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Original Article

Protective Role of Magnesium Oxide Against Orthodontically Induced Apical Root Resorption: An Experimental Rabbit Study

Sarmad S. Salih. Al Qassar[1], Rana Mahdi Fadhil[2], Shahad A. Thanoon[3], Gada A. Taqa[4] and Roaa Elias[5]

ABSTRACT

Background: Root resorption origin by orthodontic treatment (OIRR) is a frequent side effect. Thus, preservation of cementum and remodeling of the ligament (PDL) are critical in preventing such resorption. Magnesium (Mg^{2+}) a mineral that have a dramatic role in mineralization, cell growth and regulating inflammation, however its function, in OIRR is not investigated. This study aimed to investigate the impacts of magnesium oxide (MgO) supplementation on apical root resorption, cementum and PDL. **Materials and Methods:** Twenty adult male albino rabbits were randomly allocated into four groups (n = 5): negative control (no applied orthodontic force) positive control (orthodontic force applied only) low-dose MgO group (40 Mg2+/kg/day) and high-dose MgO group (80 Mg2+/kg/day). Orthodontic tooth displacement was initiated on the incisors through modified fixed orthodontic devices exerting a 40 g force over a period of three weeks. MgO was given orally once each day. Histomorphometric evaluation measured of cementoblasts, cementoclasts, fibroblasts and fibrocytes, the thickness of the cementum and PDL. Statistical analysis employed ANOVA followed by Tukey post hoc tests ($p \leq 0.05$). **Results:** The positive control group exhibited cementum reduction, elevated cementoclast quantities diminished cementoblast levels and thinner PDL relative, to the negative control ($p < 0.05$). Both MgO-treated groups presented thicker cementum and PDL and fewer cementoclasts compared to the positive control with the high-dose group displaying the strongest protective impact. The number of fibroblasts significantly increased in the MgO groups. **Conclusion:** MgO supplementation diminished OIRR with preserving cementum and PDL structure, suggested a potential protective role for magnesium during orthodontic treatment.

Keywords: Orthodontically induced root resorption, Magnesium oxide, Cementum, Periodontal ligament, Histomorphometry.

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INTRODUCTION

Orthodontic induced root resorption (OIRR) is one of the confrontation the treatment result of orthodontic treatment. The dental structure of the root apex may be permanently lost as a result of this unfavorable consequence. Orthodontic Patients usually have minor root resorption. Excessive root resorption, on the other hand, can happen in rare circumstances. Nearly 7% of orthodontic patients, according to Krishnan et al[1], who reported that at least one tooth with a root shortening of more than 4 mm. The application of a strong force[2], the length of treatment[3], the kind of root[4], and the patient's genetic predisposition have all been linked to this phenomena[5]. As a result, orthodontists must anticipate and prevent this root resoption wherever possible. In the cited studies, the use of pharmacological modulators reduced OIRR occurring with orthodontic tooth movement; however, modulator use also resulted in decreased tooth movement and velocity 1, 2 which representing a side effects of orthodontic treatment.

During orthodontic therapy, various levels of root resorption may occur[3]. According to studies, the prevalence of OIRR ranges from 3 to 100 percent 9 (li et al., 2020). Considerable apical root resorption (>2mm to 1/3 of the root length) occurs in 12-17% of orthodontic therapy patients, with 1-5% experiencing severe apical root resorption (>1/3 of the root length)[5,6].

Cementum is a mineralized connective tissue layer that replaces the enamel in the root of the teeth[7]. It differs from bone in that its thickness rises during life and it does not undergo dynamic remodeling. Historically, cementum has been divided into two types: acellular cementum, which covers the cervical root but does not contain cementocytes, and thick cellular cementum, which covers the apical root and contains cementocytes[8]. Cementoblasts are continually recruited from cemento-progenitor cells contained within resorption lacunae (pits created on the root surface during tooth root resorption)[9]. The cementum's functional cementoblasts serve crucial functions in root absorption and healing. Cementoblasts have the ability to generate new cementum and fill tooth root resorption pits during IRR. They can also express molecules associated to osteoclast differentiation, control osteoclast differentiation, and secrete extra-cellular matrix components. Cementoblasts can affect how quickly and severely root resorption occurs[10].

Magnesium is the fourth most abundant element in the human body ($Ca^{2}+ > K+ > Na+ > Mg^{2+}$) and the second most abundant cation within the body's cells after potassium. Additionally, it is crucial to the human body's structure and a number of metabolic processes. Magnesium is present in the body in amounts of 760 Mg^{2+}[11,12]. Mg^{2+} influences crystal size and formation by making the minerals that make up hydroxyapatite crystals, like Pi and Ca^{2+}, more soluble[11]. In cementum and bone, the mean Mg^{2+} concentrations are roughly 0.5 percent (w/w) and 0.5 percent (w/w), respectively[13]. Other earlier studies

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show that root resorption brought on by orthodontic forces may be influenced by the cementum's hardness and Ca/P ratio[14].

It was improved that MgO supplement has an impact on the orthodontic tooth movements and reducing post orthodontic relapse[15,16].

However, little is understood about how magnesium affects root recovery after orthodontic tooth movement. The purpose of this study was to analyze histomorphometry of the effects of magnesium supplementation on apical root resorption in a rabbit model with modeled orthodontic tooth root resorption in the form of cementoblast, cementoclast, and cementoblast. It also sought to investigate the effects of magnesium on the periodontal ligament during vigorous orthodontics tooth movement.

MATERIALS AND METHODS

Rabbits were picked as the living model for this research to be done to achieve the aforementioned goals. male albino white Rabbits that were housed in the university of Mosul's dental college's animal house for at least two weeks prior to the experiment's start were chosen for the study. The research protocol had been evaluated and approved by the University of Mosul College of Dentistry's research ethical committee (Approval No. UoM.23456).

