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Original article

Effect of Non-Surgical Periodontal Therapy on Interleukin-33 and Interleukin-1β Levels in Sever Chronic Periodontitis Patients

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ABSTRACT

Aims. *First, to determine the short-term effect of scaling and root planing on IL-33 levels in gingival crevicular fluid from patients with chronic periodontitis and compare these levels with those of IL-1β cytokine. Second, to establish the correlation between each of the clinical parameters and IL-1β levels with IL-33 levels in gingival crevicular fluid prior to and after periodontal treatment.* ***Methods****. A total of forty subjects, 20 with moderate to severe chronic periodontitis (study group) and 20 subjects with healthy gingiva (control group) were selectively collected for contribution in the present study. The chronic periodontitis patients (study group) received initial periodontal therapy (SRP). The periodontal clinical parameters including (PI, GI, BOP, PD and ALL) were measured and gingival crevicular fluids (GCF) were collected at baseline and four weeks after therapy for study group and at baseline for control group. Levels of interleukin-1β and interleukin-33 were measured using enzyme-linked immunosorbent assay kits.* ***Results****. There were statistically significant differences between the mean values of GI, PI, BOP, PD and ALL at baseline and after SRP in the study group (P < 0.001). The respective IL-β and IL-33 levels are significantly dropped from baseline to four weeks after (SRP) (96.26 ng/ml versus 33.1 ng/ml ,P=0.0001) for IL-β and (5.99 ng/ml versus 4.73 ng/ml ,P=0.0001) for IL-33. There was no significant correlation between all of the clinical parameters and interleukins levels in GCF except the significant correlation between interleukin-1β and bleeding index at 4 weeks after SRP (r=-0.448 & p=0. 048).* ***Conclusion****. Scaling and root planing (SRP) is the mainstay of treatment of periodontal diseases as SRP was effective in improving clinical parameters in patients with chronic periodontitis. This improvement was accompanied by a significant decrease in the levels of the proinflammatory cytokines IL-1β and IL-33 in GCF. IL-33 could be used as a potential diagnostic marker for periodontal disease activity in gingival crevicular fluid.*

Keywords: Non-Surgical Periodontal Therapy, Interleukin-33, Interleukin-1β, Chronic Periodontitis.

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الأهداف. أولاً، تحديد التأثير قصير المدى للتقليح وتخطيط الجذر على مستويات IL-33 في سائل اللثة الفقير من المرضى الذين يعانون من التهاب دواعم السن المزمن ومقارنة هذه المستويات بمستويات السيتوكين IL-1β ثانيًا، تحديد الارتباط بين كل من المعلمات السريرية ومستويات IL-1β مع مستويات IL-33 في سائل اللثة الفقير قبل وبعد علاج دواعم السن. الطرق. تم جمع ما مجموعه أربعين موضوعًا بشكل انتقائي، 20 مصابًا بالتهاب دواعم السن المزمن المتوسط إلى الشديد (مجموعة الدراسة) و 20 موضوعًا بلثة سليمة (مجموعة التحكم) للمساهمة في الدراسة الحالية. تلقى مرضى التهاب دواعم السن المزمن (مجموعة الدراسة) علاجًا أوليًا للدواعم (SRP). تم قياس المعلمات السريرية للدواعم بما في ذلك PI) و GI و BOP و PD و (ALL وتم جمع سوائل اللثة الفقير (GCF) في البداية وبعد أربعة أسابيع من العلاج لمجموعة الدراسة وفي البداية لمجموعة التحكم. تم قياس مستويات الإنترلوكين-1 βوالإنترلوكين-33 باستخدام مجموعات اختبار الممتز المناعي المرتبط بالإنزيم. النتائج. كانت هناك فروق ذات دلالة إحصائية بين متوسط قيم GI و PIو BOPو PDو ALLفي البداية وبعد SRP في مجموعة الدراسة (P < 0.001).انخفضت مستويات IL-β و IL-33بشكل ملحوظ من البداية إلى أربعة أسابيع بعد (SRP) (96.26 نانوغرام / مل مقابل 33.1 نانوغرام / مل، P = 0.0001لـ IL-β و 5.99) نانوغرام / مل مقابل 4.73 نانوغرام / مل، (P = 0.0001لـ IL-33. لم يكن هناك ارتباط كبير بين جميع المعايير السريرية ومستويات الإنترلوكين في GCF باستثناء الارتباط الكبير بين الإنترلوكين-1 βومؤشر النزيف بعد 4 أسابيع من (r = -0.448 & p = 0.048). الاستنتاج. يعد التقليح وتخطيط الجذر (SRP) الدعامة الأساسية لعلاج أمراض اللثة حيث كان SRP فعالاً في تحسين المعايير السريرية لدى المرضى الذين يعانون من التهاب دواعم السن المزمن. كان هذا التحسن مصحوبًا بانخفاض كبير في مستويات السيتوكينات المؤيدة للالتهابات IL-1β و IL-33 في GCF. يمكن استخدام IL-33 كعلامة تشخيصية محتملة لنشاط أمراض اللثة في سائل اللثة الفقير.

