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Relationship between clinical parameters and cytokine profiles in inflamed gingival tissue and serum samples from patients with chronic periodontitis

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Abstract

Objective: The purpose of the present study was to assess the relation between clinical parameters and concentrations of the key (IL-1β, TNF-α, IL-2, IFN-γ, IL-4, IL-10) cytokines, important in the initiation and progression of periodontal diseases, within inflamed gingival tissues and serum samples from patients with severe chronic periodontitis.

Material and Methods: Twenty-five patients with severe chronic periodontitis, who had sites with probing depths (PD) >5 mm, and 25 periodontally healthy persons were included in the study. Clinical examinations including PD, clinical attachment loss, plaque index, and bleeding index were performed before periodontal treatment. Gingival tissue biopsies were collected from one active site of each patient and from healthy individuals, and blood samples were withdrawn on the day of tissue biopsy. The concentrations of cytokines were determined by an enzyme-linked immunosorbent assay, and the relationship between their profiles in situ and in circulation with clinical parameters was analysed.

Results: The concentrations of IL-1β, TNF-α, IL-2, IFN-γ were, on average, significantly higher in serum samples and gingival tissue biopsies from periodontitis patients than in healthy controls. However, serum samples from both groups showed high individual variability of cytokine profiles, and no association between cytokine concentrations and clinical parameters of periodontitis was found. On the contrary, the levels of IL-4 and IL-10 in both kinds of samples obtained from patients and controls were generally low or even undetectable, and remained, on average, on the same level. However, the frequency of IL-4 (88% positive samples) and IL-10 (72%) was much higher in healthy gingival tissues. High concentrations of TNF-α, IFN-γ and IL-2 and, especially, a high ratio of IL-1β/IL-10 and TNF-α/IL-4 found in tissue biopsies from periodontitis patients, strongly correlated with the severity of periodontitis.

Conclusion: These results indicate that high variability of cytokine concentrations and low frequency of their detection in serum samples from periodontitis patients make these determinations useless for the detection of disease presence and/or its severity. In contrast, high absolute levels of IL-1β, TNF-α, IL-2 and IFN-γ and, especially their high ratios to IL-4 and IL-10 found in inflamed tissue biopsies, were closely associated with periodontal disease severity.

Key words: cytokines; periodontitis; serum; tissue biopsies

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Periodontal diseases are probably one of the most common chronic diseases in adults, and are initiated by an overgrowth of specific Gram-negative bacterial species, which replace the normal microbiota (Darveau et al. 1997). This may be due to a disequilibrium in the host, which may be caused by several factors, such as modification of the environmental conditions of the infected site, a significant decrease in the proportion of beneficial bacteria producing inhibitory substances and/or by decreased efficacy of the host immune system (Gendron et al. 2000). There is no doubt that the balance between local levels of key cytokines, stimulated in response to periodontopathogenic bacteria and their products, is important in determining the outcome of an immune response to a given pathogen (Jiang et al. 1999).

Cytokines, small polypeptides with a wide spectrum of inflammatory, hemopoietic, metabolic and immunomodulatory properties, are produced by a variety of cells, including the macrophage/monocyte system, dendritic cells, lymphocytes, neutrophils, endothelial cells and fibroblasts (Arai et al. 1990, Callard et al. 1999). As a consequence, cytokines, together with their receptors, form a network of high complexity that is under tight but complex biological control, including positive and negative feedback by the cytokines themselves. It is well known that immunity depends on two major types of specific immune responses, termed the cellular and humoral responses. The balance between them is strongly regulated by factors associated with antigen-presenting cells (APC) and by cytokines produced by CD4+ T helper (Th) cells, which can be divided into Th1 and Th2 subsets, with contrasting cytokine profiles (Mosmann et al. 1996). Several studies have demonstrated that some cytokines, such as interleukin (IL)-12, interleukin (IL)-1β, interferon (IFN)-γ, interleukin (IL)-6, and tumor necrosis factor (TNF)-α, are involved in Th1 immune responses and induce mainly cell-mediated immunity. In contrast, IL-4, IL-5, IL-10 and IL-13 are involved in Th2 immune responses and promote humoral immunity due to the production of B cell growth and differentiation factors (O'Garra 1998, Van der Broek et al. 2000, Belardelli & Ferrantini 2002). The characteristic cytokine products of Th1 and Th2 cells are mutually inhibitory for the differentiation and effector functions of the reciprocal phenotype. Thus, IFN-γ selectively inhibits the proliferation of Th2 cells, while IL-4 and IL-10 inhibit cytokine synthesis by Th1 cells (Mosmann & Sad 1996, Essner et al. 1998). Moreover, IL-4 suppresses the synthesis of proinflammatory cytokines, including IL-1 and TNF-α, which induce several events associated with inflammation, tissue destruction, bone resorption and the production of matrix metalloproteinases and prostaglandin E_2 (Yucel-Lindberg et al. 1999). One of the major sources of IL-1β and TNF-α in the inflamed tissue are tissue monocytes/macrophages. IFN-γ and IL-2 are produced mainly by Th1 cells, while IL-4 and IL-10 by the Th2 subset. All these cytokines play a crucial role in immune and inflammatory responses, and the outcome of infection may be attributable to the balance in the relative rate between all of them.

