## **Original Article**

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## **Evaluation of enzyme activity** and rate of tooth movement in corticotomy-accelerated tooth movement – A randomized clinical trial

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#### Abstract:

**BACKGROUND:** This study was undertaken to evaluate the enzyme activity profiles in human saliva and gingival crevicular fluid (GCF) in accelerated tooth movement when compared with normal orthodontic tooth movement (OTM) in extraction cases.

**MATERIALS AND METHODS:** Twenty patients who required premolar extractions were treated with MBT mechanotherapy. They were divided into two equal groups: conventional (Group I) and corticotomy (Group II) which was performed on both the jaw sides before initiating retraction. GCF was collected from mesial and distal aspects of canine before initiation of retraction and at 7<sup>th</sup>, 14<sup>th</sup>, 21<sup>st</sup>, and 28<sup>th</sup> days, and then at fifth and sixth weeks and third and sixth months after retraction. A total of 5 mL of unstimulated saliva was collected from the subjects after 90 min of nonoral activity (subjects were refrained from eating and drinking).

**RESULTS:** The results showed that in Group I, the peak of aspartate aminotransferase (AST) and alkaline phosphatase (ALP) enzyme activity occurred on the 14<sup>th</sup> day of force application. In Group II, the enzyme activity progressively increased from day 0 to 6 weeks, peaking at the sixth week, and then a decline in enzyme activity was observed on third and sixth months. When ALP and AST activities in GCF and saliva were compared between Groups I and II, no statistically significant difference was observed on days 0, 7, and 14.

**CONCLUSION:** Corticotomy-accelerated tooth movement is a promising technique that has many applications in orthodontic treatment of adults as it helps overcome many of the current limitations of this treatment. The enzymatic activity signifies osteoclastic and osteoblastic activities, so ALP and AST from the saliva and GCF may potentially be used as biomarkers for monitoring corticotomy-assisted OTM.

#### Keywords:

Corticotomy, gingival crevicular fluid, saliva, tooth movement

## Introduction

Due to huge demand by adults for a shorter orthodontic treatment time, an abundance of clinical orthodontic research is directed toward achieving this goal.<sup>[1]</sup> Unfortunately, adults typically require longer treatment periods because

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their metabolism is much slower than younger patients.<sup>[2,3]</sup> Also, long orthodontic treatment time poses several disadvantages like higher predisposition to caries, gingival recession, and root resorption.<sup>[1]</sup> One of the ways to shorten treatment time is to speed up the tooth movement.<sup>[4]</sup>

Orthodontic tooth movement (OTM) can occur rapidly or slowly, depending on the amount and physical characteristics

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of the applied force and biological response of the periodontal ligament (PDL) and surrounding bone.<sup>[5,6]</sup> Bone remodeling involves four main phases: activation, bone resorption, reversal, and bone formation.<sup>[7]</sup> Previous studies have shown that several enzymes are expressed during bone remodeling phases. These enzymes have been described as biomarkers during bone remodeling which includes aspartate aminotransferase (AST) and alkaline phosphatase (ALP).<sup>[8]</sup>

Many theories to increase the rate of tooth movement have been suggested in the past. One such theory is accelerated osteogenic orthodontics or periodontal accelerated osteogenic orthodontics (PAOO) (patented by W. Wilcko)<sup>[9]</sup> which is said to harness the regional acceleratory phenomenon (RAP).<sup>[4]</sup> In essence, the technique involves corticotomies around the teeth to be moved, placement of a bone graft, followed by OTM. The results showed that orthodontic force application with corticotomy promoted early rapid tooth movement.<sup>[10]</sup>

In light of the above facts, the present *in vivo* study was undertaken to assess the levels of ALP and AST in gingival crevicular fluid (GCF) during accelerated OTM and to compare it with conventional OTM.

## **Materials and Methods**

A total of 26 systemically healthy patients (12 females and 14 males) between 15 and 30 years of age who reported to the outpatient department were recruited on the basis of inclusion and exclusion criteria. Ethical clearance was obtained from the Ethical Committee (reference no. IDST/IERBC/2014-2017/13 dated 30/11/2014) and the study was conducted in accordance with the Declaration of Helsinki of 1975, as revised in 2014. This randomized parallel designed human clinical trial is registered at WHO – Clinical Trials Registry – India (CTRI/2017/05/008496). Adequate method was used to generate the random allocation sequence and block randomization was selected. The method to be used for random sequence was coin toss.

