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Original Research

Level of Cathepsin K in GCF during Orthodontic Tooth Movement

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ABSTRACT:

Background: Cathepsin K and alkaline phosphatase have been found to be significantly elevated in teeth undergoing orthodontic forces compared with untreated controls. The present study assessed the level of Cathepsin K in GCF during orthodontic tooth movement. **Materials & Methods:** This study was conducted on 12 patients age ranged 12-22 years of both genders needing orthodontic treatment. for Angle's Class I bimaxillary protrusion. From each patient 4 GCF samples were collected 1 hour before treatment, after 1 day, 7th day and 1 month after the placement of the orthodontic appliance on maxillary left canines and right canines. GCF of approximately 2 microliter was collected from the distal sulcus of the canine by extracrevicular method using a graduated micro capillary pipette. cathepsin K in GCF was estimated using ELISA method. **Results:** Out of 12 patients, there were 5 males and 7 females. The mean Cathepsin K level at 0 hour in test side was 142.5 and in control side was 140.2, at 1 day was 52.6 and at control side was 51.8, at 7 days was 341.2 and at control side was 280.4, at 30 days was 48.2 and at control side was 92.4. The difference was significant ($P<0.05$). **Conclusion:** Authors found increase level of Cathepsin K on test side as compared to control side on 7th day. The amount of Cathepsin K in GCF increased during the initial period of orthodontic tooth movement.

Key words: Cathepsin K, ELISA, Gingival crevicular fluid

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INTRODUCTION

Orthodontic tooth movement produces remodeling changes in paradental structures leading to variations in the level biochemicals like cytokines, neurotransmitters, arachidonic acid metabolites etc which are in turn reflected in the GCF of moving teeth. Assessment of these GCF biomarkers is clinically significant because it may lead to better understanding of mechanical stress resulting in shorter treatment time with minimal side effects.[1]

In the GCF, several substances such as interleukin (IL)-1b, IL-6, tumor necrosis factor (TNF)-a, b2 microglobulin, osteocalcin, cathepsin K and alkaline phosphatase have been found to be significantly elevated in teeth undergoing orthodontic forces compared with untreated controls.[2]

It has been suggested that cathepsin K orchestrates the host response to inflammatory and infectious stimuli as it stimulates the immune system by enhancing cytokine production and phagocytosis by macrophages. Thus, the overall increase in cathepsin K during inflammation and infection indicates that cathepsin K is part of the immune response and host defense mechanisms.[3] A remodeling process (resorption and apposition) takes place in periodontal tissues induced by the changes in the stress-strain distribution in the periodontium after the application of orthodontic forces. Furthermore, a local damage-repair process with inflammation-like reactions, including high vascular activity with many

leukocytes and macrophages and involvement with the immune system may occur during orthodontic tooth movement.[4] The present study assessed the level of cathepsin K in GCF during orthodontic tooth movement.

MATERIALS & METHODS

This study comprised of 12 patients age ranged 12-22 years of both genders needing orthodontic treatment for Angle's Class I bimaxillary protrusion. Patients were informed regarding the study and written consent was taken. Ethical clearance was obtained prior to the study. Data related to patients such as name, age, gender etc. was recorded. They were bonded with fixed orthodontic appliance 0.022" bracket slot, MBT prescription. Maxillary right canine was used as control tooth (CT) and maxillary left canine used as test tooth (TT). After banding and bonding was completed 0.016" NiTi wire was placed and laceback were given using 0.010 SS ligature wire only on test side with approximate force values of 200cN as measured on a Dontrix gauge.

In all patients, gingival index and periodontal disease index scores were recorded before the collection of gingival crevicular fluid. From each patient 4 GCF samples were collected 1 hour before treatment, after 1 day, 7th day and 1 month after the placement of the orthodontic appliance on maxillary left canines and right canines. GCF of approximately 2 microliter was collected from the distal sulcus of the canine by extracrevicular method using a graduated micro capillary pipette. cathepsin K in GCF was estimated using ELISA method. Results thus obtained were tabulated and subjected to statistical analysis. P value < 0.05 was considered significant.

RESULTS

Table I Distribution of patients

Total- 12		
Gender	**Male**	**Female**
Number	5	7

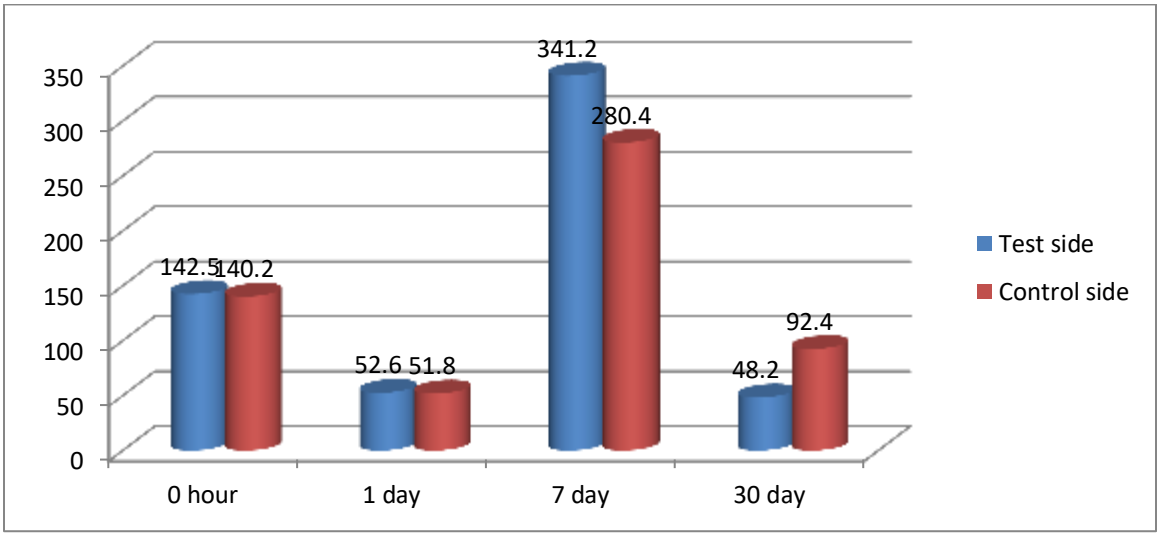
Table I shows that out of 12 patients, there were 5 males and 7 females.

