

Efficacy of low-intensity laser therapy in reducing treatment time and orthodontic pain: A clinical investigation

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Introduction: The long duration of orthodontic treatment is a major concern for patients. A noninvasive method of accelerating tooth movement in a physiologic manner is needed. The aim of this study was to evaluate the efficacy of low-intensity laser therapy in reducing orthodontic treatment duration and pain. **Methods:** Twenty patients requiring extraction of first premolars were selected for this study. We used a randomly assigned incomplete block split-mouth design. Individual canine retraction by a nickel-titanium closed-coil spring was studied. The experimental side received infrared radiation from a semiconductor (aluminium gallium arsenide) diode laser with a wavelength of 810 nm. The laser regimen was applied on days 0, 3, 7, and 14 in the first month, and thereafter on every 15th day until complete canine retraction was achieved on the experimental side. Tooth movement was measured on progress models. Each patient's pain response was ranked according to a visual analog scale. **Results:** An average increase of 30% in the rate of tooth movement was observed with the low-intensity laser therapy. Pain scores on the experimental sides were significantly lower compared with the control sides. **Conclusions:** Low-intensity laser therapy is a good option to reduce treatment duration and pain. (Am J Orthod Dentofacial Orthop 2012;141:289-97)

A major concern to orthodontic patients is treatment time.¹ Generally, the time required for fixed appliance treatment is 20 to 30 months. Reducing the treatment time requires increasing the rate of orthodontic tooth movement. Many studies have examined different methods that can increase the rate of orthodontic tooth movement, including local injections of prostaglandins,^{2,3} 1, 25(OH) 2 D₃ (the active form of vitamin D₃),⁴ osteocalcin,⁵ and relaxin⁶ around the alveolar socket. Although these substances stimulate the rate of tooth movement, they also have the undesirable side effects of local pain and discomfort during the injections. Recently, electric stimulation⁷ and resonance vibration⁸ have been tried in animals, but these methods

require an apparatus that is not routinely used in dental practice.

Ablative use of lasers has become common in dental practice. Low-intensity laser therapy has an energy output that is low enough so as not to cause the temperature of the treated tissues to rise above 36.5°C or normal body temperature.⁹ Low-intensity laser therapy in its initial days was applied only in medical sciences such as orthopedics, surgery, and medicine. It is used to accelerate the callus formation at fracture sites to facilitate wound healing.¹⁰ Saito and Shimizu¹¹ found that low-intensity laser therapy can accelerate bone regeneration in the midpalatal suture during rapid palatal expansion and stimulate the synthesis of collagen, which is major matrix protein in bone. In the last decade, many histologic studies have attempted to determine the effect of low-intensity laser therapy on the histochemical pathways directly associated with orthodontic tooth movement.¹²⁻¹⁵ Increased osteoblastic and osteoclastic activity after low-level laser therapy was observed in vivo and in vitro. Few studies in the literature have examined the effect of low-intensity laser therapy on the rate of orthodontic tooth movement, and most were short-term animal studies.

Thus, the aims of this study were to evaluate the effect of low-intensity laser therapy on the rate of

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The authors report no commercial, proprietary, or financial interest in the products or companies described in this article.

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Submitted, June 2011; revised and accepted, September 2011.

0889-5406/\$36.00

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doi:10.1016/j.ajodo.2011.09.009

orthodontic tooth movement and also to study its analgesic effect during orthodontic tooth movement.

MATERIAL AND METHODS

Our sample consisted of 20 healthy orthodontic patients (8 male, 12 female; ages, 12–23 years). Patients with a history of long-term medication were excluded because nonsteroidal anti-inflammatory drugs and hormone supplements are known to interfere with bone metabolism. Patients with unilateral chewing or parafunctional habits, skeletal crossbite, and occlusal interferences were also excluded. Periodontally compromised patients were excluded because poor bone quality can affect orthodontic tooth movement, and the development of mobility can lead to incorrect measurement of orthodontic tooth movement. Impacted canines and canines with dilacerated roots were excluded from the study because dilacerated roots make orthodontic tooth movement difficult with a greater possibility of root resorption.

The sample size was determined by power analysis based on the results of the pilot study that showed that the rate of tooth movement was twice that of the control side.

$$\eta = \frac{\{Z_{1-\alpha/2}\sqrt{P(1-P_\alpha)} + Z_{1-\beta}\sqrt{P_0(1-P_\alpha)}\}^2}{(P_\alpha - P_0)^2}$$

P_0 = Population proportion

P_α = Sample proportion

α = Significance level

$1 - \beta$ = Power

With a permissible error of 5% by using a split-mouth design, a sample size of 20 was sufficient for the study to have 80% power and be clinically significant.

