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The Impact of Fixed Orthodontic Appliance on Oxidative Status and Gingival Health Condition

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ABSTRACT

Aim: The aim of this study was to find out the effect of orthodontic treatment on the oxidative stress of patients with fixed orthodontic appliance in relation to the gingival health condition.

Material and Method: The subject population consisted of 31 participants who were in need of orthodontic treatment with fixed orthodontic appliances. Saliva samples were obtained from all individuals before treatment, at 1st month of treatment and at 3rd months of treatment. Clinical oral hygiene and Gingival (GI) parameters were measured. Samples were investigated to detect Protein Carbonyl (PC), Total Antioxidant Capacity (TAC) levels using ELISA method and Uric Acid (UA) level using spectrophotometer.

Results: All biochemical parameters levels detected in saliva at the 1st and 3rd months of orthodontic treatment is statistically significant according to baseline (P<0.05), a significant positive correlation found between GI and PC at the 1st month.

Conclusion: Employing fixed orthodontic appliances has an impact on the oral environment. Fixed orthodontic treatments result in Shifting in the oxidant-antioxidant balance with mild gingival inflammation.

Keywords: Fixed orthodontic appliance, Oxidative stress, Protein carbonyl, Gingivitis

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INTRODUCTION

Orthodontic treatments provide the best possible dent facial growth, oral functions, and dental aesthetics, by applying a constant mechanical stress to teeth [1]. The use of fixed orthodontic appliances in the treatment of numerous dental abnormalities generates a very complex environment. A limited inflammatory response surrounding the teeth that have been displaced is common to occur. The reaction to the mechanical stresses that occur during orthodontic treatment involves a high variety of inflammatory mediators [2].

The imbalance between the generation of Reactive Oxygen Species (ROS) from the inflammatory cells like PMNLs and monocytes, lymphocytes, platelets, osteoclasts, and fibroblasts; and the capacity of a biological system to detoxify the reactive intermediates or repair the damage caused by them is called oxidative stress [3-4]. Reactive Oxygen Species (ROS) induce oxidative damage by attacking lipids, proteins, and DNA. Various ways can be used to assess the damage [5]. Protein carbonyl is a frequently used parameter in measuring the oxidative damage of the proteins resulting from free radicals.

Steel alloys, titanium, and Ni-Ti are used to make fixed braces. It has been shown that various metals found in brace alloys (such as iron, chromium, copper, and vanadium) are primarily responsible for higher ROS production [6]. In human oral epithelial cells, nickel enhances the activity of intracellular lactate dehydrogenase, which changes the redox equilibrium and induces apoptosis [7].

Because of the reported connections between oxidative stress and clinical symptoms, oxidative stress has been involved in the pathogenesis of numerous diseases [8], It's unclear whether OS is the cause or the result of an illness or may be both [9]. Evidence clearly shows that oxygen-derived free radicals and their derivatives play a key role in the etiology of inflammatory diseases such as gingival diseases and Periodontitis [10].

Gingivitis is an inflammatory condition in which Oxidative Stress (OS) plays a critical role in the pathogenesis,

causing macromolecules such as proteins, DNA, and lipids to degrade [11]. Polymorph nuclear leukocytes create enormous levels of Reactive Oxygen Species (ROS) in response to bacterial microflora and local inflammation, which cause periodontal connective tissue damage by oxidizing lipids, proteins, and nucleic acids [12]. The role of redox systems in the response to Reactive Oxygen Species (ROS) is important because they are involved in a wide range of biological functions, including cell proliferation and growth stimulation, which can lead to gingival disease [13].

Higher nickel residues and protein carbonylation are seen in the gums of patients with gingival disease caused by orthodontic appliances [14]. Protein Carbonyl (PC) groups are relatively stable by-products of oxidized protein produced by a variety of ROS [15]. When compared to lipid peroxidation output, it is the most commonly utilized indicator for oxidative protein damage. Its earlier synthesis and greater stability make it a good target for laboratory measurement and storage [16-17].