Table II Comparison of cathepsin K levels in GCF between test & control sides

Time	Test side	Control side	P value
0 hour	142.5	140.2	0.92
1 day	52.6	51.8	0.97
7 day	341.2	280.4	0.01
30 day	48.2	92.4	0.02

Table II, graph I shows that mean Cathepsin K level at 0 hour in test side was 142.5 and in control side was 140.2, at 1 day was 52.6 and at control side was 51.8, at 7 days was 341.2 and at control side was 280.4, at 30 days was 48.2 and at control side was 92.4. The difference was significant (P<0.05).

Graph I Comparison of cathepsin K levels in GCF between test & control sides



DISCUSSION

Cathepsin-K is a highly expressed cysteine protease, and it plays a key role in bone remodeling and cartilage breakdown in bone. Cathepsin-K is used as a well-known marker of osteoclast activity, because this enzyme is mainly derived from osteoclasts.[5] The receptor activator for NF-κB ligand (RANKL) plays an important role in osteoclast formation. Although a recent study suggests the involvement of RANKL in the pathogenesis of periodontal disease, no one has previously examined the level of cathepsin-K in the body fluid of human subjects. If the presence of cathepsin-K, as well as RANKL, can be detected in body fluids, it would be indirect proof of the differentiation and/or activation of osteoclasts in the tissues bathed by these fluids.[6]

Cathepsins are potent proteases found in Lysosomes and get activated in low pH, thus the activation of the Cathepsin family lies within the organelles. Interestingly, exceptions such as Cathepsin K, work extracelluarly after being secreted by osteoclasts as seen during bone resorption.[7] Cathepsin K is the one of the most potent mammalian collagenase and plays a key role in bone remodeling and cartilage breakdown and is used as a well-known marker of osteoclast activity. There are studies which show increased level of Cathepsin K in GCF of patients with periodontitis.5 Early induction of Cathepsin K mRNA may cause an imbalance in the relative resorption activities on the pressure and tension side.[8] The present study assessed the level of cathepsin K in GCF during orthodontic tooth movement.

In present study, there were 12 patients with chronic periodontitis. There were 5 males and 7 females in present study. Anand et al[9] included eight bimaxillary protrusion patients undergoing orthodontic treatment with four first bicuspid extractions were selected. Retraction of the canine was initiated by giving lace back on maxillary right canine which was used as Control Tooth (CT) and maxillary left canine used as Test Tooth (TT) with no laceback. 4 GCF samples were collected 1 hour before, on 24 hours, on 168 hours, and after 30 days. The dynamics of mechanically stimulated Cathepsin K levels in GCF was assessed using enzymatic immunoassay (ELISA). Results showed significant differences between the control and treated teeth for Cathepsin K, with mean values significantly higher for treated site than control sites. On 7th day, at the test side, the levels of Cathepsin K were higher than the corresponding control sides. Another important finding was seen on the 30th day, where Cathepsin K levels were significantly higher on the control side when compared to the test side.

We found that mean Cathepsin K level at 0 hour in test side was 142.5 and in control side was 140.2, at 1 day was 52.6 and at control side was 51.8, at 7 days was 341.2 and at control side was 280.4, at 30 days was 48.2 and at control side was 92.4. The difference was significant ($P<0.05$).

Mogi et al[10] found Cathepsin B a typical lysosomal cysteine proteinase was identified immunologically with anti-human cathepsin B antibody in inflammatory exudate, gingival crevicular fluid (GCF) of adult periodontitis patients. The sensitive enzyme immunoassay (EIA) system initially developed, was rarely influenced by the presence of endogenous, cysteine proteinase inhibitors, cystatin(s), indicating that it is possible to quantify the gross amount of cathepsin B including free enzyme forms and enzyme-inhibitor complex forms using this EIA system. The cathepsin B levels in, GCF as determined by EIA and the activity measured with Z-Arg-Arg-MCA showed positive and significant correlation with various clinical parameters. Immunoblotting analysis revealed that the molecular form was a 29 kDa mature enzyme. More than 95% of Z-Arg-Arg-MCA hydrolytic activity in each GCF sample was inhibited by CA-074, specific inhibitor of cathepsin B. These results strongly suggested that the gross amount of cathepsin B in GCF as well as its activity level is closely associated with the severity of the disease and that cathepsins B play an important role in the pathogenesis of periodontitis.

CONCLUSION

Authors found increase level of Cathepsin K on test side as compared to control side on 7th day. The amount of Cathepsin K in GCF increased during the initial period of orthodontic tooth movement.

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