Original Research Article

The effects of ibuprofen and acetaminophen on orthodontic pain control and interleukin-1β levels in gingival crevicular fluid

Ganesh Prasad B R[1*], Anand K Patil[2]

[1]Senior Resident, Department of Dentistry, Dr Chandramma Dayananda Sagar Institute of Medical Eduction and Research, Harohalli Hobli, Ramnagara District, INDIA.
[2]Professor of Orthodontics and Dentofacial Orthopedics, SDM College of Dental Sciences, Dharwad, Karnataka, INDIA.
Email: ganeshprasadbr.10@gmail.com

Abstract

Background: Pain is one of the unpleasant experiences occurring during orthodontic treatment. Non Steroidal Anti Inflammatory Drug (NSAIDs) having analgesic properties minimizes discomfort caused by appliance activation. Acetaminophen with weak anti-inflammatory action, is effective in relieving discomfort without hampering Orthodontic tooth movement (OTM). Interleukin -1 β (IL-1β) a potent pro-inflammatory cytokine is reflected in Gingival Crevicular Fluid (GCF) during OTM. The study objective is to determine and evaluate effects of Ibuprofen and Acetaminophen on orthodontic pain control and IL-1β levels in GCF during initial stages of OTM. **Methodology**: A total of 30 subjects were divided into three equal groups. Initial levelling and aligning stage were carried out using 0.014'' NiTi. First and second group were prescribed with Ibuprofen and Acetaminophen respectively. Third group was control. Subjects were advised to rate average daily pain quality at (P_1)24 hours, (P_2) 48hours, (P_3)72 hours and (P_7)168 hours in all the groups. GCF samples were obtained at four time points and IL-1β levels were evaluated and correlated with pain scores. GCF samples were assayed with commercially available human IL-1β Enzyme-Linked Immunosorbent Assay (ELISA) kit. **Results:** IL-1β levels in all the groups increased significantly by 24 hours(T_1) from their respective baseline levels, decreased by (T_2)48 hours and eventually reached close to baseline levels by 168 hours(T_3). No Statistically significant correlation was found between drug groups at 48 hours(T_2). There was statistically significant correlation in all the groups at 24 hours, 168 hours. Negative correlation was found between IL-1β levels and pain scoring in drug groups indicating that IL-1β levels increased as OTM progressed, but pain decreased. Positive correlation was found between the two in control group. **Conclusions:** Ibuprofen and Acetaminophen have an inhibitory effect on the IL-1β levels and thereby cause impediment to rate of tooth movement. However, they decrease orthodontic pain during initial stages of treatment.

Keywords: Pain, Ibuprofen, Acetaminophen, IL, GCF, ELISA

[*]**Address for Correspondence:**
Dr Ganesh Prasad B R, Senior Resident, Department of Dentistry, Dr Chandramma Dayananda Sagar Institute of Medical Eduction and Research Harohalli Hobli, Ramnagara District, Karnataka -562112, INDIA.
Email: ganeshprasadbr.10@gmail.com

Received Date: 04/04/2021 Revised Date: 30/04/2021 Accepted Date: 19/05/2021
DOI: https://doi.org/10.26611/10191821

Access this article online	
Quick Response Code:	Website: www.medpulse.in
	Accessed Date: 27 May 2020

INTRODUCTION

Orthodontics being a fast-growing speciality is aimed at achieving good functional occlusion and a perfect smile. During treatment, pain has been rated as the greatest dislike and fears and apprehensions prior to orthodontic treatment.[1] Orthodontic pain is the discouraging aspect of the treatment, is one of the primary reasons to discontinue the treatment. During treatment, patients often describe the discomfort as tension, ache, pressure or soreness of the teeth. About 90-95% of the patients undergoing orthodontic treatment report pain with appliances.[3] Pain perception is part of an inflammatory reaction causing

How to cite this article: Ganesh Prasad B R, Anand K Patil. The effects of ibuprofen and acetaminophen on orthodontic pain control and interleukin-1β levels in gingival crevicular fluid. *MedPulse International Journal of Dentistry.* May 2021; 18(2): 01-04. http://www.medpulse.in/Dentistry