The study design was approved by the ethics committee of Government Dental College and Hospital, Nagpur, Maharashtra, India, according to the guidelines of Health University.

Routine orthodontic diagnostic records were collected and analyzed for all subjects. The treatment plans for these patients included extraction of the maxillary or mandibular first premolars (or both) to meet the requirements of space for the retraction of anterior teeth. A randomly assigned incomplete block split-mouth design was used to prevent interindividual biologic variation.¹⁶ In 20 patients, the maxillary first premolars were extracted, but the mandibular first premolars were extracted in only 10 patients. In each patient, the extracted right and left quadrants were randomly divided into 2 groups. The patients were blinded about the experimental and control sides. Group 1 was the control side quadrant and did not receive low-intensity laser therapy. Group 2 was the experimental

side quadrant and received laser therapy. Each group consisted of 30 quadrants.

On day 7 after the extractions, separators were placed mesially and distally to the first molars for band placement. After 2 days of separator placement, molar bands (0.180 × 0.005 in) were custom made. Triple molar tubes were welded on the buccal surfaces, and a lingual sheath was welded on the lingual surface of the maxillary molar bands. On the mandibular molar bands, double molar tubes were welded. Transpalatal arch 20-gauge (0.9 mm) stainless steel wire was adapted on the model. Maxillary bands with a transpalatal arch inserted in the lingual sheath were cemented with glass ionomer luting cement (D-tech, Pune, India). The transpalatal arch was placed for anchorage reinforcement and secured with an elastic module.

Preadjusted edgewise McLaughlin Bennett Trevisi brackets (Ortho Organizers, Carlsbad, Calif) of 0.022-in slot were bonded with Transbond XT (3M Unitek, Monrovia, Calif), and curing was done with a light-emitting diode (Dentsply International, York, Pa). Alignment and leveling were initiated with 0.016-in heat-activated nickel-titanium wire, and later sequences of wires were 16 × 22-in nickel-titanium, 17 × 25-in nickel-titanium, 17 × 25-in stainless steel, and 19 × 25-in nickel-titanium. After alignment and leveling, a final working wire was placed: 19 × 25-in stainless steel (Orthoforce; G&H Wire, Franklin, Ind).

After 21 days of 19 × 25-in stainless steel wire placement, individual canine retraction was started with a nickel-titanium closed-coil spring (G&H Wire). The incisors were consolidated by using 0.009-in steel ligature wires. The second premolar and the first molar were also consolidated to make a single anchorage unit. A constant force of 150 g was used for canine retraction on both the control and experimental sides. To maintain the force of 150 g in all patients in spite of the different widths of available extraction spaces, accurate spring selection was done by using the manufacturer's guide. The kit of the nickel-titanium closed-coil spring system (G&H Wire) contains springs of 9 and 12 mm in length. They are again subdivided into feather light, extra light, light, medium, and heavy forces. The measuring gauge supplied by manufacturer with the spring kit has a hole to simulate the eyelet of the spring. This hole is slipped over the canine hook; the closest landmark to the molar hook then shows the recommended spring size to be selected to achieve a force of 150 g. The spring was positioned from the first molar tube hook to the power arm of the canine bracket and also secured with a ligature tie to the bracket. The exerted force value was confirmed with an orthodontic dynamometer. Patients were asked to report immediately if the spring dislodged or broke; it was then replaced.

Low-intensity laser therapy was started on the selected experimental side on the same day as placement of the coil spring.

In 2 patients, the nickel-titanium coil spring became detached. In both instances, the failures occurred unilaterally, from the canine hooks. They were replaced within 12 hours.

Informed consent was obtained from each patient or parent (for patients less than 18 years of age) for laser irradiation. The laser type used was a semiconductor (aluminium gallium arsenide) diode (model LA3D0001.1; LAMBDA S.p.A., Vicenza, Italy) emitting infrared radiation with a wavelength of 808 ± 10 nm operated according to the manufacturer's recommendations. All safety precautions for the patient and the operator were followed. This medical equipment has a wide range of settings according to the required treatment.

For analgesic purposes, the settings were adjusted to a wavelength of 800 nm, a continuous wave mode, an output power of 0.7 mW, and an exposure time of 30 seconds. For bio-stimulation, the parameters were set at a wavelength of 800 nm, a continuous wave mode, an output power of 0.25 mW, and an exposure time of 10 seconds.