Although a number of studies have demonstrated that the biological activity of a variety of cytokines may be directly relevant to periodontal destruction, such as periodontal attachment loss, destruction of collagen and alveolar bone resorption (Listgarten 1987, Ishihara et al. 1997); biologic mechanisms for the progression of periodontitis are not fully understood and, despite much attention focused on this subject, still remain controversial.

The individual course of the periodontal diseases and variability of clinical parameters, which may lead to tooth loss in the absence of early and appropriate treatment, prompted us to undertake a complex study on the key cytokines responsible for the initiation, progression and/or suppression of the inflammatory response.

The purpose of our study was to assess: (1) whether any correlation exists in serum and/or biopsy specimens from periodontal patients between the concentration of cytokines that are important for disease course (IL-1β, IL-2, IFN-γ, TNF-α, IL-4, IL-10); (2) if any particular cytokine profile or cytokine ratio in serum and/or gingival tissue bioptates correlates with the clinical parameters of the disease; and (3) whether estimation of cytokine profiles in serum or gingival tissue could be a useful laboratory tool to detect changes preceding serious clinical complications.

Material and Methods

Patients

The study group consisted of 25 adult patients (19 females and six males; median age: 47 years; range: 22–69 years) newly referred to the Primary Attention Service, Department of Periodontology, Medical School of Warsaw, Poland, in whom, on the basis of clinical and radiographic findings, severe chronic periodontitis was diagnosed. All patients were included in the study on the following basis: (1) had at least four sites with a pocket depth (PD) exceeding 5 mm; (2) did not suffer from systemic disorders that could influence the course of periodontal disease; and (3) were not treated with antibiotics, immunomodulatory or anti-inflammatory drugs during 6 months prior to the study.

The control group included 25 periodontally healthy individuals (15 females and 10 males, median age: 36.7 years; range 20–70 years) undergoing orthodontic treatment, who were examined by an experienced clinician before inclusion in the study. All subjects had no sites with PD or clinical attachment loss (CAL) >3 mm, were systemically healthy and were not on any medication that could affect cytokine profiles.

Clinical examination

The clinical examination of patients was performed on all existing teeth, and periodontal conditions were evaluated on the basis of the following parameters: probing depths (PD), CAL, plaque index (PI) and bleeding index (BI). The examination was carried out using the Florida Probe system (Florida Probe Corporation, Gainesville, FL, USA) based on the use of a constant pressure probe connected to a computer. The FP32 system was used to measure PD (in mm); CAL was measured by using a standard, calibrated WHO periodontal probe. The plaque index and bleeding index were evaluated with the use of simplified percentage indicators according to O'Leary et al. (1972) (Table 1). The clinical parameters were performed on six sites per tooth, with the exception of PI for which four sites were examined, and the results were expressed as a mean value accompanied by standard deviation. All periodontitis sites were scaled prior to tissue sampling.

The study was approved by the Ethics Committee of the Warsaw Medical School. All patients and individuals from the control group were thoroughly informed about the purpose and methods of the study, and written consent was obtained from all of them.

