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RESEARCH ARTICLE
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The Effect of Sodium Fluoride Administration on IL-1β and TNF-α Expression on Orthodontic Teeth Movement

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ABSTRACT

Relapse in post orthodontic treatment is common in the community because resorption in the pressure side occurs excessively due to teeth being moved with an orthodontic device. Excessive resorption can be inhibited by using NaF which has been shown to inhibit osteoclast activity, thereby reducing osteoclast numbers. The purpose of this study was to analyze the effect of NaF administration on IL-1β and TNF-α expression of osteoclast in orthodontic teeth movement. The research used experimental-quantitative research type applying Randomized Posttest Only Control Group Design, by selecting the experimental group and the control group randomly. Animal model using 16 male Wistar rats given orthodontic force using NiTi closed coil spring adjusted to give 10 grams/cm^2 of mechanical strength, were applied to the palatal in the maxillary incisors of the Wistar rat teeth. Rats were divided into two groups, the control group (C group) and treatment group (T group) given topical NaF application (11.75 ppm). Immunohistochemical examination was performed to calculate IL-1β and TNF-α expression on osteoclasts on the 7th day and 14th day. The administration of NaF reduces IL-1β and TNF-α osteoclast's expression both on the 7th day ($p < 0.05$) and 14th day ($p < 0.05$). Data were tested by the Kolmogorov-Smirnov test, Levene test and the difference tested Annova followed by LSD ($p < 0.05$). Topical administration of NaF application to the gingival sulcus of male Wistar rats in orthodontic tooth movement can reduce the number of osteoclasts that express IL-1β in the alveolar bone in the pressure area. Topical administration of NaF application to the gingival sulcus of male Wistar rats in orthodontic tooth movement can reduce the number of osteoclasts that express TNF-α in the alveolar bone in the pressure region. Decreased number of osteoclasts expressing IL-1β and TNF-α significantly occurred on the 7th day and 14th day.

Keywords: IL-1β; TNF-α; NaF; osteoclast; orthodontic teeth movement

INTRODUCTION

Orthodontic tooth movement is on periodontal ligament and bone remodeling on alveolar bone induced by an external force exerted by an orthodontic appliance(1). Relapse can occur when the resorption process occurs excessively in the pressure area rather than the position in the pulling area. Orthodontic tooth movement activated osteoclast. Cytokine pro-inflamatory such as IL-1β is the most potently bone resorption and stimulate the differentiation precursors of osteoclast(1). TNF-α triggered sclerostin expression in osteocytes. Osteocyte express receptor activator nuclear factor kappa-B ligand (RANKL) therefore sclerostin increases. Hence, TNF-α has play role on osteoclast formation(2).

Relapse after using orthodontic treatment is unpredictable, The relapse can cause orthodontic treatment will be longer, the cost becomes relatively more expensive, it is necessary to do this research so that orthodontic treatment is more efficient. Fluoride can help to maintenance of bone health by stimulate proliferation osteoblast which can lead increased bone formation(3). In previous studies, sodium fluoride was effective in orthodontic teeth movement through the role of osteocalcin and osteonectin(4). In this study would to see the effect of IL-1β and

TNF-α on orthodontic teeth movement after the application of sodium fluoride. Cytokines IL-1β and TNF-α induced osteoclastogenesis from RANKL expression and directly stimulate precursor of osteoclast under the control of p38 MAPK[5].

In fact there are still many teeth that relapse after orthodontic treatment. Therefore this study would to see NaF material has an effect on IL-1β and TNF-α expression in orthodontic teeth movement. This study to prove that IL-1β and TNF-α expression in orthodontic treatment with the administration of NaF is lower than those not given NaF. The benefit of this research is to contribute to the development of science regarding the benefits of NaF administration which can reduce the expression of IL-1β and TNF-α induced by orthodontic mechanical strength lead to prevent the relapse or instability in orthodontic treatment.

