Original Article

Periodontal Condition in Patients with Rheumatoid Arthritis: Effect of Anti-rheumatic Drugs

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ABSTRACT

Statement of the Problem: Rheumatoid arthritis and periodontitis are chronic inflammatory diseases with a possible bidirectional relationship. This link may be affected by many factors like drug consumption.

Purpose: This study was designed to evaluate the periodontal condition in patients with rheumatoid arthritis, considering the effect of disease modifying anti-rheumatic drugs.

Materials and Method: This case-control study included 25 newly diagnosed rheumatoid arthritis patients with negative history of taking anti-rheumatic drugs, 25 patients who received anti-rheumatic drugs for more than three years and 50 healthy individuals as a control group. Periodontal indices, including plaque index, gingival index, probing depth, clinical attachment loss, and rheumatologic indices were recorded and compared between these groups.

Results: Rheumatoid arthritis patients were significantly more affected by periodontitis compared with healthy subjects ($p= 0.006$). There was no significant difference in rheumatologic indices between patients with and without periodontitis. Clinical attachment loss in old rheumatoid arthritis patients and gingival index in newly diagnosed ones were significantly more compared to the control group ($p= 0.003$ and $p< 0.001$ respectively). We could not find a linear relationship between the severity of rheumatoid arthritis and chronic periodontitis ($p= 0.1$, r= -0.224).

Conclusion: Periodontitis and clinical attachment loss were more in patients with rheumatoid arthritis than the healthy group, especially in drug consumers. Gingival index in patients without the history of consuming anti-rheumatic drugs was significantly higher than those who were drug consumers, indicating the effect of the medications on the signs of inflammation.

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Introduction

Periodontitis is a chronic inflammatory disease leading to the destruction of attachment apparatus and tooth loss. Gram-negative anaerobic bacteria in the dental plaque biofilm initiate the tissue destruction. Periodontitis may also be associated with systemic disorders such as diabetes, cardiovascular and respiratory diseases, and adverse pregnancy outcomes. Moreover, some studies have presented the relationships between periodontal and rheumatic diseases, especially rheumatoid arthritis (RA) [1-2]. RA is an autoimmune disease characterized by chronic inflammatory arthritis and bone erosion [3]. It affects approximately one percent of the world population, being three times more prevalent in women [4].

In both RA and periodontitis, similar chronic inflammatory reactions cause changes in the connective

tissues and bone [5]. Besides, they have common genetic and environmental risk factors, including human leukocyte antigen DRB1 (HLA DRB1) and smoking. HLA-DRB1 genomic region is crucial for the organism resistance and susceptibility to pathogenic factor [6]. RA occurs four times more in patients with periodontitis [7] and periodontitis is more prevalent in RA patients [8].

Despite similarities between RA and periodontitis, the literature regarding the relationship between these two diseases is still controversial [4, 7, 9]. One problem in assessing the periodontal condition in RA patients is the treatment of the subjects with a variety of common medications against RA that can affect the periodontal indices as well, at the time of the study [10-13]. Another problem with the identified studies can be linked to the cross-sectional nature and that the previous treatments of the periodontitis or RA and smoking history were not accounted [4]. The aim of this study was to evaluate the periodontal condition in patients with RA, considering the effect of disease modifying anti-rheumatic drugs (DMARDs) and the above-mentioned confounding factors.

Materials and Method

A total of 100 subjects (12 males and 88 females; mean age: 39.65±9.81 years) was included in this case-control study. The sample size was determined according to the most relevant study. In this study, the prevalence of periodontitis was about 60% in RA and 16% in non-RA patients. Therefore, considering a 99% confidence level and a 99% statistical power, this number of patients was assigned [14].

The study population consisted of adults with RA who satisfied American College of Rheumatology/ European League Against Rheumatism (ACR/EULAR, 2010) classification criteria for RAS from the Rheumatology Clinic of Sayyad Shirazi Hospital affiliated to Golestan University of Medical Sciences. The control group (n=50) was recruited from other departments of the hospital and were matched on age and gender. All the procedures performed in this study, involving human participants were in accordance with the ethical standards of the institution (Code: 31078693122422). All the patients participating in this study signed a written informed consent. Half of the cases (n=25) were newly diagnosed RA patients (disease duration of a

minimum of 6 weeks up to 6 months) without the history of DMARDs, non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids consumption (group A). The rest (n=25) had the history of RA and were using these medications (Methotrexate, Hydroxychloroquine, Prednisolone, NSAIDs) for more than three years (group B). We excluded patients with less than 10 teeth except for third molars, and pregnant or lactating females. The presence of systemic diseases that modifies the periodontal conditions, systemic antibiotic intake within the previous three months, and history of periodontal therapy in the last six months and smoking were also considered as exclusion criteria.

