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Levels of *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, inflammatory cytokines and species-specific immunoglobulin G in generalized aggressive and chronic periodontitis

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Background and Objective: Aggressive periodontitis pathogenesis still is not completely understood in the literature regarding the relationship between microbial and inflammatory aspects. So this study aimed to compare microbial and inflammatory patterns in the gingival crevicular fluid of generalized aggressive and chronic periodontitis patients.

Material and Methods: Forty aggressive and 28 chronic periodontitis patients were selected. Biofilm and gingival crevicular fluid were collected from a deep pocket (periodontal probing depth >7 mm) and a moderate pocket (periodontal probing depth $= 5$ mm) of each patient, and microbiological and immunoenzymatic assays were performed. Real-time PCR was used to determine quantities of *Aggregatibacter actinomycetemcomitans* and *Porphyromonas gingivalis*. Enzyme-linked immunosorbent assay (ELISA) was employed to determine gingival crevicular fluid levels of interleukin-1β, interferon-γ, prostaglandin E_2 and interleukin-10. In addition, immunoglobulin G (IgG) levels against *A. actinomycetemcomitans* and *P. gingivalis* lipopolysaccharide were also determined by ELISA. Analysis of variance/Tukey test, Mann–Whitney *U*-test and the Pearson correlation test were used to determine differences and correlations between variables analysed ($\alpha = 5\%$).

Results: Patients suffering from generalized aggressive periodontitis had their mouth colonized by higher amounts of *A. actinomycetemcomitans* and *P. gingivalis* than chronic periodontitis patients. Conversely, the gingival crevicular fluid levels of IgG against both pathogens were statistically inferior in aggressive periodontitis patients ($p < 0.05$). With regard to gingival crevicular

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fluid levels of cytokines, aggressive periodontitis patients presented reduced levels of interleukin-10 ($p < 0.05$).

Conclusion: In comparison to chronic periodontitis, generalized aggressive periodontitis patients have an imbalance in the host response, with reduced levels of interleukin-10 and IgG, and increased periodontal pathogens.

Although both chronic and aggressive periodontitis apparently derive from the same aetiological factors, they present clear differences in the development and progression of the disease (1). While chronic disease presents a slow progression, usually compatible with local factors, aggressive periodontitis is defined as an inflammatory disease that has its onset primarily during early-adult years and is characterized by rapid attachment loss and bone destruction (2). In order to explain possible differences between both forms of disease, microbiological and genetic aspects, as well as the role of the host immune response, have been studied; however, mechanisms responsible for these differences remain unclear.

Microorganisms and the host response against their antigens appear to modulate the development of aggressive and chronic periodontitis. Many studies have attributed the presence and high rates of *Aggregatibacter actinomycetemcomitans* (and in some populations, *Porphyromonas gingivalis*) to the different forms of aggressive periodontitis (3–5). Both bacteria present innumerable antigens capable of inducing an inflammatory and robust serum antibody response, consequently leading to periodontal destruction (6). However, at the same time, a deficiency in production of an adequate antibody response against these antigens has also been correlated with generalized aggressive periodontitis and recurrent chronic periodontal disease (3,7).

Despite decades of studies, the role of specific oral bacterial antibodies in the development and progression of aggressive and chronic periodontitis is still unclear. While some findings have suggested a protective character of antibodies in disease progression (6,8–10), others have shown that their simple presence is not related to periodontal protection against microbial virulence (11,12). One possible explanation could be the role of pro- or anti-inflammatory cytokines released by host defense cells during the production of specific antibodies (13).

