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RESEARCHARTICLE

EFFECT OF RHEUMATOID ARTHRITIS DRUGS ON SEVERITY OF PERIODONTAL DISEASES IN RHEUMATOID ARTHRITIS PATIENTS WITH PERIODONTITIS

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ABSTRACT

Backgrounds: An association between periodontitis (PD)and rheumatoid arthritis (RA) has been considered many years ago. RA is considered as an autoimmune disease whereas periodontitis has an infectious etiology with a complex inflammatory response. *Porphyromonasgingivalis* is a common pathogen in periodontal infection. The specific abilities of *P. gingivalis* to citrullinate host peptides can induce autoimmune responses in RA through development of anticycliccitrullinated peptide antibodies and trigger autoimmune responses in subjects with RA.The aim of this study was to detect the effect of Rheumatoid Arthritis drugs on Periodontal Parameters in Rheumatoid Arthritis patients with Periodontitis.

Materials and Methods: A group of45 rheumatic patients with periodontitis,age ranged (35 – 55) sub divided into 30 patients on routine RA treatment and 15 newly diagnosed patients (haven't taken treatment yet),.All have been subjected to clinical periodontal parameters registration.

Results: strong positive correlation between CAL and the different kind of drugs in the treated group in comparison with non – treated group, methotrexate shows weak positive correlation with G.I, P.P.D at $P< 0.05$, no correlation reported with CAL and B.O.p., While strong correlation reported between leflunamide and PL.I , G.I at $P=0.001$, $P< 0.05$ respectively.

Conclusion: An association between RA drugs and severity of periodontitis was demonstrated in regard to bone, plaque and gingival condition which were not related to dexterity loss.

INTRODUCTION

Rheumatoid arthritis (RA) is one of the most common autoimmune disease and the most frequent chronic inflammatory arthropathy. It affects around 1% of the world population,75% of patients are female. It is characterized by inflammation of the synovial membrane which spreads symmetrically from the small to large joints leading to the destruction of the joints (Anandarajah, 2010). On the other hand, periodontitis (PD) is a multifactorial infection characterized by a destructive inflammatory process affecting tooth supporting tissues and resulting in periodontal pocket formation and alveolar bone resorption, which might eventually lead to tooth loss(Cazalis *et al.,* 2009). Host tissue damage in PD is mainly due to the action of oral microbes and associated host immune-inflammatory responses(Van Dyke and Serhan, 2003; Van Dyke, 2007) whereas, combination of environmental and genetic factors with antibodies directed against cyclic citrullinated peptide (ACCP) has been associated with the onset of RA (Rodríguez-Rodríguez *et al.,* 2011). Intriguingly, both PD and RA share comparable clinical and pathological characteristics. For instance, in either condition, both connective tissue and bone are involved, and immune-inflammatory mediators are responsible for the host tissue damage, thus elevation of bone resorptive cytokines in PD and RA suggests common pathological pathway shared by the two diseases (Golub *et al.,*2006). Significant associations between the clinical parameters of PD and RA have been observed and it was suggested that both diseases possess a common underlying dysregulation of the inflammatory responses within the host (Mercado *et al.,* 2010). Rheumatoid arthritis is a chronic disorder for which there is no known cure. Fortunately in the last few years, a shift in strategy toward the earlier institution of disease modifying drugs and the availability of new classes of medications have greatly improved the outcomes that can be expected by most patients. The goal of treatment now aims toward achieving the lowest possible level of arthritis disease activity and remission if possible, minimizing joint damage, and enhancing physical function and quality of life. Types of drugs taken by patients involved in this study are:

- Corticosteroid
- Disease Modifying Anti-rheumatic Drugs (DMARD):

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1. Methotrexate
2. Hydroxychloroquine
3. Sulfasalazine
4. Leflunomide

Corticosteroids such as prednisone, have both anti-inflammatory and immune regulatory activity. Corticosteroids are useful in early disease as temporary adjunctive therapy while waiting for DMARDs to exert their anti inflammatory effects.

Disease Modifying Anti-rheumatic Drugs (DMARD)

DMARD agents have been shown to alter the disease course and improve radiographic outcomes. DMARDs have an effect upon rheumatoid arthritis that is different and may be slower. In most cases, when the diagnosis of rheumatoid arthritis is confirmed, DMARD agents should be started (Dougados *et al.,* 2005).

