Salivary Visfatin Concentrations in Patients with Chronic Periodontitis: An Analysis before and after Periodontal Therapy

Abstract

Background and Aims: Visfatin, also known as pre-B-cell colony enhancing factor, is secreted from a variety of cells and is thought to have some proinflammatory and immunomodulating effects. It is indicated that serum/plasma levels of visfatin increase in a number of inflammatory disorders. The present study aims to assess salivary visfatin concentrations and investigate its relationship in patients with chronic periodontitis before and after periodontal therapy. Methods: This prospective clinical study included a total of 20 subjects who were divided into two groups with 10 patients in each viz Group A: Periodontally healthy subjects, Group B: Chronic periodontitis subjects. In group B, the subjects were further assigned as T1 and T2 groups before and after periodontal therapy. Periodontal parameters including plaque index, gingival index, sulcus bleeding index, probing depth and clinical attachment level were recorded at baseline and patients were subjected to periodontal therapy. An ELISA analysis was performed to measure the visfatin levels in saliva in study groups before and after 12 weeks of periodontal therapy. Statistical Analysis Used: The results were evaluated statistically using Student t-test, one way ANOVA, Post-hoc Tukey’s test and Pearson’s rank correlation method. Results: The salivary visfatin concentrations were reduced significantly after periodontal therapy. There were statistically significant differences elicited in salivary visfatin levels of Group A and T1 of Group B and also between T1 and T2 of Group B. Conclusions: Salivary levels of Visfatin are reduced after periodontal therapy to the levels comparable with those found in healthy individuals. Therefore, the salivary visfatin levels may have the potential to be a target marker for assessment of responses to periodontal therapy.

Keywords: Adipokines, chronic periodontitis, saliva, visfatin

Introduction

Periodontitis is an inflammatory disease fundamentally initiated by dental biofilm and the subsequent interaction of the host defense mechanisms with the plaque microorganisms involving the progressive destruction of gingiva, periodontal ligament, cementum and alveolar bone.

Analyzing the information collected during a periodontal examination is necessary for a proper periodontal diagnosis. Traditional diagnostic measures, such as periodontal pocket depth, attachment level, plaque index, bleeding on probing and radiographic assessment of alveolar bone loss, are informative to evaluate disease severity but provide few useful determinants of disease activity.[1]

The use of biomarker based-disease diagnostics in identification of active periodontal disease from plaque biofilms, gingival crevicular fluid, saliva and serum is the recent advancement in the field of periodontal diagnostics.

Biomarkers, whether produced by normal healthy individuals or by individuals affected by specific systemic diseases, are tell-tale molecules that could be used to monitor health status, disease onset, treatment response and outcome.[2] Saliva contains locally and systemically derived biomarkers of periodontal disease. The diagnostic value of saliva has been recognized for quite some time and its appealing use in oral-related diseases is because of its easy and non-invasive nature in terms of its collection and its abundant nature.

Amongst the innumerable biomarkers that are known of date in the periodontal literature, Visfatin is one amongst them.

Visfatin, which is also known as Pre B-cell colony enhancing factor, is a protein...
secreted by adipose tissue. It is an inflammatory mediator that induces the synthesis of proinflammatory cytokines and acts as chemotactic factor. It has been suggested that during infection and inflammation, the production of interleukin-1β (IL-1β), tumour necrosis factor-α (TNF-α), and interleukin-6 (IL-6) is induced by visfatin. Several studies have indicated that serum/plasma levels of visfatin increase in a number of inflammatory disorders.

Although studies showing the raise in levels of visfatin in serum and GCF are existent in the periodontal literature there is a dearth of literature on salivary levels of visfatin in chronic periodontitis patients before and after periodontal therapy.

Till date, to the best of our knowledge there are only two studies stating that salivary visfatin levels were reduced in chronic periodontitis group of patients after non-surgical periodontal therapy. Thus, in view of the aforementioned findings, this study was undertaken to know the effect of complete periodontal therapy on salivary visfatin levels in subjects with chronic periodontitis.