Levels of cytokines in aggressive periodontitis vary depending on the type and severity of disease. Macrophages derived from blood cells of localized aggressive periodontitis patients have shown a hyper-responsiveness, releasing high levels of proinflammatory cytokines, such as prostaglandin E_2 (PGE_2), interleukin-1β (IL-1β) and interleukin-6 (IL-6; 13). At the same time, the cytokine profile of generalized aggressive periodontitis patients seems contradictory in the literature. While some studies have suggested that these patients present lower responsiveness of protective cells (3,14), other studies show no difference (15) or increased proinflammatory cytokines, such as tumour necrosis factor-α (TNF-α; 16). Moreover, the presence of *A. actinomycetemcomitans*, usually associated with aggressive periodontitis, is correlated with lower levels of serum interleukin-10 (IL-10), a cytokine that controls proinflammatory cytokine release by the host (17), modulating periodontal destruction.

Recent studies have tried to create a model in order to connect the cytokines and production of specific antibodies (13). However, only a few studies have evaluated these patterns simultaneously, especially in the gingival crevicular fluid, which could result in more conclusive results. Therefore, the present study was undertaken to evaluate the presence of *P. gingivalis* and *A. actinomycetemcomitans* and levels of specific antibodies against these periodontal pathogens in generalized aggressive and chronic periodontitis patients. The cytokine profile in these subjects was also determined in order to understand possible interactions between these factors in the pathogenesis of periodontal destruction.

Material and methods

Population screening

Subjects were selected after a screening examination that included a full medical and dental history, an intraoral examination, a full-mouth periodontal probing and radiographic evaluation. Subjects were divided by the type of periodontal disease, using the following criteria.

Group A – Generalized chronic periodontitis—Patients presented as follows: (i) diagnosis of severe chronic periodontitis characterized by the presence of periodontal pockets with a clinical attachment loss of ≥5 mm, bleeding on probing and radiographic bone loss; (ii) age over 35 years; (iii) at least eight teeth with a probing pocket depth of ≥5 mm and bleeding after pocket probing and at least two of the eight qualifying teeth must have probing pocket depth ≥7 mm; and (iv) minimum of 20 teeth in both jaws (wisdom teeth excluded).

Group B – Generalized aggressive periodontitis—Patients presented as follows: (i) diagnosis of generalized aggressive periodontitis, following the American Academy of Periodontology (AAP) classification (2), defined as the presence of periodontal pockets with a clinical attachment loss and radiographic bone loss in at least three teeth different from first molars and incisors; (ii) age less than 35 years; (iii) at least eight teeth with a moderate probing pocket depth of ≥5 mm and bleeding

after pocket probing and at least two of the eight qualifying teeth must have probing pocket depth ≥ 7 mm (deep probing pocket depth); (iv) minimum of 20 teeth in both jaws (wisdom teeth excluded); and (v) systemic general health (according to patient; absence of diabetes mellitus, cardiovascular, liver, cerebral or pulmonary disease).

Patients were not included in the study if presented with any of the following: (i) periapical alterations on qualifying teeth; (ii) medical disorders that required prophylactic antibiotic coverage or that could influence the response to treatment; (iii) scaling and root planning in the preceding 6 months; (iv) consumption of drugs known to affect periodontal status (antibiotic, anti-inflammatory, anticonvulsant, immunosuppressant and calcium channel blocker) within the past 6 months; (v) orthodontic therapy; (vi) pregnancy; and (vii) smoking habit (or former smokers).

Considering the above-mentioned criteria, a total of 28 patients presenting generalized chronic periodontitis and 40 subjects presenting generalized aggressive periodontitis were selected for analysis. During 4.5 years, about 1750 subjects were examined and among them, 40 generalized aggressive periodontitis patients were recruited to the present study (approximately 2.5% of the total number of subjects). As shown in Table 1, both groups presented a female majority (82 and 72.5% for chronic and aggressive, respectively). No differences between groups could be seen concerning the full-mouth plaque or bleeding on probing indexes nor in clinical attachment level (6.10 ± 0.20 and 6.39 ± 0.72, chronic and aggressive periodontitis, respectively). The mean age of aggressive periodontitis patients was 27.62 ± 0.88 years, which was statistically younger than that of chronic periodontitis patients (48.11 ± 1.52 years old, $p < 0.0001$).