Sample size determination:

The effect size (r = 0.16) used for sample size estimation was derived from previously published studies employing comparable experimental models and outcome measures. These studies reported effect magnitudes within a similar range, supporting the appropriateness of this value for the present investigation.

Sample size calculations were performed using the formula

$n=(z\times rD)2n = \left(\frac{z \times r}{D}\right)^2n=(Dz\times r)^2$

assuming a two-sided 95% confidence level (z = 1.96) and a predefined precision (D) of 0.2. This corresponds to a conventional statistical power of approximately 80% for detecting the specified effect size.

The calculation yielded a minimum estimated sample size of approximately 2–3 animals per group. To account for biological variability and potential experimental attrition, and in line with best practices for preclinical study robustness, the sample size was conservatively increased. Accordingly, five animals were included per group. This sample size was considered sufficient to ensure reliable detection of biologically meaningful effects while adhering to the principle of reduction in animal research.

Data sheets were created for each animal in accordance with the study's protocol, which includes (number, group, weight, anesthetic dosage, magnesium oxide dose, date of orthodontic appliance placement, orthodontic treatment starting date, orthodontic appliance removal date, and sacrifice date). Twenty white male albino rabbits (age range: 6–8 months; weight range: 1100–1450 gm) were divided into four designated metal cages in accordance with the study's design as soon as the sample size was established. They were fed 225g of pellets (Albers® Rabbit 16 percent Animal Feed) daily and kept on a 12:12 light/dark cycle. Every rabbit's weight was checked five days a week during the experiment[18]. To account for potential food type effects on the outcomes, the diet of the entire group was adjusted. Throughout the course of the trial, all rabbits were fed a regular concentrated pellet diet along with leafy greens that were weighed per kg per day. There is always water available. Four groups of five animals each were created by using a straightforward random procedure to divide the animals.

Study design

The total sample size (20) was divided into 2 main groups.

Control group:

The control group was subdivided into two groups.

C-ve: where neither magnesium supplementation was given for four weeks, nor orthodontic appliances were used, and distilled water was administered in the same way magnesium was administered to the other groups.

C+ve group: Positive control group with orthodontics device fixed on the teeth and only distilled water for 3 weeks without magnesium intake.

Treatment Group:

The treatment group was divided into two (2) groups with the following orthodontic appliances supplemented with MgO.

LD group: Low-dose of magnesium oxide suspension was in-forced on the rabbit mouth for three weeks at 40 Mg^{2+}/kg body weight[19].

HD group where the rabbits in this group received a maximum magnesium dose of 80 Mg^{2+}/kg for three weeks[20].

Orthodontic appliances

On the animals' lower incisors, a modified set of fixed orthodontic equipment was placed. Following two weeks of relaxation, each rabbit underwent three weeks of orthodontic tooth movement. Thus every appliance included two lower central incisor bands of size 000 (Dentaurum, Ispringen, Germany), a sectional arch wire of 0.017 × 0.025 stainless steel, and a continuous nickel titanium open coiled spring (IOS, USA), which was activated to achieve 4.5 mm of spacing and inserted between the bands of two lower incisors to induce a force to the two adjust teeth.

A tension gauge was utilized to determine the force in it prior to the spring being put in. When the springs were in use, they exerted a force of 40 g on the distal sides of the treated incisor roots. This put pressure on the treated roots' distal sides and tension on the PDLs of teeth with mesial surface teeth. Before inserting the appliance, ligature wire (Dentaurum, Ispringen, Germany) was kept in position in the holes of the brackets to hold each wire in place. To relax the animal's muscles, a mixture of xylazine (10 Mg^{2+}/kg IM) and ketamine (35 Mg^{2+}/kg IM) was injected. The lower incisor bands of the animal were then cemented using a glass-ionomer cement (Tokuso Inomer, Tokoyama, Japan). The orthodontic appliance was already activated when the experiment began, and it wasn't activated again while it was running. As shown in Figure 1.

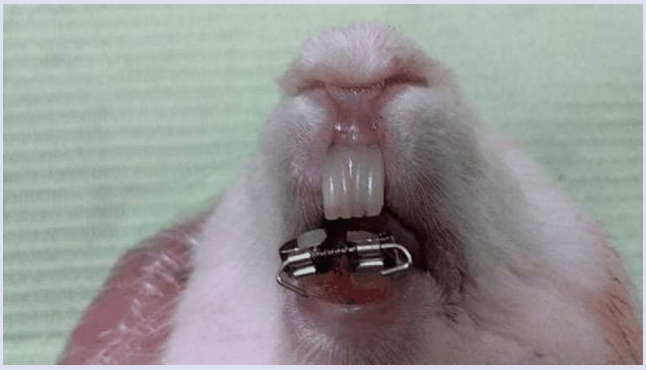

Figure 1. Illustration of modified orthodontic appliance after cementation in rabbit mouth.

Magnesium supplementation

To ensure complete administration of the recommended dose, the magnesium complement in the form of MgO tablet (250 MgO tablet, 21st century health care, AZ 85282, USA) was administered orally to the treated group by mixing one tablet with 5 ml of distilled water based on body weight for the LD group, with each 1 ml containing 50 Mg^{2+} of magnesium.

For four (3) weeks, the LD group received 0.8 ml and the HD group re ceived 1.6 ml/kg once daily at 12 p.m.