Because oxidative stress is caused by an oxidant–antioxidant imbalance, it has been suggested that the TOS to TAC ratio be used as a more accurate indication of oxidative stress in the body [18-19]. Uric acid is a heterocyclic molecule containing carbon, nitrogen, oxygen, and hydrogen that is one of the body's most powerful antioxidants [20].

The goal of this research is to find out the impact of orthodontic treatment on the oxidative stress of patients with fixed orthodontic appliance in relation to the gingival health condition and to find the correlation between fixed orthodontic treatment, salivary oxidative biomarkers and oral health parameters.

MATERIALS AND METHODS

The subject population for this observational case series study was 31 patients (19 Females, 12 Male) with age range between 18 and 23 years (mean age 19.29); being a candidate for fixed orthodontic treatment with non-extraction plan using stainless steel bracket (0.022"X0.028" slot dimension) with MBT system fitted with nickel-titanium wires. For each patient, a written informed consent was given for the participation in this follow up study after giving verbal explanation and written information about the purpose and method of the study. The study has been approved by the scientific committee of Collage of Dentistry/Baghdad University. The following inclusion and exclusion criteria were used in the study:

- Angle Class 1 malocclusion with mild dental crowding,
- Absence of any systemic diseases that can influence oxidative stress,
- No ingestion of any type of medicine or supplements,
- Maintained good oral hygiene throughout the study period,
- Not married nor pregnant female or on menstrual period,
- Not obese or smoker.

The subjects were screened in all aspects of oral hygiene by a specialized dentist before the attachment of the fixed appliances. Before and during the study period, the subjects were provided oral hygiene education on a regular basis. Unstimulated saliva sample and clinical periodontal parameters were measured three times in total before orthodontic treatment and at the first and third months of orthodontic treatment. The saliva samples were collected first before measuring the clinical parameters under standardized condition [21]. The collected samples are centrifuged at (2000-3000 RPM) for approximately 20 minutes, supernatants carefully collected and stored at −20˚C until the biochemical analysis. Silness and Loe Plaque Index (PI) and Loe and Silness Gingival Index (GI) were used to evaluate the oral hygiene and gingival health status in each patient. Biochemical Analysis of Saliva samples, were made in accordance with the package inserts using Human PC ELISA Kit (Bio search Laboratory/china) for protein carbonyl, Human T-AOC ELISA Kit (Bio search Laboratory/china) for total antioxidant capacity and Uricase-POD. Enzymatic colorimetric kit (Spin react/ Spain) for uric acid.

For all of the parameters used in this study, descriptive statistical analyses including means and standard deviations were performed separately in each period of registration. A potential difference in the parameters between three different measurements periods was analysed by Repeated Measure One Way ANOVA. As a result of these evaluations, multiple pairwise comparisons test used to detect statistical difference between two measurements on the same subject. Correlations between clinical parameters and laboratory parameters were examined by Pearson correlation. Analysis of the data was performed using MS-excel (2010) and SPSS Ver. 21.00 (SPSS Inc., IL, and USA) software packages. Statistical power analyses were conducted using G Power version 3.1.9.7. A P value of <0.05 was considered as statistically significant.

RESULTS

The mean age of a total of 31 Patients, including 12 males and 19 females with ages ranging between 18 and 23 years, is 19.29 ± 1.68 years. Among patients treated with fixed orthodontic treatment, saliva samples were collected before orthodontic treatment and at the first and third months. The mean and standard deviation of clinical gingival parameter prior to the treatment and at the first and third months and the test result on the comparison of these periods to each other are shown in (Table 1).

Table 1: clinical parameters prior to the treatment and at the first and third months.

Saliva parameters	N	Baseline	1st month of treatment	3rd month of treatment	P-value
		Mean ± std.	Mean ± std.	Mean ± std.	
PI	31	0.11 ± 0.03	0.114 ± 0.026	0.112 ± 0.038	0.47
GI	31	0.073 ± 0.064	0.309 ± 0.182	0.473 ± 0.132	0.000*

PI: Plaque Index, GI: Gingival Index, *=Significant at p<0.05.