The hand piece has a cylindrical quartz tip with a surface area of 4 mm^2 from where the laser beam is emitted. The black color-coded needle (used for therapeutic purposes) was attached to the hand piece for low-intensity laser therapy. The routine method of sterilization and disinfection was followed. In particular, the hand piece body and the optic tips were sterilized by cold sterilization.

Protection glasses were worn by both the operator and the patient. These glasses, provided by the manufacturer, were in accordance with the European norm EN 207 and had a optical density of ≥ 5 at the wavelength of emission from the diode.

Low-intensity laser therapy was started on the day of placement of the nickel-titanium coil spring for analgesia. Two irradiations were done. One irradiation was done on the middle third of the canine root on the buccal side, and the second on the palatal side holding the laser tip in direct contact with the tissues. On day 3, low-intensity laser therapy was started for bio-stimulation. A total of 10 irradiations were done: 5 on the buccal side (Fig 1) and 5 on the palatal side. To cover the entire periodontal fibers and alveolar process around the canines, the distribution and order were as follows.

On the buccal side, there were (1) 2 irradiation doses on the cervical third of the canine root (1 medial and 1 distal), (2) 2 on the apical third of the canine root (1 medial and 1 distal), and (3) 1 on the middle third (center of the root).



Fig 1. Laser irradiation.

On the palatal side, the irradiations were done similarly. The tip was held in contact with the tissue during application. The total energy density (dose) at each application was 8 J ($2 \times 40 \text{ s} \times 100 \text{ mW}$).

This procedure was followed for all subsequent appointments. The laser regimen was applied on days 0, 3, 7, and 14 in the first month. Thereafter, irradiations were done on every 15th day until complete canine retraction on the experimental side.

To prevent intraoperator variations, all irradiations were done by the same operator (D.-M.). To control the patient's behavior about the pain and maintain blindness, the hand piece was also held on the control side just to project the red guiding light with no laser emission. After 6 months, the laser side (experimental) and the control side canines were examined with periapical radiographs, which showed no undesirable changes in the adjacent periodontal ligaments and alveolar bones. Vitality tests of the retracted canines were also positive.

Three models were made for each patient. On the models, the mesial cusp tips of first molar and the canine were the reference points. The measurement recorder was blinded about the control and experimental sides. The distance between the first molar and the canine was measured on all 3 models for each patient with a digital caliper (AEROSPACE, Shanghai, China) accurate to $\pm 0.02 \text{ mm}$. These distances were recorded at T0 (after completion of alignment and leveling; day 1 of canine retraction), T1 (at the end of 3 months of canine retraction), and T2 (on completion of canine retraction on the experimental side). Descriptive statistics is presented in Table 1.

Difference between T0 and T1 was the amount of tooth movement over the period of 3 months (Table II).

The rate of orthodontic tooth movement was calculated as the amount of tooth movement divided by the

Table I. ANOVA results of the mean distances (mm) between the cusp tips of the canines and the mesial cusp tips of the first molars

	Maxillary arch		Mandibular arch	
	Control	Experimental	Control	Experimental
T0	19.81 ± 1.61	19.81 ± 1.59	21.29 ± 1.14	21.56 ± 0.94
T1	17.83 ± 1.62	15.51 ± 1.43	19.39 ± 1.47	17.04 ± 1.25
T2	15.90 ± 1.33	14.32 ± 1.26	17.52 ± 1.29	16.02 ± 1.41
F-statistics	33.03	81.26	20.86	59.08
P value*	0.0000	0.0000	0.0000	0.0000
Inference	HS	HS	HS	HS

HS, Highly significant; T0, start of canine retraction; T1, at 3 months; T2, at 4.5 months.

*Probability value denoting significance.

Table II. Amounts (mm) of canine retraction in the control and experimental sides

Variable	Control group	Experimental group	t value*	P value	Inference
T0-T1	1.98 ± 0.46	2.30 ± 0.45	2.1458	0.0381	S
T0-T2	3.96 ± 0.98	5.49 ± 0.99	4.9156	0.0000	HS

HS, Highly significant; S, significant; T0-T1, amount of canine retraction in 3 months; T0-T2, amount of canine retraction in 4.5 months.

*Paired t test applied.

time period. The rate of orthodontic tooth movement at the end of 3 months (M1) was recorded as T0 – T1 divided by 3.