Scarifying the rabbits and preparing of the histological assessments

After total anesthesia had been attained. The scarifying was accomplished in a sterile condition on the surgical table. The rabbit is placed on its back while a manual hair clipper is used to remove the hair from its lower jaw at the surgery site. Wash the shaved area with antiseptic povidone iodine and wrap a sterile cloth around the surgical region. An incision of around 1.5 cm was made above the mandibular bone using surgical blade no.15. By blunt dissection with a Hawarth periosteal elevator, the periosteum was lifted and clean bone was exposed. To prevent the bone around the target teeth from breaking down, it was dissected from the pressure side and placed in 10% neutral buffered formalin for 48 hours. The specimens were then decalcified and dehydrated before being imbedded and covered with paraffin wax. Dissection was done in a mesio-distal direction, parallel to the long axis of the root of the lower incisor, for each specimen in longitudinal serial sections with a thickness of 5 mm. On the pressure side, the specimens were stained with H&E[22].

Histological assessment

In order to ensure that the bone didn't degrade, it was dissected from the distal surface of the lower jaw from the pressure side and placed in 10 percent neutral buffered formalin for at least 48 hours. The specimens were then dehydrated and decalcified, imbedded, and covered in paraffin wax to create wax blocks. Each specimen has longitudinal serial slices cut at a thickness of 5 mm. For each specimen, they were each cut in a mesiodistal direction, parallel to the long axis of the lower incisor root. The pressure side specimens underwent H and E staining. The samples were ready for this procedure[21,22].

Quantitative assessment of histological section

Histological assessment was performed on sections obtained from the apical region of the pressure side of the roots of both right and left mandibular central incisors. Sections were examined at high power (400× objective lens), and quantitative analyses were expressed as the number of cells per microscopic field.

Inclusion criteria for cell counting

Only well-oriented histological sections exhibiting intact root surfaces, clearly defined periodontal ligament space, and absence of sectioning artifacts were included. Fields were selected from the apical third of the root on the pressure side and were required to demonstrate adequate staining contrast and cellular preservation. Overlapping cells, fragmented nuclei, or areas with tissue distortion were excluded from analysis.

Cementoblast counting

Cementoblasts were identified as mononuclear cells lining the root surface with basophilic cytoplasm and distinct nuclei. The number of cementoblasts visible within a standardized microscopic field at 400× magnification was counted and recorded for each section.

Cementoclast counting

Cementoclasts (odontoclasts) were identified based on established morphological criteria, including a multinucleated appearance, ruffled borders, clear zones, and abundant cytoplasm, consistent with osteoclast-like cells. Cementoclast/odontoclast precursors are known to originate from circulating mononuclear cells that extravasate into the periodontal ligament in response to chemotactic signals and migrate to sites of root demineralization. The number of cementoclasts visible per microscopic field at 400× magnification was recorded.

Blinding and observer reliability

All histological and histomorphometric analyses were performed by two independent observers who were blinded to the experimental groups. To assess intra- and inter-observer reliability, measurements were repeated on randomly selected sections after a two-week interval. Reliability was evaluated using the intraclass correlation coefficient (ICC), which demonstrated excellent agreement (ICC > 0.85).

Micromorphometric measurements

Micromorphometric analyses were conducted using a color USB 2.0 digital camera (Omax, ToupView 9.0-megapixel, China) coupled with image-processing software equipped with a calibrated ruler micrometer. Calibration was performed for all microscope lenses using a 0.01-mm stage micrometer (ESM-11, Japan) mounted on an Olympus CX31 light microscope, ensuring measurement accuracy across all magnifications.

Statistical analysis

The statistical analysis of the data for the number of cemntoblasts, cemntoclasts, the thickness of the PDL, and the thickness of the cemntum was performed by testing for normality and homogeneity of variance among the various groups. If the data were parametric, intragroup and intergroup analyses were conducted using the method developed by Anova and Tukey. P 0.05 was deemed to be significant. Version 25 of IBM SPSS Statistics was used for statistical analysis (IBM Corporation, USA). It was used to evaluate the variable's value. By examining 10 randomly selected slides for histomorphometrical analysis, an intraclass correlation was employed to determine the accuracy of the measurement.

RESULT

Statistical analysis of number of cementoblasts and cementoclasts found:

The statistical analysis showed that there was significant difference within each group after four week.

In apical part of the bone: Following the use of a Shapiro-Wilk test to assess the normality of distributions, there was a significant change ($p = 0.00$) in the count of cementoblasts founded of both high dose (18.5±3.9) and low dose (17.25±2.25) and control positive group (11.5±0.64) groups in comparison with control negative group (25.5±0.64) it's the normal as show in Table 1 and Figure 1.

In apical part of the bone: There was a significant rise($p = 0.00$) in the number of cementoclasts count with control positive group (2.5±0.28) in comparison both high dose (0.75±0.25) and low dose (1.25±2.05) groups which decrease number of cementoclast ,control negative group (0.00±0.0) it's the normal as show in Table 1 and Figure 1.

Histological finding

In control negative group sections of tooth of bone showed the apical side cementum (CM) with cementoblast (CB) and without cementoclast.

