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Periodontal Treatment for Chronic Periodontitis With Rheumatoid Arthritis

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ABSTRACT

Background: History of rheumatoid arthritis (RA) increases risk of periodontal diseases. A pro-inflammatory condition noted in periodontitis is considered a trigger for RA. Thus, periodontal treatment aimed at attenuating the pro-inflammatory state could aid in potentially reducing the risk of RA.

Aims: The objective of this research was to assess the effect of periodontal therapy on rheumatoid factor, Disease Activity Score-28, anti-citrullinated protein antibody, and C-reactive protein levels in patients with chronic periodontitis (CP) and RA.

Materials and methods: The sample consisted of 28 patients with CP and RA. The study was designed to be a double-blind, randomised controlled clinical study. The samples were randomly categorised to either the treatment group (n = 13) or the control group (n = 15). CP status (plaque index, bleeding on probing, probing pocket depth, clinical attachment loss), clinical rheumatologic status (Disease Activity Score), and biochemical status (C-reactive protein, anti-citrullinated protein antibody, and rheumatoid factor) were assessed at baseline and at reassessment following nonsurgical periodontal treatment as compared to the control group. However, blood serum anti-citrullinated protein antibody (P = .002) and rheumatoid factor levels (P = .351) were found to increase from baseline to 8 to 12 weeks following subgingival scaling and root planing.

Results: The treatment group showed a highly statistically significant reduction in bleeding on probing (P < .005), probing pocket depth (P < .001), plaque index (P < .001), and C-reactive protein (P < .001); a gain in the clinical attachment loss (P < .001) and an improvement in Disease Activity Score-28 (P = .001) were observed at reassessment following nonsurgical periodontal treatment as compared to the control group. However, blood serum anti-citrullinated protein antibody (P = .002) and rheumatoid factor levels (P = .351) were found to increase from baseline to 8 to 12 weeks following subgingival scaling and root planing.

Conclusions: Reduction of inflammation in the periodontium by nonsurgical periodontal therapy did not reduce anti-citrullinated protein antibody and rheumatoid factor levels. However, it has shown improvement in periodontal conditions, and remarkable changes

Key words: ACPA proteins
Chronic periodontitis
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Introduction

Periodontal disease (PD) is a bacteria-driven inflammatory destructive pathology causing periodontal pocket formation, bone loss, and tooth loss.\(^1\) In addition to oral tissues, PD affects overall systemic health. PD has been attributed to various chronic diseases, including rheumatoid arthritis (RA). According to accumulating data, there is a connection between periodontal inflammatory conditions and the progression of RA. It has been proposed that inflammation in the periodontium increases the risk of RA.\(^2\) Patients with PD may have a compromised immune system at first, making them more susceptible to infections. Furthermore, the proliferation of microbial antigens, Gram-negative anaerobic microbes, and various pro-inflammatory cytokines and opportunistic microorganisms residing in periodontal pockets can promote the development and progression of systemic diseases.\(^3\) Porphyromonas gingivalis (P. gingivalis), a unique bacterium that has been widely studied due to the presence of an endogenous peptidyl arginine deiminase enzyme,\(^4\) which is involved in arginine residual citrullination, an essential step in RA prognosis.\(^5\) In contrast to controls, P. gingivalis-associated PD is more likely to be an attributing factor for patients with RA.\(^6\)

RA represents a chronic inflammatory state of autoimmune origin. The key features include synovitis and hyperplasia, which are largely attributed to the autoantibody-mediated deterioration of the bone and cartilage. It affects 0.5% to 1.0% of the global population.\(^11\) The hypothetical example of autoimmunity progression is initiated by antibodies to proteins modified by microbial origin enzymes, known as ACPA.\(^7\) Patients with RA often have positive findings for autoantibodies such as rheumatoid factor (RF) and ACPA. Both chronic periodontitis (CP) and RA have been shown to share pathobiology in the dysregulation of host inflammatory processes, such as chronic inflammation induced by proinflammatory cytokines, connective tissue disintegration, and bone degradation.\(^13\) When ACPA levels were measured in individuals with RA, it was found that 55% to 91% of patients had positive findings for ACPA, whilst positivity for ACPA in healthy persons was only 0% to 9%.\(^14\) Literature suggests that the serum ACPA may be positive almost a decade before any clinical presentation and that it could also aid in disease prognostication.\(^15\)