**Methods**

A total of 20 subjects were divided into two groups. Sample size was calculated using G*power software considering 80% power and 95% confidence level. Group A comprised of 10 periodontally healthy subjects with no underlying systemic diseases, Group B comprised of 10 subjects diagnosed with moderate to severe chronic periodontitis (based on the American Academy of Periodontology, 1999 classification) and with no underlying systemic diseases. The purpose of the study was explained to all the participants and a written consent was taken. The study was approved by the ethical committee of the institute.

Criteria for inclusion of periodontally healthy subjects (Group A)

Subjects with uniform probing depths of three millimetres or below and with no evidence of loss of attachment, but might be showing some signs of gingival inflammation.

Criteria for inclusion of chronic periodontitis subjects (Group B)

- Age range of 25 to 65 years.
- A minimum of 20 teeth in the mouth and a minimum of four teeth in each quadrant.
- Patients diagnosed with moderate to severe periodontitis.
- Patients who had not received periodontal treatment in the past one year.

Exclusion criteria

- Patients with uncontrolled systemic disease.
- Patients with infectious diseases.
- Patients with inflammatory disorders.
- Patients with aggressive periodontitis.
- Patients who use tobacco in any form.
- Patients with BMI >25 kg/m².
- Patients with history of drug intake known to affect the periodontium.

**Study design**

All the subjects underwent baseline periodontal examination strictly according to the guidelines provided. Probing pocket depth and clinical attachment level were recorded using UNC-15 probe to the nearest millimetre.

In a specially prepared proforma, patient’s detailed case history that included medical and dental history along with patient’s Body Mass Index (BMI) was recorded. Periodontal examination was performed at baseline and at 12 weeks after periodontal therapy which included the assessment of:

- Plaque index (Silness and Löe, 1964)
- Gingival index (Loe and Silness, 1963)
- Sulcus Bleeding index (Muhlemann and Son, 1971)
- Probing depth
- Clinical attachment level.

**Collection of saliva and estimation of visfatin**

All subjects were instructed to refrain from eating and drinking one hour prior to saliva collection. Saliva samples were collected at baseline from the subjects in control group and at baseline and 12 weeks after periodontal therapy from the subjects in the test group. The patients were then asked to thoroughly rinse their mouth with water, and then expectorate unstimulated whole saliva sample into UV sterilized cups. About two millilitres (ml) to five millilitres of saliva sample was collected and immediately transferred to a two millilitres eppendorf, labelled and transferred to a portable freezer prior to centrifugation at 2,500 rpm for 10 minutes at room temperature. The supernatants thus obtained were transported and stored at -20°C to -30°C until analysis of salivary visfatin was carried out.

**Evaluation of salivary visfatin**

Analysis of salivary Visfatin was carried out through ELISA using Human Salivary Visfatin ELISA Kit; Cat. No: E0025 Hu of Bioassay Technology Laboratory. Assays were performed according to manufacturer’s instructions.

**Treatment protocol**

After the completion of periodontal examination and collection of saliva sample, periodontal treatment was provided to all the patients. All the patients included in the study received non-surgical periodontal therapy including plaque control, scaling and root planning, occlusal adjustments and elimination of any faulty dental restorations. Surgical periodontal therapy was performed under local anesthesia with 2% lignocaine containing adrenaline at a concentration of 1:2,00,000 under aseptic conditions.
Statistical analysis

All the data collected was statistically analyzed using Statistical Package for the Social Sciences software version 21.0 (SPSS). The results were expressed in means and percentages; \( P \leq 0.05 \) was considered statistically significant.

The results were evaluated statistically using the following methods:

- Comparison of the demographic variables in the study groups was done using Student \( t \)-test.
- Intergroup comparison of all the periodontal parameters and visfatin levels was done using one way ANOVA.
- Pair wise comparison of salivary visfatin levels was done using post-hoc Tukey’s test.
- Correlation between the salivary visfatin levels with other clinical parameters in all groups was done by Pearson’s rank correlation method.