alterations in blood flow following orthodontic force application.[4] Pain scale is a tool that is used to help assess a person's pain. In response to external stimuli, cytokines are actively secreted by diverse cell types and are diminutive protein molecules that regulate cell communication and function by inducing cellular proliferation and differentiation.[5,6] Interleukin (IL)-1, is a cytokine which exists in two forms alpha and beta of which in bone metabolism interleukin-1β is form pertinent.[7] In gingival crevicular fluid (GCF), inflammatory phenomena during tooth movement could be found where significant elevations in the concentrations of inflammatory mediators. Therefore, it is of great value in monitoring the outcome and efficiency of orthodontic treatment. Ibuprofen a propionic acid derivative NSAID and is well absorbed orally. It is non-selective cyclooxygenase inhibitor. It has shown to have inhibitory effect on the PGE_2 levels due to its anti-inflammatory activity.[8] However their effects on IL-1β levels in GCF is still been completely evaluated. Acetaminophen which belongs to the family of para-aminophenol, is a weak inhibitor of prostaglandin synthesis and in previous animal studies showed no effect on orthodontic tooth movement.[9] Moreover it is known to reduce the levels of prostacyclins after systemic administration in humans.[10] The orthodontist should be able to identify patients taking particular pharmaceuticals and consider any implications related to orthodontic treatment as various medications show varying effects on the rate of orthodontic tooth movement and root resorption development in human subjects.[11] The current study aims to determine and evaluate the effects of Ibuprofen and Acetaminophen on orthodontic pain control and GCF levels of IL-1β during initial stage of orthodontic tooth movement in human subjects. In

MATERIALS AND METHODOLOGY

Patients who reported to the department of orthodontics, SDM dental college and hospital, Dharwad, Karnataka for treatment were included in this study after taking approval from the ethical committee and institutional review board. The study was conducted from January 2018 to February 2019. Informed consent was obtained from all the patients included in the study. Thirty subjects (above 13 years of age; mean age:19±2years) in need of orthodontic treatment with moderate crowding in both the arches were taken for the study. The subjects were randomly divided into three equal groups. The first group was taken as the Ibuprofen group, second as the Acetaminophen group and third as the Control group.

Inclusion criteria:

1. The need for fixed orthodontic therapy.
2. No history of systemic diseases.
3. No radiographic evidence of periodontal disease.
4. No history of intake of anti-inflammatory drugs or antibiotic therapy within the past six months.

Exclusion criteria:

1. Patients who have undergone orthodontic treatment before.
2. Patients with systemic diseases.
3. Patients taking any type of medication,

Amount of dental crowding in both the arches was evaluated using Little's Irregularity index[12] in each of the patient's diagnostic casts which ranged from 4 to 6 (moderate irregularity) (Figure 1B). Fixed orthodontic therapy was started in all the patients included in the study after obtaining informed consent. Orthodontic preadjusted appliance (0.022''x0.028'' slot, MBT prescription- 3M Gemini brackets; 3M Unitek Corporation, Monrovia, California) was placed. Initial levelling and aligning was carried out using 0.014'' Nickel Titanium (NiTi) archwire (Optima, Orthodontic Supplies Ltd, Leicestershire, UK). Lacebacks were placed using 0.010'' ligature wire for crowding relieving**.** At the placement of the archwire, the subjects in the first group were given Ibuprofen, 400mg 2 times daily for 3 days. The second group received acetaminophen, 650mg 2 times daily for 3 days. The third group being control group received placebo (sugar free pills) as medication. Specific pain management instructions were given to the patients in first two groups before and immediately after initial archwire placement. The subjects were advised to rate their quality of average daily pain 24 hours after the archwire placement (P_1), 48 hours(P_2), 72 hours(P_3) and 168 hours(P_7) after the archwire placement in a pain quality rating scale evaluation sheet which was given to the patient. The patients had to rate their quality of pain on a Visual Analogue Scale (VAS) [no hurt=0, hurts worst=5], Wong Baker Faces Pain Scale, Verbal Rating Scale (0=none to 5=very severe) and six-point numerical rating scale ranging from 0 to 5.

Analysis of IL-1β Levels

GCF samples were assayed with commercially available human IL-1β ELISA (Enzyme-Linked Immunosorbent Assay) kit (Krishgen Biosystems Ltd., 3381, Paseo Drive, Brea, CA 92823, USA) to determine the concentration of IL-1β(ρg/μl).

GCF was collected at four intervals from each individual of all the three groups, amounting to a total of 120 samples.

T_0 : Before starting bonding procedure

T_1 : 24 hours after strap up

T_2 : 48 hours after strap up

T_3 : 168 hours after strap up

GCF was then diluted with 250μl sterile phosphate buffered saline (Ph 7.4) and stored at -80˚C until analysis.

