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GCF IL-1β profiles in periodontal disease

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Abstract

Objectives: Studies suggest a genetic influence on levels of interleukin-1β (IL-1β) in gingival crevicular fluid (GCF). Levels of IL-1β in GCF, however, are also dependent upon the clinical parameters at the site of collection, including probing depth (PD) and level of attachment (AL). To examine this issue, IL-1β in GCF was evaluated from patients with varying degrees of periodontal disease. The influence of both the status of the patient and the probing depth at the sampled sites were considered in the analysis.

Material and methods: GCF IL-1β was determined by ELISA at 6–8 molar sites from 29 non-smoking adults with mild, moderate, or severe periodontal disease at baseline, 2 weeks, and 24 weeks following scaling and root planing. For later analysis, patients were dichotomized on the basis of disease severity (mild/moderate vs severe). Sampled sites were classified at baseline by PD as, shallow (<4 mm), intermediate (4–6 mm), or deep (>6 mm).

Results: PD and AL were each strongly correlated with IL-1β levels at baseline. However, patients with severe disease had higher levels of IL-1β in each PD category than those with mild/moderate disease. As compared to patients with mild/moderate disease, IL-1β levels in shallow sites from patients with severe disease was elevated nearly 2 fold ($p<0.001$). IL-1β levels were reduced in all groups at 2 weeks and were still significantly reduced in patients with mild/moderate disease at 24 weeks. At 24 weeks IL-1β returned to near baseline levels in patients with severe disease.

Conclusion: While PD and AL are each associated with increased GCF IL-1β, patients with severe disease show higher IL-1β GCF levels in shallow sites, suggesting that high GCF IL-1β expression is in part a host trait, and not strictly a function of clinical parameters.

Key words: periodontitis; interleukin-1β; adult; analysis of variance; crevicular fluid; periodontal therapy

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Elevated levels of the proinflammatory cytokine IL-1 are observed in a variety of inflammatory conditions, including joint fluid from rheumatoid arthritis patients (Bunning et al. 1986), the skin of psoriasis patients (Romero et al. 1989, Debets et al. 1995), and the colonic mesynchymal tissue from Crohn's disease patients (Ligumsky et al. 1990). Furthermore, evidence suggests a critically important role for the pro-inflammatory mediator IL-1 in the molecular etiology of the periodontal diseases. Chronic inflammatory periodontal disease is initiated by Gram-negative microflora (Haffajee & Socransky 2000), and this infection elicits a host inflammatory response resulting in destruction of the periodontal attachment apparatus including non-mineralized connective tissue and bone. It is well established that various host cells are activated to release IL-1 in the presence of lipopolysacharide (LPS) and endotoxin derived from Gram-negative microorganisms. LPS is a potent inducer of IL-1 production in human peripheral monocytes (Lindemann et al. 1988). Additionally, LPS can stimulate macrophages to produce IL-1, TNF, and prostaglandin E2 (PGE2) in a dose dependent manner (Molvig et al. 1988). Polymorphonuclear leukocyte (PMN) adherence to endothelial cell monolayers increases 18 fold in the presence of elevated IL-1 levels (Bevilacqua et al. 1985). IL-1 can also promote development of an inflammatory response by up-regulating endothelial-leukocyte adhesion molecule, intercellular adhesion molecules-1 and -2, and vascular adhesion molecule-1 (VCAM-1) on the luminal surface of endothelial cells. VCAM-1 regulates PMN, monocyte, and leukocyte adhesion (for review, see

(Arend & Dayer (1990)). Endothelial cells are also capable of releasing IL-1 in response to LPS and endotoxin. Furthermore, IL-1 can induce its own gene expression in a variety of cells (Dinarello et al. 1987).

Periodontal ligament and gingival fibroblasts challenged with IL-1 in vitro release PGE2 in a dose dependent manner (Richards & Rutherford 1988), and secrete collagenase and matrix metalloproteinases (Birkedal-Hansen 1993). IL-1 up-regulates cyclooxygenase-2 (COX-2) mRNA and may increase the stability of COX-2 in vivo (Ristimaki et al. 1994). The higher tissue COX levels induced by IL-1 may in part explain the higher levels of arachadonic acid metabolite PGE2 consistently observed in the gingival crevicular fluid of patients with periodontitis.

