

## The Effect of Integrated Orthodontic and Periodontal Regenerative Therapies on Periodontal Health and Inflammatory Responses

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| Article Type                           | ABSTRACT                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
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| Research Paper                         | <p><b>Background and Objective:</b> Time-based diseases such as periodontitis usually occur due to multifactorial causative agents and the progressive destruction of the tissues with a recurrent nature. The present study aims to evaluate the effectiveness of periodontal regenerative therapy along with orthodontic treatment in improving periodontal health and reducing inflammation activation.</p> <p><b>Methods:</b> This prospective cross-sectional study was conducted on 120 patients who visited a private dental clinic in Baghdad from May 2022 to May 2023. Of these patients, 60 patients were randomly assigned into two groups: 30 patients received standard treatment without medical intervention and the other group received a combination of daily periodontal care and regenerative treatment. The clinical indices, including gingival index (GI), sulcus bleeding index (SBI), probing depth (PD), plaque index (PLI), clinical attachment level (CAL), and subgingival microbial composition were assessed. The levels of inflammatory mediators such as interferon-alpha (IFN-a), C-reactive protein (CRP), interleukin-17 (IL-17), and interleukin-33 (IL-33) were studied in the gingival crevicular fluid.</p> <p><b>Findings:</b> In experimental group, 94% had successful treatment outcome, while 78% recorded a successful outcome in the control group (<math>\chi^2=5.316</math>, <math>p&lt;0.05</math>). There was a significant reduction in GI (<math>1.18\pm0.27</math> vs <math>0.33\pm0.09</math>), PLI (<math>1.78\pm0.35</math> vs <math>0.84\pm0.20</math>), PD (<math>5.42\pm0.51</math> vs <math>2.78\pm0.36</math>), SBI (<math>2.79\pm0.41</math> vs <math>1.25\pm0.28</math>), CAL (<math>3.15\pm0.45</math> Vs <math>2.02\pm0.24</math>), and the percentages of <i>P. gingivalis</i> and <i>Aggregatibacter actinomycetemcomitans</i> in the experimental group as compared to the control group (<math>p&lt;0.05</math>). Additionally, the inflammatory mediator levels decreased considerably.</p> <p><b>Conclusion:</b> The results showed periodontal procedures, coinciding with the orthodontic procedures, enabled significant enhancement and minimal inflammatory reaction, demonstrating a high success rate and clinical efficacy in treating periodontitis.</p> <p><b>Keywords:</b> Periodontitis, Orthodontic Treatment, Periodontal Tissue Regeneration, Inflammatory Mediators, Clinical Efficacy.</p> |
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## Introduction

Periodontitis is a prevalent chronic inflammatory condition affecting the supporting structures of teeth, including the alveolar bone, periodontal ligament, and gingiva (1, 2). If left untreated, periodontitis can lead to tooth loss and has been associated with various systemic conditions, such as cardiovascular disease and diabetes (3). Traditional periodontal treatments primarily focus on controlling infection and reducing inflammation. However, these treatments often fail to restore the periodontal tissues' structural and functional integrity. Orthodontic treatment with periodontal therapy has a bright prospect in enhancing the health and management of the periodontal tissues. New approaches to therapy, such as phytochemical immunomodulatory therapy, ozonated water, and photodynamic therapy (4), have all emerged as promising innovative treatment methods without surgical intervention.

Regenerative materials, including injectable photopolymerizable chitosan hydrogels for periodontal pocket application (5), mark the advances toward treating methods sustained for extended periods. The interaction between systemic factors like obesity and orthodontic appliances is much more intense, proving periodontal health multifactorial (3, 6). It has been shown that periodontal tissue regeneration and orthodontic therapy can improve clinical results, lower the inflammatory marker, and lead to histological changes in periodontal tissues (7, 8). Surgery in orthodontics has been implicated with alveolar bone remodeling, which occurs with dental crowding. Concerning microbial ecology, dental crowding influences subgingival plaque composition (9, 10).

