Published in final edited form as:
J Periodontol. 2009 April ; 80(4): 535–540. doi:10.1902/jop.2009.080447.

Periodontal Therapy Reduces the Severity of Active Rheumatoid Arthritis in Patients Treated With or Without Tumor Necrosis Factor Inhibitors

P Ortiz[*], **NF Bissada**[*], **L Palomo**[*], **YW Han**[*], **MS Al-Zahrani**[†], **A Panneerselvam**[‡], and **A Askari**[§]

[*]Department of Periodontics, Case Western Reserve University, Cleveland, Ohio, USA

[†]Currently, Division of Periodontics, Faculty of Dentistry, King Abdulaziz University, Jeddah, Saudi Arabia

[‡]Department of Epidemiology and Biostatistics, Case Western Reserve University, Cleveland, Ohio, USA

[§]Division of Rheumatology, University Hospitals Case Medical Center, Cleveland, Ohio, USA

Abstract

Background—Rheumatoid arthritis (RA) and periodontitis (PD) are common chronic inflammatory conditions. Recent studies have shown a beneficial effect of periodontal treatment on reducing the severity of active RA. This study was undertaken to further examine the effect of non-surgical periodontal treatment on signs and symptoms of RA in patients treated with or without anti-Tumor Necrosis Factor (TNF)-α medications. The effect of anti-TNF-α therapy on periodontitis also was assessed.

Methods—Forty participants diagnosed with moderate/severe RA (under treatment for RA) and severe periodontitis were randomly assigned to receive initial non-surgical periodontal therapy with scaling/root planing and oral hygiene instructions (n=20) or no periodontal therapy (n=20). To control RA, all participants had been using disease-modifying anti-rheumatic drugs (DMARDs), and 20 had been using anti-TNF-α in addition to DMARDs before randomization. Periodontal probing depth (PD), clinical attachment loss (CAL), bleeding on probing (BOP), gingival (GI) and plaque (PI) indices, RA disease activity score (DAS-28) and erythrocyte sedimentation rate (ESR) were measured at baseline and six weeks afterwards. Linear mixed models were used to identify significant differences between subjects receiving periodontal treatment and those who did not.

Results—Patients receiving periodontal treatment showed a significant decrease in the mean DAS28, ESR ($p < 0.001$) and serum TNF-α ($p < 0.05$). There was no statistically significant decrease in these parameters in those patients not receiving periodontal treatment. Anti- TNF-α therapy resulted in a significant improvement in CAL, PD, BOP and GI.

Conclusions—Non-surgical periodontal therapy had a beneficial effect on signs and symptoms of RA regardless of the medications used to treat this condition. Anti-TNF-α therapy without periodontal treatment has no significant effect on the periodontal condition.

Corresponding Author: Nabil F. Bissada, DDS, MSD Department of Periodontics Case Western Reserve University 10900 Euclid Avenue Cleveland, OH 44106-4905 Phone: (216) 368-6752 Fax: (216) 368-3204 nabil.bissada@case.edu.

The authors report no conflicts of interest related to this study.

Keywords

Rheumatoid arthritis; Periodontitis; TNF-α therapy

Rheumatoid arthritis (RA) is a chronic systemic inflammatory disorder of unknown etiology that primarily involves joints. Periodontitis and rheumatoid arthritis (RA) share similar clinical and pathogenic characteristics.[1–3] Clinically, both diseases are characterized by local destruction of hard and soft tissues as a consequence of inflammation, and the pathogenesis includes the release of cytokines and matrix metalloproteinases (MMPs) from inflammatory cells.[4–7] The expression of proinflammatory cytokines such as TNF-α leads to propagation of the inflammation and release of a high level of inflammatory mediators that result in bone destruction.[8] TNF-α inhibitors were found to reduce recruitment of inflammatory cells, osteoclast formation, and bone loss.[9]

Recent studies suggest a relation between rheumatoid arthritis and periodontitis[10–18]; rheumatoid arthritis may have a negative impact on periodontal condition and vice versa. Mercado *et al.* reported significantly high prevalence of moderate to severe periodontitis in individuals with RA.[12] In addition, the converse also is true in that periodontitis patients have a higher prevalence of RA compared to the general population.[12] Ramamurthy *et al.* (2005), found that induction of experimental arthritis in rats resulted in periodontal destruction and increased cytokines and MMPs in the periodontal tissues.[13] Oral bacterial DNAs are detected in serum and synovial fluid of RA patients.[14] Rheumatoid arthritis patients also were found to have a significantly higher level of IgG antibody against *P. gingivalis*, *P. intermedia*, *and B. forsythus*.[13] Furthermore, two recent clinical trials suggested that treatment of periodontal disease might have a significant impact on RA severity.[16–17] Similarly, subjects with RA have significantly increased periodontal attachment loss compared to controls, and oral hygiene may only partially account for the association.[18]