Interestingly, stable inter-individual differences in IL-1 release in the presence of LPS are apparent when monocytes of differing donor lineages were compared, indicating a genetic component to the host response to a bacterial challenge (Molvig et al. 1988). Kornman and co-workers have demonstrated an association between a specific composite genotype of the IL-1 gene cluster and periodontal disease severity (Kornman et al. 1997). The genotype that was associated with adult periodontitis, is composed of a polymorphism in the gene for IL-1α (IL-1A−889 or IL-1A+4845) and in the gene for IL-1β (IL-1B+3953). Allele 2 of the IL-1B+3953 polymorphism has been linked to increased IL-1β production in vitro (Pociot et al. 1992). More recently a study from our laboratory has demonstrated that carriage of the specific IL-1 gene cluster composite polymorphism is also related to increased IL-1β expression in vivo. In that study, it was shown that among patients of similar disease severity, those with the periodontitis associated genotype (PAG) demonstrated elevated levels of IL-1β in gingival crevicular fluid (GCF) and gingival tissues (Engebretson et al. 1999).

In the present study, we evaluate the total amount and concentration of IL-1β in GCF from patients with varying degrees of periodontal disease, as well as the short and longer-term response of this mediator to treatment following scaling and root planing. The purpose of this study was to compare GCF IL-1β expression in patients with different degrees of periodontal disease, and at different sites within those patients.

Material and methods

Patient selection

The patients in this study have been described previously (Grbic et al. 1999). Briefly, 37 patients with mild (n=13), moderate (n=12), or severe (n=12) periodontitis were enrolled at baseline. Of the 37 patients, 29 completed the 24 week protocol. The following were enrollment criteria: at least 20 teeth; two sites of ⩾5 mm attachment loss in each quadrant; good general health; non-smoker; no antibiotic usage within 6 months; not a regular user of NSAIDs. A subject was considered a non-smoker if he or she had never smoked, or had stopped smoking more than 5 years previous to the date of examination and had a pack-year history of less than ten. Additional exclusion criteria were: pregnancy or lactation, diabetes, HIV infection, bleeding disorders, immunosuppressive chemotherapy, and any condition necessitating antibiotic pre-medication for dental appointments. This study was approved by the Institutional Review Board at Columbia Presbyterian Medical Center. Informed consent was obtained from all subjects. In addition to patients with periodontitis, 16 patients without evidence of periodontitis (healthy) completed baseline measures. Patients were designated healthy if their mean whole mouth attachment loss value was less than 2 mm, and there was no radiographic evidence of alveolar bone loss.

GCF collection

Each clinical evaluation was preceded by collection of GCF as previously described (Lamster et al. 1991) from the mesiolingual and mesiobuccal surfaces of all molar teeth. Briefly, teeth were air dried and isolated with cotton rolls, supragingival plaque was gently removed, and GCF was sampled with precut methylcellulose filter paper strips for 30 s. Strips were measured for fluid volume with a calibrated Periotron 6000 (Interstate Drug Exchange, Amityville, New York), then removed to separate microcentrifuge tubes containing 50 μl phosphate buffered saline-Tween 20. The tubes were stored at −20°C until eluted (maximum 48 h). Following elution, each GCF sample was analyzed separately. Values were then pooled to give a single mean value for each patient, and where appropriate, within each probing depth category.

Clinical measures

At all visits, GCF was collected first and clinical parameters were then recorded. Clinical data included probing depth (PD), attachment level (AL), plaque, and bleeding on probing (BOP) and were collected at 6 sites per tooth. PD was defined as the distance in mm from the coronal-most margin of the free gingiva to the most apical penetration of the Michigan-0 probe. AL was defined as the distance from the cemento-enamel junction to the most apical penetration of the Michigan-O probe. The presence of supragingival plaque was recorded dichotomously during PD measurements. Bleeding on probing (BOP) within 20 s was recorded dichotomously.

Treatment

Following collection of GCF and clinical parameters, subjects received full mouth root planing and scaling with curettes and ultrasonic instruments under local anesthesia for not more than 2 h. No antibiotics were prescribed following this treatment.