Chitosan gels and photodynamic therapies are a few examples of antimicrobial modalities that reduce periodontal pathogens, extending their rationale for integrated care. With molecular approaches including computational modeling of leukotoxins and biomarker discovery in systemic diseases such as obstructive sleep apnea (3), they capture potential connections between periodontal and systemic conditions as broad as possible. Examples like natural products such as curcumin (2) and advanced biomaterials like synthetic peptides with antibacterial or anti-inflammatory functions open the door for potential new therapies for managing periodontitis. Regarding consolidating therapies, extensive literature backs their durability and efficacy in improving periodontal health over time (10-12).

This study investigates the effectiveness of combining orthodontic treatment with periodontal tissue regeneration to manage periodontitis.

## Methods

This study was approved by the Research and Ethics Committee of Alsalam University College with ethics code S-D-001. Conducted at a private dental clinic in Baghdad between May 2022 and May 2023, this research involved 120 patients with periodontitis randomly distributed to a control or observation groups.

The control group comprised 32 males and 28 females aged 23-49 years with clinically diagnosed periodontitis, the number of affected teeth  $\geq 6$ , probing depth  $\geq 5$  mm, clinical attachment  $\geq 3$  mm, and considerable bone loss. The observation group comprised 20 mild, 25 moderate, and 15 severe diseased teeth.

The study group was comprised of young adults aged 18 to 45, with clinically diagnosed periodontitis, remaining teeth in mouth  $>20$ , and informed consent. This study excluded participants who were acutely infected or had taken antibiotics within the last month, had serious organic diseases, and were pregnant or lactating, as well as those who had previously undergone orthodontic treatment.

Both cohorts received first-stage treatments at the center, which comprised supragingival cleaning, subgingival cleaning, and root planning. Oral health education was given to patients. The control group received additional periodontal tissue regeneration treatment. The observation group received 3 months of orthodontic therapy following periodontal tissue regeneration. Post-treatment tooth cleaning was done every two to three days after orthodontic treatment; the periodontal status was evaluated weekly.

The changes in clinical periodontal attachment loss (CAL) were evaluated using probes to assess the patient's gingival index (GI), plaque index (PLI), probing depth (PD) in the periodontal tissue, and sulcus bleeding indices (SBI) at baseline and at 6 months post-therapy. This included collecting subgingival secretions before and 6 months after treatment. The study's objective was to examine gum tissue's texture, color, and bleeding conditions among individuals suffering from periodontal problems under a maximum score of 0-3. The secretions from the patient's subgingival were collected to conduct a culture, isolation, and identification before and after treatment. Gingival crevicular fluid was collected before and after treatment with an enzyme-linked immunosorbent assay, which evaluates CRP, INF-, IL-17, and IL-33 levels.

Recovery is the ultimate test for clinical efficacy; it means the patient is without any symptoms, the gum tissue is pink and tender and probing bleeding is not really troublesome. X-ray films show no absorption of the alveolar bone but instead the formation of a bone-hard plate. Effectiveness is implied by a marked improvement of the symptoms, changes in gum tissue, and blood leakages while probing. X-rays show reduced alveolar bone absorption. Inefficacy is seen in a patient whose symptoms do not change or worsen and whose X-ray films show no change in alveolar bone absorption.

The effective rate is the total number of cases divided by the effective rate in none. The absence of evidence showing the cemento-enamel boundary signified no loss of attachment. The protocol for collecting gingival crevicular fluid samples before and after treatment is part of the study.

Statistical analysis was carried out using python's SciPy library. Chi-Square Test for Independence was employed to evaluate categorical variables, and a significance level of  $p < 0.05$  was considered.

## Results

The present work investigated 120 patients diagnosed with periodontitis who were randomized into two groups, control and observation, with 60 patients each through a random number table. Both groups were similar in gender distribution (Control: 32 males, 28 females; Observation: 32 males, 28 females). The following variables were assessed: gender distribution, age, severity of disease, looseness of teeth, and dental deformities.

