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Periodontal infection as a possible severity factor for rheumatoid arthritis

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Abstract

Objective: Clinical effects of periodontal treatment on biochemical and clinical markers of disease severity in rheumatoid arthritis (RA) patients with periodontal disease were evaluated.

Methods: Forty-two patients were assigned to two groups, G1 ($n = 16$) and G2 ($n = 26$). G1 patients were submitted to oral hygiene instruction and professional tooth cleaning and G2 patients additionally had full-mouth scaling and root planing (SRP). Clinical periodontal measurements were obtained at baseline and 3 months after periodontal treatment. A Health Assessment Questionnaire (HAQ) was used to evaluate their performance on daily living. Rheumatoid factor (RF), erythrocyte sedimentation rate (ESR) and drug therapy were assessed.

Results: Both groups presented a full-mouth improvement in all periodontal clinical parameters ($p < 0.05$), with the exception of clinical attachment level (CAL) and probing pocket depth (PPD) > 6 mm for G1. G2 showed greater mean reductions on PPD > 4 mm than G1 ($p < 0.001$). HAQ analyses showed a reduction on the degree of disability of G2, but not statistically significant. ESR was significantly reduced for G2 after SRP although RF did not show statistical reductions.

Conclusion: The data suggest that periodontal treatment with SRP might have an effect on the ESR reduction.

Key words: basic periodontal treatment; periodontal disease/treatment; periodontal medicine; rheumatoid arthritis; risk factors

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Periodontal medicine is an emerging branch of periodontology that has been establishing a strong relationship between periodontal and systemic health or disease (Offenbacher 1996, Williams & Offenbacher 2000).

Periodontal disease (PD) and its mechanism of inflammatory reactions result in the destruction of tissue and bone in a pattern similar to that which mediate destruction of soft tissue and erosion of bone in rheumatoid arthritis (RA). In both conditions a persistent inflammatory reaction occurs in areas composed of connective tissue and bone with the activation of complement, production of cytokines and release of other inflammatory cell products (Snyderman & McCarty 1982). The similarity between RA and PD has prompted several studies of periodontal status in patients with RA although the findings reported on the relationship between RA and PD are not concordant (Malmström & Calonius 1975, Sjostrom et al. 1989, Yavuzyilmaz et al. 1992, Tolo & Jorkjend 1990, Mercado et al. 2000, 2001). Differences in disease criteria and methods for evaluation of the periodontal status form a major problem in interpretation of the literature. Most of these studies observed the influence of RA over PD but the literature on the systemic impact of periodontal treatment on RA is still scant.

Coexistence of PD and RA would offer an interesting opportunity to study the possible influence of PD inflammatory process on RA progression. The hypothesis that the destructive inflammatory disorder of PD may influence RA or vice-versa warrants consideration. The aim of this preliminary study was to evaluate the influence of periodontal treatment on the measuring parameters of the inflammatory reaction caused by RA.

Materials and Methods

Subject population

The subject population consists of a sample of 42 consecutive patients attending the University Hospital Rheumatology Clinic, with RA, diagnosed according to the parameters of the American Rheumatology Association (Arneberg et al. 1992). After approval of the University Hospital Human Research

Committee the patients were invited to take part in this pilot study. All subjects were $\geqslant 40$ years of age, had at least $\geqslant 2$ teeth and at least $\geqslant 2$ sites with pocket depths $\geqslant 5$ mm and attachment level $\geqslant 6$ mm at baseline (Machtei et al. 1992). Exclusion criteria included xerostomia, pregnancy or lactancy and systemic conditions that could affect the progression or treatment of PDs. In addition, subjects that required antibiotics for treatment during the last 6 months and smokers were excluded. Drugs used by the subjects to treat RA were assessed through their medical files.

RA clinical measurements

Patients disability status was measured by the Stanford Health Assessment Questionnaire (HAQ) Functional Disability Index (DI) (Wolfe et al. 1988). A score of one on DI indicates that, on the average, the patient has difficulty in every area of daily living (moderate disability), while a score of two indicates that he has high degree of difficulty or requires assistance in every area of daily living (severe disability).