Table 1. Clinical characteristics of patients with severe chronic periodontitis and healthy controls

	Periodontitis patients (no. 25)	Controls (no. 25)
age (years)	47 (22–69)	36.7 (20–70)
% males	24	40
mean PD (mm)	5.09 ± 1.02	1.47 ± 0.32
mean CAL (mm)	2.89 ± 1.0	0.04 ± 0.03
mean PI (%)	37.9 ± 21.3	17 ± 5.6
mean BI (%)	19.1 ± 9.8	3.89 ± 3.87

PD: probing depth; CAL: clinical attachment loss; PI: plaque index; BI: bleeding index.

Sampling of gingival tissue

Inflamed gingival tissue from patients was collected by flap operation during routine periodontal surgery with the use of a scalpel, then the wound was secured with sutures. Periodontal pockets with the PD >6 mm and bleeding on probing were determined to have active disease and were chosen for the study (one sample from each patient). Prior to surgery, all subjects underwent an initial periodontal treatment phase. Collection of gingival tissue from healthy individuals was performed before tooth extraction for orthodontic/prosthetic indications. Gingival tissue was defined as clinically healthy when the probing depth was <3 mm and there was no evidence of bleeding on probing.

The tissue was weighed, then cut into small pieces (1–2 mm^3) using scissors and solubilized in cold phosphate-buffered saline (PBS) to a final concentration of 100 mg tissue/ml. After extraction on a Vortex mixer for 10 min, each sample was centrifuged at $370 \times g$ for 5 min, and the supernatant was collected, divided into small portions and stored at $-70^{\circ}C$ until use. To avoid protease activity, the entire procedure was carried out at $4^{\circ}C$.

Peripheral blood samples were obtained from each patient and healthy individuals on the day of tissue biopsy, and the sera were isolated by centrifugation after clotting, then divided into small portions and stored at $-70^{\circ}C$ until use. Optimal conditions for sampling and retaining the materials as well as conditions for elution of tissue homogenates, giving an optical density (OD) of the remaining, i.e. ''cell-associated'' cytokines below the value of the lowest standard, had been determined in preliminary experiments.

Cytokine assays

Cytokine concentrations in serum samples and tissue supernatants were measured by an enzyme-linked immunosorbent assay (ELISA) using commercially available OptEIA sets for human IL-1β, IL-2, IFN-γ, TNF-α, IL-4 and IL-10 (PharMingen, San Diego, CA, USA), according to the manufacturer's instructions. Both intra- and inter-assay coefficients of variation were below 10%. Because of the log-normal distribution of the studied parameters, the geometric mean of concentrations (GMTs) accompanied by 95% confidence intervals (CI) was calculated for each cytokine.

Statistical analysis

All results were analyzed by applying the Kolmogorov–Smirnov, Shapiro–Wilk and χ^2 tests to determine the normality of the data distribution. According to the distribution type, the data were summarized either by mean values and standard deviations (normal distribution) or by geometric mean and confidence intervals (log-normal distribution). Comparisons between groups were performed using Student's *t*-test for independent samples (normal distribution) or by the Kolmogorov–Smirnov and Mann–Whitney tests in the case of log-normally distributed variables. The correlations among clinical parameters were analyzed using the Pearson correlation test. The Spearman rank order correlation test was used to analyze correlations between clinical parameters and concentrations of cytokines. The differences in the frequency of particular cytokines between patients and the control group were examined by the χ^2 test. A *p*-value of <0.05 was considered to be statistically significant.

Results

Concentrations of cytokines in serum samples collected from periodontitis patients and healthy controls

The comparison of mean concentrations (GMTs; CIs) of IL-1β, IL-2, IFN-y, TNF-α, IL-4 and IL-10, evaluated in serum samples of periodontal patients and healthy adult volunteers, is presented in Fig. 1. The mean concentrations of particular cytokines, except for IL-4 (p = n.s), were significantly higher in patients' sera ($p<0.05$ to $p<0.01$) than in the sera of the healthy controls. However, there were no significant differences in the frequency of detection of particular cytokines between both groups. Generally, detectable levels of particular cytokines (concentrations above the lowest value of standard) were found only in about half percent of the patients and controls (Table 2). Moreover, the pattern of cytokine profiles showed high individual variability and there was no correlation between clinical parameters and the concentration or frequency of particular cytokines.