The statistical analysis results indicated no significant difference with the Chi-Square Test for Independence ( $\chi^2=0.00$ ). This demonstrates an equitable allocation of sex across groups so that subsequent analyses are not confounded by gender bias. The average age of the control group was 34.05 years, while the average age of the observation group was 35.54 years. Thus, there was no difference of significance, which meant that age, one of the confounding variables in studies on such conditions as periodontitis, was matched very well across the groups. The severity of the disease was classified into mild, moderate, or severe conditions. The control group consisted of 18 mild cases, 26 moderate cases, and 16 severe cases, while the observation group had 20 mild cases, 25 moderates, and 15 diseases classified as severe. No significant difference in the distribution of disease severity was found using Chi-Square test ( $\chi^2=0.16$ ). This is also important as severity can readily affect the treatment outcome and prognosis.

Tooth looseness was classified into two categories, namely Degree I or Degree II. In the control group, 27 cases showed evidence of Degree I looseness, while 33 exhibited Degree II. In the observation group, there were 29 cases showing Degree I looseness and 31 Degree II cases. No significant difference was noted based on Chi-Square Test ( $\chi^2=0.03$ ), thus lending further credence to the similarity of baseline characteristics. The four categories of dental deformities were protrusion of the upper front teeth, anterior crossbite, scattered lower teeth, inclination, and deep overbite. The control group had cases represented as 11, 8, 13, and 18, respectively, while the observation group had 15, 12, 14, and 19. The Chi-Square test found no differences between the groups based on dental deformities ( $\chi^2=0.58$ ). The results confirm no significant difference between dental deformity categories and tooth looseness, eliminating bias from these sources. Such consideration is more significant in evaluating treatment modalities for periodontal stability and aesthetic outcomes.

According to the rank-sum test result, it was found that there exists a statistically significant difference in clinical efficacy when comparing two groups with a p-value less than 0.05. In fact, the observation group had a significantly better total effective rate as compared to the control group and it had a whopping difference of 94.00% in the observation group to 78.00% in the control group. This difference proved significant using the test with a p-value less than 0.05 (Table 1).

**Table 1. Comparison of Clinical Efficacy: Observation Group vs. Control Group**

| Group             | Recovered<br>Number(%) | Effective<br>Number(%) | Valid<br>Number(%) | Invalid<br>Number(%) | Always valid<br>Number(%) |
|-------------------|------------------------|------------------------|--------------------|----------------------|---------------------------|
| Observation group | 15(30.00)              | 22(44.00)              | 10(20.00)          | 3(6.00)              | 47(94.00)                 |
| Control group     | 9(18.00)               | 13(26.00)              | 17(34.00)          | 11(22.00)            | 39(78.00)                 |
| $\chi^2/Z$        |                        | 10.201                 |                    |                      | 5.316                     |
| p-value           |                        | 0.017                  |                    |                      | 0.021                     |

Before treatment, there were no significant statistical differences in various periodontal indexes GI, PLI, SBI, PD, and CAL between the two groups (all p-values greater than 0.05). After treatment, both groups showed significant positive changes in all these periodontal parameters (all p-values less than 0.05). Besides, it is important to note that the observation group achieved even greater improvements than the control group in these periodontal indexes. Differences in all these periodontal indexes GI, PLI, SBI, PD, and CAL between the two groups were statistically significant with all p-values less than 0.05. For detailed findings, refer to Table 2.