C-reactive protein (CRP) is a systemic inflammation marker that can be used to monitor the progression of RA disease development. RF was observed in patients who have both these chronic inflammatory diseases.\(^7\) CRP, which is elicited in PD-affected lesions and appears to be amplified by systemic inflammatory responses, can contribute to RA production. Published literature suggests that the use of nonsurgical modalities for PD therapy could potentially attenuate the RA activity score by suppressing inflammation.\(^16\) A major hurdle in such studies is the difficulty in controlling confounding factors. With these limitations in mind, the current study was formulated to evaluate the outcome of ACPA, RF, CRP, and Disease Activity Score, including 28 joint counts (DAS-28) levels following phase 1 periodontal therapy in patients with RA and CP.

Materials and methods

The present investigation is a double-blinded randomised controlled clinical study in which 30 patients with both RA and CP were included from the Rheumatology Department with collaboration from the Periodontology Department. All of the participants were found to have mild to severe chronic periodontitis, which was categorised in accordance with the American Academy of Periodontology classification criteria.\(^17\)

Due to personal reasons, 2 patients withdrew from the research. The sample consisted of 28 patients (23 female and 5 male, ranging from 34 to 55 years in age with 46.7 years as the mean age). The research was carried out between July 2017 and October 2017. The institutional ethical committee accepted this original research.

The sample size was calculated with the assumption of 80% power at a 95% confidence interval. Based on the calculation, each group was allotted 11 patients.\(^18\) Informed consent was obtained from all the included patients. The participating patients satisfied the revised American Rheumatism Association criteria of 1987 and the American College of Rheumatology and European League Against Rheumatism criteria of 2010.\(^19,20\)

Inclusion criteria

Inclusion criteria were as follows: At least one active joint has been confirmed to have inflammation in the synovium, there should not be any alternative diagnosis that can replace synovial inflammation with another diagnosis, and a total score of 6 or more out of 10 should be attained from the independent scores in all 4 areas: total number of involved joints (0 to 5), area of complex joints (0 to 5), serologic abnormality (0 to 3) increased acute-phase reaction (0 to 1), and total duration of symptoms (bilevels; range: 0 to 1). Patients must have been under treatment for RA for the past month and advised to continue with the same prescription for RA during the 8- to 12-week time span of the study without any modifications. The patient should have a minimum of 20 natural teeth. In patients with RA, a minimum of 30% of the overall PD site must be involved. Finally, the existence of periodontal...
inflammation was determined by holding at the minimum 1 site per tooth with PD ≥5 mm and clinical attachment loss (CAL) ≥4 mm.\textsuperscript{21}

**Exclusion criteria**

The exclusion criteria followed in the study are as follows: (1) the presence of pregnancy and any other systemic diseases beyond RA and PD, (2) having undergone antibiotic prophylaxis within the 3 months before the treatment, and (3) having a previous record of periodontal therapy and consumption of mouthwash within the 3 months prior to treatment.

**Patient selection and preparation of the patient**

Assessments were carried out at baseline and at follow-up of 8 to 12 weeks. All the patients were taking RA medications such as disease-modifying anti-rheumatic drugs (DMARDs), corticosteroids, and nonsteroidal anti-inflammatory drugs (NSAIDs). They were arbitrarily separated into 2 groups: the treatment and control groups. The treatment group comprised 13 patients (9 female and 4 male; mean age, 38.08 ± 9.2 years) who obtained oral prophylaxis, including proper toothbrushes and other auxiliary aids; full-mouth supragingival and subgingival ultrasonic scaling and root planing was done. During these 8- to 12-week periods, patients were asked to maintain appropriate oral disinfection. These phase 1 periodontal therapies were executed only after the assessment of periodontal and rheumatologic examinations at baseline. The control group comprised 15 patients with RA (14 female and 1 male; mean age, 46.7 ± 13.5 years). The control group was not given any periodontal therapy from baseline to 8 to 12 weeks but planned for a phase 1 periodontal management session succeeding the termination of the investigation.