Methotrexate is now considered the first-line DMARD agent for most patients with RA. The anti-inflammatory effects of methotrexate in rheumatoid arthritis appear to be related at least in part to interruption of adenosine and possible effects on other inflammatory and immune regulatory pathways. The immunosuppressive and toxic effects of methotrexate are due to the inhibition of an enzyme involved in the metabolism of folic acid, dihydrofolate reductase.

Hydroxychloroquine is antimalarial drug which is relatively safe and well-tolerated agent for the treatment of rheumatoid arthritis. The mechanism of action of antimalarials in the treatment of patients with rheumatoid arthritis is unknown but is thought to involve changes in antigen presentation or effects on the innate immune system

Sulfasalazine is an effective DMARD for the treatment of RA It is also given in conjunction with methotrexate and hydroxychloroquine as part of a regimen of "triple therapy" which has been shown to provide benefits to patients who have had inadequate responses to methotrexate alone.

Leflunomideis an immunosuppressive DMARD, used in active moderate to severe rheumatoid arthritis and psoriatic arthritis. It is a pyrimidine synthesis inhibitor (Pinto P, Dougados, 2006)

MATERIALS AND METHODS

In a cross sectional study, fourty-five (45) patients aged (35-55) years old, who fulfill the 1987 ACR criteria for RA with chronic periodontitis. sub divided into 30 patients on routine RA treatment and 15 newly diagnosed patients were recruited in this study. They were from attendants seeking treatment in the rheumatology clinic in Baghdad Teaching Hospital, Baghdad. Patients were subjected to questionnaire about name, age, gender, type and duration of treatment with full registration of periodontal parameters

The periodontal Examination

Oral examination was performed at four surfaces of each tooth except 3rd molar according to the following criteria:

1. Assessment of dental plaque by (PL.I) of Silness and Loe(1964).
2. Assessment of gingival condition by (G.I) of Loe and Silness (1963); Löe, 1976.
3. Probing Pocket Depth (P.P.D):It is the distance from the gingival margin to the point at which periodontal probe stop in the gingival crevice. Williams periodontal probe was allowed to fall by its own weight without any pressure.
4. Clinical Attachment Level (CAL):It is the distance from the cement-enamel junction (CEJ) to the location of the inserted probe tip (bottom of periodontal pocket).The distance was measured indirectly by subtracting the distance from the gingival margin to the CEJ from PPD. In some cases when there was gingival recession, distance measured by adding the distance from the gingival margin to the CEJ to the PPD. Estimation of CAL was done by using William periodontal probe
5. Bleeding on probing (B.O.P):A blunt periodontal probe inserted to the bottom of the gingival pocket and is moved gently along the root surface. If bleeding occure within 30 seconds after probing, the site was given positive score(1),and a negative score for the non bleeding site.

RESULTS

Periodontal parameters for the main group and the two subgroups showed in detailes in both Table 1 and 2.Table 3 found no differences in PPD and B.O.P between the two subgroups. Table 4 express the correlation between different kinds of drugs and the periodontal parameters in the treated subgroup. Regarding methotrexate it shows weak positive correlation with G.I, P.P.D at $P< 0.05$, no correlation reported with CAL and B.O.p.No correlation at all was found between prednisolone, hydroxychloroquine and sulphasalazine with the periodontal parameters. While strong correlation reported between leflunamide. and PL.I, G.I at $P=0.001$, $P< 0.05$ respectively. Table 5 found a strong positive correlation between CAL and the different kind of drugs in the treated group in comparison with non – treated group.