Analysis of IL-1β in GCF

GCF samples were analyzed for IL-1β using a commercially available enzyme-linked immunosorbant assay (Multikine Kit, Cistron Biotechnology, Pine Brook, New Jersey). This assay is a sandwich ELISA and was performed according to manufacturer's instructions using human recombinant standards. Results are reported as total amount of IL-1β (in pg±SD) per sample, or as concentration by converting Periotron units to μl using calibration curves as described previously (Lamster et al. 1988) and expressed as pg/μl. Where IL-1β levels are compared between patient groups, mean whole mouth IL-1β values are used. Where IL-1β is reported by probing depth, IL-1β values from each probing depth category are pooled within each patient.

Statistical analysis

Categorization of patients and sites was based on the clinical data collected at baseline. For comparison, patient disease severity was categorized on the basis of mean whole mouth AL as healthy (AL<2 mm), mild (AL<3 mm), moderate (AL 3–4 mm), or severe

Table 1. Characteristics (mean±SD) of the study population

Disease status	Health	Mild	Moderate	Severe	All
no. subjects	16	13	12	12	53
age (years)	26.2±4.7	37.4±13.4	43.6±9.8	38.7±7.7	41.6±11.2
gender (% female)	50.0%	51.5%	50%	50%	51.0%
probing depth (mm)	1.64±0.19	2.39±0.37	3.26±0.34	3.98±0.64	3.33±0.80
attachment loss (mm)	1.70±0.23	2.47±0.21	3.45±0.28	4.57±0.64	3.61±1.0
% plaque	13.6±9.7	52.9±28.6	75.7±22.3	78.6±11.1	69.7±30.8
% BOP	1.26±2.8	40.8±21.8	71.4±21.0	80.6±10.6	54.5±30.8

Table 2. Mean (±standard deviation) patient GCF IL-1β levels in pg/sample

		AL⩾4 (mm)						
PD	*n*	Baseline	SD	2 weeks	SD	24 weeks	SD	Change 0–24
<4 mm	16	37.5	49.9	36.5	42.5	38.7	45.6	NS
4–6 mm	20	79.5	69.8	75.8	71.2	47.1	47.9	$p<0.01$
>6 mm	10	115.7	96.6	61.0	62.5	58.0	51.6	$p<0.01$
		AL⩽4 (mm)						
<4 mm	7	72.0	51.5	37.1	28.3	63.0	61.6	NS
4–6 mm	9	104.2	67.7	39.8	43.9	82.6	80.3	NS
>6 mm	9	131.9	92.8	37.6	44.1	100.9	84.5	NS

Stratification by attachment loss category and probing depth of the sampled sites at baseline, 2 weeks, and 24 weeks. The *n* reflects that samples were not available from each probing depth category in every patient.

(AL>4 mm) periodontitis and compared by ANOVA. Correlations were calculated between mean patient PD, AL, BOP, plaque, and GCF IL-1β. The Fischer *r* to *z* transformation was used to establish correlation coefficients significantly greater than 0.

For the longitudinal analysis, patients with severe AL (AL>4 mm) are compared with the mild and moderate periodontitis groups (mild/moderate; AL⩽4 mm). We compared sites within attachment loss groups by pooling mean GCF IL-1β values within each patient and categorizing these values by probing depth as shallow (<4 mm), intermediate (4–6 mm), or deep (>6 mm). ANOVA was used to compare GCF IL-1β expression by probing depth category within AL groups. The effect of treatment on IL-1 levels over time was determined by repeated measures ANOVA. Data analysis for this study was accomplished using STATVIEW 5.0 (SAS Systems, Inc. Cary, North Carolina) software.

Results

Clinical parameters

A total of 53 patients completed the baseline evaluation. The 16 patients without periodontitis received no treatment and are only included in the baseline comparison. For all patients, 27 (50.5%) were females. The mean age was 41.6 years with a range of 21–62 years. The age of the moderate and severe patients was greater than the healthy and mild patients, however, age was not significantly associated with the outcome variable GCF IL-1β (not shown). 37 periodontitis patients began the treatment arm of the study. Of these 37, 29 finished the 24-week protocol. Demographic and clinical parameters of the individuals in the study (mean± standard error) are provided in Table 1.

IL-1β in GCF

GCF IL-1β was determined at 6–8 molar sites from each patient prior to therapy (baseline) and except for the healthy group, at the same sites 2 weeks, and 24 weeks following scaling and root planing. In total, GCF samples were taken from 421 surfaces at the baseline examination, and detectable amounts of GCF IL-1β were obtained from 381 of the 421 GCF samples. 228 GCF IL-1β samples were available from the 29 patients who completed the 2-week and 24-week examinations. Detectable amounts of GCF IL-1β were obtained from all of these samples.

