Journal of Lasers in Medical Sciences

J Lasers Med Sci 2016 Summer;7(3):146-151

Original Article

http://www.journals.sbmu.ac.ir/jlms

doi 10.15171/jlms.2016.25

Low-Level Laser Action on Orthodontically Induced Root Resorption: Histological and Histomorphometric Evaluation

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Published online 18 July 2016

Abstract

Introduction: Studies have been conducted to develop a means of preventing, controlling or reducing orthodontically induced root resorption. Phototherapy has demonstrated effectiveness as an anti-inflammatory and, considering the inflammatory origin of this pathology, this study evaluated the effects of laser on root resorption.

Methods: The research was conducted among 54 80-day-old male Wistar rats, with weights of 280 ± 40 g. Phototherapy consisted of a diode laser (Ga-Al-As), calibrated with a wavelength of 808 nm, an output power of 100 mW, 2.1 J or 96 J of energy and area of 0.0028 cm^2. The application was continuous, punctual and with contact. The left first maxillary molar was moved by a super-elastic closed spring with a pre-calibrated and constant force of 25 g. The specimens were irradiated every 48 hours, totaling three or six times, depending on the group to which they belonged. Euthanasia was made in the 7th or 10th day after the onset of movement. The histological and histomorphometric examination was performed with sections of 6 µm stained with hematoxylin and eosin (H&E).

Results: Considering the dosimetry studied, when compared the subgroups with the same time of movement, 7 or 10 days, the low-level laser (LLL) has no statistically significant effect on the root resorption. As expected, differences were found between groups with different time of movement.

Conclusion: Based on the result, this dosimetry does not seem to be clinically recommended to avoid or reduce inflammatory root resorption, but it also does not induce any root surface alteration.

Keywords: resorption; root; laser therapy; tooth movement; phototherapy.

Introduction

Inflammatory root resorption, a dependent process that may occur when the cementoblast layer is damaged,[1] can be the result of an inadequate orthodontic stimulus. When the radicular dentine becomes exposed, the inflammatory components and the clasts cells become activated, which can remove this tissue and cause the resorption.[2,3] This pathology appears in varying intensities[4] in 90% of orthodontic treatment cases and has been studied without complete success up to now.[5-9]

Phototherapy and its biomodulator effect are known to improve inflammatory control, reducing the edema and number of inflammatory cells in the conjunctive tissue.[10-12] Despite this, few studies are present to demonstrate the low-level laser (LLL) effect on root resorption. The phototherapy action on root resorption was evaluated after dental avulsion, prior to its reimplantation, showing contradictory results.[13,14] The light emitting diode (LED) effect to reduce inflammatory root resorption was tested and demonstrated success.[15]

Considering the inflammatory origin of root resorption and the satisfactory results of phototherapy in achieving inflammatory control, this study analyzed the laser diode effect, with two different energy densities, over the root resorption induced by tooth movement in rats.

Methods

Fifty-four 80-day-old male Wistar rats that weighed 280-320 g were used for this experiment. During the experimental period, the animals remained inside appropriate cages at a constant temperature that ranged between 20°C and 24°C, in a 12-hour light/dark environment. They were also provided with food and water ad libitum.

The animals were divided into two groups: experimental

Please cite this article as follows: Vasconcelos EC, Henriques JF, Sousa MV, et al. Low-level laser action on orthodontically induced root resorption: histological and histomorphometric evaluation. *J Lasers Med Sci.* 2016;7(3):146-151. doi:10.15171/jlms.2016.25.

(E), with 36 specimens, and control (C), with 18 specimens. The experimental group (E) was divided into two subgroups of 18 animals each, according to the laser irradiation doses, high (HD) or low (LD). Within both groups, half of the sample was euthanized on the seventh day and the other half on the tenth day. The experimental subgroups received laser irradiation every 48 hours, beginning on the day when springs were installed. The subgroups distribution is presented in Table 1 and the irradiation protocol is assessed in Table 2. All procedures were carried out under general anesthesia, with 0.1 mL/100 g body weight intramuscular injection of ketamine hydrochloride 100 mg/mL and xylazine hydrochloride 20 mg/mL.

A modified model described by Heller and Nanda was used to move the left first maxillary molar in both groups.[16] The appliance consisted of a super-elastic closed coil spring (25 g; wire diameter, 0.15 mm; eyelet diameter, 1.5 mm; GAC International, Bohemia, NY, USA) that was placed between the left first maxillary molar and incisors while using both central maxillary incisors as anchors. The coil was fixed to the teeth with a 0.25 mm stainless steel wire ligature (Morelli, Sorocaba, SP, Brazil). The closed coil spring was stretched five millimeters until a force of 25 g was achieved in accord with manufacturer instruction and confirmed by a dynamometer (Zeuzan 300 g, São Paulo, Brazil, PN 800). The teeth were covered by photo-cured resin around the ligature wire to improve the coil spring retention.