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INTRODUCTION

Periodontal diseases, including chronic periodontitis, are inflammatory conditions of the supporting tissues of the teeth induced by micro-organisms that stimulate the host immune and inflammatory responses [1.2]. The interplay between periodontal pathogens and the inflammatory-immune system leads to the development of chronic inflammation, progressive destruction of connective tissues and resorption of the alveolar bone [3,4].

A small group of predominantly gram-negative anaerobic or microaerophilic bacteria within the biofilm are often associated with disease initiation and progression [5]. Host reactions to these pathogens result in the production of inflammatory mediators by cells like neutrophils, macrophages, T cells, mast cells and fibroblasts [6].

These inflammatory mediators or cytokines play a key role in a number of biologic activities including development, proliferation, regeneration, repair and inflammation [7,8]. Contributing inflammatory mediators and tissue destructive molecules have been detected in the gingival tissues, gingival crevicular fluid and saliva of patients affected by periodontitis [9]. Qualitative and quantitative changes in the composition of these biomarkers could have diagnostic and therapeutic significance [10].

Of the humoral factors influencing immuno-inflammatory reactions within periodontal tissues, a crucial role is played by interleukin-1β (IL-1β). IL-1β promotes development of an inflammatory response, amplifies inflammation and modulates a lot of immunological processes [11]. Some of its biological effects include stimulation of fibroblast proliferation, stimulation of prostaglandin E2 production by monocytes and fibroblasts and activation of different cells populations to release matrix metalloproteinases (MMPs) that degrade extracellular matrix proteins [12]. This cytokine also promotes osteoclast formation, affects neutrophils chemotaxis and activation and is a potent inducer of bone demineralization [12,13].

The IL-1 family of cytokines is affective in destructive inflammatory disorders, such as periodontitis, and these cytokines are important therapeutic targets [14]. IL-33 is the most recently discovered member of the IL- 1 family [15]. It has been reported that IL-33 is expressed at sites of immune-mediated pathologies [16]. Schmitz et al. [15] reported that modest levels of IL-33 were detected in lipopolysaccharide (LPS) - activated human monocytes and dendritic cells of unknown phenotype.

Additional published evidence demonstrates that biologically active IL-33 is released from damaged endothelial cells, suggesting that this cytokine may function as an ‘‘alarmin,’’ providing an endogenous signal activating innate immunity during tissue damage and infection [17]. This was indeed confirmed in another study, reporting that stimulation of monocytes with *Escherichia coli* LPS and LPS from *Porphyromonas gingivalis* upregulated IL-33 at both messenger ribonucleic acid and protein levels [18]. Morover, IL-33 has been suggested to increase production of IL-6, IL-1β, tumor necrosis factor (TNF) by bone-derived mast cells [19].

It is generally accepted that receptor activator of nuclear factor-kB ligand (RANKL) is essential for osteoclast formation and function also in alveolar bone resorption seen in periodontitis [20,21]. In an *in vitro* study, Mun et al. [22] demonstrated that IL-33 was equally potent in stimulating osteoclast differentiation from human CD14+ monocytes as RANKL and independently of RANKL/RANK. Therefore, IL-33 may be expected to act in alveolar bone resorption in periodontitis by its independent role in osteoclast differentiation.

At present, the expression and regulation of IL-33 in periodontal tissue cells have not been clarified. Buduneli et al. [23] investigated the levels of IL-33 in the gingival crevicular fluid, saliva and plasma levels and reported that neither gingival crevicular fluid nor salivary levels of IL-33 could differentiate chronic periodontitis from clinically healthy periodontium. However, the understanding of the function of IL-33 remains the question of where, when, and how this cytokine plays a role in the immune-mediated periodontal tissue destruction. Therefore, the present

study was designed to analyze another cytokine from the IL-1 family such as IL-1β along with IL-33 to particularly provide better insight to the possible role of this novel cytokine in chronic periodontitis.