Table 1. Patient characteristics (means ± SEM) in each group

	Chronic	Aggressive	*p* value
Age	48.11 ± 1.52	27.62 ± 0.88	< 0.0001*
Sex (% female)	82.0%	72.5%	0.52
Full-mouth plaque index	36.96 ± 2.65	38.10 ± 2.07	0.72
Full-mouth bleeding on probing index	29.65 ± 2.64	26.35 ± 1.69	0.38
Clinical attachment level	6.10 ± 0.20	6.39 ± 0.72	0.69

*Mann–Whitney *U*-test (α = 5%).

Sample collection

After a full-mouth examination, all sites presenting periodontal probing depth ≥5 mm were analysed regarding pulpar alterations and presence of furcation defects (if present, the teeth were excluded). Among them, one site presenting probing pocket depth of 5 mm and another pocket with a probing pocket depth of 7 mm were randomly selected (by a paper draw) for subgingival biofilm collection. Following the careful removal of the supragingival biofilm, the areas were washed with a water spray, isolated with cotton rolls and gently dried. A sterile paper point (no. 35) (Dentsply, Ribeirão Preto, Brazil) was inserted into the bottom of the periodontal pocket for 30 s. The paper points were placed into sterile tubes containing 300 μL of reduced transport fluid (18).

Gingival crevicular fluid was collected from the same microbiological sampling sites. Sixty to 90 s after subgingival biofilm collection, the teeth were washed again, and the area was isolated and gently dried. Gingival crevicular fluid was collected by placing filter paper strips (Periopaper; Oraflow, Plainview, NY, USA) into the pocket until a slight resistance was perceived, and then left there for 15 s. Immediately, the volume of the sample was measured with the aid of a calibrated electronic gingival fluid measuring device (Periotron 8000; Oraflow). After volume measurements, the strips were placed into sterile tubes containing 400 μL of phosphate-buffered saline (PBS) with 0.05% Tween-20 (19). Strips contaminated by visible blood were discarded and a new collection was made after 30 s.

All samples (subgingival biofilm and gingival crevicular fluid) were immediately stored at 20°C. One examiner made all clinical measurements and collected all microbial and gingival crevicular fluid samples.

Microbiological evaluation

For detection and quantification of periodontopathic bacteria, the real-time PCR technique was used. The presence and concentration of *P. gingivalis* and *A. actinomycetemcomitans* were evaluated in each site using specific primers reported in the literature (20). The primers used for *P. gingivalis* were 5′ CATAGATATCACGAGGA ACTCCGATT, 3′ AAACTGTTAGC AACTACCGATG TGG; and for *A. actinomycetemcomitans* 5′ GAACC TTACCTACTCTTGACATCCGAA, 3′ TGCAGCACCTGTCTCAAAGC.

Each paper point was placed separately in plastic tubes containing 0.01 M Tris–EDTA solution, pH 8 (TE). The DNA was then extracted from the subgingival biofilm, as described previously (21). Reaction efficiency was optimized, and primer final concentrations of 0.5 mM for *P. gingivalis* and *A. actinomycetemcomitans* were chosen. Real-time PCR was performed in the LightCycler system (Roche Diagnostics GmbH, Mannheim, Germany) with the FastStart DNA Master SYBR Green I kit (Roche Diagnostics GmbH). For each run, water was used as the negative control. Briefly, amplification was performed in a 10 μL final volume containing 2.5 μL of template DNA. The concentration of the DNA used in each run was always 10 μg/mL (22). The amplification profiles were as follows: 95/10, 55/5 and 72/4 [temperature (°C)/time (s)] and 40 cycles for *P. gingivalis*; and 95/10, 55/5, 72/3 and 40 cycles for *A. actinomycetemcomitans*. Melting peaks were used to determine the specificity of the PCR (20). Absolute quantification of target bacteria in clinical samples was performed using *P. gingivalis* (ATCC 33277) and *A. actinomycetemcomitans* (JP2) as controls. Standard curves were

made with these controls (20). The standard curves were used to convert cycle threshold scores into the number of bacterial cells using controls with known amounts of bacteria-specific DNA. The level of detection was set to 10^3 bacteria per plaque sample for all target bacteria. The determination of DNA content in controls was based on the genome size of each bacteria and the mean weight of one nucleotide pair (23).