A Gallium-Aluminum-Arsenide (Ga-Al-As) laser (Whitening Laser II – DMC, São Carlos, SP, Brazil) was used to generate LLL irradiation. The wavelength was 808 nm (infrared laser) and a continuous emission regime was used. The output power was set to 100mW, the optic fiber diameter corresponded to 0.6mm and the energy density (ED) was 25 J/cm^2/point and 580 J/cm^2/point. Irradiation was applied in three points by the punctual method with contact. The application points were the buccal, palatal and mesio-cervical aspects of the first left maxillary molar. The laser was applied 3 times for each animal during the experimental period, with 48-hour intervals.

The animals were euthanized with an overdose of anesthetic in varying groups at seven and ten days after force application. Their maxillae were submerged in a 10% buffered formaldehyde solution for 48 hours. After fixation, the samples were decalcified by using EDTA (0.05M; pH 7.4) at approximately 60 days.[17] The left maxillary hemi-arches were then divided and included in paraffin, sectioned with a rotary microtome that was 6 µm thick, parallel to the occlusal plane of the first molar up to the radicular division. At this point, eight cuts were made and the one with the most expressive tissue events and best material quality was chosen. Finally, the samples were stained with hematoxylin and eosin (H&E).

A histological evaluation was performed by using a binocular microscope (Olympus BX50, Tokyo, Japan), with a 20x magnification ocular lens. The blades were photographed by using a digital camera (Nikon, Tokyo, Japan) connected to a computer. One blind examiner performed the readings, using the ImageJ 1.45s software for histomorphometric analyzes.[18]

The analyzed area corresponded to the buccal distal root. For interpretation, the same parameters were performed in the experimental and control groups. Root resorption was determined by measuring the resorbed area, resorption extension and resorption thickness. The resorbed area was found by reducing the root area outlined inside the resorption focus from the area that virtually outlined the same focus. The proportion of resorption was also registered. The resorption extension considered the summation of all focus of resorption in the extension: it was measured in a straight line between the two more extreme points of the resorbed focus. In order to determine the thickness of resorption and its ratio to the thickness of the root, the root thickness was measured, considering an external virtual line that limited the resorbed focus and continued the root contour to the center of the pulp chamber. The resorption thickness was found using the same ex-

Table 1. Sample Distribution According to Subgroups, Dental Movement, Irradiation (Low = 25 J/cm^2, High = 580 J/cm^2), Experimental Time and Number of Specimens Per Subgroup

Subgroups	Movement	Irradiation	Time	Specimens
C_7d	No	No	7 days	4
C_10d	No	No	10 days	4
C_IDM_7d	Yes	No	7 days	5
C_IDM_10d	Yes	No	10 days	5
E_LD_7d	No	Low	7 days	4
E_LD_10d	No	Low	7 days	4
E_HD_7d	No	High	10 days	4
E_HD_10d	No	High	10 days	4
E_IDM_LD_7d	Yes	Low	7 days	5
E_IDM_LD_10d	Yes	Low	10 days	5
E_IDM_HD_7d	Yes	High	7 days	5
E_IDM_HD_10d	Yes	High	10 days	5

Abbreviations: C, control; E, experimental; d, days; IDM, induced dental movement; LD, low dose; HD, high dose

Table 2. Phototherapy Parameters

Phototherapy Parameters	Values
Frequency	Three irradiation with interval of 48 hours between them, starting on day of spring installation
ED - fluency	High dose = 580 J/cm^2 Low dose = 25 J/cm^2
Total energy	High dose = 96 J Low dose = 2.1 J
Output power	100 mW
Wavelength	808 nm
Color	Invisible (Infrared)
Emission regime	Continuous
Optic fiber diameter	0.6 mm
Distance of application	In contact/punctual
Time	High dose = 2 min 43 s per point (6 points) Low dose = 7 s per point (3 points)

Abbreviation: ED, energy density.

ternal mark at the deepest point of the focus background. To confirm and complete the quantitative analyses, three parameters were instituted: *evolutionary phase*, 0 - preserved root, 1 - repaired root (could see a cement layer recovering the resorption area), 2 - paralyzed resorption (resorption area present but no osteoclast cells in root contact), 3 - active resorption (resorption area present with osteoclast cells in root contact); *resorption thickness*, 0 - no focus, 1 - involving ¼ of the root thickness, 2 - from ¼ to ½, 3 - from ½ to ¾, 4 - more than ¾ involved; *resorption extension*, 0 - no resorption, 1 - involving ¼ root perimeter, 2- from ¼ to ½, 3 - from ½ to ¾, 4 - ¾ or more involved.