METHODS

The present study was carried out on forty subjects their age ranged from 30-50 years (both males and females) which who were selected from the Department of Oral Medicine and Periodontology, Faculty of Dentistry, Mansoura University. Those only 20 patients were diagnosed as having chronic periodontitis after obtaining proper case history, thorough clinical examination and according to the clinical and radiographic criteria and 20 healthy subjects.

The selected patients were free from any systemic disease, and receiving no medication for the present condition three months prior to the study. Furthering, none of them had previous periodontal treatment including scaling, root planning, and periodontal surgery in the last six months. On other hand, smokers and pregnant females were excluded from the present study.

Clinical measurements

The following clinical parameters were be measured before and after treatment (at baseline, after 6weeks).

- Gingival index [3].
- Plaque index [4].
- Bleeding on probing index[5].
- Clinical attachment level [6].
- Probing pocket depth[6].

Study design

A baseline visit was conducted by a periodontist for two groups, and then study group underwent an initial periodontal therapy consisting of scaling and root planing (SRP) and oral hygiene instructions. The treatments were completed in 4 weeks.

GCF samples were obtained at the two visits at baseline and after 4weeks for 20 study group. And for 20 control group GCF samples collected at baseline only.

GCF collection and processing

After being selected for the study, subjects were recalled for GCF sampling. In the CP groups, GCF samples were collected from one sites of tooth with PD≥4 (pocket). In the control group, GCF samples were collected from one site of tooth with (sulcus). Prior to GCF sampling, the supragingival plaque was removed from the interproximal surfaces with a sterile curette these surfaces were dried gently by an air syringe and were isolated by cotton rolls. GCF was sampled with filter paper (Periopaper, ProFlow, Inc., Amityville, NY, USA). Paper strips were carefully inserted into the pocket until mild resistance was felt and left there for 30 seconds[7]. Care was taken to avoid mechanical injury. Strips contaminated with blood were discarded [8]. The absorbed GCF volume of each strip was determined by electronic impedance (Periotron 8000, ProFlow, Inc., and Amityville, NY, USA), pooled and placed into a sterile Eppendorf placing containing 250µl of phosphate buffer saline (PBS), Eppendorf tube reweighed before kept at −20◦C.

Statistical analysis

Numerical data were presented as mean and standard deviation (SD) values. Data were explored for normality using Kolmogorov-Smirnov and Shapiro-Wilk tests. Age data showed parametric distribution while all clinical measurements data showed non-parametric distribution. For parametric data, Student's t-test was used to compare between age values of the two groups.

For non-parametric data, Mann-Whitney U test was used to compare between the two groups. Wilcoxon signed-rank test was used to study the changes after treatment within each group.

Gender data (Qualitative data) were presented as frequencies (n) and percentages (%). Chi-square (x^2) test was used to compare between the two groups. The significance level was set at $P \leq 0.05$. Statistical

analysis was performed with IBM[1]® SPSS® Statistics Version 20 for Windows.

RESULTS

All patients completed the entire study. No adverse effects, such as discomfort, dentin hypersensitivity, or pain related to the scaling and root planing were reported by any of the patients.

Table 1 showed the demographic characteristics and baseline data of the patients enrolled in the study. The mean value and standard deviation of the age of individuals was 37.95 ± 6.07 years in study group. Their age ranged from 30-50years. And 29.45±2.09 were in control group, their age ranged from 25-34 years.

Table 1. Baseline demographic data

Parameter	Study group (SRP) (M±SD)	Control group (M±SD)
Number of patients (n)	20	20
Average Age (year)	37.95±6.07330-50	29.45±2.09 25-35
Gender (M/F)	(10/10)	(4/16)

Tables 2 showed the variation of mean values and standard deviation of GI, PI, BOP, PD and CAL of individuals participated in the study. For the study group, the mean value and standard deviation of gingival index (GI) at baseline was 2.15 ± 0.16 and after SRP was 0.68±0.36. So, there was a statistically significant decrease in GI values post-operatively (P < 0.001). Moreover, the mean value and standard deviation of plaque index (PI) before treatment was 2.02 ± 0.31. After treatment, the mean value was 0.59 ± 0.35. So, there was a highly statistically significant difference between values of PI before and after treatment in the study group (at P < 0.001).