Biochemical measurements

Venous blood was obtained and the erythrocyte sedimentation rate (ESR) was quantified using the Westergreen method (Sox & Liang 1986). Corresponding results were registered and accessed from the patient's medical files. The RA activity was determined with ESR $\geqslant 28\,mm^3$ (Wolfe & Michaud 1994). ESR was further characterized by determining, for each patient, the first ESR at baseline and the last ESR value, 3 months after periodontal therapy.

The latex method was used to measure rheumatoid factor IgM (IgM-RF) (Singer 1961, Johnson & Faulk 1976, Baum & Ziff 1985). Results were obtained from patients' medical files. RA activity was considered positive if titers were 1:40 dilutions. Titers were grouped in three categories: low RF 1:40; medium RF 1:80; high RF 1:180 (Pincus et al. 1989).

Periodontal clinical measurements

Subjects referred to Periodontal Clinic were examined and clinical measurements were recorded at six sites per tooth at all teeth and included dichotomous measures of bleeding on probing and supragingival plaque accumulation. Clinical pocket depth and attachment level were categorized in percentage of sites <4, 4–6 and >6 mm (Haffajee et al. 1983, 1997). Clinical measurements were taken at baseline and three months after therapy. All measurements for a given subject were performed by the same examiner.

Periodontal treatment

Subjects were allocated into two groups: G1 and G2. G1 was formed with 16 patients, who were submitted to oral hygiene instructions and professional supragingival tooth cleaning. G2 was formed with 26 patients, who were additionally submitted to full-mouth scaling and root planing (SRP). SRP was completed in at most eight appointments. G1 patients were examined after one month and reinforcement of oral hygiene instructions and professional supragingival tooth cleaning were conducted. G2 were also examined after 1 month and received additional full-mouth SRP, whenever necessary. Periodontal clinical parameters and RA clinical and biochemical measures were taken 3 months after periodontal treatment.

Statistical analysis

Data analysis was conducted using the Statistical Package for the Social Sciences- SPSS®, v. 8.0. (SPSS Inc., Chicago, IL, USA) Inter- and intra-group comparisons of means for age and clinical periodontal parameters before and after treatment were obtained by the Mann–Whitney test and the Wilcoxon's test, respectively. Percentage of gender, income and education level, HAQ, RF and ESR were calculated and a chi-squared or Fisher test was conducted to evaluate differences between groups. Correlations among periodontal clinical measurements, RA severity markers and socioeconomic data were obtained using the Spearman correlation test.

Results

The sample considered involved 42 subjects in total. The 16 patients in group G1 had their RA clinical-biochemical results and clinical periodontal findings compared with the 26 patients in the age and gender matched group G2. The percentage of female subjects was 93% for G1 and 88.5% for G2 and the mean age was 47.7 ($\pm$ 9.5) and 51.6 ($\pm$ 10.3), respectively, for G1 and G2.

The baseline and 3 months post-therapy clinical periodontal parameters of the two subject groups are shown in Table 1. The percentage of sites for each subject, of bleeding on probing, visible plaque, probing pocket depth (PPD) and clinical attachment level (CAL) at baseline on three categories (<4, 4–6 and >6 mm) were averaged across subjects in each group and showed no statistical difference between groups (Mann–Whitney test). Post-therapy clinical periodontal measurements indicated a significant clinical improvement in both groups for all evaluated parameters with the exception of CAL that showed an improvement only for G2 when CAL >6 mm ($p<0.01$). Mean percentage of moderate and deep pocket depths for G2 were expressively lower than those for G1 ($p<0.001$, Mann–Whitney test). Mean percentage of sites with visible plaque and bleeding on probing was also significantly lower for G2, when compared with G1 ($p<0.001$, Mann–Whitney test). Although CAL for G2 had a higher improvement than that for G1, after treatment, no significant differences were found. Mean RA years as well as disease severity markers, at baseline and post-periodontal therapy, for both groups, are presented in Table 2. Mean RA years for G1 was 6.6 ($\pm$ 3.0) and 9.9 ($\pm$ 7.4) for G2, with no statistical difference (Mann–Whitney test). The difference in percentage of RF before and after periodontal therapy across and within groups were not statistically significant, in spite of a tendency of RF reduction on both groups after periodontal treatment. ESR levels across groups did not show a significant difference, but G2 had a significant reduction after therapy. Patient's disability status measured by HAQ improved for G2 after periodontal treatment albeit without statistical significance. In addition, ESR, used to measure RA activity, showed a significant reduction in G2 ($p<0.05$; chi-squared test, McNemar), after periodontal treatment (Table 2).