The patients' socio-demographic data and their medical history were collected. In RA patients, the disease duration and medications were recorded and factors such as erythrocyte sedimentation rate (ESR), serum C-reactive protein (CRP), serum rheumatoid factor (RF), anti-cyclic citrullinated peptide (anti-CCP antibody) were measured. A rheumatologist calculated disease activity score 28 (DAS28) based on the number of joints tender to touch, the number of swollen joints, ESR and the patient's general health. For instance, DAS28 > 5.1 indicated that the subject had a high disease activity, whereas DAS28 < 3.2 meant that the disease activity was low.

Intraoral examination

Oral examinations of the subjects with RA and the control subjects were performed by the same examiner who was blinded to the rheumatologic diagnosis, using the graded probe (Goldman/Fox Williams probe; Hu-Friedy, Chicago, IL, USA) and the readings were recorded to the nearest 1 mm. We assessed all the measurements at six points of each tooth (mesio-buccal, distobuccal, mid-buccal, mesio-lingual, mid-lingual, and disto-lingual).

Probing depth (PD) was defined as the distance from the free gingival margin to the bottom of the sulcus. Clinical attachment loss (CAL) was considered as the distance from the cemento-enamel junction (CEJ) to the bottom of the sulcus and was used as an index for the diagnosis of periodontitis. Periodontal diagnosis was set by following the criteria of the International Consensus Report on Chronic Periodontitis; where the severity of chronic periodontitis was classified as slight (1 to 2 mm of CAL), moderate (3 to 4mm CAL) or severe (5mm

CAL) [15]. Plaque index (PI) scores were expressed as the percentage of positive sites [16]. The degree of the gingival inflammation was assessed according to Loe & Silliness [17].

Statistical analysis

Frequency distributions, means, and standard deviations were used to describe the demographic information of the participants. Dental variables were compared between the subjects by using Kruskal Wallis and Mann-Whitney test.

A chi-square test was used to compare the frequency of periodontitis between the study groups. The Spearman correlation coefficients were run to find the correlatios between the periodental indices and RA diseases characteristics. The data were analyzed using the statistical packages for social sciences (SPSS) software, version 16.0 (SPSS, Chicago, IL, USA). In this study, $p < 0.05$ was considered statistically significant for all the tests.

Results

The characteristics of the participants are presented in Table 1. The age of the patients ranged from 19 to 64 years. Both groups were similar regarding the gender ($p = 0.976$) and age ($p = 0.065$) (Table 1). Patients with periodontitis were 67% and 76% were in group A and 84% in the group B. However, this percentage decreased to 54% in the control group. There was no significant difference in the prevalence of periodontitis between both sub-groups of RA patients ($p = 0.48$). Based on the groups of this study, patients with RA had chronic periodontitis more than the healthy subjects had

[40 (80%) versus 27 (54%), ($p = 0.006$)]. Table 2 shows the dental variables in patients with RA and the control group. GI was significantly higher in patients with newly diagnosed RA than the control group ($p < 0.001$). The results indicated that the mean of CAL was significantly higher in the group B of RA patients in comparison to the control group ($p = 0.001$) and PI was significantly lower in the control group in comparison with RA patients ($p < 0.001$). There was no statistically significant difference in pocket depth among all these three groups ($p = 0.05$).

Rheumatologic factors are presented in Table 3. All factors are significantly higher in the group A than group B, except for anti-CCP antibody ($p = 0.62$).