It was obviously observed that there was a statistically significant reduction in bleeding on probing (BOP) scores at baseline in study group with mean values 0.99 ± 0.02 compared to scores after treatment which was 0.26±0.09 (at P < 0.001).

The mean value and standard deviation of probing pocket depth (PD) at baseline in the study group was 4.52 ± 1.44 mm and after therapy, it was 3.53 ± 1.39 mm. As a result, there was a statistically significant decrease in mean PD post-operatively (at P < 0.001). Moreover, the mean value and standard deviation of clinical attachment level (CAL) at baseline in the study group was 5.88 ± 0.59 mm. After treatment, the mean value and standard deviation of CAL in the same group was 4.97 ± 0.64 mm. Therefore, in periodontitis patients; there was a statistically significant decrease in mean CAL post-operatively (at P < 0.001).

Table 2. The mean values (±SD) of GI, PI, BOP, PD and CAL of study group before and after (SRP) and control group

Par	Before	After	At baseline	P-value
GI	2.15 ±0.16	*0.68±0.36	0.24±0.24	< 0.001
PI	2.02±0.31	*0.59± 0.35	0.26±0.22	< 0.001
BOP	0.99 ± 0.02	*0.26±0.09	0.18 ±0.09	< 0.001
PD	4.52 ± 1.44	*3.53 ± 1.39	0.50 ±0.33	< 0.001
CAL	5.88 ± 0.59	*4.97 ± 0.64	0 ±0	< 0.001

*BOP = Bleeding on probing; P = Probability of significance; **Highly significant at P < 0.001; PD = Pocket depth in millimeters; CAL = Clinical attachment level in millimeters; M = Mean; SD = Standard deviation; GI= Gingival index; PI= Plaque index; Par= Parameter*

Table 3 showed the mean values of interleukin-1β (IL-1β) and IL-33 levels in GCF (ng/ml) in study group at baseline and after SRP compared to control group. The mean values of GCF interleukin-1β and IL-33 concentration were 96.26 ± 70.09 and 5.99 ± 0.41 ng/ml respectively in the study group. However, their values were 8.3 ± 3.1 and 4.73 ± 0.62 ng/ml respectively in the control group. Interestingly, at baseline, there were statistically significant variations of the mean values of both of IL-1β and IL-33 between study and control group (p < 0.01). After SRP, the mean values of both of IL-1β and IL-33 in GCF of study group decreased to 33.1 ± 29.4 and 5.32 ± 0.67. It

was also shown that there was a statistically highly significant reduction in mean GCF IL-1β and interleukin-33 values of the study group after SRP (at P < 0. 0001). Moreover, there were statistically significant differences between the mean values of both of IL-1β and IL-33 of the study group after treatment and control group **(at P < 0. 0001)** (table 4).

Table 3. Interleukin-1β (IL-1β) and IL-33 levels in GCF (ng/ml) in study group at baseline and after SRP compared to control group (Mean±SD)

	Study group		Control group	P-value
	Before	After		
IL-1β	96.26 ± 70.09	33.1 ± 29.4*	8.3 ± 3.1	< 0.000
IL-33	5.99 ± 0.41	5.32 ± 0.67	4.73 ± 0.62	< 0.000

**p < 0.000 i.e., There is highly significant difference. GCF = gingival crevicular fluid. IL-1β = Interleukin-1β. IL-33 = Interleukin-33 ng/ml = nanogram $(10)^{-9}$/milliliter*

DISCUSSION

Chronic periodontitis is a chronic, microbial induced inflammatory disorders that affect the structure supporting the teeth. The bacterial biofilm that forms on the surfaces of teeth provide a chronic microbial stimulus that elicits a local inflammatory response in the gingival tissues. However, long-term plaque accumulation at the dento-gingival niche results in the enrichment and maturation of the biofilm, sustained inflammatory and an irreversible loss of the supporting tooth structures [8].

