Evaluation the non-surgical periodontal therapy on periodontal status of multiple sclerosis (MS) patients

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Abstract: Aim: To evaluate the effect of non-surgical periodontal therapy on periodontal status of multiple sclerosis patients. **Patients and methods: T**his study was carried out on twenty patients divided into two groups; group 1; include tenmoderate chronic periodontitis multiple sclerosis patients and group 2; include ten moderate chronic periodontitis without multiple sclerosis. Clinical parameters were assessed at baseline, 3 and at 6 months following initial periodontal therapy Clinical parameters including Plaque Index (PI), Gingival Index (GI) Clinical Attachment Level (CAL) and Pocket Depth (PD) and TNF- α were assessed at baseline, 3, 6, months following non-surgical periodontal therapy. Descriptive analysis, paired and unpaired t-test were performed. **Results:** All patients complete the study with no sign of any complications. There were non-significant difference of Plaque Index (PI) scores between the two groups at baseline, 3 and 6 months unpaired t- test. There was very highly significant difference regarding mean scores of Gingival Index between the two groups at baseline and these significant become non-significant at3 and 6 months. The levels of TNF- α revealed a very highly significant deference between the two group at the base line and this difference gradually decreased to become highly at 3 months and significant at 6 months. **Conclusions:** The present data suggest that reduction of gingival inflammatory condition in chronic periodontitis multiple sclerosis patients compared to chronic periodontitis patients without MS disease. In addition the non-surgical periodontal therapy leading to improve the periodontal status and reduction of crevicular fluid TNF-α levels in chronic periodontitis patients with and without MS disease.

[Fathey Abdel Aziem Ebrahiem Abo Zaid, Hossam Emam and Gamil Mohamed Abdullah. **Evaluation the non-surgical periodontal therapy on periodontal status of multiple sclerosis (MS) patients.** *J Am Sci* 2017;13(6):115-121]. ISSN 1545-1003 (print); ISSN 2375-7264 (online). http://www.jofamericanscience.org. 13. doi:10.7537/marsjas130617.13.

Keywords: Evaluation; non-surgical periodontal therapy; periodontal status; multiple sclerosis (MS); patient

1-Introduction

Periodontitis is chronic localized oral infection that triggers a systemic as well as local host immune-inflammatory response and that can be a source of bacteraemia, because of the large epithelial surface with ulcerated periodontal pockets [(1)]. Periodontitis, especially in its severe clinical form, is currently considered to influence the pathogenesis or increase the risk of some systemic diseases [(2)]. Oral bacteria have been associated with systemic diseases, such as infective endocarditis, rheumatoid arthritis or pulmonary diseases. Oral bacteria are able to reach the circulation and cause bacteremia following dental procedures such as tooth extraction, pocket curettage or even tooth polishing as flossing, brushing, and mastication particularly when periodontitis is present [(3,4).] *Aggregatibacter actinomycetemcomitans*, *P. gingivalis*, and *T. denticola* were recovered in atherosclerotic plaque [(5)]. Periodontal pathogen bacterias like *P. gingivalis* may also play a role in central nervous system diseases much like MS [(6)].

The multiple sclerosis (MS) is chronic inflammatory, autoimmunity disease often progressive and attacks the myelin sheath of the CNS. MS is a destructive disease that affects the oral and maxillofacial complex as well. Oral and facial manifestation in MS patients may include trigeminal neuralgia, trigeminal sensory neuropathy and facial palsy [(7)]. The cause of MS is unknown; however, it is believed to occur as a result of a combination of geographic location, environmental factors such as infectious agents and genetics [(8).]

Although the role of systemic infections in exacerbating clinical relapses and the associated image findings are well documented, systemic infection increases T-cell proliferation, leading to higher levels of inflammatory response [(9)]. Silent dental infections, frequent use of corticosteroids, immunomodulators and immunosuppressants, and the use of other drugs that may affect the oral mucosa may all add to the underlying abnormal immunological condition of these patients, thus influencing the course of MS and oral status. [(10)]

The treatment of MS is divided into three categories which include the symptomatic, acute attacks and diseases modifying [(11)].