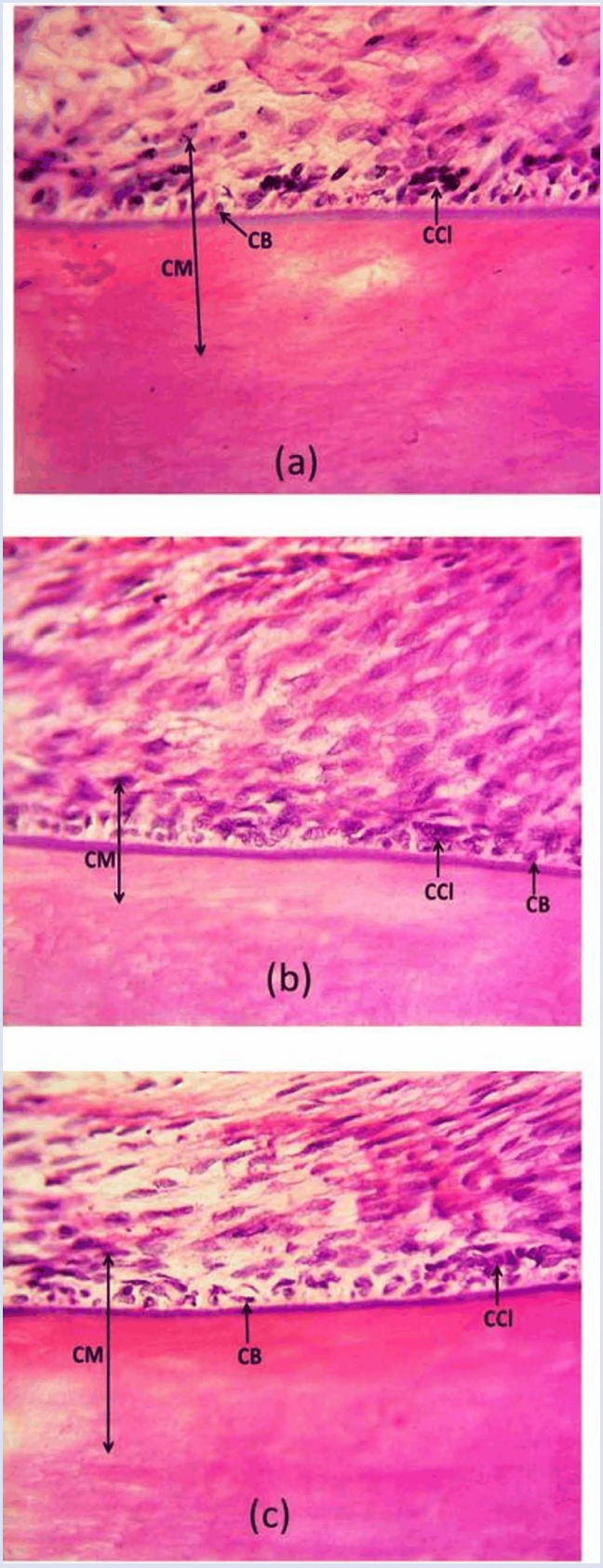

Figure 2. illustrated Microscopic examination of tissue sections by, H&E stain, 400X revealed presence of (a)photomicrograph of the tooth of control positive group of apical side shows the cementum (CM) with cementoblast (CB) and cementoclast. (b)photomicrograph of the tooth of low dose group of apical side shows the cementum (CM) with cementoblast (CB) and cementoclast. (c)photomicrograph of the tooth of high dose group of apical side shows the cementum (CM) with cementoblast (CB) and cementoclast

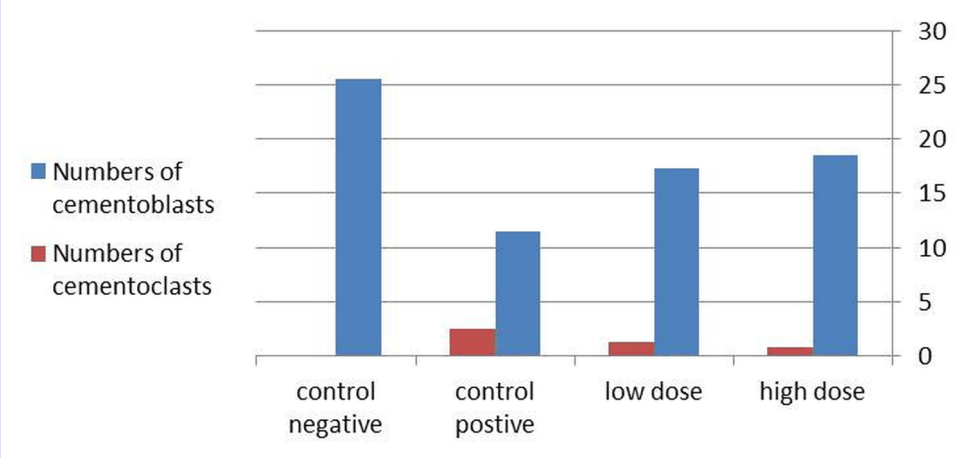

Figure 3. The histogram of statistical analysis of number of cemntoblast and cementoclast founded in the apical region.