The rate of orthodontic tooth movement on completion of canine retraction (M2) on the experimental side was recorded as T1 – T2 divided by the number of months. The M1 and M2 readings were calculated for both the experimental and control sides and compared (Table III).

Each patient's response after nickel-titanium coil-spring placement was ranked according to a visual pain scale (Fig 2) on day 1 (immediately after placement), day 3, and day 30.

To calculate errors in measurements, the measurements were repeated by another operator. The error of the measurements was calculated according to Dahlberg's formula: $Se = \sqrt{\sum d^2/2n}$, where $\sum d^2$ is the sum of the squared differences between pairs of recordings and n is the number of duplicate measurements.¹⁷ This difference was within 0.05 mm; this was insignificant.

Statistical analysis

Master sheets were prepared to facilitate analysis of the data. The data were tabulated and analyzed by statistical software (version 10.0; StataCorp, College Station, Tex). The descriptive statistics of mean differences, standard deviations, and standard errors were calculated for all variables (Table I).

The paired t test was used to compare the variables within the groups. One-way analysis of variance (ANOVA; F statistics) was used for comparing the distances at T0, T1, and T2 in both groups. Multiple comparisons were done with the Bonferroni test. After analysis, the data were sorted into various tables based on the objectives of the study. The results are expressed as levels of significance.

Significance was determined at the 0.05 and 0.01 levels of confidence.

RESULTS

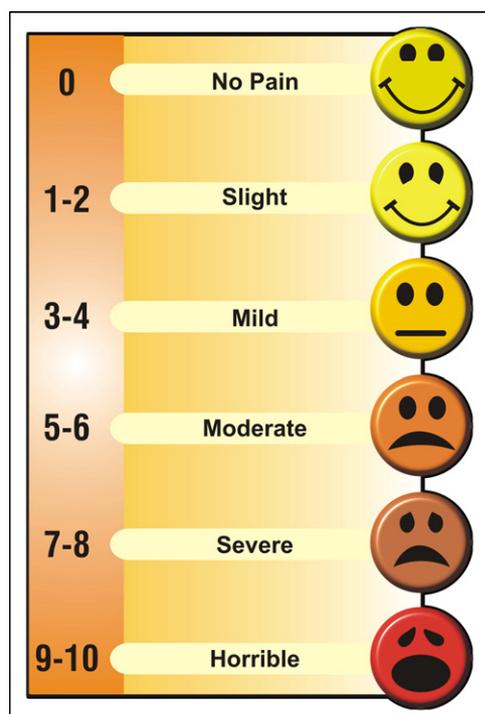
The amounts of M1 were 0.65 mm per month on the control side and 1.46 mm per month on the experimental side. The amounts of M2 were 0.81 mm per month on the control side and 1.15 mm per month on the experimental side (Table III). There was a highly significant positive difference in the rates of tooth movement on the experimental side compared with the control side (Fig 3). The mean increase in the rates of tooth movement at 3 months was 54% in the maxillary arch and 58% in the mandibular arch. Mean increase in the rate of tooth movement after canine retraction was 29% in the maxillary arch and 31% in the mandibular arch (Fig 4).

As illustrated in Figure 5 on day 3, there was a nonsignificant rise in the pain score on the control side, but there were highly significant decreases in the pain scores on the experimental sides. On day 30, there was a highly significant decrease in the pain score on both sides

Table III. Comparison of the rates of canine retraction

	M1 (mm/mo)			M2 (mm/mo)		
	Control	Experimental	Result	Control	Experimental	Result
Maxillary	0.66 ± 0.55	1.43 ± 0.15	HS	0.84 ± 0.21	1.17 ± 0.22	HS
Mandibular	0.63 ± 0.28	1.51 ± 0.18	HS	0.75 ± 0.09	1.11 ± 0.17	HS
Combined mean	0.65 ± 0.18	1.46 ± 0.16	HS	0.81 ± 0.18	1.15 ± 0.21	HS

HS, Highly significant; M1, rate at end of 3 months; M2, rate at end of canine retraction.

**Fig 2.** Visual analog pain scale.

(Table IV). The pain score on the experimental side was significantly lower compared with the control side on day 3 as well as on day 30 (Table V).

DISCUSSION

In this study, we used the semiconductor with a wavelength of 800 nm, a continuous wave mode, an output power of 0.25 mW, and an exposure time of 10 seconds because the results of Takeda¹⁸ and Bradley et al¹⁹ had indicated significant bio-stimulatory effects on bone metabolism around this dosage, whereas higher dosages had bio-inhibitory effects, and lower dosage showed nonsignificant results. A 15-day regimen was used because it coincides with normal recall visits. Ngan et al²⁰ proved that, after an orthodontic procedure, pain and soreness occur after 24 to 48 hours. Thus,

the first follow-up score after low-intensity laser therapy was recorded on day 3.