The inclusion criteria were as follows:

- 1. Patients without any systemic disease and nonsmokers
- 2. Gingiva showed no signs of inflammation
- 3. Good periodontal health with generalized probing depth less than 3 mm
- 4. No radiographic evidence of periodontal bone loss
- 5. Patients ruled out for pregnancy.

Six patients failed to meet the selection criteria to participate in the study in which four had periodontal bone loss and two were chronic smokers. All patients were informed about the purpose of the study and signed a consent letter. Patients were divided randomly into two equal groups [Figure 1]:

- Group I: Extraction cases treated with conventional tooth movement
- Group II: Extraction cases treated with corticotomy-assisted tooth movement.

The patients requiring premolar extractions (crowding 7–14 mm, bimaxillary protrusion, overjet more than 9 mm) were selected. All patients were treated with MBT mechanotherapy ( $0.022 \times 0.028$  slot). Pretreatment study models, lateral cephalogram with teeth in centric occlusion, OPG, and intraoral and extraoral photographs were taken, and case history was recorded carefully. Oral prophylaxis was performed, and oral hygiene maintenance instructions were given. The extractions of both (upper and lower) first premolars were done early to allow enhanced enzyme activity to subside by the time canine retraction was initiated.

Initial leveling and alignment was performed with 0.016 round nickel titanium wires. Leveling was completed in 3.5 months (average) from the start of treatment. In cases where anchorage requirement was high, transpalatal and lingual arches were used to enhance anchorage. After 4 weeks of placement of  $0.019 \times 0.025$  stainless steel wire, retraction was initiated in both the groups. Corticotomy was performed in Group II before the retraction was initiated. A crevicular incision was made and a full-thickness flap was reflected only on the buccal aspect of maxillary and mandibular teeth, from the distal margin of right canine to the distal margin of left canine with releasing incisions. Flaps were carefully reflected beyond the tooth apices, the cortical bone was exposed, and osteotomies were performed by partial cut of cortical plate in the form of decortication lines and dots without penetrating the medullary bone. The procedure was then



Figure 1: Flowchart showing the study layout

completed by repositioning the flap and suturing with Vicryl 3.0 thread.

## **Collection of sample**

A total of  $5 \,\mu$ L of unstimulated whole saliva was collected from the subjects after 90 min of nonoral activity like brushing or eating. The saliva was collected in a sterile container and saliva samples were centrifuged for 10 min at 4°C to remove insoluble materials. The supernatant was then transferred to a new sterile container and stored at -20°C.

GCF was collected using volumetric micropipettes of 100  $\mu$ L capacity. The patients were asked to gargle vigorously with sterile water to cleanse the oral cavity. The cheek retractor was placed, and sites were isolated and dried using cotton rolls. The micropipette was placed extra crevicularly and 1  $\mu$ L of GCF was collected from mesial and distal sites.

The salivary and GCF samples were collected on 0,  $7^{th}$ ,  $14^{th}$ ,  $21^{st}$ , and  $28^{th}$  days and at fifth and sixth weeks and after third and sixth months.

## Sample preparation and storage

One microliter of GCF was made to 100  $\mu$ L with Sorensen's medium containing 0.05% bovine serum albumin in phosphate-buffered saline. The samples were collected in eppendorf tubes and centrifuged in a refrigerated micro centrifuge for 1 min to remove the bacterial and cellular debris. These samples were then stored at -70°C until assayed for enzyme activities.

## **ALP** estimation

The kit for estimation of ALP was "Alkaline Phosphatase Assay Kit-Colorimetric" (ERBA Mannheim, Germany).

About 40  $\mu$ L per well of biological samples containing ALP were added. ALP dilution buffer was used to dilute the samples. Afterward, 40  $\mu$ L of serially diluted ALP standard solution from 100 to 0 ng/mL to the wells was added. The final amount of ALP standard was 10, 5, 2.5, 1.2, 0.6, 0.3, 0.15, and 0 ng per well.