Cytokine levels in gingival tissue supernatants collected from periodontitis patients and healthy controls

The mean concentrations (GMT; 95% CI) of cytokines in tissue supernatants are shown in Fig. 2. In all samples collected from patients and healthy controls, a minimum of three or more studied cytokines were present. The levels of IL-1β, TNF-α, IFN-γ and IL-2 were significantly higher ($p<0.001$ to $p=0.01$) in periodontitis patients when compared with healthy controls. In contrast to serum samples, there were statistically significant differences in the frequency of detection of particular cytokines. IL-1β was detected in 100% of samples in both groups (p = NS), but its mean concentration in periodontitis patients was ca. nine-fold higher than in healthy subjects. The frequency of IFN-γ was similar in patients and healthy controls (p = NS), but its concentration was ca. six-fold higher in periodontitis patients. In addition to their higher concentrations, the frequency of detection of IL-2 and TNF-α differed significantly between patients and healthy controls (IL-2, $p=0.002$; TNF-α, $p=0.025$) (Table 2).

In contrast, IL-4 and IL-10 responses were very low and remained at similar levels in both groups, but there were significant differences in their frequency between patients and healthy subjects. IL-4 was detected in 88% of healthy tissue supernatants versus 35% of samples from periodontitis patients ($p=0.001$), while IL-10 was present in 72% of healthy controls and in 45%

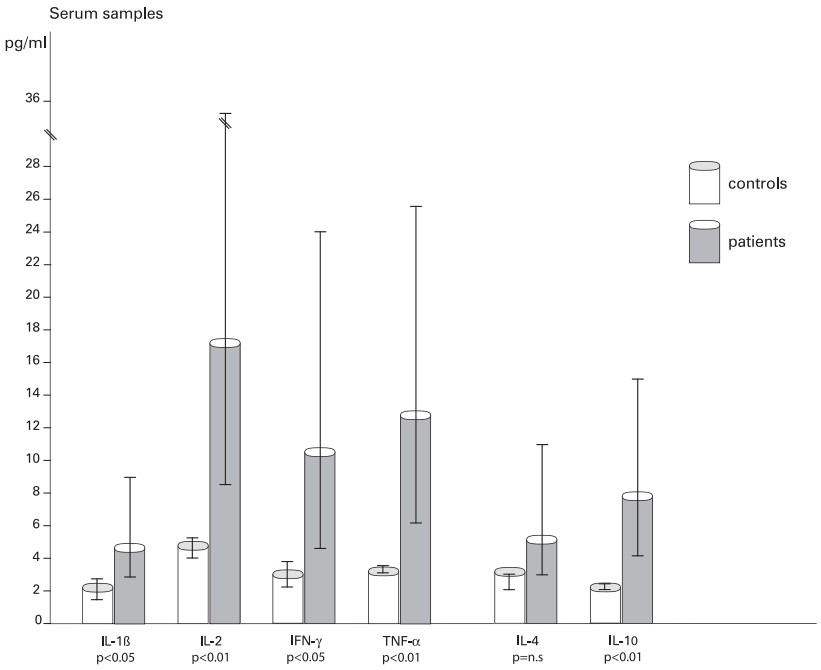

Fig. 1. Concentrations of cytokines studied in serum samples of periodontitis patients and healthy controls.

Table 2. Frequency of detection of particular cytokines in serum and gingival tissue supernatants from periodontitis patients and healthy controls

Sample		IL-1β (%)	IL-2 (%)	IFN-γ (%)	TNF-α (%)	IL-4 (%)	IL-10 (%)
serum (no. 25)	P	52	68	56	56	40	60
	C	36	44	60	40	48	40
gingival tissue supernatants (no. 25)	P	100	92	82	76	35	45
	C	100	72	68	52	88	72

P: periodontitis patients; C: healthy controls.

of samples from patients ($p = 0.002$). As a consequence, the simultaneous presence of high levels of IL-1β, IL-2, IFN-γ and TNFα with very low or nondetectable IL-4 and/or IL-10 was a predominant cytokine profile, observed in 60% of gingival tissue supernatants from periodontitis patients. In the remaining 40% of the samples, one of the following cytokine patterns predominated: IL-1β, TNF-α, IL-2 or IL-1β, TNF-α and/ or IFN-γ.