In chronic periodontitis, the host immune response is believed to play an essential role in the breakdown of connective tissue and bone [9]**.** The immune and inflammatory responses are critical for understanding the pathogenesis of periodontal diseases, and they are orchestrated by a number of host-related factors, either intrinsic or induced [10]**.** Moreover, It has been recently found that evaluation of various biologically specific proteins or markers in oral fluids (GCF and saliva) as well as in the blood circulation (serum or saliva) by using immunologic or biochemical methods may be helpful in the diagnosis of periodontal diseases [11,12]**.**

Although periodontitis can be diagnosed on the basis of the clinical parameters and radiographical findings, however, these measurements provide information about the past periodontal tissue destruction and do not elucidate the current state of the disease activity nor predict the future [12]**.**

In this study, GCF samples were used to analyze the level of IL-1β and IL-33. This is because GCF is considered a window for non-invasive analysis of periodontal conditions, including markers of connective tissue and bone destruction [13]. It is also suggested that the measurement of these mediators in GCF could be helpful to estimate the effect of periodontal treatment [14]**.** GCF has been extensively investigated in periodontal disease for the release of host response factors. It includes a mixture of molecules from blood, host tissue, and plaque biofilms, such as electrolytes, small molecules, proteins, cytokines, antibodies, bacterial antigens, and enzymes [15]**,** host cell-derived enzymes such as MMPs [16]**.**

In this study GCF samples were obtained from each subject by using absorbent filter paper point. The paper points were inserted into crevices or pockets until minimum resistance was felt only for 30 seconds [17]**.** This provides a sample of sufficient size for analysis without changing the protein concentrations of GCF, which approach those of serum. Furthermore**,** any longer time stimulates GCF flow resulting in dilution of the residual fluid in the gingival crevice [18]**.**

Moreover, careful isolation and plaque removal was performed prior to GCF collection to prevent saliva or plaque contamination, and any filter paper with saliva, plaque or blood contamination was discarded**.** As it is proved that contamination with dental plaque led to a marked change in the GCF volume determination [19]. Furthermore, It was found that contamination with saliva or blood not only affected the volume determination, but also gave false results in a GCF analysis procedure [20].

The levels of IL-1β and IL-33 in the GCF samples were determined using commercially available human-

specific ELISA in accordance with the manufacturer's instructions. ELISA tests are considered highly sensitive and specific [21] and favorably comparable to other methods used to detect substances in the body, such as radioimmune assay (RIA) tests. Moreover, they have the added advantages of not needing radioisotopes (radioactive substances) or a costly radiation counter (a radiation-counting apparatus) [22].

None of the subjects had taken medication such as antibiotics that could affect their periodontal status for at least 6 months before the study [23]. Moreover, smokers were excluded from the present study as it was found that tissues exposed to tobacco carcinogens respond by expressing elevated levels of cytokines in those tissues presumably as a part of the injury response mechanism [24]. Females, who were lactating or pregnant, were also excluded as it was assumed that circulating levels of cytokines are affected by pregnancy [24].

At the end of the study, subjects of the study group were recalled four weeks post-therapy, to resample GCF. Four weeks were agreed upon as a study period to allow for initial healing and reduce the risk of re-infection and disease reactivation [25].

All clinical parameters including GI, PI, PD and CAL of the study group, either at baseline or 4 weeks after SRP, were statistically significantly higher than those of the control group. This result was coincidental with the result of Gamonal et al., 2000 who found that healthy group showed statistically significant lower clinical parameters than chronic periodontitis groups [26]. It should be noted that reduced GI and PI in control group indicates a high state of oral hygiene and a history of regular prophylaxis.

In group I, all clinical parameters showed statistically significant reduction four weeks after treatment. This goes in line with the results of several studies who confirmed the success of non-surgical therapy by an observed reduction in whole mouth probing pocket depth, percentage of bleeding sites on probing [27,28] and clinical attachment level [29]. This may be related to the fact that non-surgical mechanical therapy has proven to be effective in reducing the bacterial load, thus resulting in clinical improvement [30].

In the present study, it was found that, compared with the healthy control subjects, patients with chronic periodontitis demonstrate significantly higher levels of IL-1β in gingival crevicular fluid. It should be pointed out, however, that in control subjects there is no correlations between IL-1β and clinical parameters were found. In chronic periodontitis patients, there were only correlations between IL-1β and bleeding index 4 weeks after SRP. Our observation is in line with previous studies. It has been found that patients with chronic periodontitis have higher IL-1β gingival crevicular fluid levels compared with control subjects [26,31], and the amounts of this cytokine do not correlate with clinical parameters [32]. Only Goutoudi et al.[33] stated that the total amounts of IL-1β were positively correlated with gingival index, while Hou et al. observed a positive correlation between the total amount of IL-1β, but not IL-1β concentration, and gingival index as well as pocket depth [34].