Around 40  $\mu$ L of pNPP substrate solution was added to each well. The reagents were used by gently shaking the plate for 30 s. End-point reading was assessed by incubation reaction at the desired temperature for 30–60 min. Finally, 50  $\mu$ L of stop solution (Component C) into each well was added. The plate was shaken on a plate shaker for 1 min before the reading.

The absorbance of reaction at 405 nm was measured using photospectrometer, and the color changes were observed.

#### **AST** estimation

The samples were analyzed spectrophotometrically. After the samples were centrifuged, they were transferred into jacketed sample cups, which were then placed into sample wheel and then placed into the analyzer with magazine loaded with reagent for analyzing the sample. AST reagent was used to analyze the enzyme activity of AST. After analyzing, the used sample was sealed into the cuvette cartridges. Quantitative estimation of enzyme levels of AST was carried out in unit per liter. The GCF AST activity was determined spectrophotometrically at a constant 30°C with less than 0.05°C fluctuation.

The kit consisted of

- a) Single-step enzymatic reagent bottle
- b) Aqua-4 bottle (double deionized, 0.2 μm, particle free reagent grade water for reconstitution of the ingredients in enzymatic reagent bottle).

### Rate of tooth movement

The rate of tooth movement was measured at TO – before retraction, T1 – after 30 days of retraction, and T2 – after 90 days of retraction. All measurements were done at different time intervals, and the mean was recorded to decrease the bias.

## **Statistical analysis**

The data were analyzed using SPSS software (Statistical Package for Social Sciences). Mean and standard deviation for AST and ALP for each group were calculated. One-way analysis of variance test was performed to compare AST and ALP enzyme activities among the two groups. Independent *t*-test was applied for comparison between AST and ALP enzyme activities for upper and lower canines within both groups at each time intervals. Bonferroni's multiple comparison test was done for each group. Significance between groups was calculated at 5% level, that is,  $P \leq 0.05$  was counted as statistically significant.

## **Results**

The quantitative estimation of enzyme levels of ALP and AST activities was carried out in unit per liter. The level of significance was set at the level of 0.05.

## ALP activity in GCF

In Group I, at upper canine, before retraction, the average basal ALP activity was  $3.60 \pm 1.01$  IU/L and in Group II was  $3.33 \pm 1.20$  IU/L on day 0. After initiation of retraction, the enzyme activity from day 0 to day 7 was not statistically significant in both the groups. Enzyme activity peaked on day 14 and then showed a rapid fall by day 21 in Group I; and after initiation of retraction, the activity increased from day 0 to sixth

week in Group II. The values at the third and sixth months showed a decreased enzyme activity in both the groups [Table 1].

#### ALP activity in saliva

Before retraction, the average basal ALP activity in saliva in Group I was  $13.02 \pm 4.81$  IU/L and in Group II was  $13.01 \pm 8.13$  IU/L on day 0. The difference in enzyme activity from day 0 to day 7 was not statistically significant in both the groups. Enzyme activity peaked at the 14<sup>th</sup> day and then showed a rapid fall by 21<sup>st</sup> day in Group I, and after initiation of retraction there was a progressive increase in enzyme activity from day 0 to sixth week in Group II. The values at third and sixth months showed a decreased enzyme activity in both the groups [Table 2].

# Comparison of ALP activity between Groups I and II in GCF and saliva

In GCF at all sites, no significant difference was observed on days 0, 7, and 14. When comparing Groups I and II, the increase in ALP enzyme activity was highly statistically significant from day 21 to sixth month in Group II. A similar pattern was observed when enzymatic activity was assessed in the salivary sample [Table 3].

#### AST activity in Groups I and II in GCF

At upper canine, before retraction, the average basal AST activity in Group I was  $11.59 \pm 4.56$  IU/L and in Group II was  $17.75 \pm 10.66$  IU/L on day 0. After initiation of retraction, there was no statistical significance in enzyme activity from day 0 to day 7 in both the groups. Enzyme activity peaked on  $14^{\text{th}}$  day ( $16.82 \pm 7.16$ ) and then showed a rapid fall by  $21^{\text{st}}$  day ( $13.93 \pm 6.47$ ) in Group I, and after initiation of retraction there was progressive increase in enzyme activity from day 0 to sixth week in Group II. The values at third and sixth months showed a decreased enzyme activity in both the groups [Table 1].