RESULTS

Table 1: IL-1β levels in different groups at different time periods

Time period	summary	Ibuprofen group(ρg/µl)	Acetaminophen group(ρg/µl)	Control group(ρg/µl)
T_0	Mean	0.069950	0.070010	0.070080
	SD	0.0001900	0.0002183	0.0002201
T_1	Mean	0.072180	0.075440	0.080800
	SD	0.0003011	0.0015579	0.0009487
T_2	Mean	0.071480	0.072540	0.076860
	SD	0.0001033	0.0005232	0.0021386
T_3	Mean	0.070240	0.070710	0.071010
	SD	0.0001430	0.0002998	0.0001729

Table 2: Subjective perception of pain levels in different groups at different time points

Time period	summary	Ibuprofen group	Acetaminophen group	Control group
P_1	Mean	2.50	2.8	4.2
	SD	0.849	0.632	0.788
P_2	Mean	2	2.2	4.2
	SD	0.66	0.632	0.788
P_3	Mean	1.3	1.5	3.4
	SD	0.483	0.707	0.516
P_7	Mean	0.4	0.5	1.7
	SD	0.516	0.527	0.674

DISCUSSION

Pain is a complex experience that includes sensations evoked by reactions to noxious stimuli. During orthodontic treatment it is also necessary to assess how well patients accept the treatment and whether they experience any side effects. Common methods for assessing patients experiences of pain are questionnaires that incorporate different unidimensional pain scales such as the Visual analogue scale (VAS), numerical rating scale, verbal rating scale and Wong baker pain rating scale. IL-1β biomarker has attracted interest from researchers. It is a cytokine that falls under the interleukin group and is said to be the earliest marker of bone resorption and a part of the inflammatory process.[13] This cytokine determines the amount of OTM dependent on the alveolar bone remodeling efficiency, as the fusion, survival and activation of osteoclasts corresponds with it.[58] Also, IL-1β is directly associated with bone resorption as it stimulates the differentiation of osteoclast precursors and induces the expression of RANKL in osteoblasts and human PDL cells.[14,15] For the pain related to fixed orthodontic appliances, use of NSAID's has been the preferred method.[4,16] Therefore, it may appear that administration of anti-inflammatory drugs such as ibuprofen, by reducing the level of PGE, may interfere with orthodontic tooth movement. Acetaminophen also known as paracetamol, a para-aminophenol derivative is a potent antipyretic and has analgesic action, but in contrast to NSAIDs drug family it is a weak anti-inflammatory and showed no effect on orthodontic tooth movement.[8,9] The mechanism of action of acetaminophen is not very well understood. It has been recommended as the analgesic of choice for relieving pain associated with orthodontic treatment as it showed no effect on orthodontic tooth movement in previous studies.[8,17] Gingival crevicular fluid (GCF) is chosen in the study for analysis. It offers a rich potential in obtaining diagnostic information regarding the periodontal status.[18] Therefore, this study was chosen to determine the effects of therapeutic doses of Ibuprofen and acetaminophen on orthodontic pain control which is an integral part of the orthodontic treatment and to check IL-1β levels of GCF during initial stage of the treatment

Table 1: Summary of IL-1β scores in all three groups at different time intervals

In the Ibuprofen group, IL-1β levels in the GCF at baseline(T_0) was 0.069950(ρg/µl). In the Acetaminophen group it was 0.070010(ρg/µl) and in the Control group it was 0.070080(ρg/µl). At 24 hours(T_1), in the Ibuprofen group these levels increased to 0.072180(ρg/µl), in the acetaminophen group it was 0.075440(ρg/µl) and in the control group it was 0.080800(ρg/µl). By 48 hours(T_2), the mean decrease in the IL-1β levels in all the three groups was noticed which stood at 0.071480(ρg/µl), 0.072540(ρg/µl) and 0.076860(ρg/µl) in the Ibuprofen, Acetaminophen and Control groups respectively. At 168 hours(T_3), the average IL-1β levels in all three groups decreased almost to their corresponding baseline levels. In the Ibuprofen group it was 0.070240(ρg/µl), in the Acetaminophen group it was 0.070710(ρg/µl) and in the Control group it was 0.071010(ρg/µl).

Table 2: Summary of Pain perception scores in all three groups at different time intervals

The average daily pain recorded by the patient 24 hours after the initial archwire placement was more in the

Control group when compared to the other two groups suggests that analgesics decreased the subjective perception of pain levels. However, the pain perception levels decreased by 168 hours(P_7) in the Control group as well suggests that the Orthodontic pain perception is part of an inflammatory reaction caused from the orthodontic force application.

CLINICAL IMPLICATIONS

Currently patients seeking orthodontic treatment has been increasing and the usage of these OTC drugs may increase. Henceforth, proper therapeutic usage of these drugs without hampering tooth movement can be beneficial during orthodontic treatment.