The increased level of Interleukin-1β in GCF of chronic periodontitis subjects may be due to the role of IL-1β in the inflammatory process. IL-1β was found to promote the development of an inflammatory response, amplify inflammation and modulate a lot of immunological processes. Some of its biological effects include stimulation of fibroblast proliferation, stimulation of prostaglandin E2 production by monocytes and fibroblasts and activation of different cell populations to release MMPs that degrade extracellular matrix proteins. This cytokine also promotes osteoclast formation and is a potent inducer of bone demineralization. It affects neutrophil chemotaxis and activation. An increasing body of evidence indicates that all of these IL-1β-dependent mechanisms may contribute to the inflammation and destruction of bone and to attachment loss, which are characteristic features of periodontal disease [35].

In this study, it was found that scaling and root planing significantly reduced the amounts of IL-1β in gingival crevicular fluid. It should be stressed, however, that 4 weeks after nonsurgical therapy the

amounts of IL-1β were still significantly higher ($p < 0.0001$) than in control groups. The effect of nonsurgical therapy on IL-1β levels has been studied previously, and it has been shown that scaling and root planing resulted in reduction of gingival crevicular fluid IL-1β [36,37,26].

As regards the level of IL-33 in GCF, it was found to be statistically significantly higher in group I, at base line and 4weeks post therapy, than that of group II. It was also found that scaling and root planing significantly reduced the amounts of IL-33 in gingival crevicular fluid in the study group after four weeks of SRP. This result was in line with the result of other study that investigate the effect of periodontal therapy on cytokine levels (IL-1, IL-8, and IL-10 and RANTES) in GCF and found that there was an increase in IL-33 levels in periodontitis patients when compared to the healthy control group. On the contrary, [38] found lower GCF IL-33 level in chronic periodontitis patients when compared with healthy controls [39]. The same was noted by [39], where no significant difference in GCF IL-33 level and conclude that it could not differentiate chronic periodontitis from clinically healthy periodontium. Disagreement with other study that did not detect IL-33 in GCF samples of chronic periodontitis patients [40].

The increased level of IL-33 in chronic periodontitis patients may be due to its role in inducing inflammation. IL-33 most likely has three roles in relation to periodontal disease: as an alarmin, a chemoattractant, and a systemic cytokine. The release of IL-33, when acting as an alarmin, results in the destruction of several cells by necrosis, mainly fibroblasts and epithelial cells [41,42]. In the context of inflammatory disease, IL-33 will induce other responses: mast cell degranulation and the production of proinflammatory cells (i.e., macrophages, eosinophils, and basophils). The release of inflammatory mediators and IL-33 will induce the activation of osteoblasts, which leads to the production of RANKL [43] and the subsequent activation of osteoclasts. Importantly, IL-33 most likely induces osteoclast activation by increasing osteoclast transcription factors. On the other hand, IL-33 is involved in the anti-inflammatory response as an augmentation of the Th2 response. However, it is believed that, in the context of periodontal disease, the levels of proinflammatory cytokines are extremely high due to the bacterial infection and, therefore, the osteoclastogenesis is favored [44].

Additionally, the degranulation of mast cells in addition to the inflammation state produces awareness of the circulating monocytes, and, in this microenvironment, they will differentiate into osteoclasts. This finding is in accordance with other studies that found a protective role of IL-33 inhibition in RA-induced animals [45,46] and increased bone erosion in RA patients with IL-33 increased serum levels [47].

CONCLUSION

Scaling and root planing (SRP) is the mainstay of treatment of periodontal diseases as SRP was effective in improving clinical parameters in patients with chronic periodontitis. This improvement was accompanied by a significant decrease the levels of the proinflammatory cytokines IL-1β and IL-33 in GCF. IL-33 could be used as a potential diagnostic marker for periodontal disease activity in gingival crevicular fluid.

REFERENCES

1. Pihlstrom BL, Michalowicz BS, NW. Periodontal diseases. Lancet 2005; 366: 1809-20.
2. Merchant AT, W. Reseaching periodontitis: challenges and opportunities. J Clin Periodont 2007; 34: 1007-15.
3. LÖe H. periodontal disease in pregnancy. ActaOdontolScanad. 1963; 21: 533.
4. Silness P. periodontal disease in pregnancy. . Odontol Scanad. 1964; 22: 121.
5. Mühleman H. Gingival sulcus index. A leading symptom in initial gingivitis. . HelvOdontolActa. 1971; 15: 107-13.
6. Ramfjord. The Periodontal Disease Index J Periodontol,. 1967; 38: 602.
7. LB, L.J, R.L. Evaluation and modification of spectrophotometric procedures for analysis of