Baseline comparison

Among all patients at baseline, GCF IL-1β was correlated with PD ($r=0.419$, $p<0.0001$) and AL ($r=0.414$, $p<0.0001$), and to a lesser extent with % sites BOP ($r=0.406$, $p<0.0001$) and % sites with plaque ($r=0.246$, $p<0.0001$). A comparison was made at baseline between AL groups. The values given are for mean total patient GCF IL-1β±standard deviation (SD). Baseline mean GCF IL-1β values were as follows: healthy 8.9 pg±8.8, $n=16$; mild 40.6 pg±54.6, $n=13$; moderate 78.1 pg±75.9, $n=12$; and severe 121.9 pg±87.2, $n=12$ (Fig. 1). The difference was statistically significant ($p<0.0001$) between all groups by ANOVA. When examined as concentration, there were similar differences in mean GCF IL-1β between AL groups (healthy 18.1 pg/ul±25.9, mild 87.1 pg/ul±85.3, moder-

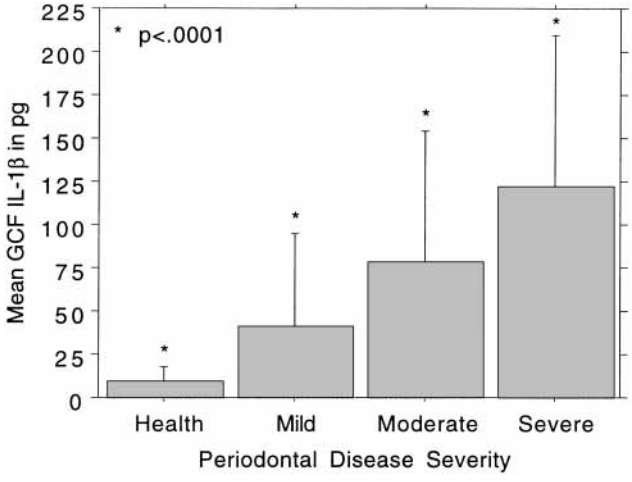

Fig. 1. ANOVA was used to compare mean patient levels of GCF IL-1β (pg/sample±SD) according to mean attachment loss category. All groups were significantly different ($p<0.001$). The patient was the unit of observation in this analysis.

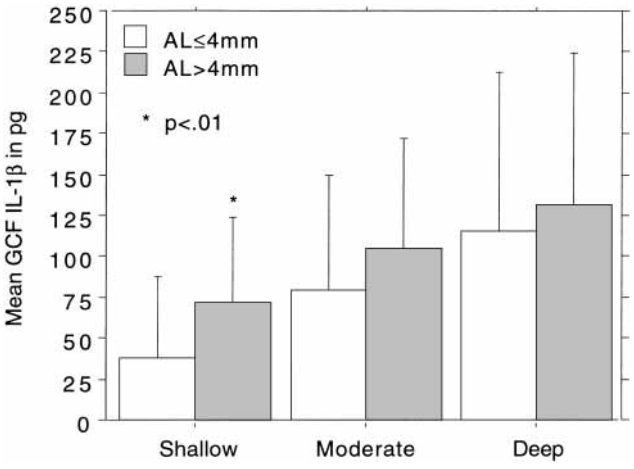

Fig. 2. For this analysis patients in the mild and moderate categories were combined to create a new category (mild/moderate; AL≤4). This new category was compared with the severe category (AL>4). ANOVA was used to compare mean levels of GCF IL-1β by attachment loss category and by probing depth category determined at baseline. The patient was the unit of observation in this analysis. GCF IL-1β is expressed in pg/sample±SD.