Cytokine levels in gingival crevicular fluid

Aliquots of each gingival crevicular fluid sample were assayed by an ELISA using commercially available kits (R&D Systems Inc., Minneapolis, MN, USA) for IL-1β, PGE_2, interferon-γ (IFN-γ) and IL-10, according to the manufacturer's instructions. Previously, samples were diluted with the diluent of the kit. The dilution was used to calculate the concentration of each gingival crevicular fluid substance. This concentration was calculated with a standard curve, which was prepared using the standard proteins in the kit. The standard curve range used for IL-1β measurement was 8–0.125 pg/mL; for PGE_2 125– 19.26 pg/mL; for IFN-γ 1000–15.60 pg/mL and for IL-10 50–0.78 pg/mL. The ELISAs were run in duplicate, and mean values were used to calculate concentrations of each cytokine.

Levels of IgG antibodies in gingival crevicular fluid

An ELISA was used to determine the levels of total IgG antibodies against *A. actinomycetemcomitans* and *P. gingivalis* in gingival crevicular fluid, according to the following protocol. A 96-well plate was covered (37°C for 75 min) with *A. actinomycetemcomitans* (JP2) and *P. gingivalis* (ATCC 33277) lipopolysaccharide (kindly donated by Dr Fatiha Chandad). After blocking free sites, samples and standard were incubated for 60 min at 37°C. Then, an alkaline phosphatase-conjugated antibody was added and the plates incubated for 60 min at 37°C. After that, a substrate solution (4-nitrophenyl phosphate disodium salt hexahydrate; Sigma) was added and incubated (60 min at 37°C) and the reaction was stopped (2 N H_2SO_4). The plate was read at a wavelength of 450 nm within 30 min and the values expressed as ELISA units. All microbiological and immunological laboratory procedures were performed blind, without knowledge of the clinical status of the study subjects or of the periodontal sites sampled.

Statistical analysis

The homogeneity of data was tested through the Shapiro–Wilk test. Since a heterogeneity was achieved for all parameters, non-parametric Mann–Whitney *U*-tests and Wilcoxon tests were used for inter- and intragroup analysis, respectively. To determine the equality of sex between groups, chi-square test was used. In order to correlate the subgingival levels of *A. actinomycetemcomitans* and *P. gingivalis* with species-specific IgG, the Pearson rank correlation test was used. A *p*-value of ≤ 0.05 was required for statistical significance.

Results

Cytokine levels

Table 2 shows that gingival crevicular fluid levels of IL-1β and PGE_2 of aggressive periodontitis patients were similar to those of chronic periodontitis patients in moderate and deep pockets ($p > 0.05$). With regard to IL-10 levels, aggressive periodontitis patients presented statistically lower levels compared with chronic periodontitis patients in moderate (0.45 ± 0.07 and 2.08 ± 0.63 pg/mL, respectively) and in deep pockets (0.33 ± 0.06 and 2.11 ± 0.74 pg/mL, respectively). Moreover, a comparison between strata of pockets shows that in aggressive periodontitis lower levels of IL-10 were found in deep pockets ($p = 0.04$), in contrast to observations in chronic periodontitis subjects ($p = 0.82$).

Gingival crevicular fluid IFN-γ levels were similar between the two types of periodontitis (Table 2). However, only aggressive periodontitis presented a statistical difference between moderate (0.67 ± 0.07 pg/mL) and deep pockets (0.46 ± 0.05 pg/mL).

