صـــور									
1 لون	4 لون								
رقم المقالة	33	الترقيم		عدد الصفحات		ص الألوان			

VISFATIN LEVELS IN GINGIVAL CREVICULAR FLUID OF PATIENTS WITH PERIODONTAL DISEASE

Sarah El Banna* ; Azza Ezz el Arab** and Noha Ghalab***

ABSTRACT

Periodontal disease is defined as an inflammatory disease of the supporting tissues of the teeth caused by specific microorganisms or groups of microorganisms, resulting in progressive destruction of the periodontal ligaments and alveolar bone with clinical attachment loss. The etiopathology of periodontal disease is considered a multifactorial process, where tissue destruction is caused by an interplay between the invading pathogenic microorganisms and the host defense mechanism. Although microorganisms are implicated as the etiologic agent that brings about the inflammatory lesion, chemical mediators of inflammation play a pivotal role in the loss of connective tissue as well as supporting alveolar bone. Visfatin, an adipocytokine produced by white adipose tissue, was found to be increased in patients with inflammatory bowel disease, rheumatoid arthritis and some metabolic disorders as Diabetes Mellitus. It was suggested that Visfatin may play a role in regulation of immune and defense functions. Thus, the evaluation of GCF Visfatin might enhance the understanding of the pathogenesis of different periodontal diseases. The present study was conducted on three groups including healthy subjects (n=10), patients with plaque induced gingivitis (n=15), and others with chronic periodontitis (n=15). This study aimed at evaluating GCF Visfatin levels in the three groups. Clinical parameters including gingival index, plaque index, probing pocket depth, and clinical attachment level were measured for each patient. GCF samples were collected from the most periodontally affected site. Visfatin detection in GCF was performed using a commercial ELISA kit. At the end of the study, clinical and laboratory data were collected for statistical analysis. The present study observed that there was statistically significant difference between control group and both plaque induced gingivitis and chronic periodontitis groups. Although GCF Visfatin levels in chronic periodontitis group were higher than those of plaque induced gingivitis, this difference was not statistically significant. In this investigation, no statistically significant correlation was observed between all clinical parameters recorded and GCF Visfatin levels in both plaque induced gingivitis and chronic periodontitis groups.

* Demonstrator O. Medicine and Periodontology
** Professor O. Medicine and Periodontology
*** Asistant Professor O. Medicine and Periodontoloy

INTRODUCTION

Gingivitis and periodontitis are the 2 major forms of inflammatory diseases affecting the periodontium. Their primary etiology is bacterial plaque, which can initiate destruction of the gingival tissues and periodontal attachment apparatus **(The American Academy of Periodontology, 2004)**.

The role of the host response in periodontal bone loss is complex. There is evidence that a deficient host response increases periodontal destruction and that also a too vigorous response leads to periodontal disease. The first conclusive evidence that the host response played an important role was shown when treatment with a prostaglandin inhibitor reduced the amount of bone loss **(Williams et al., 1985)**.

The incidence and progression rate of periodontal disease depends on complex interaction between periodontopathic bacteria and cells of the host immune system **(Schroeder et al., 1973)**. These interactions are mediated by cytokines and chemokines, which are produced by both resident and emigrent cells at the site of inflammation. Cells that produce cytokines include macrophages/ monocytes, dendritic cells, lymphocytes, neutrophils, endothelial cells and fibroblast **(Abbas et al., 2003)**.

Fat cells secrete a variety of proteins with the functional and structural properties, of cytokines; these are termed "adipocytokines". Adipokines have autocrine , paracrine, and endocrine effects and may be an important link between the immune response and metabolism, predisposing individuals to increased risk of disease **(Bray, 2004 and Tilg and Moschen, 2006)**.

The adipocytokine family has been extended by a novel member, Visfatin as one of the most recently identified adipokines. Visfatin was first described by **Fukuhara et al. (2005)** and was previously identified as pre-B-cell colony enhancing factor, which is a growth factor involved in the early development of B lymphocytes.

Visfatin has been identified in multiple tissues of humans, dogs, laboratory rodents, and pigs. Visfatin has been previously reported to be produced in adipose tissue, bone marrow, skeletal muscles and liver **(Sethi et al., 2005)**.