The results were analyzed (STATISTICA version 7), by performing three-way analysis of variance (ANOVA), followed by Tukey test, with a 5% significance level. The Kappa index was adopted to evaluate the accuracy of the evaluator in the semi-quantitative data. In order to verify the intra-examiner *systematic error*, a paired *t* test was performed. Dahlberg formula was used to estimate the *casual error.* It was implemented in 30% of the sample, randomly, with a 30-day interval between measurements.

Results

No significant difference in weight was found among the subgroups during the initial and final phases.

The results can be seen in Figures 1 and 2, which represent a specimen of each subgroup that was studied.

Comparing the subgroups with no movement; at 7 or 10 days; and high dose and low dose or no irradiation, the laser was innocuous to the roots and, causes no damage. No statistical or descriptive difference among the categories was found.

In the same way, comparing the subgroups with induced dental movement, the subgroup E_IDM_HD_10D revealed higher statistically significant values in the following criteria: percentage of total resorbed area, resorption extension and percentage of resorption extension in relation to radicular perimeter (Tables 3, 4 and 5). In the remaining criteria that were analyzed, there was no significant statistical difference.

Discussion

Among the results found in quantitative and semi-quantitative analysis, there was no statistically significant difference when the subgroups with different irradiation doses were compared, when considering the same experimental time.

The experimental times of seven and ten days were defined based on literature reports. On the seventh day extensive areas of root resorption are expected to be found. After the ninth day, there is a progressive reduction of these phenomena with a reorganization of bone resorption and cemental areas due to the loss of coil spring force.[18] Employing a descriptive analysis, the results of this study showed similar cellular events at the seven-day group, but differences at the 10-day group, which presented large hyaline areas and clasts cells inside or near from resorbed cavities. The authors believe that this may have occurred because the super-elastic closed coil spring used did not allow a rest period.

Differences occurred among the subgroups moved and

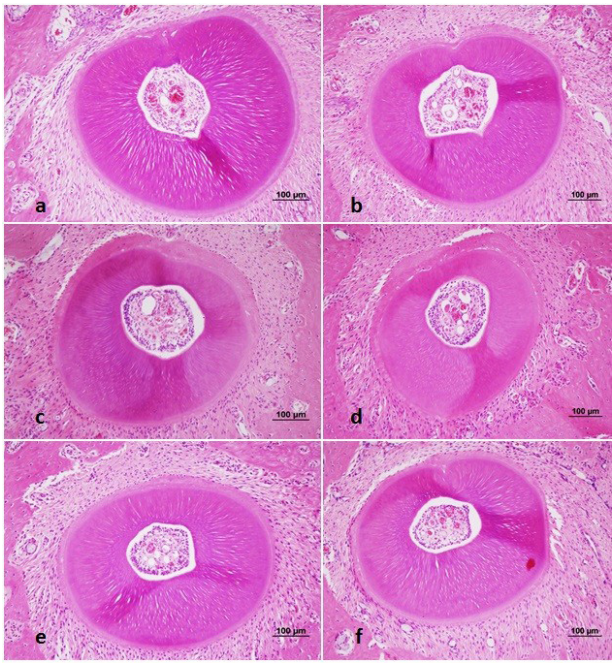

Figure 1. Photomicrography From Subgroups With No Movement. Letters represent each subgroup: (**a**) Control seven days subgroup; (**b**) Control ten-day subgroup; (**c**) High dose seven-day subgroup; (**d**) High dose ten-day subgroup; (**e**) Low dose seven-day subgroup; (**f**) Low dose ten-day subgroup. X200. HE.

