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# **O**riginal **R**esearch

# Assessment of levels of TNF-a in patients undergoing fixed orthodontic treatment

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## ABSTRACT:

**Background:** Orthodontic forces cause an initial inflammatory response followed by alterations in the vascular and neural envelope and perpetual bone and tissue remodelling accompanied by paracrine release of bioactive mediators. The pro-inflammatory cytokines include Interleukin 1b (IL-1 b), IL-2, IL-5, IL-6, IL-8, interferon  $\gamma$  (IFN  $\gamma$ ), tumor necrosis factor alpha (TNF $\alpha$ ) and granulocyte macrophage colony stimulating factor (GM-CSF), which induce classic inflammation markers. Hence; the present study was conducted for assessing the levels of TNF- $\alpha$  in patients undergoing fixed orthodontic treatment. **Materials & methods:** A total of 20 patients scheduled to undergo fixed orthodontic treatment were enrolled in the present study. Complete demographic details of all the patients were obtained. During the pre-treatment phase, all the patients were recalled in the morning and GCF samples were obtained. All the samples were sent to laboratory where auto-analyser was used for assessing TNF- $\alpha$  level. Assessment of TNF- $\alpha$  levels was done one month after starting of the fixed orthodontic treatment and six months after starting of the fixed orthodontic treatment. **Results:** Mean TNF- $\alpha$  level at pre-treatment, one month post-treatment and six months post-treatment were found to be 6.72 pg/mL, 6.51 pg/mL and 6.59 pg/mL respectively. In the present study, while comparing the mean TNF- $\alpha$  s at different time intervals, non-significant results were obtained. **Conclusion:** Fixed orthodontic treatment doesn't alter the TNF- $\alpha$  levels.

Key words: Fixed orthodontic treatment, Tumour necrosis factor

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## INTRODUCTION

Orthodontic forces cause an initial inflammatory response followed by alterations in the vascular and neural envelope and perpetual bone and tissue remodelling accompanied by paracrine release of bioactive mediators. During orthodontic tooth movement (OTM), host-derived enzymes are released at various stages of activation, resorption, reversal and deposition of osseous elements and degradation of the extracellular matrix. Some of these enzymes have been identified in the periodontal (pdl) tissue of orthodontically moved teeth. Gingival crevicular fluid (GCF) is however a better choice for assessing biomolecules or mediators as sample collection is simple, sensitive, convenient, repetitive and non-invasive.<sup>1-3</sup>

In general, cytokines are categorized into pro-inflammatory and anti-inflammatory cytokines. The pro-inflammatory cytokines include Interleukin 1b (IL-1 b), IL-2, IL-5, IL-6, IL-8, interferon  $\gamma$  (IFN  $\gamma$ ), tumor necrosis factor alpha (TNF $\alpha$ ) and granulocyte macrophage colony stimulating factor (GM-CSF), which induce classic inflammation markers. Pro-inflammatory cytokines act primarily at the onset of orthodontic tooth movement by inducing vasodilatation and increasing vascular permeability and inflammatory response. These mediators cause bone resorption and deposition at the pressure and tension sites.<sup>4-</sup> <sup>6</sup> Hence; the present study was conducted for assessing the levels of TNF- $\alpha$  in patients undergoing fixed orthodontic treatment.

#### **MATERIALS & METHODS**

The present study was planned for assessing the levels of TNF- $\alpha$  in patients undergoing fixed orthodontic treatment. A total of 20 patients scheduled to undergo fixed orthodontic treatment were enrolled in the present study. Complete demographic details of all the patients were obtained. During the pre-treatment phase, all the patients were recalled in the morning and GCF samples were obtained. All the samples were sent to laboratory where auto-analyser was used for assessing TNF- $\alpha$  level. Assessment of TNF- $\alpha$  levels was done one month after starting of the fixed orthodontic treatment. All the results were summarized in Microsoft excel sheet and were analysed by SPSS software. Student t test was used for evaluation of level of significance.

#### RESULTS

In the present study, a total of 20 patients scheduled to undergo fixed orthodontic treatment were enrolled. Mean age of the patients was 18.4 years. 60 percent of the patients belonged to the age group of less than 20 years. 55 percent of the patients were males while the remaining were females. Mean TNF-  $\alpha$  level at pre-treatment, one month post-treatment and six months post-treatment were found to be 6.72 pg/mL, 6.51 pg/mL and 6.59 pg/mL respectively. In the present study, while comparing the mean TNF-  $\alpha$ s at different time intervals, non-significant results were obtained.