Microbiological and immunological assays

Real-time PCR analysis revealed that aggressive periodontitis pockets presented higher amounts of *P. gingivalis* and *A. actinomycetemcomitans* when compared with chronic periodontitis pockets (Table 3). The *A. actinomycetemcomitans* log concentration in moderate pockets was 3.06 ± 0.46 and in deep pockets was 2.75 ± 0.46; these values were statistically higher than those found in chronic periodontitis (0.99 ± 0.34 and 1.40 ± 0.45 for moderate and deep pockets, respectively). No difference between pocket strata was found between aggressive and chronic periodontitis.

Conversely, quantities of IgG against *A. actinomycetemcomitans* were statis-

Table 2. Mean (pg/mL ± SEM) of interleukin-1β, prostaglandin E_2, interferon-γ and interleukin-10 levels in moderate (periodontal probing depth 5 mm) and deep pockets (probing pocket depth ≥7 mm) of chronic and aggressive periodontitis

	Chronic		Aggressive	
	Moderate	Deep	Moderate	Deep
Interleukin-1β	117.31 ± 19.18	99.64 ± 12.11	124.22 ± 30.22	131.22 ± 30.28
Prostaglandin E_2	462.16 + 93.78	540.85 + 165.08	328.92 + 88.03	324.78 + 88.41
Interferon-γ	1.20 ± 0.25	0.96 ± 0.24	0.67 ± 0.07	0.46 ± 0.05[a]
Interleukin-10	2.08 ± 0.63	2.11 ± 0.74	0.45 ± 0.07[b]	0.33 ± 0.06[ab]

[a]Statistical intragroup difference between moderate and deep pockets (Wilcoxon test, $p < 0.05$).
[b]Statistical intergroup difference between chronic and aggressive periodontitis (Mann–Whitney *U*-test, $p < 0.05$).

Table 3. Amounts (log_{10} ± SEM) of *A. actinomycetemcomitans* and *P. gingivalis* and IgG against them (ELISA units ± SEM) in moderate and deep pockets of chronic and aggressive periodontitis

	Chronic	Aggressive
A. actinomycetemcomitans		
Moderate		
log_{10}	0.99 ± 0.34	3.06 ± 0.46[a]
IgG	216.79 ± 47.34	114.52 ± 20.58[a]
Deep		
log_{10}	1.40 ± 0.45	2.75 ± 0.46[a]
IgG	276.94 ± 107.90	94.29 ± 14.09[a]
P. gingivalis		
Moderate		
log_{10}	3.47 ± 0.54	5.15 ± 0.53[a]
IgG	76.46 ± 16.65	75.84 ± 13.26
Deep		
log_{10}	3.59 ± 0.51	5.65 ± 0.55[a]
IgG	95.72 ± 25.89	59.34 ± 8.26

[a]Statistical difference between chronic and aggressive periodontitis (Mann–Whitney *U*-test, $p < 0.05$).

tically lower in aggressive compared with chronic periodontitis, both in moderate (114.52 ± 20.58 and 216.79 ± 47.34 ELISA units, respectively) and in deep pockets (94.29 ± 14.09 and 276.94 ± 107.90 ELISA units, respectively). No statistical difference was observed between the two types of periodontitis or pocket strata with regard to the total IgG amounts against *P. gingivalis* (Table 3).

Immunoglobulin G levels and microbiological/cytokine quantities in gingival crevicular fluid

Table 4 displays the results of the correlation between species-specific IgG levels and the amounts of *A. actinomycetemcomitans* and *P. gingivalis* in chronic and aggressive periodontitis. As it can be seen from Table 4, the Pearson correlation test did not find significant correlations between the periodontopathic bacteria and the amount of bacteria-specific IgG ($p > 0.05$).