Visfatin was originally cloned in 1994 from human peripheral blood lymphocytes. The maximum level of Visfatin mRNA was found in the liver tissue and the next highest amount was found in muscle tissue. Antigen presenting cells might be a major source of Visfatin **(Moschen et al., 2007)**. The high expression and secretory property of Visfatin in peripheral vascular adipose tissue (PVAT) indicate that Visfatin may have a potential role in local regulation of blood vessels **(Revollo et al., 2007)**.

On the functional level, it plays a key role in the persistence of inflammation through its capacity to inhibit neutrophil apoptosis. Neutrophils harvested from the circulation of septic patients show marked inhibition of the apoptotic process in association with evidence of enhanced respiratory burst capacity**(Rongveaux et al., 2002)**.

Visfatin can also be considered as a proinflammatory adipokine because it has been observed in inflammatory cells as well as in a variety of inflammatory conditions **(Jia et al., 2004)**.

On one hand, TNF-α seemed to decrease Visfatin expression in adipocytes **(Fukuhara et al., 2005 and Stephens et al., 2006)**.On the other hand, the periodontal inflammation up regulates some pro-inflammatory cytokines such as IL-6 and IL-1β from macrophages and T-helper cells. This, in turn, can lead to a high expression of Visfatin in periodontal tissues, suggesting that Visfatin is regulated differently in different cell **(Pradeep et al., 2011).** However, higher concentrations of Visfatin augment the expression of anti-inflammatory cytokines, e.g. IL10 **(Moschen et al. 2007).**

Some studies showed that inhibition of Visfatin induced activation of certain kinases, which led

to vascular endothelial growth factor production, along with a significant reduction in endothelial proliferation **(Adya et al., 2008).**

Visfatin has been suggested to have a pathological link between some systemic diseases and periodontitis. Some indicate that Visfatin is produced in the periodontium. Oral microorganisms seem to stimulate Visfatin synthesis, suggesting a possible pathogenic role for this adipokine in periodontal diseases **(Pradeep et al., 2011)**.

Serum levels of Visfatin were correlated with obesity and type 2 diabetes mellitus, and have a positive correlation with body mass index. In addition, it has been suggested that obesity, after smoking, is the strongest risk factor for inflammatory periodontal tissue destruction **(Nishida et al., 2005)**

Levels of Visfatin in serum and gingival crevicular fluid (GCF) were explored in patients with periodontal health, periodontal disease with and without type 2 diabetes mellitus.It was found that Visfatin was elevated with periodontal disease, and was correlated with periodontal clinical parameters **(Pradeep et al., 2012).**

In summary, there is currently evidence in the literature examining Visfatin as an inflammatory biomarker in patients with periodontal disease. Based on the knowledge available in the literature, rare studies have been formed comparing GCF level of Visfatin in patients with periodontal disease. According to the above mentioned data, the present study evaluated Visfatin as a marker of periodontal tissue destruction in different periodontal conditions.

Aim of the study

This study was conducted to determine Visfatin levels in the GCF of patients with plaque induced gingivitis and chronic periodontitis subjects, in an attempt to evaluate Visfatin as a biomarker of periodontal tissue destruction.

MATERIALS AND METHODS

The study population consisted of 3 groups of forty patients selected as follows: Group A included 10 healthy control subjects presented with clinically healthy periodontium. Group B (Plaque induced gingivitis patients) included 15 patients who had plaque induced gingivitis with bleeding on probing and no clinical attachment loss nor radiographic evidence of bone loss (Armitage 1999). Group C (Chronic periodontitis group) included 15 chronic moderate to severe periodontitis patients selected according to the criteria currently adopted by ***Armitage 1999***.

The age of the selected patients ranged from 23-50 years, both sexes were included.

After gently drying the area, supragingival plaque was removed without touching the marginal gingiva, and the area was isolated with cotton rolls to avoid saliva contamination. GCF was collected using filter. GCF was collected at the entrance of the gingival sulcus. Samples contaminated with blood or saliva were excluded. GCF was extracted from the filter paper with phosphate buffer saline for detection of Visfatin by ELISA technique.