Results

In the present study, a total of 20 patients (12 males and 8 females) were included and were divided into two groups, i.e. periodontally healthy group (Group A, 10 subjects; 6 males and 4 females), chronic periodontitis group (Group B, 10 subjects; 6 males and 4 females). In group B, salivary visfatin levels were measured before and after periodontal therapy which were further assigned as \( T_1 \) and \( T_2 \) groups respectively. These visfatin levels were compared between healthy subjects (Group A) and \( T_1 \) of (Group B), between \( T_1 \) and \( T_2 \) groups of (Group B) and also between Group A and \( T_2 \) of Group B.

As controversy does exist in the literature regarding the relationship of visfatin with age and body mass index (BMI),\(^{[13]}\) the normal standard range of BMI (18.5 to 25 kg/m\(^2\), according to WHO)\(^{[14]}\) was considered as the inclusion criteria in an attempt to eliminate the confounding effects of these variables [Table 1].

In the present study, the results have shown that plaque index, gingival index, sulcus bleeding index scores along with pocket depth and clinical attachment values were decreased in Group B after complete periodontal therapy in comparison with baseline values and were almost similar to those in periodontally healthy individuals. There were statistically significant differences in the mean values of periodontal variables between group A and \( T_1 \) of group B and also between \( T_2 \) and \( T_1 \), respectively [Table 2].

The mean salivary visfatin levels were 27.33 ± 7.19 ng/ml in Group A, and in Group B, the mean salivary visfatin levels were 45.96 ± 7.08 ng/ml and 30.13 ± 12.20 for \( T_1 \) and \( T_2 \), respectively [Table 2].

Analysis of visfatin concentrations in the groups demonstrated the highest levels of visfatin in the \( T_1 \) group.

### Table 1: Comparison of demographic variables (Age and Body mass index) between the study groups

| Parameters | GROUPS | Mean  | Std. Deviation | \( t \)  | \( p \) |
|------------|--------|-------|----------------|--------|------|
| Age        | GROUP A | 44.1000 | 8.41229          | 0.961  | 0.352|
|            | GROUP B | 43.9000 | 9.65459          | 0.961  | 0.352|
| BMI        | GROUP A | 24.3700 | 2.54211          | 0.792  | 0.430|
|            | GROUP B | 24.6800 | 2.64567          | 0.792  | 0.430|

Salivary visfatin levels decreased significantly after surgical periodontal treatment. \( (P = 0.000) \)

At the end of the 12 weeks period, the visfatin scores decreased significantly compared to the pre-treatment values in the study group. Pair wise comparison of visfatin levels between the groups revealed significant reduction of visfatin levels in \( T_1 \) group when compared to \( T_2 \) and the visfatin levels in \( T_2 \) group are compared to those in Group A [Table 3].

The Pearson’s rank correlation between salivary visfatin levels and clinical parameters after complete periodontal therapy showed no significant relationship between clinical periodontal parameters and visfatin concentrations [Table 4].

Discussion

In the journey of achieving an accurate diagnosis of periodontal disease, it being a multifactorial condition research has also focused on the objective measures such as biomarkers in assessing the current disease status and predicting the risk and outcome of the treatment provided.

As per the literature, the successful periodontal therapy tends to reduce systemic inflammation and the concentration of local and systemic load of biomarkers offer the basis for the detection of periodontal disease activity.

Along with the identification of various molecules like inflammatory mediators, host derived enzymes, leucocyte breakdown products and antimicrobial peptides some adipokines such as leptin, adiponectin and visfatin have also been identified in oral fluids like the saliva and GCF. As per the literature, these molecules might play a role in the cell death along with the regulation of inflammation.