#### AST activity in Groups I and II in saliva

The average basal AST activity of saliva in Group I was  $26.60 \pm 10.22$  IU/L and in Group II was  $51.10 \pm 21.10$  IU/L on day 0. After initiation of retraction, there was no statistical significance in enzyme activity from day 0 to day 7 in both the groups. Enzyme activity peaked on 14<sup>th</sup> day and then showed a rapid fall by 21<sup>st</sup> day in Group I, and after initiation of retraction there was a progressive increase in enzyme activity from day 0 to sixth week in Group II. The values at third and sixth months showed a decreased enzyme activity in both the groups [Table 2].

## Comparison of AST activity between Groups I and II in GCF and saliva

No significant difference was observed on days 0, 7, and 14, when comparing the enzyme activity in Groups I and II. The increase in AST enzyme activity was highly statistically significant from day 21 to sixth month in Group II. A similar pattern was observed when enzymatic activity was assessed in the salivary sample [Table 3].

#### Rate of tooth movement

In this study, the rate of tooth movement was measured at T0 (before retraction), T1 (after 30 days of retraction), and T2 (after 90 days of retraction) stages. The mean calculated rate of movement in different time intervals is tabulated in Table 4. The significant difference was found between Groups I and II at T2 stages (P = 0.045, P = 0.043, P = 0.035, and P = 0.042).

## Discussion

OTM is an inflammatory mechanism characterized by cell death, osteoclastogenesis, and osteogenesis. Many biomarkers of GCF are reported representing remodeling of bone during OTM.<sup>[11]</sup> AST is one of these biomarkers, and variation in its level shows the biological activity in periodontium during orthodontic treatment. Aminotransferase would be expected to pass

Table 1	: ALP	and AST ac	ctivities in g	jingival cre	vicular fluid	in Groups	I and II (IU	/L) ± SD		
Variable	Group	0 <sup>th</sup> Day	7 <sup>th</sup> Day	14 <sup>th</sup> Day	21 <sup>st</sup> Day	28th Day	5 <sup>th</sup> Week	6 <sup>th</sup> Week	3 <sup>rd</sup> Month	6th Month
	I									
ALP	UC	3.60±1.01	3.70±1.00	4.12±0.83	3.33±0.98	2.90±1.06	2.64±0.80	2.45±0.75	2.14±0.67	1.86±0.67
	LC	3.30±0.80	3.34±0.74	3.79±0.64	2.94±0.51	2.65±0.60	2.48±0.53	2.25±0.53	1.85±0.56	1.32±0.61
	П									
	UC	3.33±1.20	3.62±1.56	4.41±1.69	5.01±1.87	4.98±1.55	5.36±1.73	5.94±2.09	4.98±1.23	3.92±1.27
	LC	3.54±2.80	3.72±1.95	4.24±1.75	4.56±2.36	4.74±2.10	5.27±1.87	5.73±2.75	4.94±1.72	3.85±1.26
	I									
AST	UC	11.59±4.56	14.0±6.0	16.82±7.16	13.93±6.47	11.62±5.85	11.50±6.81	10.03±6.92	7.64±4.84	6.24±3.72
	LC	10.40±4.13	11.33±6.40	16.78±6.56	12.77±5.89	9.59±6.52	8.78±6.18	7.75±4.74	6.36±4.80	5.34±4.25
	П									
	UC	17.75±10.66	22.62±14.18	24.95±14.26	30.50±15.37	30.0±17.71	34.08±20.87	42.48±22.72	32.05±13.52	24.97±10.68
	LC	18.41±13.8	21.41±14.01	24.87±12.95	29.72±11.21	32.21±14.31	34.37±12.85	39.70±21.03	29.89±11.76	23.26±12.15

ALP – Alkaline phosphatase; AST – Aspartate aminotransferase; UC – Upper canine; LC – Lower canine; SD – Standard deviation

from periodontal tissues as an inflammatory exudate into GCF. Increased level of this enzyme may provide evidence of cell death within the periodontal tissues as a result of inflammation or OTM.<sup>[12,13]</sup>