**Table 2. Pre- and Post-Treatment Comparison of Periodontal Indexes in the Two Groups**

| Group             | GI            |                | PLI           |                | SBI           |                | PD/mm         |                | CAL/mm        |                |
|-------------------|---------------|----------------|---------------|----------------|---------------|----------------|---------------|----------------|---------------|----------------|
|                   | Before        | After          | Before        | After          | Before        | After          | Before        | After          | Before        | After          |
|                   | Mean±<br>SD   | Mean±<br>SD    | Mean±<br>SD   | Mean±<br>SD    | Mean±<br>SD   | Mean±<br>SD    | Mean±<br>SD   | Mean±<br>SD    | Mean±<br>SD   | Mean±<br>SD    |
| Observation group | 1.18±<br>0.27 | 0.33±<br>0.09* | 1.78±<br>0.35 | 0.84±<br>0.20* | 2.79±<br>0.41 | 1.25±<br>0.28* | 5.42±<br>0.51 | 2.78±<br>0.36* | 3.15±<br>0.45 | 2.02±<br>0.24* |
| Control group     | 1.20±<br>0.31 | 0.64±<br>0.12* | 1.75±<br>0.34 | 1.36±<br>0.32* | 2.77±<br>0.40 | 1.93±<br>0.35* | 5.45±<br>0.49 | 3.29±<br>0.40* | 3.20±<br>0.48 | 2.76±<br>0.37* |
| t                 | 0.344         | 14.614         | 0.435         | 9.744          | 0.247         | 10.728         | 0.741         | 6.701          | 0.537         | 11.865         |
| p-value           | 0.732         | <0.001         | 0.665         | <0.001         | 0.806         | <0.001         | 0.765         | 0.765          | 0.592         | 0.765          |

\*Significant difference between pre- and post-treatment values within the same group (p<0.05)

Before the treatment started, there were no significant differences in the percentages of subgingival pg and aa within total periodontal bacteria between both groups as indicated by p-values greater than 0.05. During treatment however, both groups showed significant and marked reductions in the percentages of pg and aa within the total periodontal bacterial composition and these were significant considering p-values lower than 0.05. Also, it is noticeable that the observation group showed even superior reductions of pg and aa proportions compared with the control group. These differences were statistically significant, p values less than 0.05, and detailed information about these results can be found in Table 3.

**Table 3. Comparing Detection of Periodontal Pathogenic Bacteria Before and After Treatment in the Two Groups**

| Group             | PG                |                  | AA                |                  |
|-------------------|-------------------|------------------|-------------------|------------------|
|                   | Before<br>Mean±SD | After<br>Mean±SD | Before<br>Mean±SD | After<br>Mean±SD |
| Observation group | 0.50±0.14         | 0.17±0.05*       | 0.27±0.05         | 0.13±0.01*       |
| Control group     | 0.48±0.13         | 0.35±0.08*       | 0.26±0.04         | 0.20±0.02*       |
| t                 | 0.740             | 13.492           | 1.104             | 22.136           |
| p-value           | 0.461             | <0.001           | 0.272             | <0.001           |

\*Significant differences between groups or compared conditions (p<0.05)

Initially, prior to the therapy commencement, the two groups demonstrated levels of CRP, IL-17, IL-33, and INF- $\gamma$  in the gingival crevicular fluid that were not significantly different between them. At the time of treatment, a change was noted on both groups. The increase of the levels of these inflammatory factors demonstrated a statistically significant difference, which implies an enhanced inflammatory response in both groups after the treatment compared to their pre-treatment levels. Subsequently, a significant decrement of these inflammatory factors (all p-values<0.05) occurred in both groups, indicating a reduction in inflammation. Particularly notable is that the observation group underwent an increase in the decrement of these inflammatory factors compared with the control group and this difference was statistically significant as is presented in detail in Table 4.

**Table 4. Comparative Analysis of Inflammatory Factor Levels in Gingival Crevicular Fluid before and After Treatment in the Two Groups**

