



Effect of ultrasonic oscillation in combination with laser microsurgery on chronic periapical periodontitis

Original Study

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Abstract

Introduction. We aimed to evaluate the effect of ultrasonic oscillation in combination with laser microsurgery on chronic periapical periodontitis.

Materials and Methods. Ninety patients with chronic periapical periodontitis admitted from January 2020 to March 2023 were divided into a control group (n=45) and a treatment group (n=45) using a random number table. The control group was treated with laser microsurgery, while the treatment group was given ultrasonic oscillation plus laser microsurgery.

Results. At 4 weeks and 8 weeks after treatment, the visual analogue scale (VAS) score significantly declined, while the mean gray value (MGV) significantly rose in both groups (P<0.05). The treatment group had a lower VAS score and a higher MGV than those of the control group at 4 weeks after treatment (P<0.05). Old-periapical index (O-PAI) of the treatment group was lower after treatment than that before treatment, and it was lower at 8 weeks after treatment than that of the control group (P<0.05). After treatment, the levels of serum calcium, phosphorus, and alkaline phosphatase in the treatment group were higher than those in the control group (P<0.05). After treatment, their levels declined in both groups, and they were lower in the treatment group than those in the control group (P<0.05).

Conclusions. Ultrasonic oscillation plus laser microsurgery can treat chronic periapical periodontitis effectively and safely, relieve pain and inflammatory response.

Keywords

laser • microsurgery • oscillation • periodontitis • ultrasound

1. Introduction

Chronic periapical periodontitis is a common oral disease characterized by a long-term inflammatory response of periapical tissues, which is usually caused by root canal infection or incomplete root canal treatment, resulting in discomfort and oral dysfunction [1,2]. Periapical pain, gingival swelling, and periapical abscess are the main clinical manifestations, and it is usually diagnosed by clinical symptoms, oral examination, and imaging examination, such as periapical film and cone-beam computed tomography [3]. If there is a long-standing neglect of the treatment of chronic periapical periodontitis, inflammation may spread to adjacent tissues, causing more serious infection and pathological changes, followed by serious consequences such as periodontal disease progression, bone resorption, adjacent tooth loosening, and jaw bone destruction. Therefore, early intervention and effective treatment are crucial for the management of chronic apical periodontitis.

In recent years, minimally invasive techniques using lasers have been the modern standard of care and have been successfully applied to tooth replantation [4] and the management of recurrent aphthous ulcers [5]. Laser has also been used in microsurgery to cut, sterilize and repair periapical tissues, thereby eliminating the source of infection and promoting the

healing of periapical tissues [6]. However, laser microsurgery alone has some limitations in the treatment of periapical periodontitis, such as a low cure rate and high recurrence rate.

Ultrasonic oscillation is characterized by simple operation, small trauma, and no radiation [7]. During the treatment of periapical periodontitis, it can effectively remove the bacteria in the root canal and the dirt on the root canal wall by the mechanical action of ultrasonic waves and the energy of micro-shock waves, thereby eliminating the source of infection [8]. To further improve the treatment outcomes, ultrasonic oscillation may be combined with laser microsurgery which can remove periapical lesions and make the treatment more accurate and complete [9]. Until now, chronic periapical periodontitis has never been treated by this combination.

Therefore, we herein evaluated the clinical efficacy of ultrasonic oscillation plus laser microsurgery on chronic periapical periodontitis, aiming to provide new ideas and directions for improving the treatment outcomes.

2. Materials and methods

2.1. General data

The sample size was calculated according to the formula $n=2 \times (\sigma)^2 \times (Z_{\alpha/2} + Z_{\beta})^2 / (\mu_1 - \mu_2)^2$, where n is the sample size, σ is the

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estimated standard deviation, $Z_{\alpha/2}$ is the Z-score corresponding to the desired confidence level ($1-\alpha$), Z_{β} is the Z-score corresponding to the desired statistical power ($1-\beta$), and $(\mu_1-\mu_2)$ is the expected difference between population means. The confidence level was 95%, and the margin of error was 0.05. Ninety patients with chronic periapical periodontitis admitted to our hospital from January 2020 to March 2023 were divided into a control group (n=45) and a treatment group (n=45) using a random number table. This study had been approved by the ethics committee of our hospital (approval No. XJU202001004). Written informed consent has been obtained from all patients.