RESULTS

In the present study the mean (± SD) values of Visfatin in clinically healthy, plaque induced gingivitis and chronic periodontitis groups were 6.7 (±7.4), 44.1 (±42.2) and 73.99 ng/ml (±37.23) respectively (Fig. 1). Plaque induced gingivitis group showed higher Visfatin levels compared to control group and this difference was statistically significant (P value=0.036). In addition, chronic periodontitis group showed higher Visfatin levels than control group and this difference was also statistically significant (P value=0.001). While, when plaque induced gingivitis group was compared to chronic periodontitis group, no statistical significance was observed although Visfatin level was higher in chronic periodontitis group (P value =0.082).

The correlation between Visfatin level in GCF and the age was direct; as the age increases, the Visfatin level is higher. However this correlation was moderate and statistically insignificant

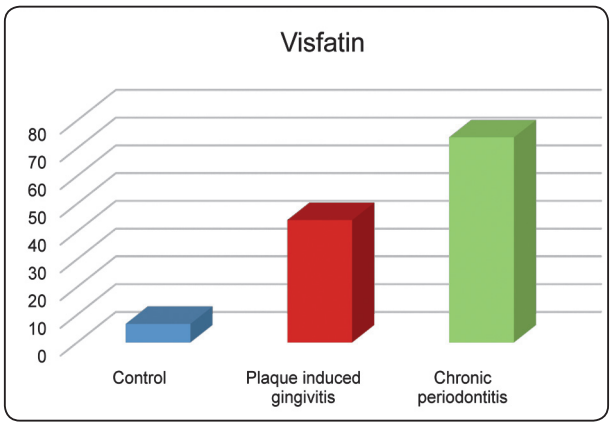

FIG. (1)

DISCUSSION:

The present study has evaluated the Visfatin level in GCF of patients with plaque induced gingivitis, chronic periodontitis and also in periodontally healthy subjects.

The current study demonstrated that mean Visfatin levels in GCF of control, plaque induced gingivitis and chronic periodontitis groups were 6.7, 44.1, 69.7 ng/ml respectively. The highest levels of Visfatin concentrations in GCF were obtained in chronic periodontitis group and the least levels were found in the control group with a statistically significant difference between them. These results came in accordance with **Pradeep et al. (2011)** who proved that concentrations of Visfatin in the GCF increased proportionally with the severity of the disease as estimated by the increase in clinical parameters. This study showed superior values of GCF Visfatin in diseased groups and inferior levels in the control group compared to those observed by **Pradeep et al. (2011).** These differences may be due to the micropapillary pipettes which were used in their study as the method of GCF collection.

Although in this study all participants were selected free from any systemic diseases, low Visfatin levels were found in GCF of healthy subjects in absence of diseased sites. This might be related to the presence of visceral fat in some of those patients.

Although the data presented in this study showed that Visfatin levels in plaque induced gingivitis group was of lower levels when compared to chronic periodontitis group; this difference was of no statistical significance. These results were different with those reported by **Pradeep et al., (2011)** who found a statistical significance between plaque induced gingivitis and chronic periodontitis regarding GCF Visfatin concentrations. This difference might be due to the amount of GCF that has been obtained in the sample.

In addition, the data presented here showed a statistically significant difference between control group and plaque induced gingivitis group as well as between control and chronic perioodntitis group regarding GCF Visfatin concentrations. These results came in accordance with those observed by **Pradeep et al. (2011)**.

Results of Pearson correlation showed negative correlations between PI, GI and GCF Visfatin concentrations, in plaque induced gingivitis group but without statistical significance. These results were similar to those found by **Pradeep et al., (2011)** who found insignificant negative correlation between GI and GCF Visfatin levels within the same group. This might be due to the multifactorial nature of periodontal disease which involves both host and bacterial interactions.

In view of the aforementioned findings, the present investigation suggested that Visfatin concentrations in GCF can be considered as a possible biomarker of inflammation in periodontal disease. In addition it might be an inflammatory mediator indicating periodontal disease progression.

Further longitudinal studies involving a larger population are needed to confirm the findings of the present study and to better understand the role of Visfatin in the pathogenesis of periodontal disease. Also addressing the clinical implication and pathological mechanism of Visfatin in periodontal disease progression are warranted.