METHODS

Rat Model of Orthodontic Tooth Movement

The research used experimental-quantitative research type applying Randomized Posttest Only Control Group Design, by selecting the experimental group and the control group randomly. Animal model in this study were sixteen male Wistar rats, healthy, age range from three to four months and 250-300 grams (0.25-0.3 kg) body weight and teeth movement forced by orthodontic devices which inserted between first molar and incisors maxillary teeth for 7 days (group 1) and 14 days (group 2). NiTi closed coil spring adjusted to give 10 grams/cm2 of mechanical strength were applied to the palatal of the Wistar rat teeth in the maxillary incisors using, determined by tension gauge (Ormco® Glendora, USA).

The animal model was divided into a control group which not given NaF (group C: consist C1 on 7 days and C2 on 14 days teeth movement) and a treatment group which given NaF (group T: consist T1, 7 days and T2, 14 days teeth movement). Rats have sacrificed at the end of the treatment for immunohistochemical examination of IL-1β and TNF-α expression. The protocol was approved by the Health Research Ethics Committee (KEPK), Faculty Dentistry, Jember University.

Immunohistochemical Procedures

The area around the maxillary incisor was taken and then fixed and decalcified for 30 days then processed into tissue embedded in paraffin. The slide was cut distal incisors in a direction extending from the root to the crown with a thickness of less than 180 µm. The slides were stained immunohistochemically with IL-1β and anti-TNF-α goat monoclonal antibodies.

Statistical Analysis

Before being analyzed, normality, and homogeneity data were tested by the Kolmogorov-Smirnov test and Levene test. The difference of mean was analyzed by the ANOVA test followed by LSD. Significances were determined if $p<0.05$.

RESULTS

The immunohistochemistry stained preparations with specific antibodies IL-1β and TNF-α were observed under a microscope, the expression of the cytokine in the cell was characterized by the cells absorbing a brownish color. The immunohistochemistry staining results in each group can be seen in figure 1 and figure 2.

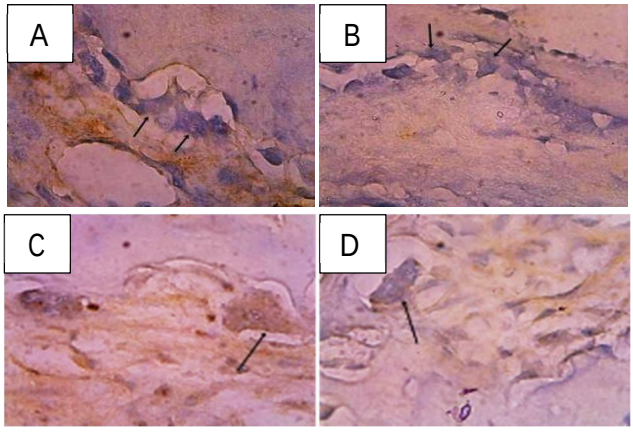

Figure 1. Immunostaining IL-1β in furcation of the distal root of upper incisor tissue section: A). Control group on 7th day (C1); (B). Control group on 7th day (C2); (C). Treatment group on 7th day (T1); (D). Treatment group on 14th day (T2). The arrow point cell with the expression of IL-1 β (IHC IL-1β, 1000x)

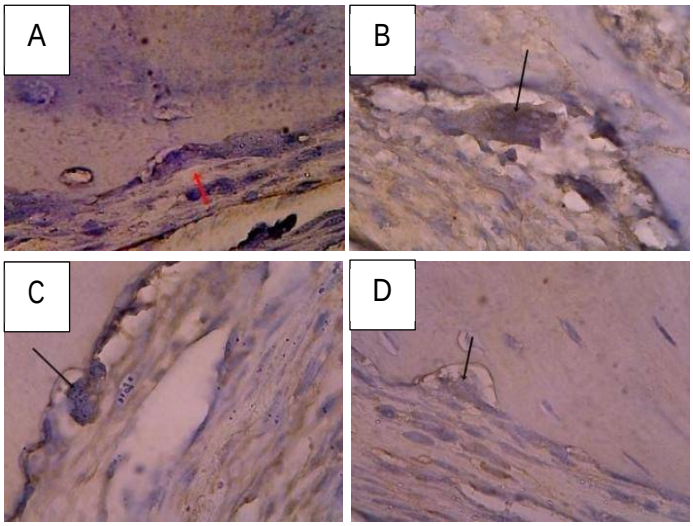

Figure 2. Immunostaining TNF-α in furcation of the distal root of upper incisor tissue section: A). Control group on 7th day (C1); (B). Control group on 7th day (C2); (C). Treatment group on 7th day (T1); (D). Treatment group on 14th day (T2). The arrow point cell with the expression of TNF-α (TNF-α, 1000x)