LIMITATIONS OF THE STUDY: Pain scoring being a subjective study, the results depend on patients' perception and therefore pain threshold may vary from each individual. The results of the study may have been influenced from this inter-individual variability. Hormones, gender differences and age could have played a role in affecting the values of IL-1β. Inspite of strict oral hygiene maintainence, some degree of gingivitis can occur and affect the IL-1β production.

CONCLUSION

Both the OTC drugs, Ibuprofen and Acetaminophen were effective in relieving the discomfort of pain during the initial stages of orthodontic treatment. IL-1β levels in the GCF peaked at 24 hours after appliance activation and decreased nearly to baseline levels by 168 hours. Both Ibuprofen and Acetaminophen was found to affect and inhibit the IL-1β levels significantly when compared to the control group at all the time points during the experimental period. Both these OTC drugs have an inhibitory effect on the release of pro-inflammatory cytokine IL-1β during initial stages of the orthodontic treatment and thereby may interfere in the orthodontic tooth movement.

REFERENCES

1. O'Connor PJ. Patients' perceptions before, during, and after orthodontic treatment. J clin Orthod 2003;34(10):591-2.
2. Oliver RG, Knapman YM. Attitudes to orthodontic treatment. Br J Orthod 1985;12:179-88.
3. Lew KK. Attitudes and perception of adults toward orthodontic treatment. J Clin Orthod 1992; 26:311-3.
4. Krishnan V. Orthodontic pain: from cause to management-a review. Eur J Orthod 2007;29:170-9.
5. Blesta A, Berggreen E, Brudvik P. Interleukin-1 alpha and Tumor necrosis factor-alpha expression during the early phases of orthodontic tooth movement in rats. Eur J Oral Sci. 2006;114:423-429.
6. Ren Y, Hazemeijer H, de Haan B, Qu N, de Vos P. Cytokine profiles in crevicular fluid during orthodontic tooth movement of short and long durations. J Periodontaol. 2007;78:453-458.
7. Krishnan V, Davidovitch Z. Cellular, molecular, and tissue- level reactions to orthodontic force. Am J Orthod Dentofacial Orthop. 2006;129:1-469.
8. Shetty *et al.*: Comparision of the effects of ibuprofen and acetaminophen on PGE_2 levels in the GCF during orthodontic tooth movement: a human study. Progress in orthodontics 2013;14:6
9. Arias OR, Marquez-Orozoc MC. Aspirin, acetaminophen and ibuprofen: their effects on orthodontic tooth movement. Am J Orthod Dentofacial Orthop 2006;130:364-70.
10. Green K, Drvota V, Vesterqvist O. Pronounced reduction of in vivo prostacyclin synthesis in humans by acetaminophen (paracetamol). 1989;37(3):311-5.
11. Kaklamanos EG, Makrygiannakis MA, Athanasiou AE. Does medication administration affect the rate of orthodontic tooth movement and root resorption development in humans? A systematic review. Eur J of Orthodontics. 2019,1–8.
12. Little RM. The irregularity index: a quantitative score of mandibular anterior alignment. Am J Orthod. 1975 Nov;68(5):554-63.
13. Sánchez GA, Miozza VA, Delgado A, Busch L. Salivary IL-1β and PGE2 as biomarkers of periodontal status, before and after periodontal treatment. J Clin Periodontol 2013;40(12):1112–7.
14. Teixeira CC, Khoo E, Tran J, Chrtres I, Liu Y, Thant LM, *et al.* Cytokine expression and accelerated tooth movement. J Dent Res. 2010;89:1135-41.
15. Saito M, Saito S, Ngan PW, Shanfeld J, Davidovitch Z. Interleukin 1 beta and prosyaglandin E are involved in the response of periodontal cells to mechanical stress in vivo and in vitro. Am J Orthod Dentofacial Orthop. 1991; 99:226-240.
16. Krukemeyer AM, Arruda AO, Inglehart MR. Pain and Orthodontic Treatment. Angle Orthod, 2009;79,6.
17. Kehoe NJ, Choen SM, Zarrinnia K, Cowan A. The effect of acetaminophen, ibuprofen and misoprostol on prostaglandin E_2 synthesis and the degree and rate of orthodontic tooth movement. Angle Orthod 1996;66(5):339-50.
18. Offenbacher S, Collins JG and Heasman PA. Diagnostic potential of host response mediators. Adv Dent Res.1993;7:175-81.

Source of Support: None Declared
Conflict of Interest: None Declared