Accordingly, it has been determined that there was a significant difference between the periods in the gingival index at different stages of the treatment (P<0.05). No significant difference in plaque index between the periods (P>0.05) was found.

The mean and standard deviation of biochemical parameters of saliva before the treatment and at the first and third months and the test result on the comparison of these periods to each other are shown in (Table 2).

Table 2: Biochemical salivary parameters prior to the treatment and at the first and third months.

Saliva parameters	N	Baseline	1st month of treatment	3rd month of treatment	P value
		Mean ± std.	Mean ± std.	Mean ± std.	
PC	31	53.586 ± 16.050	86.612 ± 28.49	82.774 ± 39.003	0.000*
TAC	31	5.872 ± 1.583	9.414 ± 3.426	10.406 ± 4.161	0.000*
UA	31	0.088 ± 0.051	0.109 ± 0.058	0.116 ± 0.047	0.002*

PC: Protein Carbonyl, TAC: Total Antioxidant Capacity, UA: Uric Acid, *=Significant at p<0.05.

As a result, a significant difference between the periods in terms of all the parameters measured in saliva at different stages of the treatment (P<0.05) was found.

The results of multiple pairwise comparisons test to determine any significant difference between the periods in statistically significant parameters according to the one way ANOVA test are shown in (Table 3).

Table 3: The results of multiple pairwise comparisons to determine any significant difference between the periods in statistically significant parameters according to the one way ANOVA test.

Variable	Baseline–1st month		Baseline– 3rd month		1st month – 3rdmonth	
	MD	P-value	MD	P-value	MD	P-value
GI	-0.236	0.000*	-0.4	0.000*	-0.164	0.000*
PC	-33.027	0.000*	-29.189	0.001*	3.838	0.650^
TAC	-3.542	0.000*	-4.534	0.000*	-0.992	0.262^
UA	-0.021	0.018*	-0.027	0.001*	-0.006	0.498^

GI: Gingival Index, PC: Protein Carbonyl, TAC: Total Antioxidant Capacity, UA: Uric Acid, *=Significant at p<0.05

Consequently, in Saliva measurements, a significant increase has been shown in all biomarkers levels between pre-treatment and first month of treatment and between pre-treatment and third month of treatment (P<0.05), while, a significant increase has been shown between all the periods in GI level (P<0.05).

There was a significant positive correlation between gingival index and salivary protein carbonyl level after one month of the fixed orthodontic treatment as shown in (Table 4).

Table 4: The correlations between salivary oxidative biomarker and gingival health condition.

Periods	Variable	PC		TAC		UA	
		r	p-value	r	p-value	r	p-value
Baseline	GI	0.179	0.344	0.053	0.781	0.13	0.494
1st month	GI	0.401	0.025*	0.104	0.585	0.231	0.22
3rd month	GI	0.103	0.589	0.142	0.455	0.13	0.493

GI: Gingival Index, PC: Protein Carbonyl, TAC: Total Antioxidant Capacity, UA: Uric Acid, *=Significant at p<0.05.

DISCUSSION

The aim of this study was to evaluate oxidative stress in the unstimulated saliva of patients treated with fixed orthodontic appliances; the harmful effects of free radicals are utilized by an antioxidant system.

A change in this balance in favour of free radicals result in oxidative tissue damage associated with oxidative stress [24].

In the literature, there was no previous human prospective study measuring protein carbonyl as oxidative stress biomarker that may occur as a result of inflammation in tissues with orthodontic treatment. Therefore, this study is the first on this issue.

Protein carbonylation is one of the most essential oxidative changes, which is recognized as a unique characteristic of oxidative stress-related disorders. It refers to an irreversible oxidative modification caused by Reactive Oxygen Species (ROS) in which a carbonyl group is introduced into the polypeptide chain, causing changing in structure formation, that have a significant impact on protein function [25-26].