A direct comparison between this study and previous studies was limited by a number of factors, such as different laser parameters and various animal models. Some researchers omitted descriptions of important aspects related to the study designs. The force to move teeth also differed across studies, as did the methods used for measuring movement.

The rate of tooth movement after 3 months on the experimental side showed a 1.3-fold increase. In other words, the rate was 56% more compared with the control side. Similar findings were reported by Kawasaki and Shimizu²¹ and Yoshida et al.²² They reported a 1.3-fold increase in movement in their experimental laser group over periods of 12 and 21 days in rats. Fujita et al¹⁵ also demonstrated a 1.5-fold increase in their irradiated group over only 7 days. However, their study was on rat molars, and the orthodontic force was not specified.

Kim et al²³ reported a higher rate of tooth movement than that in our study over a period of 2 months in dogs. They found a 2.08-fold increase in tooth movement for their experimental low-intensity laser therapy sample compared with a 1.3-fold increase over 3 months in our study. They used a pulsed mode rather than the continuous mode that we used. Yoshida et al²² stated that laser units show more bio-stimulatory response when functioning in pulsed mode, but Bradley et al¹⁹ and Takeda¹⁸ used the continuous mode effectively. The continuous mode also has peaks and valleys because the laser unit cannot emit continuously in real time. In 2004, Cruz et al²⁴ was the first to carry out a human study on the effect of low-intensity laser therapy on orthodontic tooth movement. They showed that the irradiated canines were retracted at a rate 34% greater than the control canines over 60 days. In our study, the rate of retraction was 54% greater on the experimental side but over a period of 3 months.

Goulart et al²⁵ did a split-mouth study in dogs with 3 groups, 1 control and 2 experimental. In 1 experimental group, they used an energy density of 5.25 J per square centimeter; in the second experimental group, they used

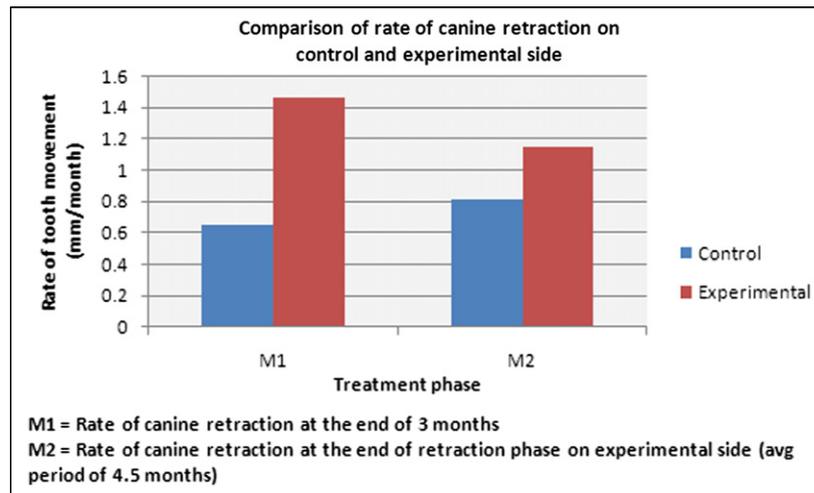


Fig 3. Rates of tooth movement in the control and experimental groups.

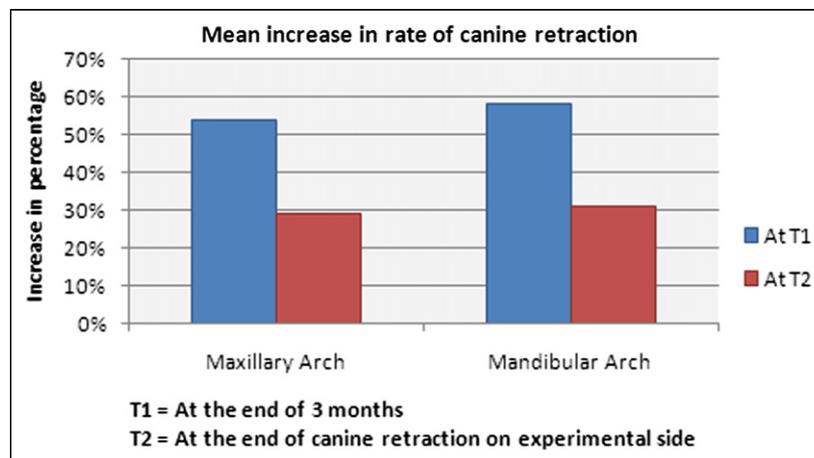


Fig 4. Increases in the rates of tooth movement.