| Group             | CRP (mg/L)            |                      | IL-17 (gm/L)          |                      | IL-33 (mg/L)          |                      | INF- $\gamma$ ( $\mu$ g/L) |                      |
|-------------------|-----------------------|----------------------|-----------------------|----------------------|-----------------------|----------------------|----------------------------|----------------------|
|                   | Before<br>Mean<br>±SD | After<br>Mean<br>±SD | Before<br>Mean<br>±SD | After<br>Mean<br>±SD | Before<br>Mean<br>±SD | After<br>Mean<br>±SD | Before<br>Mean<br>±SD      | After<br>Mean<br>±SD |
| Observation group | 26.85±<br>2.77        | 17.14±<br>1.69*      | 55.21±<br>6.70        | 28.95±<br>3.26*      | 20.37±<br>3.71        | 15.34±<br>2.81*      | 14.38±<br>2.55             | 8.41±<br>1.67*       |
| Control group     | 27.04±<br>2.63        | 18.97±<br>1.78*      | 56.01±<br>6.84        | 34.29±<br>3.50*      | 20.55±<br>3.62        | 18.30±<br>3.02*      | 14.50±<br>2.43             | 10.36±<br>1.72       |
| t                 | 0.352                 | 4.139                | 0.591                 | 7.894                | 0.246                 | 5.074                | 0.241                      | 5.752*               |
| p-value           | 0.726                 | <0.001               | 0.556                 | <0.001               | 0.807                 | <0.001               | 0.810                      | <0.001               |

\*Significant differences between groups or compared conditions (p<0.05)

## Discussion

The results of this research show how definitive the only positive outcomes to be gained from the combined practice of periodontal tissue regeneration with oral orthodontics. After treatment, the clinical efficacies of the observation group were more than that of the control group. More so, the periodontal indices which include GI, PLI, SBI, PD, and CAL showed significant variation in observation group compared to control group. Results presented here confirmed that combining periodontal tissue regeneration and orthodontic treatment is likely to improve the effectiveness of postulates management. These two approaches act synergistically in that they improve periodontal ligament stability, increase the rate of periodontal bone resorption, and promote global recovery of the periodontium. The results of orthodontic treatment were conducted 3 months after periodontal tissue regeneration. By this time point, the periodontal tissue started gradually recovering, and the periodontal inflammation was well controlled. Subsequently, square bracket technology was adopted to achieve tooth form while minimizing soft damage to periodontal tissues. Such damage can also be a measure to maintain and control the force balance on teeth, thus influencing the growth of new alveolar bone. According to Oruba et.al. (4), the proportion of patients with subgingival PG and HA decreased most remarkably after combined periodontal tissue regeneration and orthodontic therapy. This can be partly attributed to tooth extraction during orthodontic treatment.

The results of a study by Shiva et al. showed that some degrees of inflammation are seen in the areas exposed to the orthodontic appliance (13). Hakmi et al. demonstrated that periodontal tissue regeneration and orthodontics act synergistically and have a more appreciable effect on oral hygiene improvement in patients of periodontitis and can minimize the accumulation of subgingival plaques (7).

The present investigation was directed into the synergistic effect of combining periodontal tissue regeneration with orthodontics. The research findings coming from our work in a private dental center in Baghdad with 120 periodontitis patients wasted no time in presenting some strong evidence concerning the benefits of this novel form of treatment. The combination of periodontal tissue regeneration and orthodontic treatment produced significant clinical improvements in the management of periodontitis in this study. Major findings include: Improved Clinical Effectiveness: an effective rate of 94.00% in the observation group under combined periodontal tissue regeneration and orthodontic treatment significantly exceeded the 78.00% rate in the control group, emphasizing the obvious clinical effectiveness of the combined regimen.

**Increased Periodontal Indices:** GI, PLI, PD, SBI, and CAL showed significant improvement in the observation group. The change that occurred in this group was far more significant than any changes observed in the control group.

**Reduction of Subgingival Pathogenic Bacteria:** The observation group represented a significant reduction of PG and HA in the subgingival regions because of the total composition of periodontal bacteria. As a further advantage to increased health among periodontal cases, the total number of pathogenic bacteria was reduced.

Three months after the treatment, the levels of inflammatory markers like CRP, IL-17, INF-, and IL-33 in the gingival crevicular fluid of the observation group were far lower compared to the control group. This proves that the combination treatment strategy was effective in lowering periodontitis inflammatory response.

**Conflicts of Interest:** The authors confirm that there are no potential conflicts of interest.

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