Recently, TNF-α blocking agents have been developed and used for managing RA.[19] Studies in animals[20,9] and in humans[21] suggested that anti-TNF-α therapy may reduce the severity of periodontitis. The present study was undertaken to evaluate the effect of periodontal therapy on serum TNF-α levels and on the clinical status of rheumatoid arthritis patients treated with or without TNF-α blocking agents. The effect of anti-TNF-α therapy on the periodontal condition of RA patients was also evaluated.

MATERIALS AND METHODS

Participants

This study was conducted from February 4th to Nov 20th, 2007 and informed consent was obtained from all subjects before their enrollment. The study was approved by the Institutional Review Board of University Hospitals Cleveland/Case Medical Center (No. 10-06-41 on 1-24-2007).

Inclusion criteria included ≥30 years of age, confirmed diagnosis of active RA, generalized severe chronic periodontitis, and at least 20 teeth present. Exclusion criteria were antibiotic use during the previous 3 months before the study, smoking, diabetes, severe xerostomia, and pregnancy.

Forty subjects, recruited from the Rheumatology Division at University Hospitals of Cleveland, were enrolled. Of these, 20 subjects were taking disease-modifying anti-rheumatic drugs (DMARDs) alone; the other 20 subjects were on a combination of DMARDs and anti TNF-α medication for management of their RA. Each of these groups of 20 participants were then

randomized to either the treatment (n=10) or the control (n=10) groups. This resulted in the following four groups (10 subjects each): Periodontal Treatment only (group A), No Periodontal Treatment and No Anti TNF-α drug (group B), Periodontal Treatment and Anti TNF-α drug (group C), and Anti TNF-α drugs only (group D). DMARDs consisted of the following drugs: methotrexate, hydroxychloroquine, leflunomide, and sulfasalazine, whereas Anti NF-α drugs included Infliximab, Etanercept, and Adalimumab. The dosages of the previous medications were determined by the treating rheumatologist based on the patients' needs.

Data Collection

The following information was obtained from subjects' medical records: age, gender, medical history and medications used by the subjects. Periodontal and RA status as well as serum TNF-α level were assessed at baseline and at 6 weeks thereafter. To assess periodontal status, the following data were recorded by a calibrated examiner: probing depth (PD) and clinical attachment level (CAL) at 6 sites per tooth, plaque index (PI) of Sillness and Loe, gingival index (GI) of Loe and Sillness[22,23], percentage of sites with bleeding on probing (BOP), and number of teeth present. To assess RA status, the following data were extracted from patients' records: number of tender (TJ) and swollen (SJ) joints, patients' general assessment of their condition scored on Visual Analog Scale (VAS), erythrocyte sedimentation rate (ESR) and Disease Activity Score 28 joints (DAS28). DAS28 is a numeric index that was introduced and validated in 1995.[24] DAS28 score is calculated using TJ, SJ, VAS, and ESR. At present, it is a widely used method for assessment of RA disease activity in daily practice. To assess TNF-α, 2 ml of blood was drawn at each visit and enzyme linked immunosorbent assay (ELISA) was used for TNF-α analysis. Subjects in the periodontal treatment groups (A and C) received oral hygiene instruction along with full mouth scaling/root planing immediately after the baseline assessment. Participants in the control groups (B and D) scheduled an appointment for periodontal treatment after the completion of the study.

Statistical Analysis

Characteristics of the study participants (age, gender and RA severity) were compared between groups using Kruskal-Wallis and Chi-square tests. Differences in PD, CAL, PI and GI within groups were compared using linear mixed models adjusted for age, gender, rheumatoid factor (RF), tooth type, and random effect from patients. The analyses were performed on the average values of measures from each tooth. For BOP, the difference in percentage of bleeding sites was calculated for each subject and a linear regression model adjusted for age, gender, and RF was used to examine within group differences. To compare the intra-group differences in ESR and DAS-28, linear regression models adjusted for age and gender were used. The within group difference in the TNF-α level was tested using a two-sided t-test. To examine the intergroup differences in PD, CAL, PI and GI, linear mixed models adjusted for baseline values, age, gender, RF, tooth type, and random effect from patients were used. A linear regression model adjusted for baseline values, age, gender, and RF was used to compare BOP between groups. To compare differences in ESR and DAS-28 between groups, linear regression models adjusted for baseline values, age, and gender were used. Linear mixed models were fitted using Proc Mixed in SAS statistical software[1].