lactate dehydrogenase, beta-glucuronidase and arylsulphatase in human gingival crevicular fluid collected with filter-paper strips, . Oshrain, Arch Oral Bioi 1985; 30: 235-42.
8. G, S. Method of collection, . Crevicular Fluid Updated. 1983: 29-36.
9. D. Cytokines that promote periodontal tissue destruction. J Periodontol 2008; 79(8): 1585S-91S.
10. Taubman MA, Valverde P, Han X. Immune response: The key to bone resorption in periodontal disease. J Periodontol. 2005; 76(11): 2033-41.
11. Kinney J. S, Ramseier C. A, and Giannobile. Oral fluid-based biomarkers of alveolar bone loss in periodontitis. Annals of New York Academy of Sciences. 2007; 1098: 230–51.
12. Buduneli N, D.F. Host-derived diagnostic markers related to soft tissue destruction and bone degradation in periodontitis. J Clin Periodontol. 2011; 38(11): 85–105.
13. V.J. gingival crevicular fluid- an introduction. Periodontology 2003; 31: 9–11.
14. Konopka L, Pietrzak A, E. Effect of scaling and root planing on interleukin-1β, interleukin-8 and MMP-8 levels in gingival crevicular fluid from chronic periodontitis patients. J Periodont Res. 2012; 47: 681-8.
15. Soder B, Jin LJ, S. Granulocyte elastase, matrix metalloproteinase-8 and prostaglandin E2 in gingival crevicular fluid in matched clinical sites in smokers and non-smokers with persistent periodontitis. J Clin Periodontol. 2002; 29(5): 384–91.
16. Engebretson SP, Hey-Hadavi J, FJ. Gingival crevicular fluid levels of interleukin-1beta and glycemic control in patients with chronic periodontitis and type 2 diabetes. J Periodontol. 2004; 75: 1203-8.
17. Lamster IB, J. Analysis of gingival crevicular fluid as applied to the diagnosis of oral and systemic diseases. Ann N Y Acad Sci. 2007; 1098: 216–29.
18. GS. Formation, collection and significance of gingival crevice fluid. Periodontol 2000 2003; 31: 32-42.
19. Stoller N.H, Karras D.C., L.R. Reliability of crevicular fluid measurements taken in the presence of supragingivalplaque. JPeriodontal. 1990; 61: 670-3.
20. Griffiths G, Wilton J.M, M. contamination of human gingival crevicular fluid by plaque and saliva. Arch Oral Biol. 1992; 37: 559-64.
21. Bostanci N, I˙lgenli T, Emingil G, Afacan B, Han B, To¨z H, et al. Gingival crevicular fluid levels of RANKL and OPG in periodontal diseases: implications of their relative ratio. J Clin Periodontol. 2007; 34: 370–6.
22. L. Clinical laboratory methods for detection of antigens and antibodies. Medical Immunology. 2001: 221-2.
23. Lopez N. J, Socransky S. S, Da, Japlit M. R, Haffajee. Effects of metronidazole plus amoxicillin as the only therapy on the microbiological and clinical parameters of untreated chronic periodontitis. Journal of Clinical Periodontology. 2006; 33: 648–60.
24. Rhodus NL, B Cheng, W Bowles, al. Proinflammatory cytokine levels in saliva before and after treatment of (erosive) oral lichen planus with dexamethasone. Oral Dis. 2005; 12(2): 112-6.
25. Iglhaut J, Aukhil I, DM. Progenitor cell kinetics during guided tissue regeneration in experimental periodontal wounds. J Clin Periodontol. 1998; 25: 475-81.
26. Gamonal J, Acevedo A, Bascones A, Jorge O, A. Levels of interleukin-1β, -8, and -10 and RANTES in gingival crevicular fluid and cell populations in adult periodontitis patients and the effect of periodontal treatment. J Periodontol. 2000; 71: 1535–45.
27. I.L.C., J.B. The role of reactive oxygen and antioxidant species in periodontal tissue destruction. Periodontology 2000. 2007; 43: 160-232.
28. Grant MM, Brock GR, Matthews JB, IL. Crevicular fluid glutathione levels in periodontitis and the effect of non-surgical therapy. J Clin Periodontol. 2010; 37(1): 17-23.
29. Duarte PM, da Rocha M, Sampaio E, Mestnik MJ, Feres M, Figueiredo LC, et al. Serum levels of cytokines in subjects with generalized chronic and aggressive periodontitis before and after non-surgical periodontal therapy: a pilot study. J Periodontol. 2010; 81(7): 1056-63.
30. Petersilka GJ, Ehmke B, TF. Antimicrobial effects of mechanical debridement. Periodontol 2000. 2002; 28: 56-71.
31. Yu¨ cel OO, Berker E, Garibog˘ lu S, H. Interleukin-11, interleukin-1b, interleukin-12 and the