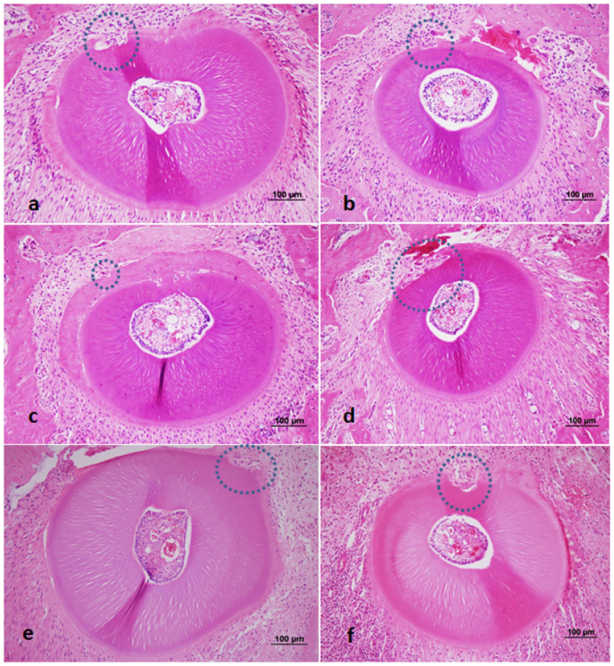

Figure 2. Photomicrography From Subgroups With Movement. Letters represent each subgroup: (**a**) Control seven days subgroup; (**b**) Control ten-day subgroup; (**c**) High dose seven-day subgroup; (**d**) High dose ten-day subgroup; (**e**) Low dose seven-day subgroup; (**f**) Low dose ten-day subgroup. X200. HE.

Table 3. Percentage of Resorbed Area

Dosis	Movement	Time	Mean ± SD (%)	N
Control	No	7 days	0.0 ± 0.0[a]	4
Control	No	10 days	0.1 ± 0.2[a]	4
Control	Yes	7 days	0.6 ± 0.7[ab]	5
Control	Yes	10 days	2.9 ± 3.5[ab]	5
Low	No	7 days	0.02 ± 0.05[a]	4
Low	No	10 days	0.0 ± 0.0[ab]	3
Low	Yes	7 days	1.6 ± 1.6[ab]	4
Low	Yes	10 days	2.1 ± 1.9[ab]	3
High	No	7 days	0.0 ± 0.0[ab]	3
High	No	10 days	0.0 ± 0.0[a]	4
High	Yes	7 days	0.2 ± 0.4[a]	5
High	Yes	10 days	3.9 ± 1.8[b]	4

Abbreviation: SD, Standard deviation; N, number of specimens.
*Statistically significant for $P<0.05$
Different letters represent statistically significant differences.
Three-way ANOVA followed by Tukey tests.

Table 4. Extension of Resorption

Dosis	Movement	Time	Mean ± SD (μm)	N
Control	No	7 days	0.0 ± 0.0[a]	4
Control	No	10 days	13.5 ± 27.0[a]	4
Control	Yes	7 days	78.1 ± 73.8[ab]	5
Control	Yes	10 days	108.5 ± 145.6[ab]	5
Low	No	7 days	12.9 ± 25.8[a]	4
Low	No	10 days	0.0 ± 0.0[a]	3
Low	Yes	7 days	104.9 ± 108.3[ab]	4
Low	Yes	10 days	139.7 ± 155.0[ab]	3
High	No	7 days	0.0 ± 0.0[a]	3
High	No	10 days	0.0 ± 0.0[a]	4
High	Yes	7 days	15.9 ± 29.7[a]	5
High	Yes	10 days	243.6 ± 122.4[b]	4

Abbreviation: SD, Standard deviation; N, number of specimens.
*Statistically significant for $P<0.05$
Different letters represent statistically significant differences.
Three-way ANOVA followed by Tukey tests.

Table 5. Percentage of Resorbed Extension in Relation to the Radicular Perimeter

Dosis	Movement	Time	Mean ± SD (%)	N
Control	No	7 days	0.0 ± 0.0[a]	4
Control	No	10 days	0.7 ± 1.4[a]	4
Control	Yes	7 days	4.1 ± 3.9[ab]	5
Control	Yes	10 days	5.6 ± 7.4[ab]	5
Low	No	7 days	0.7 ± 1.4[a]	4
Low	No	10 days	0.0 ± 0.0[a]	3
Low	Yes	7 days	5.6 ± 6.2[ab]	4
Low	Yes	10 days	7.8 ± 9.0[ab]	3
High	No	7 days	0.0 ± 0.0[a]	3
High	No	10 days	0.0 ± 0.0[a]	4
High	Yes	7 days	0.8 ± 1.5[a]	5
High	Yes	10 days	14.3 ± 6.9[b]	4

Abbreviation: SD, Standard deviation; N, number of specimens.
*Statistically significant for $P<0.05$
Different letters represent statistically significant differences.
Three-way ANOVA followed by Tukey tests.

not moved; such differences were justified by known microscopic changes after an induction of movement.[19,20] Furthermore, among subgroups moved for different experimental time and irradiated with the same dose, a variation occurred (Tables 3, 4 and 5). Previous studies that show the evolution of the tissue changes during tooth movement and its resolution explained this result.[18-20]