The mean expression of IL-1β in C1 was 8.3±0.250 and C2 was 5.1±0.838. The mean of expression of IL-1β in T1 was 6.6±0.864 and T2 was 4.1±0.629. The expression of TNF-α means in C1 was 6.3±0.341 and C2 was 5.3±0.258 whereas in T1 was 5.1±0.200 and T2 was 4.3±0.346. The mean expression of IL-1β and TNF-α of the control and treatment group in 7th day and 14th-day teeth movement is illustrated in figure 3 and figure 4**.** The mean expression of IL-1β in the control group and treatment group on the 7th day and 14th day showed in figure 5. The result showed decrease in IL-1β and TNF-α expression day 7th and day 14th. And seen more pronounced decrease IL-1β and TNF-α after administration on NaF on dat 7th and 14th.

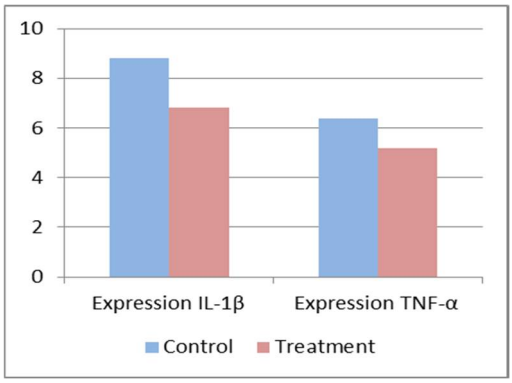

Figure 3. The mean expression of IL-1β and TNF-α on 7th-day teeth movement on osteoclast

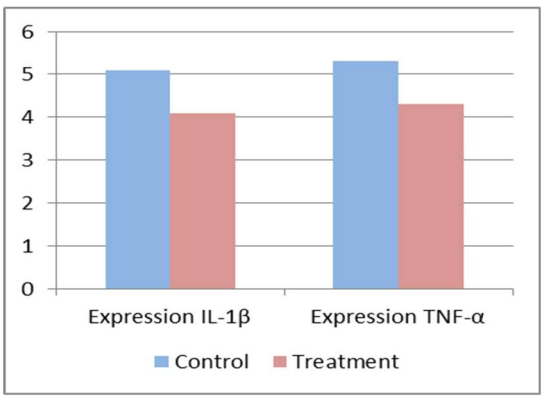

Figure 4. The mean expression of IL-1β and TNF-α on 14th-day teeth movement on osteoclast

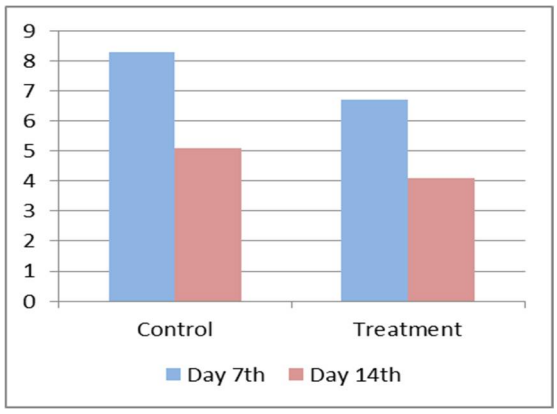

Figure 5. The mean expression of IL-1β of control group and treatment group on 7th day and 14th day

The statistical analysis using the SPSS program showed that the data of this study are normally distributed and homogeneous in each group (p= 0.507 in IL-1β and p= 0.760 in TNF-α). The result of one way Anova test showed a significant difference among the group (p <0.05). The expression IL-1β and TNF-α on the 7th day and 14th day are significantly different, this can be interpreted that there is a significant decrease between control group and treatment group.