RESULTS

The distribution of the baseline variables (Age, Gender, and RA severity) is given in Table 1. There was a significant difference in the age of the patients between the four groups: groups

[1]SAS system for widows, version 9.1, SAS institute, Gary, NC.

A and D have older patients compared to groups B and C. No differences were found between the groups in the distribution of gender and RA severity.

Table 2 presents the differences in periodontal and RA parameters at baseline and at 6 weeks. Subjects receiving periodontal therapy (groups A and C) showed a statistically significant improvement in ESR, DAS-28, PD, BOP, PI, and GI when pre- and post-treatment visits were compared. No significant changes between the visits were observed in the control groups (groups B and D). When subjects receiving periodontal therapy (groups A and C) were compared to the control subjects (groups B and D), statistically significant differences in DAS-28, PD, CAL, BOP, PI, and GI were observed between groups ($P<0.01$), whereas ESR was not significantly different between groups ($p=0.64$). When subjects on the anti-TNF-α therapy (groups C and D) were compared to those not receiving TNF-α therapy (groups A and B), ESR, PD, CAL, BOP, and GI were significantly different between groups ($p< 0.05$). DAS-28 and PI were not significantly different between those receiving TNF-α therapy or not ($P>0.05$).

Subjects receiving periodontal therapy (groups A and C) showed a statistically significant decrease in number of swollen joints (SJ) and in VAS values after periodontal therapy. Subjects in group C also showed statistically significant decrease in number of tender joints (TJ) after periodontal therapy. No improvement in SJ, TJ, or VAS was seen in groups B and D. Subjects receiving periodontal therapy (groups A and C) showed significant improvement in SJ ($p<0.001$), TJ ($P=0.2$) and VAS ($P <0.001$) as compared to the control subjects (groups B and D). The previous parameters were not significantly different between those treated with or without anti-TNF-α drugs ($P>0.05$). Table 3 presents number of subjects showing a decrease in serum TNF-α level between baseline and 6-weeks visits. Fifty percentof the subjects in groups A and 40% in group C showed a decrease in serum TNF-α level after periodontal treatment, whereas only 20% of the subjects in groups B and D showed such a decrease. The decrease in the mean TNF-α level between baseline (77.79 ± 53.99) and 6-weeks (42.48 ± 42.95) visits was significantly different ($P<0.001$) in the periodontally treated subjects (groups A and C). In the control subjects (groups B and D), such difference was insignificant ($P=0.2$), the mean TNF-α at baseline and 6-weeks, was 37.13 ($\pm$ 39.94) and 77.89 ($\pm$93.59), respectively.

DISCUSSION

Non-surgical periodontal treatment of subjects suffering moderate/severe chronic periodontitis and RA was found to reduce severity of RA as measured by disease activity score (DAS-28). An improvement in ESR, number of swollen and tender joints, and VAS also was observed in periodontally-treated subjects. No such improvement was seen in untreated controls. The difference between periodontally-treated and non-treated subjects was statistically significant. These findings are in agreement with previous studies,[16,17] that suggest a beneficial effect of periodontal therapy on RA status. They also support the concept that periodontal disease is a systemic inflammatory condition.[25–28] Periodontal treatment was shown to decrease systemic inflammatory products.[29] Thus, the improvement in RA condition after periodontal therapy might be attributed to a reduction in these markers. Another possible explanation is that elimination of periodontal pathogens by scaling and root planing might reduce exposure of the joints structures to bacteria and their toxins and subsequently lead to improved RA conditions.[30]

Subjects on anti-TNFα therapy showed a statistically significant improvement in ESR, CAL, PD, BOP, and GI as compared to those not receiving this therapy. This is consistent with findings of a previous study in RA subjects that showed an inverse association between anti-TNF-α therapy use and severity of periodontitis.[21] However, severity of RA, as measured by DAS-28, was not significantly different in subjects treated with or without anti-TNF-α drugs.

This could be attributed in part to the prolonged use of anti-TNF-α therapy before initiation of the study.