DAS-28 was used to determine the RA disease activity. DAS-28 is divided into 4 categories: remission (DAS28 <2.6) and low (≥2.6 to <3.2), moderate (≥3.2 to <5.1), and high disease activity (≥5.1).\textsuperscript{26}

**Methodology**

From the antecubital fossa through venipuncture, using a 20-gauge needle, 2 mL of blood was collected at baseline and 8 weeks following periodontal therapy, using heparin tubes and directly shifted to the research lab. The collected blood sample was clotted at room temperature. About an hour later, serum collection was carried out through a 20-minute centrifuging at 3000 revolutions/minute. Serum anti-cyclic citrullinated peptide (anti-CCP) antibodies, RF, and CRP were assessed by enzyme-linked immunosorbent assay (ELISA).

Clinical periodontal examinations were performed with all the involved participants at baseline and 8 to 12 weeks later. Standardisation was done before and after for both the groups using stents for calibration. CAL, probing pocket depth (PPD), plaque index (PII), number of teeth present, and bleeding on probing (BOP) were recorded. BOP and the supragingival plaque were assessed on 6 sites per tooth. A calibrated examiner assessed PPD and CAL on 6 sites per tooth using Williams’ periodontal probe.\textsuperscript{22}

**Statistical analyses**

Kolmogorov–Smirnov and Shapiro–Wilk test assessed normality. Based on the mixed results, a combination of parametric and nonparametric methods was applied. Intergroup mean value comparison was conducted through independent-samples t test. Intragroup mean value comparison was conducted through paired t test. Intergroup proportion comparison was carried out with chi-square test, whilst Fisher exact test was employed if the expected cell frequency was lower than 5. In normally distributed values, Mann–Whitney U test was applied for intergroup comparison, and for intragroup comparison Wilcoxon signed-rank test was used. SPSS (IBM SPSS Statistics for Windows, Version 22.0, IBM Corp.) was employed for data analysis. Five percent (\(\alpha = 0.05\)) was set as the significance level.

**Results**

Demographic data, clinical periodontal, and RA study characteristics assessed at baseline are summarised in Table 1. Participants with RA and periodontal treatment did not elicit significant differences in demographic profiles concerning age and sex in either the treatment or control groups. Clinical periodontal parameters (PII, PPD, CAL, and BOP) and the number of teeth present were assessed. Insignificant differences were noted in periodontal parameters except for the PII (\(P = .001\); Table 1). Not many remarkable differences were found in rheumatologic parameters except for anti-CCP antibodies serum levels (\(P = .005\)) and anti-CCP antibody positivity (\(P = .001\); Table 1).

The treatment group demonstrated a highly significant reduction in PII (\(P < .001\)), BOP (\(P < .005\)), PPD (\(P < .001\)), and CAL (\(P < .001\)) at reassessment following phase 1 periodontal therapy (Table 2). Insignificant remarkable changes were observed in the control group’s periodontal parameters following reassessment (Table 2).

The intergroup comparison is tabulated in Table 3; the treatment group exhibited a more highly significant reduction in PII, PPD, CAL, and BOP from baseline to reassessment than the control group (Table 3).

The treatment group intragroup analysis elicited a significant attenuation in CRP levels (\(P < .001\)) and DAS-28 (\(P = .001\)). Statistically significant changes were observed in serum RF (\(P = .013\)) at 8 to 12 weeks following supra- and subgingival scaling and root planing; however, serum anti-CCP antibody levels were found to increase from baseline (\(P = .001\); Table 4).

An improvement was seen in the CRP levels and DAS-28 in patients with RA (Table 4). Table 5 demonstrated intergroup analyses, which reported that the treatment group showed significantly reduced CRP levels (\(P = .001\)) and DAS-28 (\(P < .001\)). In contrast, serum anti-CCP antibodies (\(P = .002\)) and serum RF (\(P = .351\)) were found to increase from baseline to reassessment more than in the control group (Table 5).
Table 1 – Demographic data for chronic periodontal and rheumatologic characteristics of patients with rheumatoid arthritis (RA) with and without periodontal treatment at baseline.  