DISCUSSION

This study showed that NaF application reduced the expression both of IL-1β and TNF-α in 7th day and 14th day in the bone around maxillary incisor teeth Wistar rats which give an orthodontic teeth movement strength of 10 gram/cm^2. Excessive resorption can be inhibited by using NaF which has been shown to inhibit osteoclast activity. Fluoride play role in calcium metabolism and bone turn over [(6)]. Thereby reducing osteoclast numbers a dose of 11.34 ppm. NaF was obtained from the calculation of equalization between the optimal dosages of NaF topical application used by humans, which is 400 ppm at a dose of experimental animals, in this case, Wistar rats.

IL-1β and TNF-α are osteotropic cytokines, these cytokines can directly and indirectly initiating bine resoprtion [(7)]. IL-1β may be involved in bone resorption by activasting reseptor on osteoblast cells on PDL and also triggering differentiation of osteoclast and activation of mature osteoclast [(1)]. Orthodontic tooth movement is followed by the inflammatory responses of the tissue because of the mechanical forces that have been carried out and regulated by IL-1β and TNF-α as an activator and inhibitor [(7)].

IL-1β is produced as an inflammatory responses to the mechanical forces of orthodontic to make osteoclastogenesis process. By induction of TNF-α and upregulation of RANKL and MMPs, IL-1β participates in several processes of osteclastogenesis and result in bone remodeling [(8)].

IL-1β is a highly-expressed pro-inflammation cytokine in the periodontal ligament in areas of pressure both human and animal adjacent to the alveolar bone in the early stages of orthodontic tooth movement. [(9)] Orthodontic strength can induce chemical and physical responses to periodontal tissues. In the early stages of orthodontic tooth movement, mechanical stimuli can cause acute inflammatory reactions in periodontal tissues, which can trigger a biological process in the form of bone resorption to accommodate tooth movemen [(10)].

IL-1β can induce osteoclast cell formation directly from osteoclasts precursors under in vitro and TNF-α stimulation at the biomolecular level, IL-1β has the potential to induce a resorption process and decrease bone formation process because it strongly inhibits osteoblastogenesis. [(11,12)] In another in vitro study also explained that IL-1 supports osteoclast cell formation by increasing the production of macrophage colony-stimulating factor (M-CSF), PGE2, and decreasing OPG production by osteoblasts. [(11)] The inhibition of IL-1β could be done by the anti-inflammatory agent from papaya seeds. [(13)]

A study conducted by Yakoya, Sasaki, and Shibasaki [(14)] proved an increase in osteoclasts due to TNF-α expression on the first day after tooth movement was given until the 7th day in the pressure area. They also proved that there were osteoclasts in the pulling area on the first day until the 14th day and there was no increase. [(15)] Then the peak increase in cytokine IL-1β during the initial stages of orthodontic tooth movement is 24 hours (1 day) and 168 hours (7 days). The statistical tests performed showed that there was a dramatic increase after 168 hours (7 days). [(16)]

The mean description results showed that TNF-α expression in the treatment group was lower when compared to the control group. Test results meaning that there is difference between the control group, which is the tooth that is moved and not topically treated with NaF, and the treatment group is the tooth group moved and given topical NaF. The expression in both variables decreases between the 7th day and 14th day.

TNF-α was suggested to stimulate bone resorption and bone-cell replication. TNF-α induces several biological responses via 2 receptor cell surfaces, called, type 1 TNF receptors (p55) and type 2 TNF receptors

(p75). In addition to changing the direct processes associated with tooth movement, TNF-α can also induce mediators in the inflammatory process, which can affect osteoclasts and their function. [17]

CONCLUSION

Topical administration of NaF application to the gingival sulcus of male Wistar rats in orthodontic tooth movement can reduce the number of osteoclasts that express IL-1β and TNF-α. It decreased the number of osteoclasts expressing IL-1β and TNF-α occurred on the 7th day and 14th day.

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