A significant reduction in serum TNF-α level between baseline and 6 weeks follow-up visits was observed in periodontally-treated subjects but not among untreated controls. This is consistent with findings of two recent studies[31,32] in which treatment of subjects suffering from moderate to severe chronic periodontitis was found to significantly reduce level of circulating TNF-α. However, they contradict findings of other studies in which periodontal treatment was not found to affect circulating TNF-α level.[33, 34] None of the aforementioned studies, however, was in RA patients. TNF-α is suggested to play an important role in the process of inflammation with systemic effects and is implicated in the pathogenic mechanisms of RA.[19] Thus, the reported reduction in the level of serum TNF-α in the present study could be another possible mechanism by which periodontal treatment reduces severity of RA.

In conclusion, the present findings indicate that control of periodontal infection and inflammation by means of scaling and root planing and oral hygiene in subjects with moderate severe periodontal disease might contribute to a reduction in signs and symptoms of active rheumatoid arthritis as well as to a reduction in the serum levels of TNF-α.

SUMMARY OF KEY FINDINGS

Non-surgical periodontal therapy had a beneficial effect on signs and symptoms of RA irrespective of the medications used to treat this condition.

Acknowledgments

This study was sponsored by the Department of Periodontics at Case Western Reserve University and NIH grants DE14924, DE16102, and DE17165.

REFERENCES

1. Grassi W, De Angelis R, Lamanna G, Cervini C. The clinical features of rheumatoid arthritis. Eur J Radiol 1998;27:S18–S24. [PubMed: 9652497]
2. Mercado FB, Marshall RI, Bartold PM. Inter-relationships between rheumatoid arthritis and periodontal disease. A review. J Clin Periodontol 2003;30:761–772. [PubMed: 12956651]
3. Falcini F, Cimaz R. Juvenile rheumatoid arthritis. Curr Opin Rheumatol 2000;12:415–419. [PubMed: 10990178]
4. Kjeldsen M, Holmstrup P, Bendtzen K. Marginal periodontitis and cytokines: A review of the literature. J Periodontol 1993;64:1013–1022. [PubMed: 8295085]
5. Birkedal-Hansen H, Moore WGI, Bodden MK, Windsor LJ, DeCarlos A, Engler JA. Matrix metalloproteinases: A review. Crit Rev Oral Biol Med 1993;4:197–250. [PubMed: 8435466]
6. Bendtzen K. Cytokines and natural regulators of cytokines. Immunol Lett 1994;43:111–123. [PubMed: 7737681]
7. Havemose-Poulsen A, Holmstrup P. Factors affecting IL-1- mediated collagen metabolism by fibroblasts and the pathogenesis of periodontal disease: A review of the literature. Crit Rev Oral Biol Med 1997;8:217–236. [PubMed: 9167094]
8. Lerner UH. Inflammation-induced bone remodeling in periodontal disease and the influence of post-menopausal osteoporosis. J Dent Res 2006;85:596–607. [PubMed: 16798858]
9. Assuma R, Oates T, Cochran D, Amar S, Graves DT. IL-1 and TNF antagonists inhibit the inflammatory response and bone loss in experimental periodontitis. J Immunol 1998;160:403–409. [PubMed: 9551997]