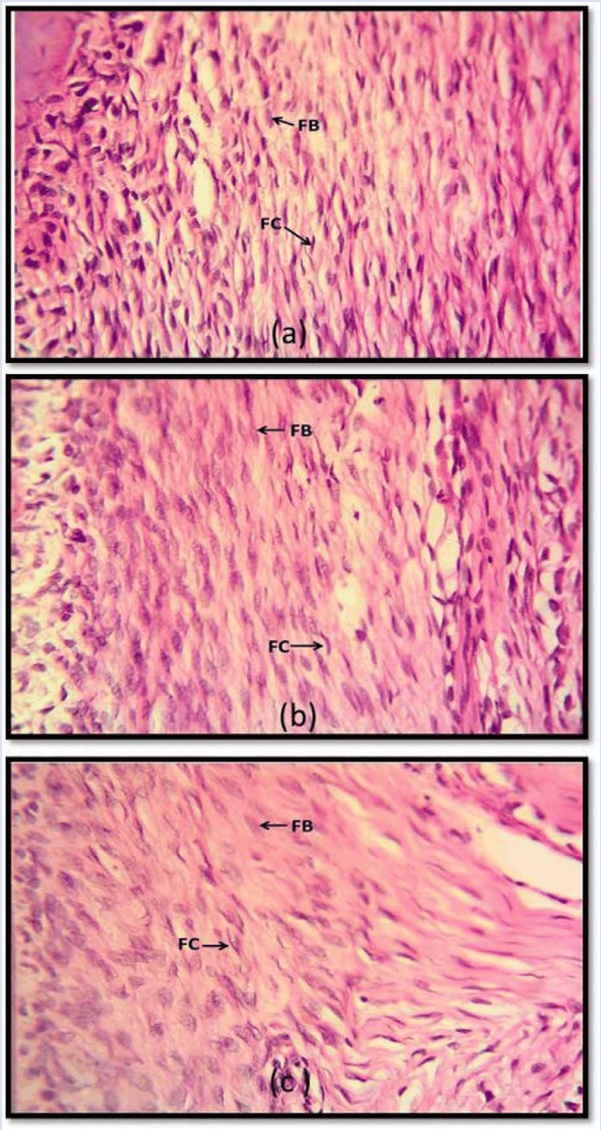

Figure 4. illustrated Microscopic examination of tissue sections by, H&E stain, 400X revealed presence of (a) photomicrograph of tooth of the positive control group showing the periodontal ligament with fibroblast (FB) and fibrocytes (FC) surrounding tooth(b)): photomicrograph of tooth of the low dose group showing the periodontal ligament with fibroblast (FB) and fibrocytes (FC) surrounding tooth.(c) photomicrograph of tooth of the high dose group showing the periodontal ligament with fibroblast (FB) and fibrocytes (FC) surrounding tooth.

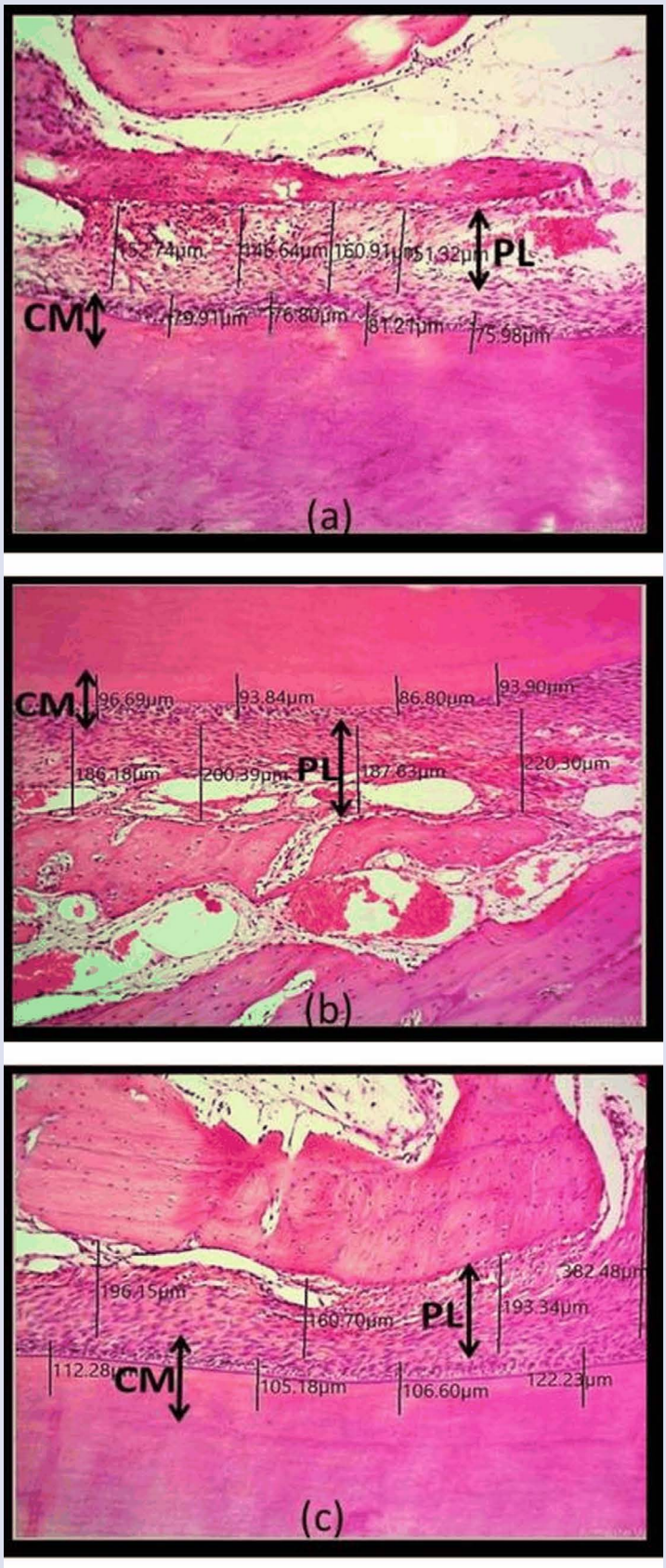

Figure 5. illustrated Microscopic examination of tissue sections by, H&E stain, 400X revealed presence of (a)photomicrograph of the tooth of control positive group of apical side shows the thicknesses of periodontal ligament (PL) and cementum (CM). Omax ToupView program..:(b) photomicrograph of the tooth of low dose group of apical side shows the thicknesses of periodontal ligament (PL) and cementum (CM). Omax ToupView program. (c) photomicrograph of the tooth of high dose group of apical side shows the thicknesses of periodontal ligament (PL) and cementum (CM). Omax ToupView program.