Association between cytokine concentrations, cytokine balance and clinical parameters

Because the balance between APC, Th1 and Th2 cytokine responses during infection may be as important, if not more important, than the concentration of particular cytokines alone, we compared the ratios of particular cytokines produced in situ with clinical parameters.

In tissue supernatants from periodontitis patients, a positive correlation was found between high concentrations of TNF-α and the PD value ($R = 0.42$; $p = 0.03$), and between a high ratio of IL-1β to IL-10 and BI ($R = 0.56$; $p = 0.016$). These correlations were even more evident when the severity of clinical parameters was taken into consideration. Eleven out of 25 patients with a mean PD value >5 mm showed positive correlations between high values of CAL and high levels of IL-2 ($R = 0.66$; $p = 0.02$), IFN-γ ($R = 0.63$; $p = 0.04$), TNF-α ($R = 0.75$; $p = 0.007$) and the ratio of TNF-α to IL-4 ($R = 0.53$; $p = 0.006$). Moreover, in patients with a BI value exceeding 15% (No. 12), positive correlations were found between CAL and high levels of IL-2 ($R = 0.58$; $p = 0.04$), and IFN-γ ($R = 0.66$; $p = 0.01$), while in the remainder (BI $< 15\%$) a positive correlation was found between a high PD value and concentration of TNF-α ($R = 0.66$; $p = 0.03$). It is worth noticing that in tissue supernatants from healthy controls, most cytokine ratios were significantly lower (2–10-fold) than in inflamed tissue, indicating a delicate balance between cytokines secreted in normal conditions (Table 3).

Discussion

In this study, we analyzed the expression of key (IL-1β, TNF-α, IFN-γ, IL-2 IL-4 and IL-10) cytokines that seem to play an important role in the initiation and progression of periodontitis. The study was performed on simultaneously collected serum samples and gingival tissues from 25 patients with documented severe chronic periodontal disease and 25 periodontally healthy subjects. It extends and supplements earlier information on cytokine synthesis in response to periodonthopathogenic bacteria and their products, which were mostly derived from in vitro experiments or were based on data derived from studies performed on a narrower range of selected parameters (Ishihara et al. 1997, Kent et al. 1999, Gamonal et al. 2000), and which provide inconclusive results. Data from several in vivo and in vitro experiments performed in patients with periodontitis and other infectious diseases clearly show that secretion of cytokines involved in cell-mediated inflammatory reactions is essential for clearance of pathogens from the host, but that these cytokines must be down-regulated at the appropriate point in the infection to prevent pathology (Essner et al. 1998, Kabashima et al. 2001). In other words, the time and site of antagonistic cytokine release and their relative concentrations contribute to successful resolution of infection.

Our study with the use of serum samples shows the considerable variability of cytokine levels and their profiles seen among individual patients and healthy subjects. Although the concentrations of cytokines studied were significantly higher in patients