10. Kaber UR, Gleissner C, Dehne F, Michel A, Willershausen-Zonnchen B, Bolten WW. Risk for periodontal disease in patients with longstanding rheumatoid arthritis. Arthritis Rheum 1997;40:2248–2251. [PubMed: 9416864]
11. Mercado F, Marshall RI, Klestov AC, Bartold PM. Is there a relationship between rheumatoid arthritis and periodontal disease? J Clin Periodontol 2000;127:267–272. [PubMed: 10783841]
12. Mercado FB, Marshall RI, Klestov AC, Bartold PM. Relationship between rheumatoid arthritis and periodontitis. J Periodontol 2001;72:779–787. [PubMed: 11453241]
13. Ramamurthy NS, Greenwald RA, Celiker MY, Shi EY. Experimental arthritis in rats induces biomarkers of periodontitis which are ameliorated by gene therapy with tissue inhibitor of matrix metalloproteinases. J Periodontol 2005;76:229–33. [PubMed: 15974846]
14. Moen K, Brun JG, Valen M, et al. Synovial inflammation in active rheumatoid arthritis and psoriatic arthritis facilitates trapping of a variety of oral bacterial DNAs. Clin Exp Rheumatol 2006;24:656–63. [PubMed: 17207381]
15. Ogrendik M, Kokino S, Ozdemir F, Bird PS, Hamlet S. Serum antibodies to oral anaerobic bacteria in patients with rheumatoid arthritis. MedGenMed 2005;7(2):2. [PubMed: 16369381]
16. Riberio J, Leao A, Novaes AB. Periodontal infection as a possible severity factor for rheumatoid arthritis. J Clin Periodontol 2005;32:412–416. [PubMed: 15811060]
17. Al-Katma MK, Bissada NF, Bordeaux JM, Sue J, Askari AD. Control of periodontal infection reduces the severity of active rheumatoid arthritis. J Clin Rheumatol 2007;13(3):134–7. [PubMed: 17551378]
18. Pishon N, Pischon T, Kroger J, et al. Association among rheumatoid arthritis, oral hygiene, and periodontitis. J Periodontol 2008;79(6):979–86. [PubMed: 18533773]
19. Toussirot E, Wendling D. The use of TNF-alpha blocking agents in rheumatoid arthritis: an update. Expert Opin Pharmacother 2007;8(13):2089–107. [PubMed: 17714062]
20. Di Paola R, Mazzon E, Muia C, et al. Effects of etanercept, a tumour necrosis factor-alpha antagonist, in an experimental model of periodontitis in rats. Br J Pharmacol 2007;150:286–97. [PubMed: 17200677]
21. Kiarash O, Bissada NF, Arauz-Dutari J, et al. Impact of anti-TNF therapy on periodontitis in rheumatoid arthritis patients. J Dent Res. 2007 Abst. #2506.
22. Loe H, Silness J. Periodontal disease in pregnancy. I. Prevalence and severity. Acta Odontol Scand 1963;21:532–551.
23. Loe H. The gingival index, the plaque index and the retention index systems. J Periodontol 1967;38 (suppl):610–616. [PubMed: 5237684]
24. Prevoo ML, van't Hof MA, Kuper HH, van Leeuwen MA, van de Putte LBA, van Riel PLCM. Modified disease activity scores that include twenty-eight joint counts: development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. Arthritis Rheum 1995;38:44–8. [PubMed: 7818570]
25. Ebersole JL, Machen RL, Steffen MJ, Willmann DE. Systemic acute-phase reactants, C-reactive protein and haptoglobin, in adult periodontitis. Clin Exp Immunol 1997;107:347–352. [PubMed: 9030874]
26. Loos BG, Craandijk J, Hoek FJ, Wertheim-van Dillen PM, van der Velden U. Elevation of systemic markers related to cardiovascular diseases in the peripheral blood of periodontitis patients. J Periodontol 2000;71:1528–1534. [PubMed: 11063384]
27. Slade GD, Ghezzi EM, Heiss G, Beck JD, Riche E, Offenbacher S. Relationship between periodontal disease and C-reactive protein among adults in the Atherosclerosis Risk in Communities study. Arch Intern Med 2003;163:1172–1179. [PubMed: 12767953]
28. Noack B, Genco RJ, Trevisan M, Grossi S, Zambon JJ, De Nardin E. Periodontal infections contribute to elevated systemic C-reactive protein level. J Periodontol 2001;72:1221–1227. [PubMed: 11577954]
29. D'Aiuto F, Nibali L, Parkar M, et al. Short-term effects of intensive periodontal therapy on serum inflammatory markers and cholesterol. J Dent Res 2005;84:269–273. [PubMed: 15723869]
30. Simelyte E, Rimpilainen E, Lehtonen L, et al. Bacterial cell wall induced arthritis: chemical composition and tissue distribution of four *Lactobacillus* strains. Infect Immun 2000;68:3535. [PubMed: 10816508]

31. Yun F, Firkova EI, Xun H, Jun-Qi L. Effects of surgical periodontal therapy on serum levels of TNF-alpha in patients with chronic periodontitis. Folia Med (Plovdiv) 2007;49(12):37. [PubMed: 18018468]

32. Wang Y, Yang PS, Qi XM, Ren JM, Ge SH. [Change of circulating TNF-alpha in patients with advanced periodontitis before and after periodontal initial therapy]. Shanghai Kou Qiang Yi Xue 2003;12(2):85–7. Chinese. [PubMed: 14661505]

33. Ide M, McPartlin D, Coward PY, Crook M, Lumb P, Wilson RF. Effect of treatment of chronic periodontitis on levels of serum markers of acute-phase inflammatory and vascular responses. J Clin Periodontol Apr;2003 30(4):334–40. [PubMed: 12694432]