Discussion

In this study, the relationship between RA and chronic periodontitis was assessed, considering DMARDS therapy among the study patients. A previous study mentioned medications for the treatment of RA could reduce gingival inflammation [18]. We eliminated smoking as an important confounding variable in investigating the possible relationship between these two chronic diseases. Demographic characteristics of our participants were consistent with other studied populations, meaning that RA was more common in middle-aged females [19]. Similar to the other studies, periodontitis was significantly more frequent in RA patients than in healthy individuals [18-21]. Patients in the group B indicated more CAL and disease severity than newly diagnosed ones. This may be due to the cumulative periodontal destruction, which occurs during these years. Kasser *et al.* [22]

Table 1: Comparison of demographic characteristics between the cases and the control group (SD= standard deviation)

Characteristic	Case (n=50)		Control (n=50)	p Value
	A (n=25)	B (n=25)		
Gender (n [%])				
Male	3(12)	3(12)	6(12)	0.976
Female	22(88)	22(88)	44(88)	
Age(years; mean±SD)	42.20±10.84	40.72±8.37	37.84±9.76	0.065

Table 2: Dental examination results in rheumatoid arthritis patients and the control group (SD= standard deviation)

Variable	Case		Control	p Value
	A	B		
GI † ((mean±SD)	0.9±0.42	0.7±0.52	0.54±0.28	0.02
PI‡	88.48±18.58	83.36±20.46	68.56±17.08	<0.001
PD§	1.34±0.36	1.22±0.28	1.42±0.30	0.058
CAL¶	2.08±1.93	2.88±2.08	1.32±1.58	0.004

†Gingival index, ‡plaque index, § probing depth, ¶ clinical attachment loss

Table 3: Rheumatologic factors in rheumatoid arthritis patients (SD= standard deviation)

Variable	Case		p Value
	A	B	
Anti-CCP[†] (mean±SD)	59.53±75.26	58.19±78.44	0.621
ESR [‡]	35.16±23.67	21.44±16.78	0.034
CRP [§]	8.22±4.68	6.02±3.96	0.013
DAS28 [¶]	4.03±1.53	3.29±0.99	0.033

† Anti-Cyclic Citrullinated peptide, ‡ Erythrocyte sedimentation rate, § C-reactive protein,   ¶ disease activity score 28

also revealed that CAL increased by 173% in patients with long-standing, active RA. Furthermore, cytokine profile of both diseases, including persistent high levels of pro inflammatory cytokines and low levels of anti-inflammatory cytokines may be responsible for active periods of tissue destruction; Group B presented a higher frequency of sites with CAL equal to 4-5 mm.

In contrast, some population-based and clinical studies showed no correlation between RA and the prevalence of periodontitis [9]. This discrepancy seems to be a dependent variable in different ethnic groups and adjustments for confounding variables among different populations.

We could not find any significant correlation between the severity of RA and periodontitis severity, which is in line with previous studies [12, 23]. On the contrary, Khantisopon [20] reported significant relationship among Thai patients. These differences may be attributed to the various classification of periodontal disease in the study patients and high prevalence of periodontitis in the general Thai population.

Both groups presented higher PI than the control group, which may be due to upper body disabilities and poor manual dexterity of patients with RA to remove supragingival plaque [24]. Although RA patients had more bacterial plaque, no significant statistical difference was observed regarding GI between DMARDS users and the healthy population. This difference might be due to the consumption of anti-inflammatory and anti-rheumatic drugs for a long time, which is in accordance with the result of Ishi Ede *et al.* [25].

In contrast, Torkzaban *et al.* [26] could not find any significant correlation between RA and the mean percent of PI because the status of oral hygiene among all the patients was poor, which could be considered as a confounding factor of their study.

Moreover, patients in the group A had more ESR,

CRP, and DAS28 level compared to the patients in the group B. This can justify the effect of drugs in the control of the disease. Our results demonstrated no significant differences in rheumatologic factors between periodontitis and periodontally healthy ones in the RA group, which are similar to the results of a clinical review [27]. The current study did not check the oral hygiene practice of all patients, which can be concerned as the limitation of our study. Longitudinal multicenter studies with larger sample size are recommended to evaluate the effect of related risk factors including; stress, nutritional factors, lifestyle, and DMARDs consumption in more details. Close cooperation between dentists and rheumatologists might be beneficial to improve the patient's status.

Conclusion

According to our findings, CAL was higher and periodontitis was more prevalent in patients with RA compared with the control group, particularly in medication consumers. GI in RA patients with negative history of consuming DMARDs was high which reveals the positive impact of the medication in the control of inflammation.

Acknowledgement

Conflict of Interest

None declared.

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