This review found only one study that assessed the phototherapy on the inflammatory root resorption, but with LED.[15] Considering that LED and laser phototherapy exhibit similar effects[21] and the coherence of light generate a benefit particularly in the deeper tissue layers,[22] these studies were compared. Fonseca et al[15] investigated the effect of phototherapy on inflammatory root resorption, in Wistar rats. Their study applied a power density of 4 J/cm² on the day two, three and four, with the euthanasia on the seventh day of tooth movement. The movement was achieved with a nickel titanium spring and 50 g of force on the upper first molars.[15] The results presented an increase of periodontal tissue repair, reduced inflammation and reduced root resorption by phototherapy, thus contradicting the results of the present study. Despite the fact that the methodology was distinct, the difference found between these two studies could be due to different doses and wavelengths employed.

Currently, it is conclusive that phototherapy causes changes in cellular metabolism, but the way it operates is still being investigated.[23] The difficulty of finding the correct dose for each therapy is related to the mechanism of the laser action. In drawing an analogy with the pharmacology, each wavelength is thought to correspond to a different drug. Then after the drug is chosen, it is necessary to establish the optimum dose and the best treatment regimen.[21]

The laser effect on the inflammatory response in the control of chronic and acute inflammation has been positive.[11] It seems to control the number of cells involved in this process and to reduce pro-inflammatory mediators,[10] especially prostaglandins.[24]

Tooth movement needs the local inflammatory process to occur, and this inflammation can cause the loss of root tissue when the cementoblast layer is lost.[25,26] The action of the cells involved in the removal process of necrotic tissue and bone tissue, can damage the root in the denuded surface.[27] Accordingly, it supposes that the same mechanism that causes the acceleration of induced tooth movement stimulates a more intense root resorption, and the opposite would also be true. Nevertheless, some studies confirm this assumption,[7,8] while others show that the mechanism that regulates tooth movement may be different from the mechanism of the root resorption.[6] Consequently, it would be possible to accelerate the teeth movement without increasing the root resorption.

The LLL can stimulate osteoclasts[28,29] during the induced tooth movement, but this effect seems contradictory for root resorption process. Osteoclasts are important to remove the hyaline area, responsible for keeping the resorption process after the interruption of the force.[30] Suppos-

edly, a faster removal of the hyaline area could facilitate the tooth movement and the paralyzation of the resorption. Despite this, while removing the hyaline area with greater speed, could also damage the root tissue, enhancing the resorption.

The positive laser effect on the fibroblasts,[31] collagen matrix[32] and capillarity,[28] in the periodontium, may accelerate the repair and rehabilitation of the root fibers, thus reducing the exposed area to the action of osteoclasts and macrophages.[33] However, the dose in this study showed no statistically significant difference between the irradiated and the control groups. Perhaps the applied doses in this study were ineffective because they are in a neutral or slightly modulator level for the cells in question.

For phototherapy to be effectively used in orthodontics for preventing inflammatory root resorption, the mechanism of the laser action on the pathology and the appropriate dosimetry for humans, must be defined. For that reason, based on the results obtained in this study, its clinical use for this purpose could not be recommended. Even so, it is interesting to note that the wavelength tested show to be safe for tooth movement without causing or stimulating resorption.

It is suggested that future investigation of resorption may be accompanied by the quantification of tooth movement, since the ideal would be that the dose used to prevent resorption would not cause, or could predict, a delay in the movement. Furthermore, a longer experiment is proposed to determine the action of phototherapy in the process of repairing resorbed roots after the removal of the force and with persistence of hyaline regions.

Conclusion

Based on the result, this dosimetry does not seem to be clinically recommended to avoid or reduce inflammatory root resorption, but it also does not induce any root surface alteration.

Ethical Considerations

This study was approved by the Ethics on Teaching and Research in Animals Committee of the University of São Paulo under protocol number 010/2012. Authors herein attest that all animal studies undertaken as part of research from which this manuscript is derived, are in compliance with the regulations of our institution and generally accepted guidelines governing such work. Authors warrant that this manuscript contains no violation of any existing copyright or other third party right or any material of an obscene, indecent, libelous, or otherwise unlawful nature and that to the best of our knowledge the manuscript does not infringe the rights of others previous publications. Authors certify that neither this manuscript nor one with substantially similar content under our authorship has been published or being considered for publication elsewhere in any language (neither local nor international journals).

Conflict of Interests

Authors warrant that any financial interests, direct or indirect, that exist or may be perceived to exist for individual contributors in connection with this manuscript have been disclosed in the covering letter.

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