| Parameters                  | Control group (n = 15) | Treatment group (n = 13) | P value  |
|-----------------------------|------------------------|--------------------------|---------|
| Age, y                      | 46.73 ± 13.5           | 38.08 ± 9.2              | .057    |
| Female, %                   | 49.3 (93.3)            | 9 (69.2)                 | .155    |
| PII, mm                     | 2.68 ± .54             | 3.62 ± .77               | .001    |
| BOP, median (min, max)      | 1.00 (0.00, 1.00)      | 1.00 (0.00, 1.00)        | .556    |
| PPD, mm                     | 6.67 ± .97             | 7.38 ± 1.4               | .131    |
| CAL, mm                     | 9.13 ± 1.3             | 10.08 ± 1.6              | .104    |
| No. of missing teeth, median (min, max) | 1.00 (0.00, 3.00) | 1.00 (0.00, 7.00) | .772    |
| Duration of RA, median (min, max) | 2.00 (1.00, 3.00) | 2.00 (1.00, 3.00) | .605    |
| CRP, mg/L                   | 39.17 ± 7.6            | 40.67 ± 8.1              | .619    |
| DAS-28, median (min,max)    | 4.10 (1.81, 7.40)      | 2.06 (1.20, 8.10)        | .112    |
| Serum RF levels, IU/mL      | 49.5 (1572.25)         | 186 (8,1641.60)          | .231    |
| RF positive, %              | 9 (60.0)               | 7 (53.8)                 | .743    |
| Serum anti-CCP titer, U/mL  | 13.00 (5,154)          | 86.80 (8,212.90)         | .005    |
| Anti-CCP antibody positive, | 6 (40)                 | 13 (100)                 | .001    |

Anti-CCP, anti-cyclic citrullinated peptide; BOP, bleeding on probing; CAL, clinical attachment loss; CP, chronic periodontitis; CRP, C-reactive protein; DAS-28, Disease Activity Score, including 28 joint counts; PII, plaque index; PPD, probing pocket depth; RA, rheumatoid arthritis; RF, rheumatoid factor.  
* Significant at P < .05.

Discussion

A remarkable number of studies have found a close correlation between RA and CP. In the present study, the treatment (38.08 ± 9.2 years) and control (46.73 ± 13.5 years) groups did not differ significantly in mean age when demographic data and clinical periodontal and rheumatologic features were analysed at baseline. A high percentage of female patients participated in this study, which was in accordance with previous studies stating that women experience higher rates of RA. There were statistically significant differences concerning the PII (P = .001), serum levels of anti-CCP antibodies (P = .005), and anti-CCP antibody positivity (P = .001) at baseline between the 2 groups. Many of the patients in this research were taking corticosteroids, DMARDs, or NSAIDs; these medication regimens were unchanged during the study. The use of several biologic DMARDs, either alone or in combination, has significantly attenuated joint degeneration. Given the close association between RA and CP, PD may exert a positive impact upon RA and vice versa.

Our study has proved that the intensity of RA was reduced following phase 1 periodontal therapy in the treatment group. This observation was in association with the positive development in response to the periodontal parameters. The treatment group showed a highly significant reduction in PII, BOP, PPD, and CAL at reassessment following nonsurgical periodontal therapy. Our study findings were in conjunction with those of earlier research. Kaur et al, in a systematic review on the interrelationship between CP and RA, observed that CAL was significantly found to be increased in patients with RA when compared to individuals without RA, which is suggestive of the intensity with which CP exerts its effect on patients with RA. In our current study, on comparing the intragroup analysis, the treatment group showed an increase in CAL at baseline. Still, after phase 1 periodontal treatment, there was a more significant decrease in the CALs, exhibiting high statistically significant changes during reassessment after 8 to 12 weeks in the treatment group in comparison with the control group.

Consequently, the current meta-analysis revealed that after phase 1 periodontal therapy, such as Scaling and root planing (SRP), there is a downsizing of the DAS-28 in patients with RA and CP substantiating the outcome of periodontal

Table 2 – Intragroup analysis of periodontal parameters in patients with rheumatoid arthritis with and without periodontal treatment at baseline and reassessment.  

| Parameters                  | Baseline | Reassessment | P value |
|-----------------------------|----------|--------------|---------|
| PII, mm                     | 2.68 ± 0.54 | 2.77 ± 0.62  | .150    |
| BOP, median (min, max)      | 3.00 (0.00, 3.00) | 3.00 (0.00, 3.00) | .564    |
| PPD, mm                     | 6.67 ± 0.97 | 6.87 ± 1.06  | .082    |
| CAL, mm                     | 9.13 ± 1.35 | 9.13 ± 1.35  | 1.000   |

BOP, bleeding on probing; CAL, clinical attachment loss; PII, plaque index; PPD, probing pocket depth.  
* Significant at P < .05.