35 J per square centimeter. The first experimental group had a 50% increase, but the second experimental group had a 90% decrease during the first 21 days. They concluded that low-intensity laser therapy with an energy density of 5 J per square centimeter and a total dose of 1.89 J had a stimulatory effect when compared with the controls, and an energy density of 35 J per square centimeter and a total dose 12.6 J had a bio-inhibitory effect when compared with the controls. In our study, an energy density of 5 J per square centimeter and a total dose of 8 J were used.

However, the findings of Limpanichkul et al²⁶ differed from ours. They showed no difference between the experimental low-intensity laser therapy subjects and the controls in a split-mouth study with human subjects over 4 months. The reason could be the higher

energy density of 25 J per square centimeter that they used.

The average time required for canine retraction on the experimental side was 4.5 months. Thus, the rate on the experimental side was 1.5 times, or 30%, more compared with the control side. However, Youssef et al²⁷ reported a rate of canine retraction almost twice as fast as that of the control canines over a 6-month period in human subjects using a split-mouth design. The reason could be the increased irradiation frequency of 4 times per month until the end of canine retraction compared with 4 times per month in the first month and 2 times per month in subsequent months in our study.

In this study, in the first 3 months, a 56% increase in rate of tooth movement was observed, whereas the average increase during the entire period of canine retraction

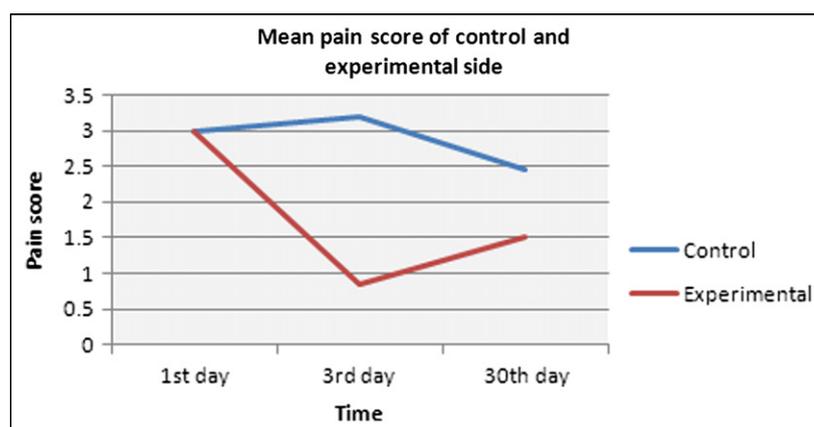


Fig 5. Pain scores in the control and experimental groups.

Table IV. Pain scores in the control and experimental groups (Wilcoxon signed rank test)

Comparison	Control group			Experimental group		
	Z value	P value	Inference	Z value	P value	Inference
Day 1 vs day 3	1.508	0.1317	NS	4.028	0.0001	HS
Day 1 vs day 30	3.162	0.0016	HS	4.056	0.0000	HS

HS, Highly significant; NS, nonsignificant.

Table V. Mean changes of pain scores at days 3 and 30 from baseline between the control and experimental groups

	Control group	Experimental group	Z value	P value	Inference
Day 3	0.25 ± 0.71	2.15 ± 0.98	5.246	0.0000	HS
Day 30	0.5 ± 0.51	1.5 ± 0.76	4.1000	0.0000	HS

HS, Highly significant.

was only 30%. This indicates a decrease in the rate of tooth movement in later time periods; this could be explained as analogous to the normal lag phase in orthodontic tooth movement.

No study has compared the rate of orthodontic tooth movement in the maxillary and mandibular arches. In our study, the mean increases in the rates of tooth movement at 3 months were 54% in the maxillary arch and 58% in the mandibular arch. Mean increases in the rates of tooth movement after canine retraction were 29% in the maxillary arch and 31% in the mandibular arch. These differences were not statistically significant but clinically thought provoking. The smaller increase in the maxillary arch might be because the periodontal ligament of the canines is farther from the site of irradiation on the palatal side. Esnouf et al²⁸ showed a significant reduction in intensity in the first millimeter of penetration: ie, up to 66%. The clinical implication will

be that more energy density should be used on the palatal surfaces of the maxillary teeth.