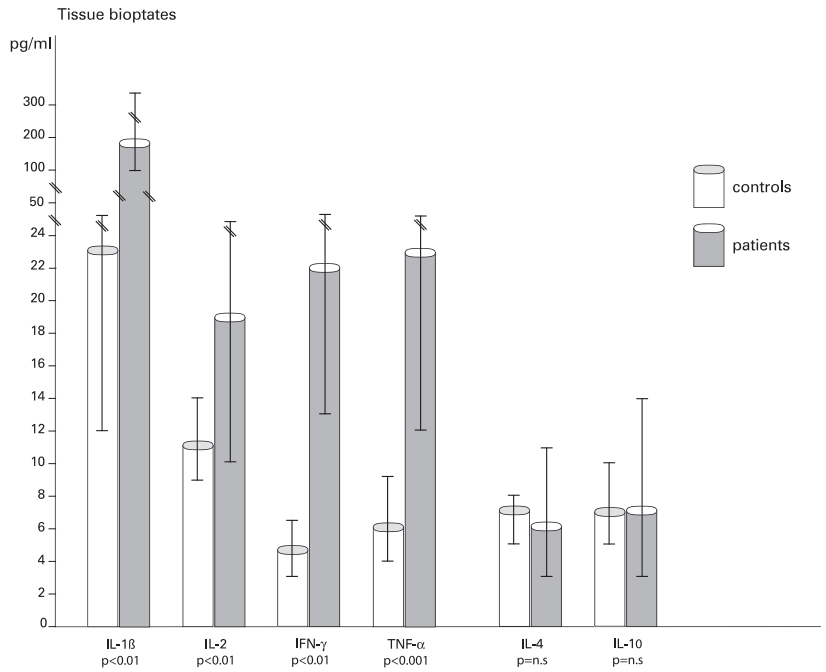

Fig. 2. Concentrations of cytokines studied in gingival tissue supernatants from periodontitis patients and healthy controls.

Table 3. Comparison of the ratios of cytokines in gingival tissue from periodontitis patients and healthy controls

	Cytokine ratios (±95% CI)		*p*-value
	patients (no. 25)	controls (no. 25)	
IL-1β to IL-4	35.8 (1.10–888.30)	0.96 (0.24–2.36)	<0.001
IL-1β to IL-10	32.4 (1.24–206.50)	0.96 (0.50–2.36)	<0.001
TNF-α to IL-4	4.06 (0.04–92.31)	1.43 (0.79–2.10)	<0.001
TNF-α to IL-10	2.91 (0.03–64.10)	1.45 (0.75–2.10)	<0.01
INF-γ to IL-4	3.31 (0.03–123.08)	1.27 (0.78–11.79)	<0.05
INF-γ to IL-10	2.74 (0.10–30.77)	1.28 (0.55–11.80)	NS
IL-2 to IL-4	3.37 (0.05–56.41)	1.92 (1.49–6.00)	<0.01
IL-2 to IL-10	2.26 (0.04–47.28)	1.94 (0.98–3.87)	NS

NS: not significant.

than in controls ($p<0.05$ to $p<0.01$), still in about half of the individuals in both groups only one or two different types of cytokines were present simultaneously. However, there was no significant domination of any cytokine profile that could be of predictive value for disease progression. Consequently, we could not find any association between the expression of particular cytokines in serum samples and clinical parameters. These results are in agreement with earlier observations suggesting that serum levels of such cytokines as IL-1β and/or IL-6 do not reflect the presence or severity of periodontitis (Chen et al. 1997). Thus, because all our patients presented severe chronic periodontitis, we suggest that serum is useless for cytokine determination in this disorder, and results may lead to controversial conclusions.

In contrast, we found high concentrations and frequency of detection of IL-1β, TNF-α, IFN-γ and IL-2 in tissue supernatants collected from patients with advanced periodontitis when compared with healthy controls. Interestingly, IL-1β, unlike in sera, was detected in 100% of tissue supernatants, obtained both from patients and controls. However, these two groups differed significantly in the concentration of this cytokine that was nine-fold higher, on average, in samples from patients ($p<0.001$). Similarly, a significant difference in the mean concentration between both groups was observed for TNF-α ($p<0.01$), which was detected in 76% of tissue supernatants collected from patients. Moreover, the other two cytokines studied by us, IFN-γ and IL-2, which both mainly represent Th1 cell-mediated responses, were also found in a high percentage of tissue supernatants from patients (82% and 92%, respectively). The high production of these cytokines in our patients with severe chronic periodontitis may, in part, be a marker of continuous Th1 response against bacterial pathogens colonized in gingival tissue, with simultaneous suppression of Th2 cell activity. Significantly higher concentrations and frequency of IL-1β, TNF-α, IFN-γ and IL-2 found in inflamed tissue in comparison with healthy tissue and serum samples support the local production of these cytokines, and thus, may indirectly indicate strong activation of the monocyte/macrophage system and Th1 cells in inflamed gingival sites. These results are consistent with previous studies reporting that the biological activity of these cytokines seems to be directly relevant to periodontal destruction, such as periodontal attachment loss, destruction of collagen and alveolar bone resorption (Stashenko et al. 1991, Ishihara et al. 1997, McGee et al. 1998). Also, Kabashima et al. (2001) found in periapical granulation tissue a high percentage of CD4+ T cells positive for IFN-γ, but not for IL-4, whereas in regeneration tissue, Th cells were positive for IL-4, but negative for IFN-γ. However, our findings are in contrast with the observations of Gemmell & Seymour (1994), who found low levels of IL-2 and IFN-γ in periodontal lesions, and suggested decreased Th1 responses.