 Table 1: Demographic data

| Parameter            |              | Number<br>patients | of Percentage<br>patients | of |
|----------------------|--------------|--------------------|---------------------------|----|
| Age group<br>(years) | Less than 20 | 12                 | 60                        |    |
|                      | More than 20 | 8                  | 40                        |    |
| Gender               | Males        | 11                 | 55                        |    |
|                      | Females      | 9                  | 45                        |    |

**Table 2:** Mean TNF-  $\alpha$  level

| TNF-α   | Pre-      | One month | Six months |
|---------|-----------|-----------|------------|
| levels  | treatment | post-     | post-      |
| (pg/mL) |           | treatment | treatment  |
| Mean    | 6.72      | 6.51      | 6.59       |
| SD      | 7.11      | 8.36      | 7.41       |

#### DISCUSSION

The level of  $TNF\alpha$  increases in gingival crevicular fluid (GCF) during OTM and it induces bone resorption at the

pressure site. GCF is a biological exudate, and measuring its components is a current method for identifying specific biomarkers with reasonable sensitivity. A chemical cascade that mediates the transmission of signals from extracellular matrix leading to genetic modulation is interceded by the release of mediators in paracrine environment. These signals are responsible for a change in the cytoskeletal structure, leading to alteration of nuclear protein matrix and eventually gene activation or suppression.7-9 Detection of an indicator of active phases of tissue destruction, particularly, that of alveolar bone during periodontal disease is the dream of dental investigators. The shortcoming of current clinical indices that assess periodontal disease has led to the development of more precise, non-invasive means of determining active disease, prediction of sites of future deterioration, and response to treatment.<sup>8-10</sup> Hence; the present study was conducted for assessing the levels of TNF- $\alpha$  in patients undergoing fixed orthodontic treatment.

| Table 2. | Compania  | n of TNE of | larva1 |
|----------|-----------|-------------|--------|
| Table 5: | Compariso | n of TNF-αl | level  |

| Comparison  | t-    | p-    |
|---|-------|-------|
|   | value | value |
| Pre-treatment versus One month post-<br>treatment         | 12.36 | 0.12  |
| Pre-treatment versus six months post-<br>treatment        | 11.85 | 0.81  |
| One month post-treatment versus six months post-treatment | 16.45 | 0.44  |

In the present study, mean age of the patients was 18.4 years. 60 percent of the patients belonged to the age group of less than 20 years. 55 percent of the patients were males while the remaining were females. Mean TNF-  $\alpha$  level at pre-treatment, one month post-treatment and six months post-treatment were found to be 6.72 pg/mL, 6.51 pg/mL and 6.59 pg/mL respectively. Tumor necrosis factor-a, another pro-inflammatory cytokine, was shown to elicit acute or chronic inflammation and stimulate bone resorption. Studies have shown that TNFa directly stimulates the differentiation of osteoclast progenitors to osteoclasts in the presence of macrophage colonystimulating factor (M-CSF). Davidovitch et al and Saito et al demonstrated marked increases in TNFa in cells of the PDL and alveolar bone during OTM in cats.<sup>8-11</sup> In the present study, while comparing the mean TNF-  $\alpha$ s at different time intervals, non-significant results were

different time intervals, non-significant results were obtained. Atuğ Özcan SS et al examined the changes in the levels of interleukine-1 beta (IL-1 $\beta$ ), tumor necrosis factor alpha (TNF- $\alpha$ ), malondialdehyde (MDA), nitric oxide (NO), and 8-hydroxydeoxyguanosine (8-OHdG) in saliva and IL-1 $\beta$ , TNF- $\alpha$ , and NO in gingival crevicular fluid (GCF) samples of patients with fixed orthodontic appliances. The subject population consisted of 50 volunteers who were in need of orthodontic treatment with fixed orthodontic appliances. GCF and saliva samples were obtained from all individuals before treatment, at 1st month of treatment and at 6th month of treatment. Periodontal clinical parameters were measured. Samples were investigated to detect IL-1 $\beta$ , TNF- $\alpha$ , and 8-OHdG levels using ELISA method and NO and MDA levels using spectrophotometric method. Since IL-1 $\beta$  level detected in GCF at the 6th month of orthodontic treatment is statistically significant according to baseline (P < 0.05), all other biochemical parameters detected both in saliva and in GCF did not show any significant change at any measurement periods. Orthodontic treatment do not lead to a change above the physiological limits that is suggestive of oxidative damage in both GCF and saliva.<sup>12</sup>

### CONCLUSION

From the above results, the authors concluded that fixed orthodontic treatment doesn't alter the TNF- $\alpha$  levels. However; further studies are recommended.

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