2.2. Inclusion and exclusion criteria

The inclusion criteria were as follows: patients meeting the diagnostic criteria for chronic periapical periodontitis [10]; those aged 18-60 years and with indications for laser microsurgery; those whose periapical low-density radiographs remained unhealed after complete root canal therapy or retreatment; those with root canal filling materials beyond the apex and unable to be removed from the root canal and with obvious clinical symptoms of the affected teeth.

The exclusion criteria included: patients with severe periodontal disease, vertical alveolar bone absorption $>1/3$ of root length or tooth loosening \geq degree II; those with periapical periodontitis caused by tooth fracture, root canal lateral wall perforation or instrument fracture; those with diseases of the heart, liver, kidney or other important organs; those with contraindications to surgery; and pregnant or lactating women.

2.3. Treatment method for control group

Laser microsurgery was performed, specifically as follows. The incision position was designed according to the preoperative reconstruction data of cone-beam computed tomography. Flap surgery was then performed using an erbium (Er: YAG) laser (Biolase, model: WaterLase iPlus, EPIC X) to expose the root apex, and the root was severed 4 mm away from the apical region. The inner wall structure of the root canal was removed with Er: YAG laser under the following parameters: wavelength: 2940 nm, pulse width: 50 ms, power: 0.3 W, energy: 20 mJ, and frequency: 15 Hz. Then, the infected tissue was disinfected using a neodymium (Nd:YAG) laser (Lutronic, model: ADVANTAGE series) 1 mm away from the bone and tooth tissue of the lesion area under the following parameters: wavelength: 1064 nm, pulse width: 150 ms, power: 0.5 W, energy: 50 mJ, and frequency: 10 Hz. Following retrograde filling using mineral trioxide aggregates (MTA) (Avalon Biomed Inc., model: MTA Angelus), the incision was sutured. Subsequently, photobiological stimulation was performed using a low-energy Nd:YAG laser in the surgical area under the following parameters: wavelength: 1064 nm, pulse width: 100 ms, power: 1.5 W, energy: 50 mJ, and frequency: 15 Hz. The sutures (Medtronic, model: Silkam) were removed 7 d postoperatively.

2.4. Treatment method for treatment group

Ultrasonic oscillation plus laser microsurgery was performed. Before the operation, the patients needed to be informed in detail of the treatment process and possible discomfort, ensuring that they fully understood the treatment content and expected effect. The patients were informed that some discomfort, such as mild toothache or pressure, may occur during root canal preparation, but this is normal, and that there may be some irritation when the sodium hypochlorite solution is instilled into the dental pulp cavity, but it will soon subside. Ultrasonic oscillation may produce some vibration, but it helps clean the root canal and reduces the risk of infection. There may be some discomfort when the paste is filled into the root apex and root canal, but these pastes are important for the healing of the periapical tissue. Some slight pressure may be felt when the cavity is closed after operation, but it helps protect the treated area and promote healing.

Before treatment, periapical films were taken to learn about the apical lesions. The root canal was then dredged using 10# and 15# K-files to prepare the root canal for subsequent treatment. At the same time, the working length was measured by an electronic apex locator combined with periapical films. According to the measured working length, the root canal preparation was completed using the step-down method. The root canal was lubricated with EDTA during root canal preparation to reduce friction and facilitate root canal cleaning. After root canal preparation, 2% sodium hypochlorite solution was dripped into the dental pulp cavity for cleaning and disinfecting the root canal. Then, the root canal was oscillated for 30 s using a P5 ultrasonic instrument connected with a 15# file so as to effectively remove the bacteria in the root canal and the dirt on the root canal wall. Afterwards, an appropriate amount of Vitapex paste was introduced into the root apex to promote periapical tissue healing. Then, calcium hydroxide iodoform paste was sealed into the root canal to provide further disinfection and protection. After root canal therapy, the cavity was temporarily sealed with ZOE to protect the treated area and promote healing. Depending on the patient's condition, the medical staff may recommend some postoperative adjunctive medications, such as antibiotics or painkillers. The patients were instructed to pay attention to oral hygiene, avoid excessive eating or chewing, keep the mouth clean, and avoid hot or irritating foods to promote healing. The patients in the two groups were followed up after 2 months of treatment.