The activation phase is essential for the initiation of tooth movement. During this phase, inflammation and cell necrosis occur and produce the enzyme AST. During OTM, two processes occur simultaneously and lead to recruitment of osteoblasts and osteoblast progenitors. The ALP activity signifies osteoclastic and osteoblastic activities, so ALP acts as a biomarker of osteoblastic activity during bone deposition.<sup>[14,15]</sup>

Orthodontic force induces a cellular response in PDL, which leads to resorption on the pressure side and bone deposition on the tension side. This occurs through induction of osteoclasts by activating the RANK–RANKL pathway in the presence of various inflammatory mediators such as interleukin (IL)-1, IL-8, and tumor necrosis factor (TNF)-alpha.<sup>[16-18]</sup> Surgical methods have been used to accelerate tooth movement. These methods were based on the principle that when bone is irritated surgically, an inflammatory cascade is initiated which caused increased osteoclastogenesis, hence causing faster tooth movement (RAP or PAOO).<sup>[19]</sup>

There are limited number of studies in GCF and saliva which shows the changes in levels of ALP and AST activities during OTM. Therefore, the current longitudinal study was aimed to evaluate both ALP and AST activity changes in GCF during conventional versus periodontally accelerated OTM.

#### ALP and AST in GCF and saliva

In Group I (conventional group), very slight difference in ALP and AST enzyme activities was observed on day 7 compared with day 0 values, that is, enzyme value was found to be lying close to pretooth movement value. The seventh-day enzyme activity coincides definitively with lag phase of tooth movement when hyalinization sets in and the 14<sup>th</sup> and 21<sup>st</sup> day enzyme activities are pointers to the beginning of post lag phase. The enzyme activity peaked on 14th day. This finding is supported by Batra et al.[15] and Perinetti et al.[20] who examined ALP activity in GCF during OTM and demonstrated that ALP activity was significantly higher on 14<sup>th</sup> day, showing peak enzymatic activity. Similarly, this finding is also supported by Dannan et al.,<sup>[21]</sup> Tomizuka et al.,<sup>[22]</sup> and Rohaya et al.<sup>[23]</sup> who examined AST activity in GCF.

Furthermore, there was a rapid fall from 21<sup>st</sup> day till sixth week. The fall in cellular response that occurred after 14<sup>th</sup> day of activation could be related to cellular activity and thereby affecting the enzyme activity. The

Table 2	: ALP and A	AST activities	in saliva in Group:	s I and II (IU/I	-) ± SD					
Variable	Group	0 <sup>th</sup> Day	7 <sup>th</sup> Day	14 <sup>th</sup> Day	21st Day	28 <sup>th</sup> Day	5 <sup>th</sup> Week	6 <sup>th</sup> Week	<b>3rd Month</b>	6 <sup>th</sup> Month
ALP	_	13.02±4.81	17.21±6.16	17.65±5.46	15.79±3.55	15.26±5.37	14.95±4.41	14.81±4.32	10.58±3.74	9.45±5.14
	=	13.01±8.13	$15.90 \pm 9.35$	18.65±13.15	23.93±15.6	30.89±19.8	36.70±22.60	44.80±27.5	31.78±18.29	28.31±15.43
	٩	0.9974	0.7157	0.8267	0.1250	0.0269	0.0079	0.0031	0.0021	0.0018
AST	_	26.60±10.22	33.50±14.75	41.30±15.18	28.50±10.99	25.50±13.39	27.90±20.20	20.10±30.90	17.10±10.17	13.61±8.90
	=	51.1±21.10	43±17.70	52.30±21.21	64.90±21.82	67.50±19.78	77.50±22.68	91.90±24.06	54.90±13.37	46.00±12.6
	٩	0.0039	0.2087	0.1989	0.0002	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
ALP – Alka	line phosphatas	e; AST – Aspartate	aminotransferase; SD – Si	tandard deviation						