Periodontitisis a peripheral, chronic, infectious disease result from the interaction between periodontopathic bacteria and the host response characterized by production of inflammatory molecules including interleukin-1β (Il-1β), interleukin-6 (Il-6), and tumor necrosis factor-α (TNF-α) [12]. These cytokinescan play an important role as diagnostic or prognostic markers for periodontal disease activity and wound healing [13]. TNF-α is the first cytokine secreted by endotoxin-activated macrophages exerts cytotoxic effect as well as participates in differentiation and growth modulatory activities on many different target cells. TNF-α is now known as a pleiotropic mediator and angiogenic cytokine that stimulate and enhances the production of other cytokines, activates inflammatory leukocytes, resulting in production of other proinflammatory cytokine such as IL-1, IL-6, and IL-8 and additional TNF-α. [14]. Also TNF-α can induce/up-regulate MMP-8 expression via gingival fibroblasts [15].

The etiopathogenesis of MS have not been completely characterized although inflammation is thought to play a significant role. Increased brain inflammatory molecules such as Il-1β, Il-6 and TNF-α participate in activating and perpetuating molecular pathways that may contribute to diseases activity [16, 17]. They have a potential to damage myelin, directly or indirectly with consequent axonal damage. So, cytokines are important mediators of immune response in MS [18]. Furthermore, TNF-α is one of the most potent inflammatory cytokines with the confirmed role in direct myelin damage [19]. It induces secretion of interferon gamma and other inflammatory cytokines activate macrophages and microgial cells to stimulate the production of reactive oxidative species, nitric oxide and lytic enzymes [20,21].

This study aimed to evaluate effect of non-surgical periodontal treatment on the periodontal status of chronic periodontitis patients with and without multiple sclerosis manifestations.

2- Patients and methods

Patient selection

All patients were selected from those patients attending at the out-patients clinic of Oral Medicine and Periodontology Department, Faculty of Dental Medicine, Al-Azhar University (Assiut Branch). The study protocol was explained in detail to all patients and their consent for participating study was taken. Twenty chronic periodontitis patients were included in this study divided into two groups.

Group 1: comprised of 10 chronic periodontitis patients diagnosed as relapsing remitting of MS (clinically and radiological by neurogist).

Group 2: comprised of 10 chronic periodontitis patients without manifestations of MS.

Inclusion criteria were chronic periodontitis patients previously diagnosed with MS and subjected to the suitable treatment and continuous follow up by the neurogist.

Exclusion criteria were includes: the presence of other systemic diseases, smoker, pregnancy or nursing, mental retardation, antibiotics administration and periodontal treatment previously 6 months. All patients were recruited for the study if they signed informed consent to study participation, received adequate information regarding the study's design. Attention was paid to ensuring that the patients were free from an acute attack at the time of examination. The patients of group 2 to bematched to group 1 regarding age, sex and plaque index.

Clinical intervention

The periodontal examinations were recorded on four sites (mesial, distal, buccal and lingual) for all teeth except the third molar; the periodontal parameters included Plaque Index (PI) [22], Gingival Index (GI) [23], Clinical Attachment Level (CAL) [24] and Pocket Depth (PD). The periodontal parameters were recorded 1 day before sampling collection and the initial therapy was started immediately after sampling (baseline).

All patients subjected to through scaling and root planning for all periodontal disease teeth in 2 to 4 visit with maximum period one month according to the treatment need, using standard rigid Gracey curettes and ultrasonic instrumentation. Subjects were followed up at 3 and 6 months. At each visit, clinical parameters and GCF samples collection at the same sites of baseline and oral hygiene instructions were carried out.

Gingival Crevicular Fluid sampling

Complete isolation of sampling sites: gingival crevicular fluid samples were taken using absorbent paper points. Paper points were inserted into the gingival crevice until mild resistance was felt, and kept in place for 30 seconds. Samples collected from two periodontal disease sites with plaque index scores more than 2 in different quadrants of the mouth of each patient. Samples were always taken from the same sites at the three visits. Following collection of GCF the paper point placed in eppendroffs tubes contain (300 micro liter) phosphate buffer saline. GCF was eluted from paper point by centrifugation at 3000 rpm for 15 minutes after that the paper point was removed and GCF sample kept at -40 ˚C till analysis.

For their analysis, samples were eluted and the concentrations of TNF-α (pg/ml) were measured by an enzyme linked immunosorbent assay (ELISA) using a specific commercial test (ELISA kit R & D System, Inc. USA & Canada) following the manufacturers' instructions.

Statistical analysis

Results were expressed as mean values ± standard deviation, and means of difference for each variable and analyzed by Graph pad prism (windows version 6; Graph pad software 2007) to produce paired and unpaired t-test of the two groups. The level of significance was at (P< 0.05).