Correlation of clinical parameters with severity markers of RA for the two groups, did not show a significant association ($p>0.05$; Spearman's correlation).

For demographic variables, it was observed that the lower the level of RF the higher was the family income ($p>0.05$; Spearman's correlation).

Table 1. Mean percentages (± SD) of clinical parameters for G1 and G2 patients, before and after periodontal treatment

Clinical parameters	G1 (n = 16)		G2 (n = 26)	
% sites with:	Initial	Final	Initial	Final
Visible plaque	57.9 ± 32.8	22.8 ± 26.3	54.7 ± 28.4	13.0 ± 13.7
Bleeding on probing	58.0 ± 28.8	37.4 ± 26.6	51.4 ± 27.9	8.5 ± 5.8
PPD				
< 4 mm	70.8 ± 20.7	74.8 ± 18.4	71.9 ± 14.4	90.0 ± 7.3
4–6 mm	27.5 ± 18.2	23.2 ± 16.4	25.9 ± 13.0	9.7 ± 7.1
> 6 mm	1.7 ± 4.4	2.3 ± 4.4	2.2 ± 3.3	0.4 ± 1.0
CAL				
< 4 mm	81.5 ± 11.2	63.8 ± 25.5	81.7 ± 13.1	75.9 ± 19.1
4–6 mm	13.5 ± 10.3	30.1 ± 16.6	11.8 ± 8.2	22.0 ± 16.1
> 6 mm	5.0 ± 3.6	6.3 ± 4.4	6.5 ± 6.4	2.1 ± 4.3

*p< 0. 05(significant) **p<0. 01(significant), Wilcoxon test.

*p< 0. 001(significant), Mann–Whitney test.

G1, plaque control and professional tooth cleaning; G2, plaque control, scaling and root planing; PPD, probing pocket depth; CAL clinical attachment level.

Percentages of the different drugs used by the patients for RA treatment, steroidal and non-steroidal anti-inflammatory drugs, imunosuppressor, antineoplasic and sulfa, were compared between the two groups. No significant statistical differences were found by the end of periodontal treatment, except for an increase in the use by group G1 of the steroidal anti-inflammatory drug (SAID) – prednisone, between initial and final examination (p<0.001; chi-squared test).

Discussion

Socioeconomic status of the sample, inspite of the differences found in educational level, showed sufficient homogeneity between the two groups. The high proportion of female patients involved in this study is also in accordance with the prevalence of RA (Arnett et al. 1988, Currey 1988). Clinical periodontal parameters for the two groups, measured at the baseline examinations, showed a similar degree of disease, presenting a low level of PD severity with low prevalence of deep pockets. This could either be explained by the frequent use of non-steroidal anti-inflammatory drugs (NSAID) by these groups (Hamberg 1972, Waite et al. 1981, Feldman et al. 1983, Weiss 1989, Heasman & Seymour 1990), or else could be related to the high number of lost teeth observed in the sample (data not shown). The second possibility and its association with RA is controversial (Malmström & Calonius 1975, Laurell et al. 1988, Tolo & Jorkjend 1990, Arneberg et al. 1992, Storhaug 1992). Periodontal treatment applied to G2 (SRP) led to a significant improvement on all periodontal clinical parameters. Likewise, for G1 (OH) improvement was significant for plaque, bleeding on probing and moderate pockets. This is in accordance with previous studies (Mousques et al. 1980, Sigrist & Kornman 1982, Badersten et al. 1984, Beltrami et al. 1987, Dahlen et al. 1992, Katsanoulas et al. 1992, Rishein et al. 1992, McNabb et al. 1992). The improvement observed was not influenced by the RA drug therapy used, since there were no prescription changes during the study.

A questionnaire and biochemical parameters were used to describe RA severity including: HAQ, RF and ESR. In this study, for these parameters, no statistical difference was found across groups before and after periodontal therapy. However RF was reduced, although not significantly, for both G1 and G2. In addition ESR showed a significant reduction for G2 that had all its clinical periodontal parameters reduced after periodontal treatment (p<0.01). That might be related with the reduction of periodontal inflammatory status, suggesting that other inflammatory conditions may stimulate a systemic inflammatory response.