Th2 cytokines, IL-4 and IL-10, are implicated in suppressing the destructive actions of Th1 and other cell-mediated inflammatory responses (de Waal Malefyt et al. 1993, Mosmann et al. 1996, Essner et al. 1998). Both cytokines can target macrophages and inhibit the release of IL-1, TNF-α, reactive oxygen intermediates and nitric oxide (Report of the American Academy of Periodontology 2002), but they also are growth and differentiation factors for activated B-cells, found in increased proportions in progressive periodontal lesions (Seymour, 1991). In our study, we did not observe vigorous production of these two cytokines nor their higher frequency in tissue supernatants obtained from patients with chronic periodontitis, while they were present most often in biopsies collected from normal tissues.

One of the interesting observations was the correlation between high ratios of IL-1β to IL-10, and TNF-α to IL-4 and high BI, PD and CAL found in inflamed tissue. Moreover, we found positive associations between severe CAL and high levels of TNF-α, IFN-γ and IL-2 in periodontitis patients who had pocket depths exceeding 5 mm. Our findings point to continuous stimulation of monocytes/macrophages and the Th1 subset by pathogens and confirm earlier observations that evidenced IL-4 deficiency in diseased periodontal tissues (Fujihashi et al. 1993, Kabashima et al. 2001).

In conclusion, this study demonstrated that inflammatory cytokines, such as IL-1β, TNF-α, IL-2 and IFN-γ, dominated in the response to periodontopathogenic bacteria in inflamed gingival tissue from patients with severe chronic periodontitis. The other consistent observation was the association between high ratios of IL-1β and TNF-α to IL-4 and IL-10, and high values of PD, CAL and BI, which are strong clinical markers of disease activity. We also suggest that the high ratio of IL-1β to IL-10 that was most characteristic for inflamed gingival sites and was found in all samples studied, could be used as a laboratory tool for assessing disease progression.

Moreover, our results clearly show that determination of the cytokines studied by us in serum samples is useless as an indicator of periodontal disease presence and/or severity.

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Zusammenfassung

Beziehung zwischen klinischen Parametern und Cytokin-Profilen der entzündeten Gingiva und den Serumproben von Patienten mit chronischer Parodontitis

Ziele: Der Zweck der vorliegenden Studie war es, bei Patienten mit schwerer chronischer Parodontitis die Beziehung zwischen klinischen Parametern und Konzentrationen der Schlüssel-Cytokine (IL-1β, TNF-α, IL-2, IFN-γ, IL-4, IL-10), die für das Auslösen und die Progression von Parodontalerkrankungen wichtig sind, in der entzündeten Gingiva und den Serumproben zu beurteilen.

Material und Methoden: Fünfundzwanzig Patienten mit schwerer chronischer Parodontitis, welche Stellen mit >5 mm Sondierungstiefe aufwiesen und 25 parodontal gesunde Personen wurden in die Studie aufgenommen. Vor der Parodontalbehandlung wurde eine klinische Untersuchung mit Sondierungstiefe (PD), klinischem Attachmentverlust (CAL), Plaque-Index (PI) sowie Blutungs-Index (BI) durchgeführt. Die Gingivabiopsien wurden von einer aktiven Tasche bei jedem Patienten in von den gesunden Personen entnommen und am gleichen Tag entnahm man Blutproben. Mittels eines Enzym-linked-Immunosorbent-Assays (ELISA) wurden die Konzentrationen der Cytokine bestimmt und die Beziehung zwischen ihren Profilen in situ sowie im Blutkreislauf und den klinischen Parametern wurde analysiert.