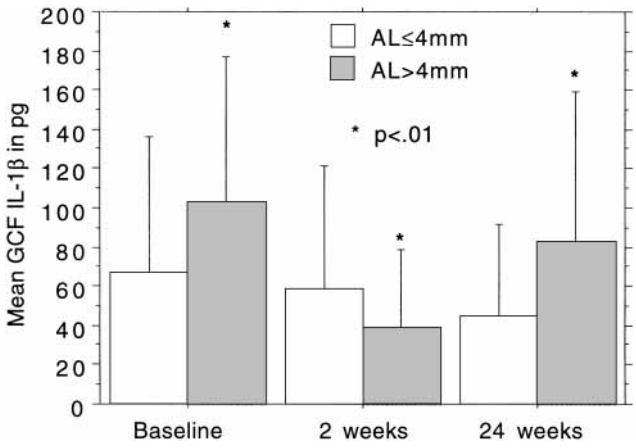

Fig. 3. The mean patient GCF IL-1β levels in pg/sample±SD at baseline, 2 weeks and 24 weeks following scaling and root planing. AL≤4 mm are compared with AL>4 mm by ANOVA. The patient was the unit of observation in this analysis.

ate 107.2 pg/ul±95.5, and severe 141.1 pg/ul±93.6). These differences between groups were also significant at the $p<0.001$ level by ANOVA. Since the differences between groups were more pronounced for total IL-1β in GCF versus concentration, only total IL-1β activity is reported hereafter.

Baseline comparison by AL group and PD category

The following data are for the 29 patients who completed the 24-week protocol. For these subsequent analyses, patients from the mild and moderate categories are combined (AL≤4 mm, $n=20$) and compared with patients in the severe category (AL>4 mm, $n=9$). Differences were observed when probing depths were considered in the analyses. In shallow sites (<4 mm), total IL-1β levels were nearly 2× higher for patients with more severe attachment loss compared to the shallow sites from patients with mild/moderate attachment loss (71.9 pg±26.0, $n=16$, versus 37.4 pg±29.5, $n=7$; $p<0.01$) (Fig. 2). GCF IL-1β from patients in the severe group showed a trend towards higher levels of IL-1β in the intermediate and deep sites but these differences were not significant.

The effect of treatment on total IL-1β in GCF (Fig. 3)

In this analysis, we examined the effects of treatment on mean patient IL-1β levels. At baseline, these two groups were significantly different with regard to mean total GCF IL-1β expression by ANOVA (mild/moderate 66.2 pg±69.9, versus severe 101.8 pg±73.8, $p<0.001$). GCF IL-1β levels were reduced at the 2-week follow-up for both groups, but proportionately more so for the group with more severe disease (mild/moderate 58.6 pg±62.8, versus severe 38.5 pg±39.9, $p<0.0001$). 24 weeks after therapy, IL-1β levels were again significantly higher in the severe disease group compared with the mild/moderate group (82.2 pg±77.1, versus 44.8 pg±44.8, $p<0.0001$). Mean GCF IL-1β values were reduced between the baseline and 24-week examinations for those in the AL≤4 mm group (66.2 pg±69.6, versus 44.8 pg±47.2 (baseline versus 24 weeks, $p=0.0001$)). Mean GCF IL-1β values for the AL>4 mm group at the 2-week examination were significantly reduced compared with baseline but were not significantly different from baseline at the 24-week examination −103.0 pg±73.8, vs. 38.5 pg±39.9 (baseline versus 2 weeks, $p<0.0001$), versus 82.2 pg±77.2 (baseline versus 24 weeks, $p=0.07$).

The effect of treatment on total IL-1β in GCF with respect to probing depth (Table 2)

Using repeated measures ANOVA, differences were also observed in GCF IL-1β levels following treatment for probing depth categories. When compared to baseline, GCF IL-1β levels were reduced at 24 weeks for the moderate and deep sites of patients in the mild/moderate group. In the severe group, no differences were seen between sites in any probing depth category when comparing the baseline and 24-week examinations.

Discussion

The purpose of this study was to establish baseline levels of the proinflammatory cytokine IL-1β in GCF from untreated patients of varying periodontal disease severity, and to monitor IL-1β activity in GCF of those patients at two time points following scaling and root planing. These comparisons were made in consideration of recent findings that suggest individual variation in GCF cytokine expression (Engebretson et al. 1999).

Regardless of disease severity, clinical parameters such as probing depth and clinical attachment loss at baseline were significantly associated with total IL-1β and IL-1β concentration in GCF. 2 weeks following scaling and root planing, levels of IL-1β in GCF were reduced in all patients. This reduction was more pronounced for patients with more severe disease. At 24 weeks, IL-1β continued to decrease for patients with less disease severity, while cytokine activity in individuals with more severe disease had rebounded and approached baseline levels.