3- Results

This study was carried out on twenty patients divided into two groups; group 1 tenmoderate chronic periodontitis patient with multiple sclerosis manifestations (6 females and 4 male with age mean (37+ 4.56) and group 2 include ten moderate chronic periodontitis without multiple sclerosis manifestations (6 females and 4 male with age mean (38+ 5.33) with non-significant difference between the age and sex and plaque index. All patients complete the study with no sign of any complications.

The clinical periodontal parameters (PI, GI, CAL and PD) revealed high scores in all clinical periodontal parameters at baseline and then gradually decrease within the period of study (table-1 and figures 1, 2, 3 & 4).

The means scores of PI at baseline were 2.25± 0.408 then decrease to 0.725± 0.299 and 0.375±0.186 at 3 and 6 months respectively in group 1. While in group 2, the means scores of PI at baseline were 2.23± 0.35 then decrease to 0.555± 0.163 and 0.342 ±0.096 at 3 and 6 months respectively.

Regarding GI, the means scores in group 1 at baseline were 1.8± 0.387 then decrease to 0.534± 0.188 and 0.44±0.018 at 3 and 6 months respectively. While in group 2the means scores of GI at baseline were 2.475± 0.142 then decrease to 0.49 ± 0.088 and 0.443±0.157 at 3 and 6 months respectively. In group 1, the means levels of TNF-α were 14.39 ± 1.107, 12.46± 0.972 and 10.79±0.651 (pg/ml) at baseline, 3 and 6 months respectively. While in group 2the means scores at baseline were 16.94± 1.316 then decrease to 13.9 ± 1.031 and 10.49±0.962 at 3 and 6 months respectively.

Table (1): Means ± standard deviations (SD), of clinical parameters (PI, GI, CAL and PD) and TNF-α levels in both groups at baseline (BL), 3 and 6 months.

		Baseline (BL)		3 months		6 months	
		G 1	G 2	G 1	G 2	G 1	G 2
PI	Mean	2.25	2.3	0.725	0.555	0.375	0.342
	SD	0.408	0.35	0.299	0.163	0.186	0.092
GI	Mean	1.8	2.475	0.534	0.49	0.44	0.443
	SD	0.387	0.142	0.188	0.088	0.018	0.157
CAL	Mean	3.726	3.512	2.892	2.252	2.564	1.685
	SD	0.165	0.179	0.288	0.384	0.555	0.312
PD	Mean	4.795	4.809	3.626	3.052	3.285	2.591
	SD	0.351	0.426	0.324	0.518	0.359	0.563
TNF-α	Mean	14.39	16.94	12.46	13.9	10.79	10.49
	SD	1.107	1.316	0.972	1.031	0.651	0.962

Table (2): P- value and level of significance of clinical parameters (PI, GI, CAL and PD) and TNF-α levels in within each group at baseline (BL), 3 and 6 months (Paired t-test).

Parameter		Group 1			Group 2		
		Blvs 3 m	Blvs 6 m	3 m vs 6 m	Blvs 3 m	Blvs 6 m	3 m vs 6 m
PI	P value	<0.0001	<0.0001	0.022	<0.0001	<0.0001	0.012
	Level of significance	****	****	*	****	****	*
GI	P value	<0.0001	<0.0001	0.151	<0.0001	<0.0001	0.455
	Level of significance	****	****	NS	****	****	NS
CAL	P value	<0.0001	<0.0001	0.034	<0.0001	<0.0001	<0.0001
	Level of significance	****	****	*	****	****	****
PD	P value	<0.0001	<0.0001	0.0003	<0.0001	<0.0001	0.012
	Level of significance	****	****	***	****	****	*
TNF-α	P value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
	Level of significance	****	****	****	****	****	****

There were very high significant difference between the plaque score in group1 at baseline versus 3 month and between baseline versus 6 months but this difference decline to significant at 3 month versus 6 months. Similarresults were recorded in group 2.

There were very high significant differences between the means of gingival index scores in group1 at baseline versus 3 and 6 months but this difference becomesnon-significant (NS) at 3 months versus 6 months. Similar result was recorded in group 2. As regard to TNF –α; there were very high significant difference between the means of its levels in group1 at baseline versus 3 and 6 months and at 3 month versus 6 months as well as similar results were recorded in group 2(table- 2).

Table (3): P- value and level of significance of clinical parameters (PI, GI, CAL and PD) and TNF-α levels between the two group at baseline (BL), 3 and 6 months (unpaired t-test).

