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Study On Evaluation Of Salivary Tumor Necrosis Factor-Alpha Level In The Treatment With Fixed Appliances And Clear Aligners

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Abstract

Background: *Tumor necrosis factor-alpha (TNF-α), a key pro-inflammatory cytokine, plays a significant role in orthodontic tooth movement by mediating periodontal and bone remodeling processes. The level of TNF-α in saliva may serve as a non-invasive biomarker for monitoring inflammatory responses during orthodontic treatment with different appliances.*

Objective: *This study aimed to evaluate and compare salivary TNF-α levels in patients undergoing orthodontic treatment using fixed appliances and clear aligners over a 3-month treatment period.*

Methodology: *A total of 60 orthodontic patients aged 18–30 years were recruited and divided into two equal groups: Group A (fixed appliances) and Group B (clear aligners). Unstimulated saliva samples were collected at baseline (T0), 1 week (T1), 1 month (T2), and 3 months (T3) post-application of appliances. TNF-α concentrations were measured using ELISA. Clinical parameters such as plaque index and gingival index were also recorded. Data were analyzed using repeated-measures ANOVA and independent t-tests.*

Results: *Both groups showed a significant increase in salivary TNF-α at T1 (Group A: 48.2 ± 6.3 pg/mL; Group B: 41.7 ± 5.8 pg/mL; $p < 0.001$) compared to baseline (Group A: 12.3 ± 2.9 pg/mL; Group B: 11.9 ± 3.1 pg/mL). Levels declined gradually by T3 but remained elevated compared to T0. At all time points, Group A exhibited significantly higher TNF-α levels than Group B ($p < 0.05$). Plaque and gingival indices were also higher in Group A throughout the study period.*

Conclusion: *Fixed appliances induce a greater inflammatory response as indicated by elevated salivary TNF-α levels compared to clear aligners. Monitoring salivary TNF-α can be a valuable, non-invasive biomarker for assessing orthodontic treatment-associated inflammation.*

Keywords: *TNF-alpha, saliva, fixed orthodontic appliances, clear aligners, inflammation, biomarker*

INTRODUCTION

Orthodontic tooth movement is a complex biological process involving controlled mechanical forces that stimulate remodeling of periodontal ligament and alveolar bone. This process is accompanied by a cascade of cellular and molecular events characterized by the release of inflammatory mediators, among which tumor necrosis factor-alpha (TNF-α) is a critical cytokine [1]. TNF-α is secreted by macrophages, monocytes, and fibroblasts in response to mechanical stress and is involved in osteoclast activation and matrix degradation during tooth movement [2].

Saliva is an attractive diagnostic medium as it contains a variety of biomarkers reflective of systemic and local inflammatory states. Among these, salivary TNF-α has gained attention due to its role in periodontal inflammation, bone remodeling, and immune modulation during orthodontic treatment [3]. The non-

invasive nature of salivary collection makes it suitable for repeated measures and longitudinal monitoring in orthodontic patients **[4]**.

Orthodontic appliances—whether fixed (brackets and wires) or removable (clear aligners)—induce varying degrees of force and tissue response. Fixed appliances, due to their constant application of force and challenges in maintaining oral hygiene, may induce a greater inflammatory response compared to clear aligners which allow intermittent force application and better hygiene maintenance **[5]**. Recent studies have suggested that differences in appliance type may result in variable levels of inflammatory cytokines, though direct comparative evidence remains limited **[6]**.

Despite the growing popularity of clear aligners, there is insufficient data comparing their biological impact with conventional fixed appliances, particularly in terms of inflammatory mediator expression in saliva. Understanding this relationship is crucial in tailoring orthodontic strategies and improving patient outcomes.

Objective: This study aims to evaluate and compare the levels of salivary TNF-α in patients undergoing orthodontic treatment with fixed appliances and clear aligners over a 3-month period, and to assess associated clinical periodontal parameters.

MATERIALS AND METHODS

Sample Size and Participant Selection

Sixty orthodontic patients aged between 18 and 30 years, requiring mild-to-moderate alignment correction, were recruited. Participants were randomly assigned into two groups (n=30 each):

- **Group A:** Fixed orthodontic appliances (0.022-inch slot MBT brackets)
- **Group B:** Clear aligners (commercially fabricated using polyurethane material)

Inclusion Criteria:

- Healthy individuals with Class I malocclusion
- No systemic diseases or history of smoking
- Good periodontal health (plaque index <1)

Exclusion Criteria:

- Periodontal disease or caries
- Antibiotic or anti-inflammatory therapy within 1 month
- Pregnancy or lactation
- Previous orthodontic treatment

Materials Used

- ELISA kits specific for human TNF-α (R&D Systems)
- Sterile Salivette tubes for saliva collection
- Calibrated periodontal probes
- Digital stopwatch

Experimental Procedure

Saliva Collection:

Unstimulated saliva was collected from all participants between 9–11 AM to control for diurnal variation. Participants were instructed to refrain from eating, drinking, or oral hygiene procedures for 90 minutes prior.