Table 3 – Intergroup analysis of changes in periodontal parameters in patients with rheumatoid arthritis at baseline and reassessment.  

| Parameters                  | Control group (n = 15) | Treatment group (n = 13) | P value |
|-----------------------------|------------------------|--------------------------|---------|
| PII, mm                     | 0.093 ± 0.23           | –0.88 ± 0.36             | <.001*  |
| BOP, median (min, max)      | 0.00 (–1.00, 1.00)     | –1.00 (–1.00, 0.00)      | .005    |
| PPD, mm                     | 0.200 ± 0.414          | –2.23 ± 0.725            | <.001*  |
| CAL, mm                     | 0.202 ± 0.58           | –2.07 ± 0.64             | <.001*  |

BOP, bleeding on probing; CAL, clinical attachment loss; PII, plaque index; PPD, probing pocket depth.  
* Significant at P < .05.
management in patients with RA. Results from preceding clinical studies strongly suggested that thorough SRP may positively affect the disease severity of RA \(^1\),\(^2\),\(^3\),\(^4\). The previous studies’ observations correlated with our study reports exhibiting a highly statistically significant change in DAS-28 \((P = .001)\) in the treatment group compared from baseline to reassessment. The benefit of 8 to 12 weeks of SRP on the clinical status of patients with RA was highlighted, as the control group showed no substantial improvements in DAS-28. PD is a systemic inflammatory condition; thereby controlling the periodontal infection and inflammation could lead to reduced serum levels of specific inflammatory mediators, which reduces the severity of disease activity in individuals with RA by downgrading the scores of excruciating joints, and attenuating morning joint stiffness and effusion. Thus, the clinical improvement was better in RA affected individuals with CP.\(^2\) Therefore, the development in RA disease activity could be because of SRP, which might have decreased the systemic inflammatory mediators.\(^1\),\(^4\),\(^9\),\(^2\),\(^3\) On the flip side, the elimination of periodontal pathogens by the phase 1 treatment could have reduced the joints’ vulnerability to microbes and their toxins, resulting in improved disease activity in individuals with RA.\(^3\)

The intra- and intergroup analysis showed that the ACPA levels significantly increased from baseline to reassessment in the treatment group. Our results are supported by the earlier study of Okada et al.\(^4\). Our research presented the impression that the severity of ACPA increases in patients with RA, and they do not harmonise with the clinical periodontal parameters even after periodontal therapy. Our study report observed no significant reduction of ACPA levels in patients with RA treated with phase 1 periodontal treatment over the control groups. The reason for this might be the minimum number of participants incorporated in this study. Furthermore, a comparatively short period for observation (8 to 12 weeks) was in accordance with studies that revealed the development in RA disease activity at a minimum of 4 to 6 weeks after periodontal management.\(^6\) In previous reports, the etiophasic phase of periodontal therapy has been reported to significantly decrease the levels of biochemical markers such as ACPA in CP patients without RA, though; these findings are not proved in patients with active RA.\(^3\),\(^3\) Our results contradict those of Lappin et al, who found substantial reductions in ACPA levels 6 months after periodontal treatment.\(^3\) Another study report by Salemi et al reported that a case of ACPA positivity showed a decline in the ACPA levels following nonsurgical periodontal therapy.\(^7\)

In well-established RA, ACPA specificity can be as high as 95%, and during the early stages of RA it can be as low as 40% to 55%.\(^3\) The levels of ACPA in the blood will fluctuate depending on how active RA is, indicating that the status of ACPA will not have any consequence on the prevalence or the intensity of periodontitis. Also, it might have been thought that the periodontal infection by itself is not enough to instigate RA.\(^6\)