Immunoglobulin G levels against *A. actinomycetemcomitans* were also correlated with the gingival crevicular fluid levels of IL-1β, IFN-γ, PGE_2 and IL-10 (Table 5). A stronger and statistically positive relationship between *A. actinomycetemcomitans*-specific IgG and IFN-γ, PGE_2 and IL-10 could be seen in aggressive periodontitis, both in moderate and in deep pockets. The amounts of IL-10, PGE_2 and IFN-γ were greater in the gingival crevicular fluid when the quantity of *A. actinomycetemcomitans*-specific IgG was also higher. In chronic periodontitis, a significant positive correlation was observed between IFN-γ and PGE_2 levels and in IgG against *A. actinomycetemcomitans* in deep pockets (Table 5).

With regard to *P. gingivalis*-specific IgG, a significant correlation with cytokine levels was only observed in aggressive periodontitis, in both strata of pockets. Higher levels of IL-1β, PGE_2, IFN-γ and IL-10 correlated with higher quantities of *P. gingivalis*-specific IgG (Table 6). No correlation was observed in chronic periodontitis.

Table 4. Correlation between gingival crevicular fluid levels of bacterial species-specific IgG and amounts (log_{10}) of *A. actinomicetemcomitans* and *P. gingivalis* in moderate and deep periodontal pockets

	Chronic log_{10} × IgG against		Aggressive log_{10} × IgG against	
	Moderate	Deep	Moderate	Deep
A. actinomicetemcomitans	−0.20	−0.21	−0.10	−0.18
P. gingivalis	0.21	−0.03	0.08	−0.11

Pearson rank correlation test ($p > 0.05$).

Discussion

Several studies have attempted to explain the differences in development and progression of aggressive and chronic periodontitis. However, discrepant results found in the literature regarding microbial and cytokine profile and production of antibodies complicates the comprehension of the differences between the bacteria–host relationship of each form of the disease. Therefore, this study aimed to evaluate the local presence, i.e. in the gingival crevicular fluid, of *A. actinomycetemcomitans* and *P. gingivalis* and their IgG species-specific antibodies, as well as inflammatory cytokine levels, in patients suffering from generalized aggressive and chronic periodontitis.

In the present study, higher concentrations of both microorganisms were found in periodontal pockets of aggressive than of chronic periodontitis. Although some studies did not find any difference in microbial profiles between the diseases (24), others corroborate the present results, showing higher levels of *A. actinomycetemcomitans* in aggressive periodontitis (5,25). A previous study evaluated the bacterial profile of aggressive periodontitis in a Brazilian population, finding 72% of aggressive periodontitis individuals infected with *A. actinomycetemcomitans*; a percentage that was statistically greater than that found in chronic periodontitis (41.6%; 4). Our results also corroborate other microbiota screening studies carried out in Chilean (26) and Japanese periodontitis patients (27).

The relationship between *P. gingivalis* and aggressive periodontitis is uncertain in the literature. The 1999 AAP Periodontal Disease Classification states that *P. gingivalis* may be associated with aggressive periodonti-

Table 5. Correlation (*r*) between IgG against *A. actinomycetemcomitans* and gingival crevicular fluid level of interleukin-1β, prostaglandin E_2, interferon-γ and interleukin-10 (pg/mL) in chronic and aggressive periodontitis (moderate and deep pockets)

	Chronic IgG against *A. actinomicetemcomitans*		Aggressive IgG against *A. actinomicetemcomitans*	
	Moderate	Deep	Moderate	Deep
Interleukin-1β	0	−0.14	0.1	0.26
Prostaglandin E_2	0.34	0.54*	0.44*	0.62**
Interferon-γ	0.32	0.56*	0.57**	0.68**
Interleukin-10	0.01	−0.15	0.56**	0.37*

Pearson rank correlation test, $*p < 0.02$ and $**p < 0.001$.