Table 1. Descriptive statistic and ANOVA-test comparisons of number of cementoblast and cemntoclast found in the field /400X field in the cementum

Group	C-ve	C+ve	HD	LD	P -value
	mean±SD	mean±SD	mean±SD	mean±SD	
Numbers of cementoblasts	25.5 ± 0.64	11.5 ± 0.64	18.5 ± 3.9	17.25 ± 2.05	0
	A	B	C	CD	
Numbers of cementoclasts	0.0 ± 0.0	2.5 ± 0.28	0.75 ± 0.25	1.25 ± 0.25	0
	A	B	AC	C	

Different letter mean there is significant difference, while same letter mean there in no significant difference at $P \leq 0.05$. Data expressed as mean ± standard error after four week ,Data expressed as Mean ± stander error

Table 2. Dfescriptive statistic and ANOVA test comparisons of number of fibroblast and fibrocyte found in the apical tooth in the 400X field

Group	C^{-ve}	C^{+ve}	LD	HD	P value
Count	mean±SD	mean±SD	mean±SD	mean±SD	
Fibroblasts	118.75 ±23.07	56±15.32	86.75±14.79	142±5.59	0
fibrocyte	27±4.69	63.25± 7.13	55.25±9.06	40±6.16	0

Different letter mean there is significant difference, while same letter mean there in no significant difference at $P \leq 0.05$. Data expressed as mean ± standard error after four week ,Data expressed as Mean ± stander error

Table 3. Descriptive statistic and ANOVA-test comparisons of Thickness of cementum and periodontal ligament in micrometer µm100X field) in the apical region

Group	C-ve	C+ve	HD	LD	P -value
Thickness	mean±SD	mean±SD	mean±SD	mean±SD	
Cementum	166 ± 7.1	77.75 ±1.37	111.25 ± 3.9	94 ± 2.34	0
	A	B	C	D	
periodontal ligament	225 ± 35.97	115 ± 14.15	172 ± 32.78	146.12 ± 20.06	0
	A	B	B	C	

Different letter mean there is significant difference, while same letter mean there in no significant difference at $P \leq 0.05$. Data expressed as mean ± standard error after four week ,Data expressed as Mean ± stander error

In control positive group section of bone of tooth showed the apical side the CM with CB and cementoclast.

In low dose group section of bone of tooth showed the apical side the CM with CB and cementoclast.

In high dose group section of bone of tooth showed the apical side CM with CB and cementoclast. H&E stain, 400X as shown in Figure 3.

Statistical analysis of number of fibroblasts and fibrocytes found

The statistical analysis showed that there was significant difference (p = 0.00) within each group after four week

in periodental ligament after a Shapiro-Wilk test was used to assess the normality of distributions there was significant increase(p = 0.00) in number of fibroblast founded of both high dose(142±5.59) and low dose(86.75±14.79) in comparison with control posative group(56.75±15.32) where the control positive group(118.75±23.07) groups it's the normal as show in Table 2 and Figure 4.

in periodental ligament after a Shapiro-Wilk test was used to assess the normality of distributions there was increase of number of fibrocyte founded with control positive group(63.25±7.13) in comparison both high dose(40±6.16) and low dose(55.25±9.06) groups which decrease number of fibrocyte ,control negative group(27±4.69) it's the normal significantly (p = 0.00) as show in Table 2 and Figure 2.

Histological finding

In control negative group showing the periodontal ligament with fibroblast (FB) and fibrocytes (FC) surrounding tooth.

In control Positive group showing the periodontal ligament with fibroblast (FB) and fibrocytes (FC) surrounding toot.

In the low dose group showing the periodontal ligament with fibroblast (FB) and fibrocytes (FC) surrounding tooth.

the high dose group showing the periodontal ligament with fibroblast (FB) and fibrocytes (FC) surrounding tooth. H&E stain, 400Xas shown in Figure 4.

The statistical analysis Thickness of cementum and periodontal ligament in micrometer

Showed that there was significant difference within each group after four week

In apical part of the bone: there was significant decrease(p = 0.00) thicknesses of cementum founded of control positive group(77.75±1.37) µm in comparison with both high dose(111.25±3.9) µm and low dose(94±2.34)µm groups,control negative group(166±7.1) it's the normal

In apical part of the bone: there was significant decrease thicknesses of of periodontal ligament (PL) founded of control positive group (115±14.15)µm groups in comparison with both high dose(172±32.78) µm and low dose(146.12±20.06)µm ,control negative group(225±235.97)µm it's the normal as show in Table 2.

Histological finding

In control negative group sections of tooth of bone showed the apical the thicknesses of periodontal ligament PL and cementum (CM).

In control positive group section of bone of tooth showed the apical side shows the thicknesses of PL and CM.

In low dose group section of bone of tooth showed the apical side the shows the thicknesses of PL and CM.

In high dose group section of bone of tooth showed the apical side the thicknesses of PL and CM. Omax ToupView program. H&E stain, 100X. as shown in Figure 5.

DISCUSSION

Animal studies can help researchers understand more about the effects of natural compounds and pharmaceuticals on the body, as well as avoid some of the issues that can arise when trying to treat humans. However, it's critical that the experimental circumstances remain consistent. Although, Monkeys are the closest models to humans in terms of oral architecture and physiology, however, their use is restricted due to ethical and financial concerns[23,24].

Rabbits are a popular animal candidate for dental implants researches due to their small size, ease of handling, short lifespan, and low cost of purchase and maintenance. They are also placid and non aggressive[24].