2.5. Observation of indicators

Criteria for evaluating treatment outcomes [11]: Cured: The patient felt no discomfort and had good tooth function, the clinical examination results were normal, the X-ray film showed tight and smooth root canal filling, and the original apical shadow disappeared. Improved: The patient had no occlusal pain or percussion pain, no gingival swelling or sinus tract and other symptoms, the X-ray film showed that the periapical transparent

Table 1. General data (n, $\bar{x} \pm s$)

Group	n	Age (year)	Apical foramen diameter (mm)	Gender	Tooth position/n	Etiology/n
				M/F	Maxillary anterior teeth/mandibular premolar/maxillary premolar	Dental trauma/caries/central cusp deformity
Control	45	26.28±4.27	1.18±0.31	26/19	15/21/9	13/6/26
Treatment	45	25.91±4.30	1.20±0.33	24/21	12/23/10	14/8/23
$t/2$		0.410	0.296	0.180	0.477	0.506
P		0.683	0.768	0.671	0.788	0.776

shadow was significantly reduced, and there were non-intact lamina dura and wide periodontal ligament space. Ineffective: The physical examination showed percussion pain or occlusal pain, and the X-ray film showed no significant reduction or increase in periapical transparent shadow.

The visual analogue scale (VAS) score was recorded at different time points (before treatment, 4 weeks after treatment, and 8 weeks after treatment) [12]. No pain, mild pain (within the tolerance range), worsened pain (affecting sleep), and severe pain (beyond the tolerance range) were scored as 0 points, <3 points, 4-6 points, and 7-10 points, respectively. Mean gray value (MGV) was detected in X-ray films by the same radiologist before treatment and at 4 weeks and 8 weeks after treatment.

Imaging for healing: The same X-ray imaging system with the same exposure settings was used before treatment and at 2 weeks, 4 weeks, and 8 weeks after treatment. The old-periapical index (O-PAI, grade 1-5) was used to reflect the changes in periodontal ligament space, periapical bone, and apical foramen [13].

Serum biochemical indicators of bone formation: Serum calcium (Ca), phosphorus (P), and alkaline phosphatase (ALP) were measured 4 weeks after treatment by an automatic biochemical analyzer.

Inflammatory factors in gingival crevicular fluid (GCF): Before and 4 weeks after treatment, GCF was collected using a micropipette or special GCF collection paper. The sampler was gently placed in the gingival sulcus for a few seconds until the GCF was absorbed or collected into the sampler. Then, the levels of tumor necrosis factor- α (TNF- α) and interleukin-6 (IL-6) were measured by enzyme-linked immunosorbent assay, and the level of C-reactive protein (CRP) was measured by immunoassay.

After treatment, the incidence of adverse reactions such as local swelling, infection and nerve injury was recorded.

2.6. Statistical analysis

Normal distribution was confirmed using the Shapiro-Wilk test. The normally distributed measurement data (including age, mean apical foramen diameter, VAS score, MGV, biochemical indicators of bone metabolism, and inflammatory factors) were described by mean \pm standard deviation ($\bar{x} \pm s$). They were

compared by the paired t -test at different time points within the same group and by the independent t -test at the same time point between two groups. One-way repeated measures analysis of variance was performed for comparisons at multiple time points. Subsequently, Bonferroni correction can be used for multiple comparison. The count data (gender, tooth position, etiology, efficacy, and incidence of adverse reactions) were described by rate and percentage (%), and analyzed by the χ^2 test. $P < 0.05$ was considered statistically significant. SPSS 23.0 software was used for statistical analysis.