pathogenesis of inflammatory periodontal diseases. J Clin Periodontol. 2008; 35: 365–70.
32. Toker H, Poyraz O, K. Effect of periodontal treatment on IL-1b, IL-1ra, and IL-10 levels in gingival crevicular fluid in patients with aggressive periodontitis. J Clin Periodontol 2008; 35: 507–13.
33. Goutoudi P, Diza E, M. Effect of periodontal therapy on crevicular fluid interleukin-1b and interleukin-10 levels in chronic periodontitis. J Dent. 2004; 32: 511–20.
34. Hou LT, Liu CM, EF. Crevicular interleukin-1b in moderate and severe periodontitis patients and the effect of phase I periodontal treatment. J Clin. 1995; 22: 162–7.
35. Hou LT, Liu CM, Liu BY, Lin SJ, Liao CS, EF. Interleukin-1β, clinical parameters and matched cellular histopathologic changes of biopsied gingival tissue from periodontitis patients. J Periodont Res. 2003; 38: 247-54.
36. Engebretson SP, Grbic JT, Singer R, IB. GCF IL-1b profiles in periodontal disease. J Clin Periodontol. 2002; 29: 48–53.
37. Buduneli N, Buduneli E, Cetin EO, Kirilmaz L, N. Clinical findings and gingival crevicular fluid prostaglandin E2 and interleukin-1b levels following initial periodontal treatment and short-term meloxicam administration. Expert Opin Pharmacother. 2010; 11: 1805–12.
38. Beklen , G. Interleukin-1 superfamily member, interleukin-33, in periodontal diseases. The Biological Stain Commission Biotechnic & Histochemistry. 2013; 89(3): 209–14.
39. Buduneli N, O¨ zgu¨n O¨ zcxaka, Nalbantsoy. Interleukin-33 levels in gingival crevicular fluid, saliva, or plasma do not differentiate chronic periodontitis. J Periodont 2012; 83: 362-8.
40. Papathanasiou E, Teles F, Griffin T, Arguello E, Finkelman M, Hanley J, et al. Gingival crevicular fluid levels of interferon-c, but not interleukin-4 or -33 or thymic stromal lymphopoietin, are increased in inflamed sites in patients with periodontal disease. J Periodont Res 2014; 49: 55–61.
41. Schmitz J, Owyang A, Oldham E, Song Y, Murphy E, McClanahan TK, et al. IL-33, an interleukin 1-like cytokine that signals via the IL-1 receptor-related protein ST2 and induces T helper type 2-associated cytokines. Immunity. 2005; 23: 479–90.
42. Joshi AD, Oak SR, Hartigan AJ, Finn WG, Kunkel SL, Duffy KE, et al. Interleukin-33 contributes to both M1 and M2 chemokine marker expression in human macrophages. BMC Immunol. 2010: 11-52.
43. Saidi S, Bouri F, Lencel P, al. IL-33 is expressed in human osteoblasts, but has no direct effect on bone remodeling. Cytokine. 2011; 53(3): 347–54.
44. Felipe Andrés Cordero da Luz, Ana Paula, Lima Oliveira, Daniella Borges, Paula Cristina Brígido, Silva. The Physiopathological Role of IL-33: New Highlights in Bone Biology and a Proposed Role in Periodontal Disease. Mediators of Inflammation. 2014: 8 pages.
45. G. Palmer, Talabot-Ayer, al. Inhibition of interleukin-33 signaling attenuates the severity of experimental arthritis. Arthritis and Rheumatism. 2009; 60(3): 738–49.
46. Xu D , Jiang HR , Kewin P , Li Y , Mu R , Fraser AR , et al. IL-33 exacerbates antigeninduced arthritis by activating mast cells. Proc Natl Acad Sci USA. 2008; 105: 10913 – 8.
47. Xiangyang Z, Lutian Y, Lin Z, Liping X, Hui S, L. Increased levels of interleukin-33 associated with bone erosion and interstitial lung diseases in patients with rheumatoid arthritis. Cytokine. 2012; 58(1): 6–9.