In present study, there was an increase in the level of protein carbonyl after one month of orthodontic treatment followed by a decrease at the third month [14]. Reported that there is greater PC in patients with fixed orthodontic appliance or have history of orthodontic treatment [27].

Found that despite the decrease in oxidative stress biomarker after three months it remains higher to the baseline values also, [28]. reported that Oxidative Status Index (OSI) was elevated one week after orthodontic treatment and then decreased through the next six months of orthodontic treatment.

The increase in the PC level is due to nickel and iron released from orthodontic appliances to the oral environment producing Hydroxyl radical which reacts rapidly with DNA, lipids, and proteins causing structural damage, which is often irreversible [14,29-30].

Antioxidants (enzymatic and non-enzymatic) protect against free radical effects caused by harmful metals.

In vitro, antioxidant prevents protein oxidation even in the presence of redox-active iron (or copper), according to previous findings [29].

The present study results revealed continuous increase in total antioxidant capacity and uric acid, which is one of the most antioxidants in the body [20]. In regard to UA same result was found [28].

A significant increase in TAC after one month of metallic appliances was also reported [24]. an increase in TAC after ten weeks was found [31].

Elevating salivary TAC level related to two probable reasons: First, as a defensive mechanism against tissue inflammatory alterations (a compensatory response to periodontal disease-induced oxidative stress); Second, when having oral discomfort, patients adjust their diet to include more liquid foods and juices that are generally high in nutrients, vitamins, and antioxidant components, which will improve the body's and saliva's antioxidant status [32].

Uric acid is a physiological antioxidant in saliva that represents the majority of total antioxidant capacity while also having the ability to scavenge metals and react with biological oxidants [33].

Because of the redox balance idea, even one substance, such as a small-molecule redox-active vitamin, has the potential to change the system as a whole, although Antioxidant defence systems have a high level of specificity [26].

The other aim of this study was to investigate the influence of fixed orthodontic appliance on gingival health status; in particularly only patients with good oral hygiene was included in the study, in accordance with the study [34].

With continued oral hygiene instruction throughout the treatment for patient motivation, similar to the investigations [35-36].

There were no correlation between the level of dental hygiene and oxidative stress, same result was found [31]. In this study, GI value was increased at different periods of treatment with mild gingivitis was noticed. Same result was found [37-40].

Suggested that the release of metal ions were higher at early stages of orthodontic treatments, this increase in oxidative stress levels in the early stages may be the reason of gingival tissues inflammation.

Still the measured values were within physiological limits. Orthodontic tooth movement result in a non-infectious inflammatory response after a persistent mechanical force to the Periodontal Ligament (PDL); the production of pro inflammatory-mediators, such as cytokines which are highly detected in gingival reticular fluid from the PDL of orthodontic ally forced teeth [41-43].

Facilitate the enrolment of Polymorph nuclear leukocytes at the inflammatory site to release oxidants [44].

Oxidants are important biological signals generated by mechanical cell stress and blood flow changes under physiological and pathological conditions [45-46]. Oxidative stress activates inflammatory mediator production in periodontium [47].

Orthodontic force generates oxidative stress in the PDL and dental pulp [48].

CONCLUSION

Employing fixed orthodontic appliances has an impact on the oral environment. Orthodontic treatment induced oxidative stress in saliva in some trials, but not in others. The defence mechanism of antioxidant and the body adaptation compensate the oxidative stress biomarker elevation with mild gingival inflammation. The effect of mechanical stimulation or damage to nearby tissues caused by the device attachment process on saliva's oxidative status cannot be considered out. So that better understand the function of orthodontic therapy in affecting oxidative stress in saliva, Also prescribing antioxidant supplements like vitamins during the orthodontic treatment may reduce the risk of gingival inflammation. More research is needed with bigger samples and consideration of additional risk factors.

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