When the probing depth of the sampled sites was considered, differences in GCF IL-1β between the mild/moderate and severe groups were most pronounced at shallow probing depths. In a previous study, patients with similar periodontal disease severity, but who differed by their carriage of the periodontitis associated genotype, were compared for expression of IL-1 in the GCF (Engebretson et al. 1999). It was found that IL-1β levels were 3-fold higher in the shallow probing depth sites of patients who carried the genotype. We have speculated that carriage of the periodontitis associated genotype caused a "left shift" of the normal IL-1β expression pattern, meaning that increased IL-1 expression would be greater in each probing depth category. This finding was significant in that a postulated genetic mechanism might explain this increased expression of the important inflammatory mediator, IL-1β. Since the group of patients in the current study were examined prior to description of the periodontitis associated genotype, blood samples were not collected for genotyping. Nevertheless, the different response patterns of IL-1β in GCF in the more severe patient groups suggests inherent differences in the local production of IL-1β. If the different patient groups differed just in the number of cells producing IL-1β, then the 2 groups of patients should differ only in the magnitude of the response. This was not seen, and our data suggests that the differences are due to either the amount of IL-1β produced, or a lag period during which the IL-1β is produced following removal of the microbial challenge present prior to treatment.

There is a striking similarity in IL-1β expression pattern observed in the current study and our previous study of patients with known carriage of the polymorphic variant of the IL-1 gene cluster (Engebretson et al. 1999). It is of interest that in both the present study and our previous study, differences in IL-1 levels became even more pronounced after therapy. This finding further suggests that IL-1 expression may be a patient trait since removal of the microbial challenge (scaling and root planing) enhanced this finding. These results are also consistent with the data reported by Figueredo et al. (1999) that increased IL-1 levels are found in the GCF of patients with periodontal disease regardless of the disease severity at the site. Further, in a study of the effects of stress on periodontal health (Deinzer et al. 1999), GCF IL-1 was elevated in response to stress whether gingivitis was present or not. Taken together, these studies suggest individual variability with regard to GCF IL-1 expression and that genetic variability is a plausible explanation for this occurrence.

Hence, IL-1β would seem an attractive candidate molecule for monitoring periodontal disease initiation, progression, and therapeutic outcome. McGuire & Nunn (1999) have suggested that knowledge of a patient's IL-1 genotype status could aid in establishing a prognosis. In that study, IL-1 genotype status was associated with greater risk for tooth loss. Nevertheless, while evidence suggests an important role for IL-1β in the pathophysiology of chronic adult periodontal disease, clinical studies thus far have not defined how measurement of this proinflammatory cytokine can be used diagnostically. In fact, in the present study, high IL-1 in GCF was not associated with greater incidence of attachment loss during our 24-week protocol (data not shown).

The finding of a potential genetic influence on GCF IL-1β expression has important clinical ramifications. Since genotype status is static, young children of severely affected parents can be evaluated to identify at-risk individuals. These patients could then be treated aggressively and followed more closely to avoid disease initiation. Longitudinal trials are needed to fully explore this question. Lastly, the potential benefit of the specific soluble receptors for proinflammatory cytokines in animal models of periodontitis has been demonstrated (Assuma et al. 1998), and these agents have been used in the treatment of other inflammatory diseases (Rutgeerts et al. 1999). These approaches may ultimately prove useful in the treatment of periodontitis. Topical application of such substances may offer a paractical means of delivering agents directly to the affected tissues.

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Zusammenfassung

Interleukin-1β-Profile in der Sulkusflüssigkeit bei Parodontitis

Hintergrund: Es liegen Hinweise auf eine genetische Beeinflussung der Konzentrationen von Interleukin-1β (IL-1β) in der Sulkusflüssigkeit (SF) vor. Die IL-1β-Konzentrationen in der SF sind aber ebenfalls von klinischen Parametern wie Sondierungstiefe (ST) und Attachmentverlust (AL) an den untersuchten Stellen abhängig.

Zielsetzung: Abklärung des Zusammenhanges zwischen dem Ausmaß parodontaler Erkrankung und den IL-1β-Konzentrationen in der SF.