Ergebnisse: Die Konzentrationen von IL-1β, TNF-α, IL-2, IFN-γ waren bei Parodontitis-Patienten im Serum und in den Gingivabiopsien durchschnittlich signifikant höher als bei den gesunden Kontrollen. Jedoch zeigten in beiden Gruppen die Serumproben eine individuelle Variabilität der Cytokin-Profile und es wurde keine Assoziation zwischen Cytokin-Konzentration und klinischen Parodontitis-Parametern gefunden. Im Gegensatz dazu sowohl bei den Patienten als auch bei den Kontrollen in beiden Arten von Proben die Titer von IL-4 und IL-10 im allgemeinen sehr niedrig oder sogar nicht nachweisbar und blieben durchschnittlich auf dem gleichen Niveau. Jedoch war die Häufigkeit von IL-4 (88% positive Proben) und IL-10 (72%) im gesunden Gingivagewebe viel höher. Hohe Konzentrationen von TNF-α, IFN-γ und IL-2 sowie insbesondere ein hohes Verhältnis von IL-1β/IL-10 und TNF-α/IL-4 wurde in Gewebebiopsien von Parodontitis-Patienten gefunden und korrelierte stark mit der Schwere der Parodontitis.

Schlussfolgerung: Diese Ergebnisse zeigen, dass durch die hohe Variabilität der Cytokin-Konzentrationen und die geringe Häufigkeit ihres Nachweises in Serumproben von Parodontitis-Patienten diese Tests für den Nachweis der Erkrankung und/oder ihre Schwere nutzlos sind. Im Gegensatz dazu waren die hohen absoluten Titer von IL-1β, TNF-α, IL-2 und IFN-γ die in entzündeten Gingivabiopsien gefunden wurden, und insbesondere ihr hohes Verhältnis zu IL-4 und IL-10, eng mit der Schwere der Parodontalerkrankung assoziiert.

Resumé

Objectif: Le but de cette étude était de mettre en évidence la relation entre les paramètres cliniques et les concentrations des cytokines clés (IL-1β, TNF-α, IL-2, IFN-γ, IL-4, IL-10) importantes dans l'initiation et la progression des maladies parodontales, dans les tissus gingivaux enflammés et des échantillons sériques de patients atteints de parodontites chroniques sévères.

Matériel et Méthodes: 25 patients atteints de parodontite chronique sévère qui présentaient des sites avec une profondeur au sondage >5 mm et 25 personne au parodonte sain furent inclus dans cette étude. Les examens cliniques comprenaient les profondeurs au sondage, (PD), la perte d'attache clinique (CAL), l'indice de plaque (PI), l'indice de saignement (BI) et furent réalisés avant le traitement parodontal. Des biopsies des tissus gingivaux furent prélevés sur un site actif de chaque patient et chez des individus sains, et des échantillons sanguins furent prélevés le jour des biopsies tissulaires. Les concentrations de cytokines furent déterminées par ELISA et la relation entre leurs profils in situ et dans la circulation avec les paramètres cliniques fut analysée.

Résultats: Les concentrations d'IL-1β, TNF-α, IL-2, IFN-γ étaient, en moyenne, significativement plus importantes dans les échantillons sériques et les biopsies de tissus gingivaux des patients atteints de parodontie. Cependant, les échantillons sériques des deux groupes montraient des variabilités individuelles importantes des profils de cytokines et aucune association entre les concentrations de cytokines et les paramètres cliniques des parodontites ne fut trouvée. Au contraire, les niveaux d'IL-4 et d'IL-10 dans les deux groupes d'échantillons issus des patients et des contrôles, étaient généralement bas ou même indétectables et restaient en moyenne, au même niveau. Cependant, la fréquence de l' IL-4 (88% d'échantillons positifs) et d'IL-10 (72%) était plus important dans les tissus gingivaux sains. De fortes concentrations de of TNF-α, IFN-γ et d'IL-2 et, spécialement, un fort taux d' IL-1β/IL-10 et TNF-α/IL-4 trouvé dans les biopsies tissulaires des patients atteints de parodontite était fortement corrélé avec la sévérité des maladies parodontales.

Conclusion: Ces résultats indiquent qu'une haute variabilité des concentrations de cytokine et une basse fréquence de leur détection dans le sérum des patients atteints de parodontite rendent leur mise en évidence inutile pour détecter la présence de la maladie et/ou sa sévérité. A l'inverse, les niveaux absolus d' IL-1β, TNF-α, IL-2 et IFN-γ et, particulièrement leurs fortes proportions avec l' IL-4 et IL-10 trouvés dans les biopsies de tissus inflammatoires étaient étroitement associés à la sévérité des maladies parodontales.

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