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Table 3:	Comparison	of ALP	and AST activ	vities in gingiv	al crevicular	fluid between	Groups I and	II (IU/L) ± SD			
Variable	Segment	Group	0 <sup>th</sup> Day	7 <sup>th</sup> Day	14 <sup>th</sup> Day	21st Day	28 <sup>th</sup> Day	5 <sup>th</sup> Week	6 <sup>th</sup> Week	<b>3rd Month</b>	6 <sup>th</sup> Month
ALP	nc	_	3.60±1.01	3.70±1.00	4.12±0.83	3.33±0.98	2.90±1.06	2.64±0.80	2.45±0.75	2.14±0.67	1.86±0.67
		=	3.33±1.20	3.62±1.56	4.41±1.69	5.01±1.87	4.98±1.55	5.36±1.73	$5.94\pm 2.09$	4.98±1.23	3.92±1.27
		٩	0.592	0.892	0.632	0.021	0.0021	0.0003	0.0001	<0.0001	0.0003
	ГС	_	3.30±0.80	3.34±0.74	3.79±0.64	2.94±0.51	2.65±0.60	2.48±0.53	2.25±0.53	$1.85\pm0.56$	1.32±0.61
		=	3.54±2.80	3.72±1.95	4.24±1.75	4.56±2.36	4.74±2.10	5.27±1.87	5.73±2.75	4.94±1.72	3.85±1.26
		٩	0.7973	0.5716	0.4549	0.0480	0.0073	0.0003	0.0010	<0.0001	<0.0001
AST	nc	_	$11.59 \pm 4.56$	14.0±6.0	16.82±7.16	13.93±6.47	11.62±5.85	11.50±6.81	10.03±6.92	7.64±4.84	6.24±3.72
		=	17.75±10.66	22.62±14.18	24.95±14.26	30.50±15.37	30.0±17.71	34.08±20.87	42.48±22.72	32.05±13.52	24.97±10.68
		٩	0.1102	0.0935	0.1245	0.0056	0.0060	0.0044	0.0004	<0.0001	0.0001
	LC	_	10.40±4.13	11.33±6.40	16.78±6.56	12.77±5.89	9.59±6.52	8.78±6.18	7.75±4.74	6.36±4.80	5.34±4.25
		=	18.41±13.8	21.41±14.01	24.87±12.95	29.72±11.21	32.21±14.31	34.37±12.85	39.70±21.03	29.89±11.76	23.26±12.15
		٩	0.0957	0.0532	0.0950	0.0005	0.0002	<0.0001	0.0002	<0.0001	<0.0001
Significant,	P≤0.05. P – Prob∈	ability; ALP	<ul> <li>Alkaline phospha</li> </ul>	itase; AST – Asparta	ate aminotransferas	e; UC – Upper canir	ie; LC – Lower canin	ie; SD – Standard o	leviation		

Table 4:	Comparison of	rate of	tooth	movement
between	Groups I and	I (IU/L)	±SD	

Group	Т0	T1	T2
I	6.95±0.55	5.50±0.73	2.05±0.92
П	6.99±1.35	4.10±0.65	0.42±0.55
Ρ	0.932	0.126	0.045
I	6.87±0.73	4.90±0.66	2.87±0.86
П	6.91±1.26	4.07±0.46	0.29±0.32
Ρ	0.933	0.446	0.043
I	5.94±0.75	4.20±0.70	1.05±0.84
П	5.52±0.28	3.77±0.42	0.37±0.64
Ρ	0.914	0.567	0.035
I	5.65±0.31	4.09±0.51	2.07±0.47
П	5.52±0.29	3.87±0.49	0.52±0.40
Р	0.410	0.416	0.042
	Group  I I P I I P I I I P I I I P I I I P I I I P I P I I P I P I I P I P I I P I P I I P I P I I P P I P P I P	Group         T0           I         6.95±0.55           II         6.99±1.35           P         0.932           I         6.87±0.73           II         6.91±1.26           P         0.933           I         5.94±0.75           II         5.52±0.28           P         0.914           I         5.65±0.31           II         5.52±0.29           P         0.410	Group         T0         T1           I         6.95±0.55         5.50±0.73           II         6.99±1.35         4.10±0.65           P         0.932         0.126           II         6.87±0.73         4.90±0.66           II         6.91±1.26         4.07±0.46           P         0.933         0.446           P         0.933         0.446           I         5.94±0.75         4.20±0.70           II         5.52±0.28         3.77±0.42           P         0.914         0.567           I         5.65±0.31         4.09±0.51           II         5.52±0.28         3.87±0.49           P         0.410         0.416

Significant,  $P \le 0.05$ . P – Probability; T0 – Before retraction; T1 – After 30 days of retraction; T2 – After 90 days of retraction; SD – Standard deviation

value at third and sixth months showed a decreased enzymatic activity. These findings were supported by Smitha *et al.*,<sup>[24]</sup> Asma and Melsen,<sup>[25]</sup> Insoft *et al.*,<sup>[26]</sup> and Perinetti *et al.*,<sup>[20]</sup> who also concluded that ALP enzyme activity declined up to sixth week.