Parameter		Baseline (BL)		3 months		6 months	
		G 1	G 2	G 1	G 2	G 1	G 2
PI	P value	0.772		0.132		0.621	
	Level of significance	NS		NS		NS	
GI	P value	< 0.0001		0.512		0.953	
	Level of significance	****		NS		NS	
CAL	P value	0.012		0.0005		0.0004	
	Level of significance	*		***		***	
PD	P value	0.937		0.008		0.004	
	Level of significance	NS		**		**	
TNF-α	P value	0.0002		0.005		0.429	
	Level of significance	***		**		NS	

There were non-significant difference of Plaque Index (PI) scores between the two groups at baseline, 3 and 6 months unpaired t- test. There was very highly significant difference regarding mean scores of Gingival Index between the two groups at baseline and these significant become non-significant at3 and 6 months. There was significant difference regarding mean scores of clinical attachment levels between the two groups at baseline and this significant become very highly significant at 3 and 6 months. The mean scores of Pocket Depth (PD) revealed non-significant difference at baseline and were high significant a difference between the two groups at 3 and 6 months. The levels of TNF- α revealed a very highly significant deference between the two group at the base line and this difference gradually decreased to become highly at 3 months and significant at 6 months. (table-3).

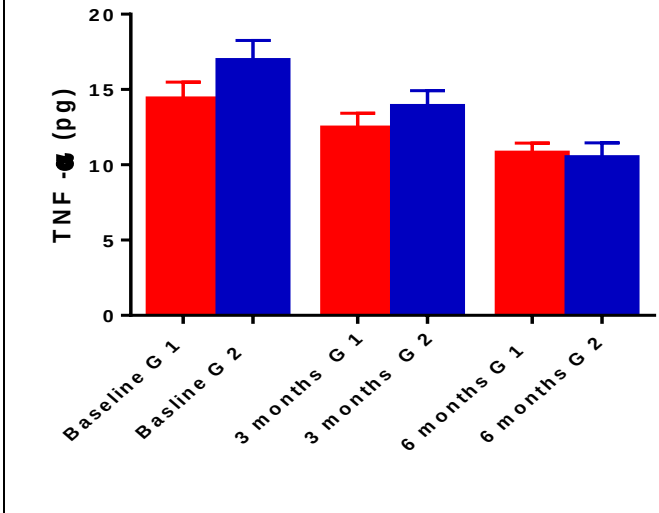

Figure- 1: Histogram illustrating means ± standard deviations TNF- α in both groups at baseline, 3 and 6 months

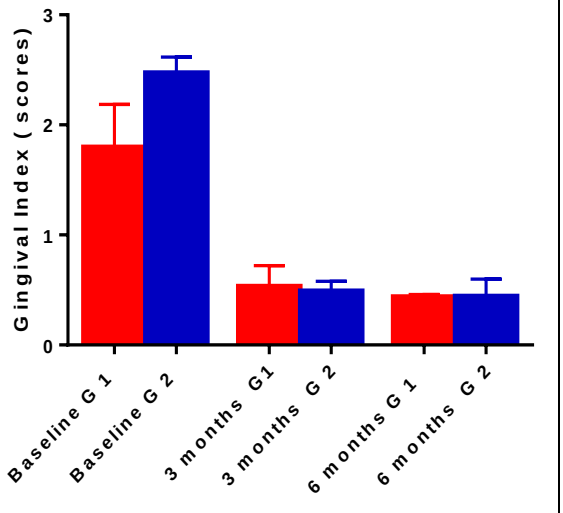

Figure- 2: Histogram illustrating means ± standard deviations GI in both groups at baseline, 3 and 6 months

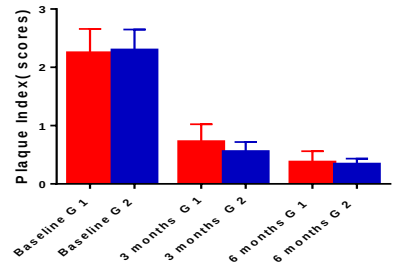

Figure- 3: Histogram illustrating means ± standard deviations PI in both groups at baseline, 3 and 6 months

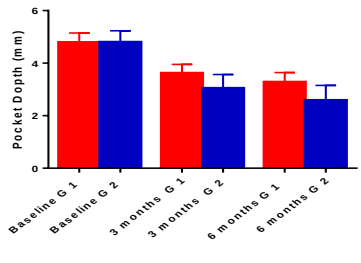

Figure- 4: Histogram illustrating means ± standard deviations PD in both groups at baseline, 3 and 6 months