Tooth root is composed of four parts: a central core of dentin covered by cementum, Alveolar bone that attached to the root cementum via the periodontal ligament. After trauma or dental orthodontic procedures rapid bone turnover including the alveolar bone of rabbit was Part of the reasons we choose it as a study[25]. Insomniac incisor orthodontic appliances were less upsetting for rabbits than other orthodontic appliances made between the first molars and lower incisors that is why we applied it to the lower incisors[26]. To rule out hormonal changes in female rabbits, we utilized male rabbits. Also, because all rabbits received the same daily diet, no weight fluctuation would be expected even if Botulinum neurotoxin (BTX) lowered food intake, as previous research by Tsai et al[26] indicated.

To the best of our knowledge, no studies have examined the effect of MgO on OIRR, and the present study is the first to investigate the effect of MgO on OIRR in rabbit model. This study investigated the effects of magnesium administration on apical root resorption Including its four parts (alveolar bone, PDL, root dentin & cementum) in albino rabbit subjected to orthodontic tooth treatment. The rabbit forcibly administered supplementation with MgO which in addition to its possible mineralization effect has anti-stress effect as demonstrated by in a study by Boyle et al.[27]

Regarding cementum part of the dental root : we found a significant decrease thicknesses of cementum in control positive group(77.75±1.37) in comparison with both high dose(111.25±3.9) and low dose(94±2.34) MgO administered groups. Control negative group(166±7.1) showed a normal cementum thickness. This signify that forceful orthodontic manipulation cause cementum resorption while cementum is relatively preserved in both MgO administered but especially in higher dose group. This finding may be explained by the effect of MgO on cementum regeneration and degradation cells (cementoblasts and cementoclasts respectively).

We demonstrate that there was significant decrease of number of cementoblasts found in both high dose (18.5±3.9) and low dose (17.25±2.25) and control positive group (11.5±0.64) groups in comparison with control negative group which has a normal value of (25.5±0.64). In addition to a significant increase of number of cementoclasts found with control positive group (2.5±0.28) in comparison both high dose (0.75±0.25) and low dose (1.25±2.05) groups which decrease number of cementoclasts While ,control negative group is (0.00±0.0).

The important ratio of the mineral content of the cementum and Mg^{2+} ratio and its association with other mineral constituent has studied previously, the inorganic chemical composition of the root cementum was reported to consist of elements such as calcium (Ca), phosphorous (P), and magnesium (Mg^{2+}) .Thus, individual variations in the hardness of cementum may be related to the chemical composition of Ca, P, and Mg^{2+}, and may influence whether may or may not resist or be susceptible to root resorption[28].

Previous studies have reported that Mg^{2+} regulates the metabolism of cementum, influencing mineralization, especially crystal growth[29], stabilizing calcium phosphate, and reducing the degradation rate of calcium phosphate. The mineralized surface of the cementum followed orthopedic force is more resorbed in the apical part after orthodontic tooth movement than in other regions[30,31].

Regarding effect of Mg^{2+} on periodental ligament, we found that there are currently no information in the literature about the use of magnesium oxide and its possible role in the enhancement of periodontal ligament thickness in vivo. However, there have been few reports on the effect of Mg^{2+} deficiency on the morphology of periodontal tissues including PDL.

In this research one of our main findings are the significant differences in the PDL thickness between the four study groups. After orthodontic intervention maximum rate of resorption of PDL is seen in control positive group (14.15Mm)

This finding is supported by research by Mortazavi et al [32]who found that forceful orthodontic procedure causes of PDL widening.

Lesser rate of resorption are seen in low and high Mg^{2+} supplement groups (20.6Mm and 32.78 Mm) respectively, reflect the importance of Mg^{2+} mineral in periodontal ligament preservation after forceful orthodontic movement.

The PDL widening after orthodontic movement could be explained by disarray of the periodontal fibers (principal fibers) and a change in fibroblasts which are responsible for PDL fibers production , beside impairment of the alveolar bone at the site of attachment and insertion of the periodontal fibers into the bone, This probably reduces the supporting capacity of the PDL against functional loading. These changes in PDL might be supported in a research by[33] who studied the effect of Mg^{2+} deficiency on PDL and found that Collagen metabolism or turnover in the PDL was damaged by Mg^{2+} deficiency. Probably because Mg^{2+} deficiency disturbs the intracellular homeostasis that influences collagen metabolism.

Moreover, Fibroblasts in culture with Mg^{2+} deficiency showed accelerated senescence and an increase in telomere attrition. These findings are also supported by another study by Ishikawa et al[34]who looked for the effect of magnesium difficiency in rats found that histological observations demonstrated a widening of the periodontal ligament space, disturbance of the periodontal fibers arrangement , and an increase in fibroblasts with collagen containing vesicles in their cytoplasm.Indicating the importance of Mg^{2+} in generation and preservation of PDL. Furthermore, Mg^{2+} also affect the the alveolar bone as it was resorbed from the periodontal side in Mg^{2+} deficient rats during the experimental period[34-36].

Another study by Brown et al, 2015[34] where PLGA scaffold (which is widely used for the production of biodegradable and biocompatible micro- and nanoparticles drug delivery scaffold used as implanted drug delivery system in different tissue. Brown et al has use it to deliver slow release of magnesium at the alveolar bone part of dental root following tooth extraction. The slow release of Mg^{2+} ion lead to provide the necessary pH buffering properties (buffer the acidic environment) thus provide an osteoconductive environment for alveolar bone growth[34].

Mg^{2+} has long been linked to tooth biomineralization[35]. Li et al[36] found that the incorporation of Mg^{2+} into pulp-capping biomaterials, allowing therapeutic Mg^{2+}ions to be released in to the cupped tooth , has been proposed as a potential method for promoting tooth tissue regeneration especially dentin matrix (of the root). They explained that the therapeutic ions activate cellular signaling, causing resident pulp cells to develop into odontoblast-like cells, dentin matrix secretion to increase, and tertiary dentin production to occur as Mg^{2+} connects cell-

surface receptor induction and cytosolic effectors as an intracellular second messenger[36,37] .