In Group II (corticotomy), 0 to 7<sup>th</sup> day, the enzyme activity was similar to pretooth value which coincides with the lag phase as mentioned earlier with ALP and AST activities. The activity was consistently increased from seventh day to sixth week. The enzymatic activity increased from day 0 to sixth week with a peak on sixth week. Findings of Group II are similar to the results of Wilcko *et al.*<sup>[9,27,28]</sup> who reported rapid tooth movement at a rate of three to four times greater than conventional orthodontic movement which is directly proportional to enzymatic activity.

These findings can be correlated with the RAP, described by previous studies<sup>[29,30]</sup> as a local response of tissues to noxious stimuli by which tissue regenerates faster than normal (i.e., without stimuli) in a regional regeneration/ remodeling process. This is an intensified bone response with increased osteoclastic and osteoblastic activity, and increased levels of local and systemic inflammatory markers in areas around cuts that extend to the marrow. It lasts for 4 months in human bone. According to Yaffe *et al.*,<sup>[31]</sup> RAP in humans begins within a few days of surgery, typically peaks at 1–2 months, and may take from 6 to more than 24 months to subside which is similar to our finding.

The enzyme activity between the two groups did not show any significant difference on days 0, 7, and 14. However, from 21<sup>st</sup> day to sixth month, enzyme activity was highly statistically significantly increased in Group II when compared with Group I. This can be justified by RAP phenomenon. Thereby further supporting the idea of accelerating OTM following corticotomy which generates intensified bone response and inflammatory markers.

#### Rate of tooth movement

In our study, measurements were done at three different intervals in both the groups (T0 – before retraction, T1 – after 30 days of retraction, and T2 – after 90 days of retraction). The results of this study demonstrated that the mean rate of retraction at T1 stage in all segments was significantly increased in Group II (experimental group) (2.10 mm/month) when compared with Group I (1.45 mm/month) but was not statistically significant (P = 0.126). The rate of tooth movement was increased in Group I at T2 stage and was statistically significant.

Our results were supported by Wilcko *et al.*<sup>[32]</sup> who had orthodontically treated within 7 months with stable results even after 8 years of retention. Yao *et al.*<sup>[33]</sup> did molar intrusion of 4 mm in 7.6 months using these temporary devices. On the other hand, the same procedure combined with corticotomy-assisted orthodontic (CAO) can achieve the same amount of intrusion in 2.5 months as found by Oliveira *et al.*<sup>[34]</sup> Sebaoun JD *et al.*<sup>[35]</sup> found that retention and stability with CAO are better than with conventional orthodontics.

## Conclusion

Corticotomy-accelerated tooth movement is a promising technique that has many applications in the orthodontic treatment of adults as it overcomes many of the limitations including lengthy duration, potential for periodontal complications, lack of growth, and the limited envelope of tooth movement. The mechanism behind this can be summarized as when the bone is irritated surgically, an inflammatory cascade is initiated which causes increased osteoclastogenesis, hence causing faster tooth movement. During tooth movement phase, inflammation and cell necrosis occur and produce the enzymes. The enzymatic activity signifies osteoclastic and osteoblastic activities, so ALP and AST act as biomarkers for bone resorption and bone formation. ALP and AST from saliva and GCF may potentially be used as biomarkers for monitoring OTM. Enzyme activity peaked at the 14<sup>th</sup> day and then showed a rapid fall by 21st day in Group I, and after initiation of retraction there was a progressive increase in enzyme activity from day 0 to sixth week in Group II. Further studies targeting large sample size and different durations for the collection of GCF are required for a better insight and understanding of the role of the said enzymes during OTMs.

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#### **Conflicts of interest**

There are no conflicts of interest.

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