A relationship between the reduction of RF titles and periodontal treatment complemented by tooth extractions was reported in the literature (Takahashi et al. 1995). In vivo and in vitro studies have shown that LPS from bacteria associated with PD can stimulate the production of RF, antierythrocytes, anti-DNA and antithymocytes antibodies (Cunningham 1974, Hammarstrom et al. 1976, Dresser 1978, Hara et al. 1996). Human studies have also indicated a relationship between PD bacteria and local or systemic production of RF in PD patients (Gargiulo et al. 1982,

Table 2. Means and percentages of RA disease severity markers, at initial and final evaluations for G1 and G2

RA disease severity markers	G1 (n =16)		G2 (n =26)	
	Initial	Final	Initial	Final
RA years of disease ($x \pm$ dp)	6.6 ± 3.0		9.9 ± 7.4	
RF (%)				
1/40	0	6.2	7.7	26.1
1/80	87.5	93.8	80.8	65.2
1/180	12.5	0	11.5	8.7
ESR (%)				
≥ 28 mm/h	75.0	75.0	84.6	53.8 *
HAQ (incapacity)				
0 (0 or little)	25.0	25.0	27.0	31.0
1 (moderate)	18.0	12.5	15.0	19.0
2 (severe)	56.0	62.5	58.0	50.0

*$p < 0.05$ chi-squared, (McNemar) test.

G1, oral hygiene instruction and professional tooth cleaning; G2, oral hygiene instruction, professional tooth cleaning, scaling and root planing; RA, rheumatoid arthritis; RF, rheumatoid factor; ESR, erythrocyte sedimentation rate; HAQ, Health Assessment Questionnaire.

Tolo & Jorkjend 1990, Thé & Ebersole 1991). It is, thus, reasonable to suggest that treatment of PD could induce a reduction in LPS production and consequently reduce the levels of RF. Comparisons of ESR levels between G1 and G2 have shown a significant reduction for G2, after periodontal treatment, possibly as a result of the decrease of infection in G2 (Table 2). That is in accordance with the literature (Ebersole et al. 1997). The infectious process stimulates the production of globulins, plasmatic proteins such as haptoglobulin, C-reactive protein, fibrinogen and consequently increases the levels of ESR. Infection caused by PD induces an increase in fibrinogen levels that can be measured by the ESR exam. Additionally the total number of plasmatic cells increases according to the severity of PD (Williams & Offenbacher 2000). Therefore, the decrease noticed in ESR levels for G2, seems to be related with the diminishing degree of PD for that group.

The effect of periodontal treatment on RA levels, measured by HAQ showed no significant differences between G1 and G2, before and after therapy (Table 2). However, after periodontal treatment, severe incapacity degree increased for G1 and decreased for G2. Such differences, although not significant, seem to reflect body response to the different treatments offered. That applies since the drugs used by patients whose final HAQ results changed were not modified or had their posology changed during the study.

Changes on functional ability degree for RA patients are (time consuming or time dependent) slowly processed and better observed in longitudinal studies. The HAQ questionnaire evaluates the effects of clinical treatment or use of drugs for long periods of time. The 3 months interval observed between HAQ application and the measurement of treatment effects, might not be enough to demonstrate differences with statistical significance.

The lack of association found in the present study among the severity markers of RA and periodontal clinical parameters may be due either to the low severity of PD observed or else to the two groups sample sizes. Few studies indicated an association between RA and PD and a comparison of their results leads to conflicting conclusions (Malmström & Calonius 1975, Gargiulo et al. 1982, Del Puente et al. 1988, Sjostrom et al. 1989, Tolo & Jorkjend 1990, Mercado et al. 2000). Such comparisons are very difficult to carry out because of a lack of standardization in the classifications used for PD and RA.

In this study, PD has shown a positive clinical response while ESR was significantly reduced with a tendency for improvement in RA. The results reported here were drawn from a small set of subjects and to reinforce them there is a need for a more elaborate and larger scale study. However, these preliminary results highlighted the potential for a relationship between two common chronic inflammatory conditions affecting humans and warrants further detailed investigation.

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