Alvarez-Perez at 2005[37] reported that the presence of Mg^{2+} influenced the Ca/P and Mg^{2+}/Ca ratios, and that the influence was inversely proportional to the Ca/P ratio. Thus, the decreased Ca/P ratio might have been involved in the increase in Mg^{2+} and vice versa.

In a study by Kong et al[38] who have found that Mg^{2+}- enriched microenvironment enhanced odontogenic differentiation in DPSCs by activating ERK/BMP2/Smads signaling via intracellular Mg^{2+} increase[38.]

other study by Salem et al[39], reveal that Mg^{2+} may promote cellular proliferation (including dental root cells) as Mg^{2+} may act as a key factor of the so-called coordinated control of cell proliferation. Mg^{2+} is involved in DNA duplication and plays a role in cytoskeleton rearrangement leading to the formation of the mitotic spindle and cytokinesis[39].

Another study proving the relationship between Mg^{2+} and cellular regeneration and proliferation is by[40] who found that Mg^{2+} is important in governing key rate-limiting steps in the cell cycle, particularly at the onset of DNA synthesis and at mitosis[40]. Magnesium also plays a role in the cytoskeleton rearrangement leading to the formation of the mitotic spindle and cytokinesis as mentioned in a study by (Zou et al 2022)[41].

Magnesium deficiency effects have been studied previously in an animal model, it was shown that after just three days of Mg^{2+} deficient diet , there was a rise in the number and activation of inflammatory cells such as macrophages, leucocytes, neutrophils, and eosinophils[42,43]. Also, raise the inflammatory cytokines, particularly TNF-and C-reactive protein, are also enhanced which may affect all the body including dental roots[44].

The lack of enough magnesium, calcium, and phosphorus in the diet is usually associated with loose teeth and premature tooth loss. In magnesium deficiency, the alveolar bone is fragile, and the gum becomes hypertrophic[44.]

Magnesium influences dental and oral health, partly by enhancing the antimicrobial microenvironment, reducing oral inflammation, enhancing calcium absorption into the teeth, and increasing tooth enamel flexibility. Some clinical scientists believe that magnesium is more important than calcium in maintaining oral and dental health. Without adequate magnesium balance,The salivary glands cannot remove excess food debris and provide a more basic environment to mitigate the effects of bacterial acid production , The immune system cannot activate vitamin D, one of its primary forces , The body cannot adequately make glutathione, an important anti-inflammatory agent that combats inflammation of teeth and gums,The teeth can no longer absorb calcium, which instead enters the gums, where it calcifies and causes inflammation, The tooth enamel lacks a primary constituent of its amorphous binding solution the magnesium ion. Magnesium deficiency, therefore, is apparently vital to protecting teeth and keeping them healthy[43-44]. Therefore, vitamin D may be of benefit in treating periodontitis because of its direct effects on bone metabolism as well as its possible anti-inflammatory effects on periodontopathogens[33], Deregulation of osteoclast differentiation, function and survival may lead to pathological conditions, such as osteoporosis or osteopetrosis[34].

Other previous study have demonstrated a moderate or subclinical magnesium deficiency can induce chronic low-grade inflammation or exacerbate inflammatory stress. This would increase the secretion of pro- inflammatory cytokines, which stimulate the resorption of bone by the induction of the differentiation of osteoclasts. The ability of Mg^{2+} to decrease the inflammatory response and oxidative stress possibly by inhibiting IL-6 pathway, NF-κB pathway, and L-type calcium channels[40,45].

However, The present study has several limitations that should be recognized. The use of an animal model may not fully replicate the complexity of human periodontal and cementum remodeling processes, and therefore, the findings should be interpreted with caution when extrapolating to clinical conditions. Additionally, the outcomes were based primarily on histological and histomorphometric assessments; no molecular or biochemical analyses were performed to validate the cellular activity or signaling pathways underlying the observed changes. The absence of such molecular confirmation limits mechanistic interpretation of the results, and future studies incorporating gene expression or protein-level analyses are warranted to further substantiate the findings.

Clinical implication

The clinical implication of this study is mainly to consider the patients under orthodontic therapy along with MgO supplementation , it's cheap and available the orthodontist could be, compromised treatment.

CONCLUSION

Under the constraints of this experimental rabbit investigation, magnesium oxide (MgO) supplementation showed an restorative impact against orthodontically induced inflammatory root resorption (OIRR). The use of force, by itself caused notable thinning of the cementum heightened cementoclast activity decreased cementoblast count narrowing of the periodontal ligament (PDL) and histological characteristics indicative of increased root resorption. Conversely rabbits given MgO supplements-at the elevated dose—exhibited maintained cementum thickness, fewer cementoclasts, comparatively increased cementoblast numbers and enhanced PDL thickness relative, to the positive control group.

These results indicate that magnesium has a function in cementum metabolism and the remodeling of periodontal tissues during orthodontic tooth movement. The noted effects could result from magnesium's impact, on mineralization, control of cell behavior stimulation of fibroblast growth and reduction of inflammatory reactions linked to intense orthodontic forces. Overall MgO supplementation seemed to lessen the extent of root resorption and maintain periodontal tissue health without disrupting the orthodontic mechanical procedures.

Therefore, magnesium supplementation may represent a promising adjunctive strategy for reducing the risk and severity of OIRR during orthodontic treatment. However, further investigations—including molecular studies, long-term evaluations, and well-designed clinical trials—are required to elucidate the precise mechanisms involved, determine optimal dosing, and assess the translational relevance of these findings to human orthodontic patients.

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