Material und Methoden: Bei 29 erwachsenen Nichtrauchern mit milder, moderate oder schwerer Parodontitis wurden die IL-1β-Konzentrationen von 6–8 Molarenstellen mittels ELISA zu Beginn der Studie sowie 2 und 24 Wochen nach Scaling und Wurzelglättung bestimmt. Für die weitere Analyse wurden die Patienten nach Schweregrad der Parodontitis dichotomisiert (mild und moderat/schwer). Die untersuchten Stellen wurden klassifiziert nach ST zu Studienbeginn in flach ($<$4 mm), mittel (4-6 mm) und tief ($>$6 mm).

Ergebnisse: ST und AL waren stark mit den IL-1β-Konzentrationen zu Studienbeginn korreliert. Allerdings zeigten Patienten mit schwerer Parodontitis höhere IL-1β-Konzentrationen in jeder ST-Kategorie als Patienten mit milder/moderater Parodontitis. Beim Vergleich mit Patienten mit milder/moderater Parodontitis zeigten die flachen Stellen der Patienten mit schwerer Parodontitis fast doppelt so hohe IL-1β-Konzentrationen ($p<0.001$). Die IL-1β-Konzentrationen waren bei allen Patienten nach 2 Wochen reduziert und blieben bei den Patienten mit milder/moderater Parodontitis auch nach 24 Wochen signifikant erniedrigt. Bei Patienten mit schwerer Parodontitis erreichten die IL-1β-Konzentrationen nach 24 Wochen annähernd die Werte, die zu Studienbeginn gemessen worden waren.

Schlußfolgerungen: Während ST und AL jeweils mit erhöhten IL-1β-Konzentrationen in der SF assoziiert waren, zeigten Patienten mit schwerer Parodontitis höhere IL-1β-Konzentrationen in der SF flacher Taschen. Dies legt den Schluss nahe, dass eine hohe IL-1β-Expression in der SF teilweise ein Wirtscharakteristikum und nicht allein eine Funktion der klinischen Parameter ist.

Résumé

Les profils IL-1β dans le fluide créviculaire gingival lors de la maladie parodontale

But: Des études ont suggéré une influence gé-

nétique sur les teneurs d'interleukine-1β (IL-1β) dans le fluide créviculaire gingival (GCF). Les niveaux d'IL-1β dans le GCF sont néanmoins dépendants des paramètres clinique au niveau du site du prélèvement incluant la profondeur de poche (PD) et le niveau d'attache (AL).

Matériaux et méthodes: Pour examiner ce phénomène, l'IL-1β du GCF a été évaluée chez des patients avec des différents degrés de maladie parodontale. Les influences tant de l'état du patient que de la profondeur au sondage au niveau des sites échantillonnés ont été considérées dans l'analyse. IL-1β dans le GCF a été déterminée par ELISA au niveau de 6 à 8 molaires de 29 adults non-fumeurs avec une maladie parodontale faible, modérée ou sévère, lors de l'examen initial et 2 et 24 semaines après le détartrage et le surfaçage radiculaire. Pour l'analyse qui s'est effectuée plus tard, les patients ont été séparés sur base de la sévérité de leur maladie (faible et modérée versus sévère). Des sites d'échantillonnage ont été classifiés lors de l'examen initial par PD: <4 mm, 4 à 6 mm et >6 mm.

Resultats: PD et AL étaient tous deux fortement en corrélation avec les teneurs en IL-1β lors de l'examen initial. Cependant les patients avec une maladie sévère avaient des teneurs supérieures en IL-1β dans chaque catégorie PD que ceux avec maladie faible ou modérée. Les teneurs en IL-1β dans les sites de faibles profondeurs des patients avec maladie sévère étaient presque 2× plus élevées ($p<0.001$) que chez ceux avec maladie faible ou modérée. Les teneurs en IL-1β ont été réduites dans tous les groupes lors de la semaine 2 et étaient toujours réduits significativement chez les patients avec une maladie faible à modérée lors de l'examen à la 24ième semaine. A ce moment, l'IL-1β retournait à des niveaux quasi identiques à ceux de l'examen initial chez les patients avec maladie sévère.

Conclusion: Tandis que PD et AL sont tous deux associés à une augmentation des teneurs en IL-1β dans le GCF les patients avec maladie parodontale sévère affichaient des teneurs plus importantes en IL-1β dans le GCF dans les sites de faible profondeur suggérant, que l'expression importante d'IL-1β dans le GCF est en partie une caractéristique de l'hôte et non-strictement une fonction des paramètres cliniques.

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