Also this adipocytokine, in particular Visfatin also known as pre-B cell colony enhancing factor/NAMPT produced by neutrophils, macrophages and lymphocytes has many pleiotropic biological activities. A study showed that visfatin induces the expression and activity of matrix metalloproteinase (MMP) and conversely, down-regulates the inhibitors of the MMPs in monocytes and endothelial cells. It has also been reported that any imbalance between these MMPs and their inhibitors play a key role in the progression of periodontitis.\(^{[17,18]}\)

From the aforementioned conditions put forth, it could be hypothesized that there is a relationship between visfatin...
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Initial studies evaluated visfatin levels in gingival crevicular fluid (GCF) and serum in periodontal health and disease and demonstrated that visfatin levels increase progressively in both GCF and serum as periodontal disease progresses\(^{19,20}\), and it was also concluded that these GCF and serum visfatin levels were reduced following non-surgical periodontal therapy.\(^{21}\)

In a study conducted to evaluate the changes in GCF visfatin levels in chronic periodontitis patients in response to non-surgical periodontal therapy, it was observed that visfatin levels significantly decreased after the therapy.\(^{22}\)

Later, it was indicated that visfatin is identifiable and measurable even in saliva\(^{24}\) wherein a study was conducted to examine the relationship between salivary visfatin concentrations and periodontitis which demonstrated that the salivary visfatin concentrations are significantly elevated in patients with chronic periodontitis.\(^{25}\)

Another study evaluated the effect of non-surgical periodontal treatment on serum and salivary levels of visfatin in patients with generalized moderate-to-severe chronic periodontitis and its findings indicated that there is a direct relationship between periodontal tissue inflammation and disease activity with salivary and serum visfatin levels.\(^{10}\)

As there are no studies comparing the salivary visfatin concentrations of chronic periodontitis patients before and after surgical periodontal therapy this present study was formulated to compare the salivary visfatin levels of chronic periodontitis patients before and after surgical periodontal therapy who requires surgical management for complete elimination of periodontal disease.

Table 2: Comparison of periodontal parameters and the salivary Visfatin levels between control and chronic periodontitis groups

| Parameter          | GROUP A | T\(_1\) | T\(_2\) | n   | Mean  | Std. Deviation | f   | p    |
|--------------------|---------|---------|---------|-----|-------|----------------|-----|------|
| Plaque index       | 10      | 0.5040  | 0.2400  | 20.177 | 0.000*           |
|                   | T\(_1\) | 10      | 1.9520  | 0.97571 |
|                   | T\(_2\) | 10      | 0.4330  | 0.28806 |
| Gingival index     | 10      | 0.2200  | 0.13840 | 24.992 | 0.000*           |
|                   | T\(_1\) | 10      | 1.4280  | 0.67475 |
|                   | T\(_2\) | 10      | 0.4040  | 0.18458 |
| Bleeding index     | 10      | 0.3080  | 0.13357 | 49.397 | 0.000*           |
|                   | T\(_1\) | 10      | 2.0080  | 0.57723 |
|                   | T\(_2\) | 10      | 0.8380  | 0.32937 |
| Probing depth      | 10      | 2.1860  | 0.16847 | 127.246 | 0.000*           |
|                   | T\(_1\) | 10      | 4.3660  | 0.55526 |
|                   | T\(_2\) | 10      | 2.0410  | 0.25155 |
| CAL                | 10      | 2.2130  | 0.16221 | 67.720  | 0.000*           |
|                   | T\(_1\) | 10      | 5.4920  | 0.84082 |
|                   | T\(_2\) | 10      | 3.2430  | 0.71578 |
| Visfatin           | 10      | 27.3370 | 7.19806 | 12.054  | 0.000*           |
|                   | T\(_1\) | 10      | 45.9610 | 7.08790 |
|                   | T\(_2\) | 10      | 30.1370 | 12.20399 |