RF expression has been found in patients with periodontal inflammation.\(^5\) It can be justified that periodontitis management could bring down lipopolysaccharide production and decreases RF levels. In the present study, the intergroup analyses demonstrated that there was a gradual rise in the blood serum RF from baseline to reassessment, stating that RF does not correlate with periodontal therapy; the nonsignificance could be due to the variations in the intensity of PD or could be because of a minimum number of sample sizes. Our findings were in accordance with 2 other studies indicating no statistical difference in RF levels after phase 1 periodontal therapy in patients with RA and periodontitis and suggesting that only SRP does not affect serologic markers for RA.\(^2\),\(^3\)

In patients with RA, CRP is a significant disease activity marker. Reduced levels of serum CRP are linked to an improved RA functional score. In patients with active RA, a persistent rise in CRP levels is connected to a deteriorated functional score.\(^3\) Various studies illustrated a statistically significant increase in the blood serum levels of CRP in patients with PD when compared with controls.\(^3\) In the present study, a high statistically significant reduction in CRP levels was noted in treatment groups following 8 to 12 weeks

### Table 4 – Intragroup analysis of changes in rheumatologic and serum parameters in patients with rheumatoid arthritis with and without periodontal treatment at baseline and reassessment

| Parameters                  | Control group (n = 15) | Treatment group (n = 13) | P value |
|-----------------------------|------------------------|--------------------------|---------|
| CRP, mg/L                   | 39.17 ± 7.6            | 37.00 ± 7.31             | .045    |
| DAS-28, median (min, max)   | 4.10 (1.81, 7.40)      | 4.10 (2.00, 7.40)        | .180    |
| Serum levels of RF, IU/mL   | 49 (5,1572.25)         | 68 (5,1765)              | .008    |
| Serum anti-CCP antibody,    | 13 (5,154)             | 13 (6,172)               | .012    |

Anti CCP, anti-cyclic citrullinated peptide; CRP, C-reactive protein; DAS-28, Disease Activity Score, including 28 joint counts; RF, rheumatoid factor.

* Significant at \(P < .05\).

### Table 5 – Intergroup analysis of changes in rheumatologic and serum parameters in patients with rheumatoid arthritis from baseline to reassessment

| Parameters                  | Control group | Treatment group | P value |
|-----------------------------|---------------|-----------------|---------|
| CRP, mg/L                   | -2.16 ± 3.82  | -7.45 ± 3.45    | .001*   |
| DAS-28, median (min, max)   | 0.05 (0.04, 0.30) | -0.78 (-1.26, -0.18) | <.001*  |
| Serum levels of RF, IU/mL   | 11 (-2,192.75) | 27 (-1,160.50)  | .351    |
| Anti-CCP antibody, U/mL     | 1.00 (0.00, 22.00) | 18.20 (5.57, 112.80) | .001*   |

Anti CCP, anti-cyclic citrullinated peptide; CRP, C-reactive protein; DAS-28, Disease Activity Score, including 28 joint counts; RF, rheumatoid factor.

* Significant at \(P < .05\).
of nonsurgical periodontal therapy; findings are in line with the study of Okada et al, which showed that the elucidation of periodontal inflammation following the etiologic phase might be the reason for reducing serum CRP levels.29 Our observations are in line with those of D’Aiuto et al, who observed a notable reduction in CRP levels 2 months following SRP and plaque control treatment procedures.40 Our results are in contrast to those of Pinho et al, who found no improvement in CRP levels after periodontal treatment in RA patients with CP.41

According to our research, the treatment group had an improvement in the DAS-28 and CRP level in patients with RA with improved clinical periodontal parameters. At 8 to 12 weeks, serum levels of ACPA and RF, on the other hand, increased dramatically. Hence, within this study’s limitations, there were statistically significant changes in the DAS-28 for RA following phase 1 periodontal therapy. Nevertheless, these outcomes are based upon the minimum number of participants. Further studies are required with a greater number of participants for more extended follow-up periods to substantiate these results.

Conclusions

After the etiologic phase, there was substantial attenuation in RA disease activity and CRP levels. Thus, it is always better to screen for oral findings in patients with RA for periodontal involvement as an adjunct to anti-rheumatoid management. It can be suggested that nonsurgical periodontal therapy could eventually be included in the treatment plan for individuals with periodontitis and RA comorbidities.

Declaration of Competing Interest

None disclosed.

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