in English. Peer-reviewed articles were targeted using the following keywords: "visfatin," "periodontal disease," "inflammatory mediator," and "biomarker." Available full-text articles were read, and related articles were also scrutinized, while a hand search was also performed. The articles written in English and published between 1985 and 2016 were selected.

DETECTION OF VISFATIN IN SALIVA AND GINGIVAL CREVICULAR FLUID

Saliva contains specific biomarkers, and specific changes in these markers might help the diagnosis of periodontitis. Salivary levels of visfatin are an acceptable alternative in the evaluation of inflammatory conditions.^[10,11] It was reported that the levels of salivary resistin, visfatin, and adiponectin was correlated with serum hormonal levels.^[12] For example, GCF is in close contact with periodontal tissues; therefore, GCF levels reflect the status of this tissue. In fact, the vast levels of cytokines present in GCF are potentially useful for diagnosis of periodontal disease.^[13] Visfatin

exists in both saliva and GCF, and its levels alter depending on physiologic and pathophysiologic conditions. In addition, visfatin levels was determined in the GCF of healthy individuals and patients with periodontitis, and the study investigated the possible relationship between this adipokine and the presence and levels of *Porphyromonas gingivalis*, *Prevotella intermedia*, *Prevotella nigrescense*, and the Epstein-Barr virus (EBV).^[14] It was concluded that the presence of EBV in oral plaque may be another factor that causes an increase in visfatin levels.

VISFATIN AND PERIODONTAL DISEASE

Despite reports on the role of visfatin as a marker in periodontal diseases,^[15] only a few studies have been conducted in this area. One study^[16] found a correlation between visfatin and the progress of periodontal disease. In this study, the relationship between the serum and GCF concentrations of visfatin and periodontal diseases was evaluated and it was eventually concluded that concentrations of visfatin in the serum and GCF progressively increased among patients suffering a range of gum diseases from gingivitis to periodontitis. In addition, the concentration of visfatin was higher in patients with periodontal disease and type 2 diabetes mellitus (T2DM) compared to individuals with the periodontal disease but without T2DM. Tabari *et al.*^[17] reported a relationship existed between salivary visfatin and chronic periodontitis in which salivary visfatin concentrations elevated during periodontal infection. Another study^[18] stated that salivary visfatin levels were significantly higher in the gingivitis and periodontitis subjects when compared to those in the healthy subjects.

In addition, Özcan *et al.*^[19] investigated the expression of visfatin, NF- κ B (NF- κ B1 and NF- κ B2), PI3k, TNF- α , and IL-1 β in the tissues of healthy individuals and patients with periodontitis. They revealed increased visfatin levels were associated with the expression of NF- κ B and PI3k, which may play a role in the pathogenesis of periodontitis. We suggest that increased visfatin may contribute to the inhibition of neutrophil apoptosis through the NF- κ B and PI3k signaling pathways.

ALTERATION IN VISFATIN LEVELS AND PERIODONTAL THERAPY

It was reported that both serum and GCF concentrations of visfatin decreased after periodontal treatment.^[20]

Decreased levels of this cytokine after periodontal therapy may lessen the risks associated with the condition, and visfatin is targeted for its therapeutic potential in the treatment of periodontal diseases. In comparison, Abolfazli *et al.*^[21] evaluated the effect of nonsurgical periodontal treatment on serum and salivary levels of visfatin. They found decreased clinical parameters of *P* laque index, gingival index, probing pocket depth, clinical attachment levels following nonsurgical periodontal treatment.

In the latest study^[22] that compared changes in the levels of visfatin, decreased amount of GCF was found in healthy subjects as well as in subjects with periodontitis, with or without controlled T2DM, after administration of nonsurgical periodontal therapy. It was concluded that visfatin levels are highest in individuals with both periodontal disease and diabetes, even after periodontal therapy. Individuals with T2DM may be at higher risk of developing periodontal disease.

THE LINK BETWEEN VISFATIN AND TYPE 2 DIABETES MELLITUS

Furthermore, one of the main risk factors for insulin resistance and T2DM is excess adiposity. Adipose tissue produces numerous adipocytokines include leptin, adiponectin, resistin, visfatin, TNF, and IL-6. In addition, it is able to modulate insulin sensitivity in diabetes, dyslipidemia, inflammation, and atherosclerosis. However, the mechanisms of adipocytokines in the pathogenesis of T2DM were not fully elicited.^[23]

The dual effects of visfatin as an adipocytokine, specifically as a global insulin-imitator and local adipogenic, have created a therapeutic challenge for visfatin in the treatment of T2DM.^[24] However, mechanisms have been introduced that explain how visfatin acts on a cellular level. In brief, visfatin binds to insulin receptors and stimulates glucose uptake in adipocytes and muscle cells while suppressing glucose release from the hepatocytes.^[25] For example, Haider *et al.*^[26] found plasma visfatin levels increased with elevated blood glucose. The expression of visfatin up-regulated in a glucose-dependent manner in cultured adipocytes.^[27] In healthy volunteers taking a glucose tolerance test, visfatin increased with deteriorated insulin secretion reactions to glucose.^[28] These results displayed the relationship between serum visfatin and the inflammatory state in T2DM.

VISFATIN AND OBESITY

It is reported that plasma visfatin is high in overweight or obese patients. The abundance of adipose tissue in these patients is responsible for elevated levels of visfatin.^[29-31] Choi *et al.*^[32] reported the level of visfatin was higher in Korean obese women participants when compared to nonobese participants. They also detected a correlation with plasma visfatin and body weight reduction using an exercise program.

VISFATIN AND POLYCYSTIC OVARY SYNDROME

Polycystic ovarian syndrome (PCOS) is a multifaceted metabolic disease associated with insulin resistance and obesity. Women exhibiting PCOS have higher plasma levels of visfatin. In addition, the visfatin level in the subcutaneous and visceral adipose tissues was higher among women with PCOS.^[33]

VISFATIN AND CARDIOVASCULAR DISEASE

One study^[34] revealed that visfatin levels increased in patients with cardiovascular disease. Visfatin plays a key role in the pathogenesis of macrovascular diseases. Moreover, visfatin levels are high in the atherogenic plaque of patients with acute myocardial infarction. Matrix metalloproteinase two and nine expressions were activated by visfatin in human endothelial cells. Therefore, there was a correlation between visfatin and atherogenic plaque instability,^[35] implying an interaction between visfatin and inflammatory atherosclerotic diseases. Visfatin was high, significantly expressed in symptomatic atherosclerotic carotid plaques, and it was localized to areas with lipid-loaded macrophages.^[36]

CONCLUSION

Visfatin in GCF, saliva, and serum can be considered an inflammatory biomarker in periodontal disease. Periodontal disease progression has been identified as a predictor of high-risk diseases such as diabetes and cardiovascular diseases. Periodontal infection influences the systemic inflammatory reaction by upregulating pro-inflammatory agents such as visfatin. Further research can be conducted to determine visfatin effects on human periodontal conditions. According to the findings of this review, it is tempting to hypothesize that visfatin levels can

be considered a possible link between periodontal infection and other systemic diseases.

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Conflicts of interest

There are no conflicts of interest.

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