\(\ast\). The mean difference is significant at the 0.05 level

Table 3: Pair wise Comparison of Salivary Visfatin levels using post-hoc Tukey’s test

| Dependent Variable | (I) group | (J) group | Mean Difference (I-J) | Std. Error | Sig. | 95% Confidence Interval |
|--------------------|-----------|-----------|-----------------------|------------|------|------------------------|
| Visfatin           | GROUP A   | T\(_1\)   | 18.6240\(^*\)        | 4.0905     | 0.000* | -28.766 - 8.4818        |
|                   |           | T\(_2\)   | -2.8000               | 4.0905     | 0.774 | -12.942 7.3422         |
|                   |           | T\(_1\)   | 15.8240\(^*\)        | 4.0905     | 0.002* | 5.6818 25.966          |

\(\ast\). The mean difference is significant at the 0.05 level

Table 4: Correlation between the salivary visfatin levels and other periodontal parameters by Pearson rank correlation method

| Parameters                     | Visfatin |
|--------------------------------|----------|
| Plaque index (PI)              | 0.227    | 0.528 |
| Gingival index (GI)            | 0.292    | 0.412 |
| Bleeding index (SBI)           | 0.499    | 0.142 |
| Probing depth (mm) (PD)        | -0.280   | 0.434 |
| clinical attachment level (mm) (CAL) | 0.015 | 0.968 |

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To the best of our knowledge, the present study is the first in its attempt to investigate alterations in the salivary concentrations of visfatin following surgical periodontal therapy in chronic periodontitis patients.

In the present study, the results have shown that plaque index, gingival index, sulcus bleeding index scores along with pocket depth and clinical attachment values were decreased in Group B after complete periodontal therapy in comparison with baseline values.

These results suggest that complete periodontal treatment could effectively improve periodontal status.

In chronic periodontitis patients (Group B) mean salivary visfatin levels at baseline were 45.96 ± 7.08 ng/ml and 30.13 ± 7.08 ng/ml at 12 weeks after periodontal therapy. These results of the current study indicated that salivary visfatin levels decreased significantly 12 weeks after complete periodontal treatment, in parallel with significant reductions in plaque index, gingival index, bleeding index, probing depth and clinical attachment levels. Moreover, the levels of salivary visfatin in individuals after receiving treatment were comparable with those in periodontally healthy individuals.

Through this, it may be speculated that changes in the microbial composition and the ongoing inflammatory process in the pocket environment might have a close relationship with the visfatin levels in saliva. Reductions in key cells for visfatin production in the periodontium, such as macrophages and inflammatory leukocytes, following treatment may be an additional reason for diminished levels of salivary visfatin concentrations after periodontal treatment.[9]

Significance of the present study

• It is the first study to evaluate the alterations in salivary levels of visfatin in patients with chronic periodontitis before and 12 weeks after surgical periodontal therapy.

Limitations of the present study

• Sample size was small, and hence results cannot be generalized to the entire population.
• Salivary visfatin analysis after non-surgical periodontal therapy (4 weeks) could have also been assayed followed by the analysis of surgical periodontal therapy.

Future directions

• Further studies with larger sample sizes must be performed in order to establish accurately the role of salivary visfatin in chronic periodontitis.
• As per the literature, GCF and serum seems to be a better tool in estimating the levels of visfatin when compared to those in saliva. Hence, further studies comparing the salivary, GCF and serum levels of visfatin must be conducted to elicit the significance of visfatin levels in saliva before and after complete periodontal therapy for better understanding of the role of salivary visfatin in monitoring responses to periodontal therapy.

Conclusion

The results of the present study showed that the salivary visfatin levels were found to be elevated in patients with chronic periodontitis and also there were significant reductions of these salivary visfatin concentrations in patients with chronic periodontitis to levels comparable with those in periodontally healthy individuals, as a result of complete periodontal therapy.

Therefore, salivary visfatin might be useful for monitoring responses to periodontal therapy. However, for visfatin to be considered as a potential therapeutic target in the treatment of chronic periodontitis, further longitudinal studies with larger sample sizes are needed.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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