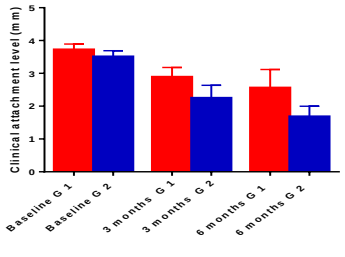

Figure- 5: Histogram illustrating means ± standard deviations CAL in both groups at baseline, 3 and 6 months

4. Discussion

The relationship between the periodontal diseases and some systemic diseases was documented in the previous decades. From this point of view; we select the patients with multiple sclerosis to two reasons in the present study, one of them little information and studies regarding this diseases and the other increase the number of patient suffering from this condition and attending to the dental clinic. There is little overlap between medical and dental research; therefore, oral examinations are present in very few medical-driven cohorts. Considering the high prevalence of Periodontal diseases in the general population (46% in adults 30 and older), even if Periodontal dresses has only a low-to-moderate effect, preventing or treating it could prevent a significant number of Alzheimer, diseases cases and, therefore, deserves unequivocal consideration [25]. Furthermore subjects with Alzheimer, diseases (AD) are more likely to have infections with periodontal bacteria than healthy persons suggesting that perhaps periodontal bacterial infection may be linked to the pathogenesis of AD and poor response to anti-dementia medications [26].

Moderate chronic periodontitis were selected in this study as initial periodontal therapy is the most prevalent form, the procedure cannot achieve the optimal effect in all cases. This is particularly the case with regard to deep periodontal pockets and complicated intraosseal defects when periodontal surgical procedures are necessary as well as antimicrobial agents [27]. Scaling and root planing (SRP) is one of the most commonly utilized procedures for the treatment of periodontal diseases and has been used as the "gold" standard therapy in comparison to other therapeutically procedures [28].

The results of the present study; showed improvement in all clinical periodontal parameters in the form of decreased gingival inflammation and bacterial plaque, pocket depth and clinical attachment level loss following the non- surgical periodontal therapy. The results of this study in agreement with the results of other studies [27,29] revealed improvement in clinical parameters following non-surgical periodontal therapy. These clinical improvements are attributed to the removal of subgingival plaque and disruption of subgingival biofilm leading to a decrease of bacterial counts [30]. Area of interest her; clinical improvement in non-MS chronic periodontitis patient were higher than that of chronic periodontitis patient with MS.

TNF- α present study showed detection of TNF-α in both group included in this study before the periodontal therapy and following the initial treatment these levels were decreased in all patients indicating that decrease in TNF-α levels were as results of removal of the microbial plaque. The results of the present study showed decrease in gingival crevicular fluid TNF-α levels in chronic periodontitis patients with multiple sclerosis than chronic periodontitis patients without MS as well as decrease the gingival inflammation in those patients in spite of the no difference in score of plaque index. These can interpret by the pattern of immune response in those patient as well as effect disease modifying therapy of multiple sclerosis that include, immunosuppressive and immunoregulatory drugs [11]. These drugs may lead to decrease the inflammatory conditions of the periodontium.

The result of the present study showed increased the TNF- α in the GCF of chronic periodontitis patients and these level were decreased after initial periodontal therapy; these result were in agreement with result of several studies that revealed high GCF concentrations of and TNF-α at sites with periodontal destruction and reduced concentrations after periodontal treatment [31, 32]. The association of dental infections and MS activity not extensively studied, perhaps because such infections have never been considered as a potential risk for MS patients. Also is

possible that, hidden infections may be one of the causes for poor response of disease modifying therapy in MS patients.

The gingival inflammatory profile in MS patients can be hidden the periodontal diseases progression, so, those patients should be instructed to frequent dental checkups and periodontal evaluations. In addition, the proper oral hygiene of these patients can be neglected because of the physical disability and depression.

Our limitation in this study was decrease the sample size and assesses the TNF- α in gingival crevicular fluid only. Other studies are needed considering the periodontal conditions in different MS subtypes and patients not yet receiving specific medications.

Conclusions

The results of present study suggest that reduction of gingival inflammatory condition in chronic periodontitis multiple sclerosis patients compared to chronic periodontitis patients without MS disease. The gingival crevicular fluid TNF- α levels in chronic periodontitis patients without MS disease were higher than patient with MS disease that may due to immunoregulatory treatment. In addition the non-surgical periodontal therapy leading to improve the periodontal status and reduction of crevicular fluid TNF- α levels in chronic periodontitis patients with and without MS disease.

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7/23/2017