3. Results

3.1. General data

There were no significant differences in the mean age, mean apical foramen diameter, gender, tooth position, and etiology between the two groups ($P > 0.05$) (Table 1).

3.2. Treatment outcomes

After 2 months of follow-up, the total effective rate of the treatment group (98%) was significantly higher than that of the control group (82%) ($P < 0.05$) (Table 2).

3.3. Pain degree and MGV

Before treatment, there were no significant differences in the VAS score or MGV between the two groups ($P > 0.05$). At 4 weeks and 8 weeks after treatment, the VAS score significantly declined, while MGV significantly rose in both groups ($P < 0.05$). The treatment group had a lower VAS score [(1.06±0.24) points] and a higher MGV (128.04±10.23) than those of the control group [(1.92±0.31) points, 108.12±10.15] at 4 weeks after treatment ($P < 0.05$), while the two groups had no significant difference in MGV at 8 weeks after treatment ($P > 0.05$) (Table 3).

3.4. O-PAI at different time points

There was no significant difference in O-PAI between the two groups before treatment ($P > 0.05$). O-PAI declined at 4 weeks and 8 weeks after treatment in both groups compared with those before treatment, and it was lower in the treatment group (1.26±0.10) at 8 weeks after treatment than that in the control group (1.49±0.15) ($P < 0.05$) (Table 4).

Table 2. Treatment outcomes [n(%)]

Group	n	Cured	Improved	Ineffective	Total effective rate
Control	45	25 (55)	12 (27)	8 (18)	37 (82)
Treatment	45	29 (65)	15 (33)	1 (2)	44 (98)
$F_{time^1 P_{time}}$					6.049
P					0.014

Table 3. Pain degree and MGV ($\bar{x} \pm s$)

Group	n	VAS score (point)			MGV		
		Before treatment	4 weeks after treatment	8 weeks after treatment	Before treatment	4 weeks after treatment	8 weeks after treatment
Control	45	7.31±1.35	1.92±0.31	0.63±0.12	77.65±9.41	108.12±10.15	136.14±14.27
$F_{time^1 P_{time}}$		800.00, <0.001			1200.00, <0.001		
$t_{time^1 P_{time}}$ (Bonferroni correction)		Before vs. 4 weeks after treatment: 26.10, <0.001			Before vs. 4 weeks after treatment: 15.13, <0.001		
		Before vs. 8 weeks after treatment: 33.06, <0.001			Before vs. 8 weeks after treatment: 19.67, <0.001		
		4 vs. 8 weeks after treatment: 26.03, <0.001			4 vs. 8 weeks after treatment: 14.65, <0.001		
Treatment	45	7.28±1.27	1.06±0.24	0.38±0.06	78.53±9.52	128.04±10.23	138.25±15.02
$F_{time^1 P_{time}}$		1200.00, <0.001			1500.00, <0.001		
$t_{time^1 P_{time}}$ (Bonferroni correction)		Before vs. 4 weeks after treatment: 32.28, <0.001			Before vs. 4 weeks after treatment: 24.55, <0.001		
		Before vs. 8 weeks after treatment: 36.41, <0.001			Before vs. 8 weeks after treatment: 22.69, <0.001		
		4 vs. 8 weeks after treatment: 18.44, <0.001			4 vs. 8 weeks after treatment: 5.45, <0.001		
$t_{between\ groups}$		0.109	14.715	12.500	0.441	9.273	0.683
$P_{between\ groups}$		0.914	<0.001	<0.001	0.660	<0.001	0.496

Table 4. O-PAI at different time points ($\bar{x} \pm s$)