Table 6. Correlation (*r*) between *P. gingivalis*-specific IgG and gingival crevicular fluid level of interleukin-1β, prostaglandin E_2, interferon-γ and interleukin-10 (pg/mL) in chronic and aggressive periodontitis (moderate and deep pockets)

	Chronic IgG against *P. gingivalis*		Aggressive IgG against *P. gingivalis*	
	Moderate	Deep	Moderate	Deep
Interleukin-1β	0.08	−0.05	0.39*	0.44*
Prostaglandin E_2	0.38	0.02	0.86**	0.84**
Interferon-γ	−0.17	0.19	0.79**	0.80**
Interleukin-10	0.31	0.01	0.65**	0.79**

Pearson rank correlation test, $*p < 0.02$, $**p < 0.001$.

tis in some populations (1), as confirmed in other studies (28). However, only a few studies have been able to find differences in the prevalence of *P. gingivalis* between aggressive and chronic disease (29,30). In our study, using quantitative analyses (real-time PCR), significantly higher quantities of this pathogen were observed in aggressive periodontitis.

It is well established that both *A. actinomycetemcomitans* and *P. gingivalis* present antigens that lead to a robust host immunological response. Several studies have shown that whole cells, lipopolysaccharide, fimbriae and carbohydrates from both bacteria are capable of increasing the production of immunoglobulin, especially subclass G (13,31,32). Localized aggressive periodontitis usually shows greater quantities of IgG, especially against *A. actinomycetemcomitans*, than generalized aggressive and chronic disease (12,33–35), although some studies did not find significant differences between the diseases (12,31–42).

Studies have found a positive relationship between the presence of periodontal pathogens and local levels of IgG (12,43). However, the present study demonstrated discrepant correlations between levels of anti-*P. gingivalis* and anti-*A. actinomycetemcomitans* IgG and the amounts of both bacteria in the periodontal pockets. With regard to *P. gingivalis*, even though aggressive periodontitis presented higher amounts of these bacteria, the IgG level was inferior but not statistically significant. In the case of *A. actinomycetemcomitans*, although statistically higher quantities of the bacteria were found in the subgingival area, the IgG level detected was significantly lower, suggesting a poorer IgG production of aggressive periodontitis patients.

Recently, the influence of the levels of cytokines on IgG production has been investigated, and a modulator potential of several cytokines has been discovered. Among these, IL-1β, IFN-γ, PGE_2 and IL-10 have all been shown to influence the production of immunoglobulins in different manners (13,32). Considering that aggressive periodontitis presented lower levels of IL-10 production, its role on infectious diseases, such as periodontitis, should be considered.

Interleukin-10 is essential to B-cell differentiation and proliferation, reducing apoptosis of immune cells and stimulating Cd8+ and natural killer cells, representing an important role in the adaptative response (44–46). At the same time, its overexpression is implicated in infectious persistence and augmentation of host susceptibility to some bacteria (46–50). Considering this, the altered IL-10 production in aggressive periodontitis should be further clarified in order to identify its relationship to disease pathogenesis.

Our results show that aggressive periodontitis subjects presented higher amounts of *A. actinomycetemcomitans* and *P. gingivalis* than chronic periodontitis patients. Conversely, the gingival crevicular fluid levels of IgG against both pathogens and the IL-10 cytokine levels were lower in aggressive periodontitis patients. These results indicate that aggressive and chronic periodontitis pathologies present several host response differences, possibly explaining their difference in progression and development. However, we must be careful when considering the results. First of all, some other factors should be considered in future studies to confirm and explain the results, for example, comparing both diseases to healthy individuals and validating the results by repetitive sampling analyses would be necessary. In addition, the influence of race also could contribute to identify populations with an imbalanced host response, as addressed by other studies (1,12).

Conclusion

In comparison to chronic periodontitis, generalized aggressive periodontitis patients have an imbalance in the host response, with reduced levels of anti-inflammatory cytokines and IgG, and increased periodontal pathogens. However, this imbalanced host response should be further clarified with additional studies which could contribute to a better under-

standing of periodontitis pathogenesis phenomena.

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