REFERENCES

1. Abbas S, Zhang YH, Clohisy JC, Abu-Amer Y. Tumor necrosis factor-alpha inhibits pre-osteoblast differentiation through its type-1 receptor. Cytokine 2003; 22(1-2):33-41.
2. Adya R, Tan BK, Punn A, Chen J, Randeva HS. Visfatin induces human endothelial VEGF and MMP-2/9 production via MAPK and PI3K/Akt signaling pathways: novel insights into Visfatin induced angiogenesis. Cardiovasc Res 2008; 78: 356–365.
3. Bray GA. Medical consequences of obesity. J Clin Endocrinol Metab 2004; 89: 2583–9.
4. Fukuhara A, Matsuda M, Nishizawa M, Segawa K, Tanaka M, Kishimoto K, Matsuki Y, Murakami M, Ichisaka T, Murakami H, Watanabe E, Takagi T, Akiyoshi M, Ohtsubo T, Kihara S, Yamashita S, Makishima M, Funahashi T, Yamanaka S, Hiramatsu R, Matsuzawa Y, Shimomura I. Visfatin: a protein secreted by visceral fat that mimics the effects of insulin. Science 2005; 307: 426-30.
5. Jia SH, Li Y, Parodo J, Kapus A, Fan L, Rotstein OD. Pre-B cell colony-enhancing factor inhibits neutrophil apoptosis in experimental inflammation and clinical sepsis. J Clin Invest 2004; 113: 1318–1327.
6. Moschen, A. R., Kaser, A., Enrich, B., Mosheimer, B., Theurl, M., Niederegger, H., and Tilg, H. Visfatin, an adipocytokine with proinflammatory and imunnomodulating properties J Immunol 2007; 178(3):1748-1758.
7. Nishida N, Tanaka M, Hayashi N, Nagata H, Takeshita T, Nakayama K. Determination of smoking and obesity as periodontitis risks using the classification and regression tree method. J Periodontol 2005; 76: 923-928.
8. Pradeep AR, Raghavendra NM, Kathariya R, Patel SP, Pradeep S, Sharma A, Raju A. Gingival crevicular fluid and serum visfatin concentration: their relationship in periodontal health and disease. J Periodontol 2011; 82(9): 1314-9.
9. Pradeep AR Rhagavendra NM, , Kathariya R, Pradeep S, Raju A, Sharma A. Association of serum and crevicular levels in periodontal health and disease with type 2 diabetes mellitus. J Periodontol 2012; 83 (5):629-34.
10. Revollo JR , Korner A , Mills KF , Satoh A , Wang T , Garten A , Dasgupta B , Sasaki Y , Wolberger C , Townsend RR , Milbrandt J , Kiess W , Imai S. Nampt/PBEF/Visfatin regulates insulin secretion in beta cells as a systemic NAD biosynthetic enzyme . Cell Metab 2007; 6: 363 – 75.
11. Rongvaux A, Shea RJ, Mulks MH, Gigot D, Urbain J, Leo O, Andris F. Pre-B cell colony-enhancing factor, whose expression is up-regulated in activated lymphocytes, is a nicotinamide phosphoribosyltransferase, a cytosolic enzyme involved in NAD biosynthesis. Eur J Immunol 2002; 32: 3225–3234.
12. Schroeder HE, Lindhe J, Hugoson A, Münzel-Pedrazzoli S.Structural constituents of clinically normal and slightly inflamed dog gingiva. A morphometric study. Helv Odontol Acta. 1973; 17(2):70-83.
13. Stephens JM, Vidal-Puig AJ. An update on visfatin/pre-B cell colony-enhancing factor, an ubiquitously expressed, illusive cytokine that is regulated in obesity. Curr Opin Lipidol 2006; 17 (2): 128-31.
14. The American Academy of Periodontology. Treatment of Plaque-induced Gingivitis, Chronic Periodontitis, and Other Clinical Conditions. J Periodontol 2004; 72:1790-1800.
15. Tilg H, Moschen AR. Adipocytokines: mediators linking adipose tissue, inflammation andimmunity. Nat Rev Immunol 2006; 6: 772-783
16. Williams RC, Jeffcoat MK, Kaplan ML, Goldhaber P, Johnson HG, Wechter WJ. Flurbiprofen: A potent inhibitor of alveolar bone resorption in beagles. Science 1985; 227:640-642.