Samples were collected at the following time intervals:

- T0 (baseline before appliance placement)
- T1 (1 week)
- T2 (1 month)
- T3 (3 months)

Collected samples were immediately centrifuged at 3000 rpm for 10 minutes and stored at –80°C until assay.

Clinical Evaluation:

- **Plaque Index (Silness and Löe)**
- **Gingival Index (Löe and Silness)**

Indices were measured at T0, T2, and T3 to correlate with TNF-α levels.

TNF-α Assay:
Salivary TNF-α concentrations were quantified using ELISA. Each sample was tested in duplicate. Concentrations were expressed in pg/mL.

Statistical Analysis
Data were analyzed using SPSS v27.0. Descriptive statistics were calculated for all variables. Intergroup comparisons were made using independent t-tests. Intragroup comparisons over time were assessed with repeated-measures ANOVA followed by Bonferroni post-hoc test. $p < 0.05$ was considered statistically significant.

RESULTS

Participant Characteristics
All 60 participants completed the study. The mean age was 22.4 ± 3.2 years in Group A and 21.9 ± 3.5 years in Group B. There were 18 females and 12 males in each group. No dropouts or adverse events were reported.

Salivary TNF-α Levels

Table 1: Mean Salivary TNF-α Levels (pg/mL)

Time Point	Group A (Fixed Appliances)	Group B (Clear Aligners)	p-value
T0	12.3 ± 2.9	11.9 ± 3.1	0.621
T1	48.2 ± 6.3	41.7 ± 5.8	<0.001
T2	35.4 ± 5.1	29.3 ± 4.7	<0.001
T3	22.8 ± 3.6	18.7 ± 2.9	<0.001

Significant increases from baseline were observed at all time points ($p < 0.001$ within groups). Group A exhibited consistently higher TNF-α levels compared to Group B throughout the study period.

Plaque and Gingival Index Scores

Table 2: Plaque and Gingival Index Scores

Index	Group A (T3)	Group B (T3)	p-value
Plaque Index	1.7 ± 0.4	0.9 ± 0.3	<0.001
Gingival Index	1.5 ± 0.5	0.8 ± 0.2	<0.001

Higher clinical index scores in Group A indicate increased plaque accumulation and gingival inflammation, correlating with elevated TNF-α levels.

DISCUSSION

This study demonstrates that salivary TNF-α levels significantly increase during the initial phase of orthodontic treatment, peaking at 1 week and gradually declining over three months. Patients treated with fixed appliances exhibited higher levels of TNF-α compared to those using clear aligners, suggesting a more intense inflammatory response [7].

Our findings align with those of Alfaqeeh and Andersson who showed elevated TNF-α in gingival crevicular fluid following orthodontic force application [8]. Similar elevations in saliva suggest that salivary TNF-α reflects periodontal remodeling and may serve as a reliable non-invasive biomarker [9].

The greater inflammatory response in fixed appliance users can be attributed to continuous force application, appliance-induced irritation, and difficulty in maintaining oral hygiene [10]. In contrast, aligners allow better plaque control and apply intermittent force, possibly reducing cytokine expression [11,12].

An important clinical implication is the potential use of salivary TNF-α for monitoring treatment progression and identifying patients at risk of excessive inflammation or periodontal breakdown. Furthermore, orthodontic strategies that minimize unnecessary inflammation could improve patient comfort and treatment outcomes.

Strengths: The study employed standardized saliva collection protocols, validated ELISA assays, and longitudinal design. Clinical indices provided supportive evidence for biochemical findings.

Limitations: Small sample size and short duration limit generalizability. Future studies should include extended follow-up, GCF analysis, and evaluation of other cytokines such as IL-1β and RANKL.

CONCLUSION

Salivary TNF-α levels rise significantly during the early phase of orthodontic treatment, particularly with fixed appliances. Clear aligners are associated with a milder inflammatory profile. Monitoring salivary TNF-α may provide a valuable tool for assessing biological responses and guiding personalized orthodontic care.

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