To relieve orthodontic pain, several methods have been used. One is drugs (nonsteroidal anti-inflammatory drugs). Although these drugs can be effective in relieving pain, they might also reduce the rate of tooth movement.²⁹ Therefore, the second aim of this study was to clinically evaluate the analgesic effect of low-intensity laser therapy after the application of an orthodontic force. We found a highly significant decrease in pain scores on the experimental sides on day 3 compared with day 1. Similar findings were reported by Koji et al.³⁰ They observed significant pain reductions with low-intensity laser therapy immediately after insertion of separators until day 4.

Lim et al⁹ also observed decreases in pain scores with low-intensity laser therapy after placement of the initial archwires. Youssef et al²⁷ evaluated orthodontic pain on

every 21st day after placement of nickel-titanium closed-coil springs until complete canine retraction and reported significant decreases in pain scores with low-intensity laser therapy during all treatment stages.

CONCLUSIONS

Low-intensity laser therapy increases the rate of orthodontic tooth movement in a physiologic manner. It causes no side effects on the vitality or the periodontium of the teeth. Thus, it can safely and routinely be used during orthodontic treatment to shorten the treatment time. Low-intensity laser therapy also is an effective method of analgesia during orthodontic treatment. It has the following clinical applications.

1. Low-intensity laser therapy can be used for differential movement of teeth. In cases of midline shift, it can be used to stimulate orthodontic tooth movement on the opposite side. Application of low-intensity laser therapy only on teeth to be moved conserves the anchorage. Because low-intensity laser therapy stimulates tooth movement by altering the biologic response and not by increasing forces or changing mechanics, it does not tax the anchorage.
2. A few studies have reported a decreased rate of tooth movement in adult patients because of decreased vascularity and cellularity of bone.³¹ Low-intensity laser therapy will be beneficial in adult patients because vascularity and cellularity of bone. With increasing numbers of adults in orthodontic practices, this application might be important.

We thank the Honourable Dean Dr. Vinay Hazary of Government Dental College and Hospital, Nagpur, India for his support throughout this study.