Table 1. Summary statistics of periodontal parameters at the studied group

Periodontal parameters	No.	Mean	Std. Dev.	Std. Error
PL.I	45	2.16	0.64	0.10
G.I	45	1.98	0.50	0.07
P.P.D.(mm)	45	4.59	0.44	0.07
CAL(mm)	45	6.67	0.92	0.14
B.O.P. (Mean of %)	45	0.73	0.45	0.07

Table 2. Summary statistics of Periodontal Parameter at the studied subgroups

Subgroups	Statistics	Periodontal Parameters				
		PL.I	G.I	P.P.D.	CAL	B.O.P.
Treated	No.	30	30	30	30	30
	Median	2	2	3	3	1
	Range	2	2	1	1	1
	Minimum	1	1	2	3	0
	Maximum	3	3	3	4	1
Non treated	No.	15	15	15	15	15
	Median	2	2	3	4	1
	Range	1	1	0	1	0
	Minimum	2	2	3	3	1
	Maximum	3	3	3	4	1

Table 3. Comparisonsfor Periodontal Parametersof the studied subgroups

Contrast Comparisons		PL.I	G.I	P.P.D.	CAL	B.O.P
Treated	X Non treated	0.131	0.402	-	0.001	-

(-) All values are less than or equal to the median. Median Test cannot be performed.

coexistence between the conditions could arise either because one is contributing to the etiology and pathogenesis of the other or because similar environmental or genetic parameters govern the manifestation and progression of both.

Table 4. Spearman's correlation between Periodontal Parametersand types of drugs at the treated subgroups

Drug	Spearman's Correlation Coefficient	PL.I	G.I	P.P.D.	CAL	B.O.P.
MTX	Correlation Coefficient	0.345	0.413	0.4	0.098	-0.175
	Sig. (2-tailed)	0.062	0.023	0.028	0.608	0.355
	No.	30	30	30	30	30
PDN	Correlation Coefficient	-0.213	-0.201	-0.067	-0.03	0.234
	Sig. (2-tailed)	0.259	0.287	0.724	0.875	0.214
	No.	30	30	30	30	30
CHQ	Correlation Coefficient	0.141	-0.080	-0.224	0.280	0.120
	Sig. (2-tailed)	0.456	0.674	0.235	0.134	0.529
	No.	30	30	30	30	30
LEFL.	Correlation Coefficient	-0.596	-0.45	-0.264	-0.067	0.161
	Sig. (2-tailed)	0.001	0.012	0.159	0.723	0.395
	No.	30	30	30	30	30
SALAZ	Correlation Coefficient	0.264	0.149	0.042	-0.224	0.134
	Sig. (2-tailed)	0.159	0.431	0.827	0.235	0.481
	No.	30	30	30	30	30

Correlation is significant at the .05 level (2-tailed).

Table 5. Spearman's correlation between Periodontal Parametersand types of drugs at the studied main group

Groups	Spearman's Correlation Coefficient	PL.I	G.I	P.P.D.	CAL	B.O.P.
RA + PD	Correlation Coefficient	-0.142	-0.172	-0.005	-0.541	0.025
	Sig. (2-tailed)	0.353	0.258	0.974	0.000	0.870

Correlation is significant at the .05 level (2-tailed).

DISCUSSION

Pathophysiologically, the same immune mechanisms, cytokines, inflammatory mediators and degradative enzymes operate in both periodontal disease and RA (Mercado, 2010) The similarity between RA and PD has prompted several studies as early as 1930s, regarding the periodontal status in patients with RA, these studies have been noted significantly high level of plaque in RA patients in comparison with the healthy controls. Table 3 express no differences in PPD and B.O.P between the two subgroups ,this might be due to effect that the extent of gingival inflammation and pseudo-pockets may have been managed through DMARDS or other anti-inflammatory agents used over longer periods of time. (de Pablo *et al*., 2000) And this finding came in contrast with a study done by Kässer *et al.* (1997) who reported increase in gingival acute inflammation in the form of gingival bleeding relevant to tissue breakdown following long-term use of corticosteroids. In their study correlation between sulcus bleeding index and the drug dosage has been found (Kässer *et al*., 1997).

The effects of DMARD agent in the management of RA are related to effects on TNF-α pathways and the inhibition of an enzyme involved in the metabolism of folic acid. Several studies reported that treatment with DMARDS improved periodontal conditions (Okada *et al*., 2011) this strongly support finding of this study, as table 5 show a strong positive correlation between CAL and the different kind of drugs in the treated group in comparison with non –treated group. DMARDs might protect periodontal tissues from destruction. Based on this, less periodontal destruction (CAL) would be expected (Biyikoglu *et al*., 2006). This association or

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