34. Yamazaki K, Honda T, Oda T, Ueki-Maruyama K, Nakajima T, Yoshie H, Seymour GJ. Effect of periodontal treatment on the C-reactive protein and proinflammatory cytokine levels in Japanese periodontitis patients. J Periodontal Res 2005;40(1):53–8. [PubMed: 15613080]

Table 1

Characteristics of the study sample

Variable	Over All (n = 40)	Groups A (n = 10)	B (n = 10)	C (n = 10)	D (n = 10)	P-value
Age (median (min, max))	55.5 (39, 87)	69 (46, 83)	49 (42, 68)	54.5 (40, 88)	63 (39, 87)	0.0337
Gender						0.3051
Male	5 (12.5%)	2 (20%)	0 (0%)	2 (20%)	1 (10%)	
Female	35 (87.5%)	8 (80%)	10 (100%)	8 (80%)	9 (90%)	
RA						0.0741
Moderate	10 (25%)	0 (0%)	3 (30%)	2 (20%)	5 (50%)	
Severe	30 (75%)	10 (100%)	7 (70%)	8 (80%)	5 (50%)	

A= periodontal treatment only; B=no periodontal treatment and no anti-TNF-a therapy; C=periodontal treatment and no anti-TNF-a therapy; D= anti-TNF-a therapy only.

Table 2

Periodontal and Rheumatoid Arthritis Parameters at Baseline and at 6 weeks.

	Group A		Group B		Group C		Group D		p-values		
Outcomes	**Baseline**	**6-week**	**Baseline**	**6-week**	**Baseline**	**6-week**	**Baseline**	**6-week**	**Between Group**	**A&C vs B&D**	**C&D vs A&B**
CAL	3.53 (0.99)	3.40 (0.88)	3.44 (1.03)	3.47 (1.00)	3.82 (1.11)	3.52* (0.95)	4.04 (1.07)	4.02 (1.03)	<0.001	<0.001	<0.001
PD	3.06 (0.80)	2.85* (0.65)	3.01 (0.71)	3.01 (0.69)	3.25 (0.70)	2.82† (0.49)	3.55 (0.83)	3.50 (0.79)	<0.001	<0.001	0.107
BOP	0.83 (1.11)	0.63† (0.93)	0.75 (0.03)	0.81 (1.01)	1.72 (1.98)	1.12* (1.49)	1.58 (1.82)	1.37 (1.68)	<0.001	0.003	<0.001
GI	0.71 (0.49)	0.61* (0.43)	0.59 (0.44)	0.62 (0.42)	0.92 (0.67)	0.74† (0.53)	0.95 (0.72)	0.88 (0.66)	<0.001	<0.001	<0.001
PI	1.09 (0.84)	0.80† (0.68)	0.82 (0.51)	0.87 (0.51)	1.17 (0.90)	0.72† (0.61)	1.07 (0.74)	1.08 (0.67)	<0.001	0.008	0.327
ESR	52.5 (19, 122)	10.5† (7, 39)	15.5 (10, 120)	10.0 (1, 61)	51.5 (11, 86)	22.5* (1, 60)	27 (9, 63)	17 (8, 60)	0.162	0.640	0.037
DAS-28	5.09 (1.01)	3.51† (1.11)	4.29 (0.95)	3.98 (0.63)	4.96 (0.99)	3.54* (1.05)	4.34 (1.34)	4.10 (1.09)	0.0269	0.005	0.596
SJ	3.5	2.1†	2.8	3.1	4.9	2.9†	4.2	3.7	<0.001	<0.001	0.268
TJ	3.1	1.8	3.8	3.7	4.3	2.3*	2.6	2.6	0.102	0.017	0.536
VAS	68	48†	54.5	60	50	30†	49.5	45	<0.001	<0.001	0.0926

A= periodontal treatment only; B=no periodontal treatment and no anti-TNF-a therapy; C=periodontal treatment and anti-TNF-a therapy; D= anti-TNF-a therapy only. ESR, mean (minimum and maximum) value of erythrocytes sedimentation rate; SJ and TJ, median number of swollen and tender joints, respectively; VAS, Patients' General Assessment of their RA condition scored on Visual Analog Scale.

*P<0.05 and

†p<0.01, statistically significant difference between baseline and 6-week visits.

Table 3

Frequency and percentage of patients with a decrease in TNF-α level within each group.

group	Number	%
A	5	50
B	2	20
C	4	40
D	2	20
Total	13	32.5