REFERENCES

1. Skidmore KJ, Brook KJ, Thomson WM, Harding WJ. Factors influencing treatment time in orthodontic patients. *Am J Orthod Dentofacial Orthop* 2006;129:230-8.
2. Shibata Y, Imai S, Tani Y, Shibasaki Y, Fukuhara T. Clinical application of prostaglandin E1 (PGE1) upon orthodontic tooth movement. *Am J Orthod* 1984;85:508-18.
3. Sefi M, Eslami B, Saffar AS. The effect of prostaglandin E2 and calcium gluconate on orthodontic tooth movement and root resorption in rats. *Eur J Orthod* 2003;25:199-204.
4. Kale S, Kocadereli I, Atilla P, Aşan E. Comparison of the effects of 1,25 dihydroxycholecalciferol and prostaglandin E2 on orthodontic tooth movement. *Am J Orthod Dentofacial Orthop* 2004;125:607-14.
5. Hashimoto F, Kobayashi Y, Mataka S, Kobayashi K, Kato Y, Sakai H. Administration of osteocalcin accelerates orthodontic tooth movement induced by closed coil springs in rats. *Eur Orthod Soc* 2001;23:525-45.
6. Madan MS, Liu ZJ, Gu GM, King GJ. Effects of human relaxin on orthodontic tooth movement and periodontal ligaments in rats. *Am J Orthod Dentofacial Orthop* 2007;131:8.e1-10.
7. Davidovitch Z, Mathew D, Finkelson BS. Electric currents, bone remodeling, and orthodontic tooth movement. *Am J Orthod* 1980;77:14-32.
8. Nishimura M, Chiba M, Ohashi T, Sato M, Shimizu Y, Igarashi K, et al. Periodontal tissue activation by vibration: intermittent stimulation by resonance vibration accelerates experimental tooth movement in rats. *Am J Orthod Dentofacial Orthop* 2008;133:572-83.
9. Lim HM, Lew KK, Tay DK. A clinical investigation of the efficacy of low level laser therapy in reducing orthodontic postadjustment pain. *Am J Orthod Dentofacial Orthop* 1995;108:614-22.
10. Mester E, Spiry T, Szende B, Tota JG. Effect of laser rays on wound healing. *Am J Surg* 1971;122:532-5.
11. Saito S, Shimizu N. Stimulatory effects of low-power laser irradiation on bone regeneration in midpalatal suture during expansion in the rat. *Am J Orthod Dentofacial Orthop* 1997;111:525-32.
12. Kim Y, Kim S, Kim S, Kwon D, Jeon E, Son W. Low-level laser irradiation facilitates fibronectin and collagen type I turnover during tooth movement in rats. *Lasers Med Sci* 2010;25:25-31.
13. Aihara N, Yamaguchi M, Kasai K. Low-energy irradiation stimulates formation of osteoclast-like cells via RANK expression in vitro. *Lasers Surg Med* 2006;21:24-33.
14. Yamaguchi M, Fujita S, Yoshida T, Oikawa K, Utsunomiya T, Yamamoto H, et al. Low-energy laser irradiation stimulates the tooth movement velocity via expression of MCSF and c-fms. *Orthod Waves* 2007;66:139-48.
15. Fujita S, Yamaguchi M, Utsunomiya T, Yamamoto H, Kasai K. Low-energy laser stimulates tooth movement velocity via expression of RANK and RANKL. *Orthod Craniofac Res* 2008;11:143-55.
16. Antczak-Boukoms AA, Tulloch JF, Berkey CS. Split-mouth and cross-over designs in dental research. *J Clin Periodontol* 1990;17:446-53.
17. Dahlberg G. Statistical methods for medical and biological students. New York: Interscience Publications; 1940.
18. Takeda Y. Irradiation effect of low energy laser on alveolar bone after tooth extraction experimental study in rats. *Int J Oral Maxillofac Surg* 1988;17:388-91.
19. Bradley P, Groth E, Gursoy B, Karasu H, Rajab A, Sattayut S. The maxillofacial region: recent research and clinical practice in low intensity laser therapy. *Lasers in medicine and dentistry*. Rijeka: Vitagraf;2000.227-42.
20. Ngan P, Kess B, Wilson S. Perception of discomfort by patients undergoing orthodontic treatment. *Am J Orthod Dentofacial Orthop* 1989;96:47-53.
21. Kawasaki K, Shimizu N. Effects of low-energy laser irradiation on bone remodeling during experimental tooth movement in rats. *Lasers Surg Med* 2000;26:282-91.
22. Yoshida T, Yamaguchi M, Utsunomiya T, Kato M, Arai Y, Kaneda T, et al. Low-energy laser irradiation accelerates the velocity of tooth movement via stimulation of the alveolar bone remodeling. *Orthod Craniofac Res* 2009;12:289-98.
23. Kim SJ, Moon SU, Kang SG, Park YG. Effects of low-level laser therapy after Corticision on tooth movement and paradental remodeling. *Lasers Surg Med* 2009;41:524-33.
24. Cruz DR, Kohara EK, Ribeiro MS, Wetter NU. Effects of low-intensity laser therapy on the orthodontic movement velocity of human teeth: a preliminary study. *Lasers Surg Med* 2004;35:117-20.
25. Goulart CS, Nouer PR, Mouramartins L, Garbin IU, de Fátima Zanirato Lizarelli R. Photoradiation and orthodontic movement: experimental study with canines. *Photomed Laser Surg* 2006;24:192-6.

26. Limpanichkul W, Godfrey K, Srisuk N, Rattanayatikul C. Effects of low-level laser therapy on the rate of orthodontic tooth movement. *Orthod Craniofac Res* 2006;9:38-43.
27. Youssef M, Ashkar S, Hamade E, Gutknecht N, Lampert F, Mir M. The effect of low-level laser therapy during orthodontic movement: a preliminary study. *Lasers Med Sci* 2008;23:27-33.
28. Esnouf A, Wright PA, Moore JC, Ahmed S. Depth of penetration of an 850nm wavelength low level laser in human skin. *Acupunct Electrother Res* 2007;32:81-6.
29. Arias OR, Marques-Orozco MC. Aspirin, acetaminophen, and ibuprofen: their effects on orthodontic tooth movement. *Am J Orthod Dentofacial Orthop* 2006;130:364-70.
30. Koji F, Toru D, Takashi M, Akihito F, Kazuhiko K, Teruko T. Clinical effect of CO₂ laser in reducing pain in orthodontics. *Angle Orthod* 2007;78:299-303.
31. Beckwith FR, Ackerman RJ, Cobb CM, Tira DE. An evaluation of factors affecting duration of orthodontic treatment. *Am J Orthod Dentofacial Orthop* 1999;115:439-47.