Group	n	Before treatment	4 weeks after treatment	8 weeks after treatment
Control	45	3.38±0.08	2.42±0.12	1.49±0.15
$F_{time^1 P_{time}}$		141.58, <0.001		
$t_{time^1 P_{time}}$ (Bonferroni correction)		Before vs. 4 weeks after treatment: 7.44, <0.001		
		Before vs. 8 weeks after treatment: 12.60, <0.001		
		4 vs. 8 weeks after treatment: 6.14, <0.001		
Treatment	45	3.41±0.09	2.37±0.11	1.26±0.10
$F_{time^1 P_{time}}$		254.04, <0.001		
$t_{time^1 P_{time}}$ (Bonferroni correction)		Before vs. 4 weeks after treatment: 8.38, <0.001		
		Before vs. 8 weeks after treatment: 17.29, <0.001		
		4 vs. 8 weeks after treatment: 9.38, <0.001		
$t_{between\ groups}$		0.284	3.346	5.144
$P_{between\ groups}$		0.777	<0.001	<0.001

3.5. Serum biochemical indicators of bone formation

After treatment, the levels of serum Ca [(3.20±0.53) mmol/L], P [(2.35±0.23) mmol/L], and ALP [(150.94±10.83) U/L] in the treatment group were higher than those in the control group [(2.54±0.41) mmol/L, (1.98±0.14) mmol/L, (120.31±8.92) U/L] (P<0.05) (Table 5).

3.6. Levels of inflammatory factors in GCF

Before treatment, the levels of inflammatory factors TNF- α , IL-6, and CRP in GCF had no significant differences between the two groups (P>0.05). After treatment, their levels declined in both groups, and they were lower in the treatment group [(2.46±0.43), (5.42±1.06), (1.05±0.32) μ g/L] than those in the control group [(2.95±0.62), (7.16±1.48), (1.38±0.41) μ g/L] (P<0.05) (Table 6).

Table 5. Serum biochemical indicators of bone formation ($\bar{x} \pm s$)

Group	n	Ca (mmol/L)	P (mmol/L)	ALP (U/L)
Control	45	2.54±0.41	1.98±0.14	120.31±8.92
Treatment	45	3.20±0.53	2.35±0.23	150.94±10.83
<i>t</i>		6.607	9.218	14.645
P		<0.001	<0.001	<0.001

Table 6. Levels of inflammatory factors in GCF ($\bar{x} \pm s$, µg/L)

Group	n	TNF-α		IL-6		CRP	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control	45	7.65±0.94	2.95±0.6 ^a	15.68±2.74	7.16±1.4 ^a	2.68±0.48	1.38±0.4 ¹ a
Treatment	45	7.72±1.03	2.46±0.4 ³ a	15.73±2.85	5.42±1.0 ⁶ a	2.71±0.53	1.05±0.3 ² a
<i>t</i>		0.337	4.356	0.085	6.412	0.281	3.860
P		0.737	<0.001	0.933	<0.001	0.779	<0.001

^aP<0.05 vs. the same group before treatment

Table 7. Incidence of adverse reactions [n(%)]

Group	n	Local swelling	Infection	Nerve injury	Incidence rate
Control	45	2 (4)	2 (4)	1 (2)	5 (10)
Treatment	45	1 (2)	0 (0)	1 (2)	2 (4)
²					1.394
P					0.238

3.7. Incidence of adverse reactions

No significant difference was found in the incidence rate of adverse reactions between the two groups (10% vs. 4%) ($P>0.05$), and all symptoms disappeared after 2 days without special treatment (Table 7).

4. Discussion

Traditional apical surgery is commonly performed to remove the periapical pathological tissue and resect the root apex, followed by root canal preparation with a ball-shaped drill. Then, the cavity was filled with silver amalgam to achieve tight isolation between the root canal and the periapical tissue [14]. However, due to the lack of proper lighting and magnifying equipment in traditional surgery, it is often hard to observe the fine structure at the end of the root canal and the imprecision of amalgam filling, resulting in a fluctuation of surgical success rate. With a focused light source, the dental operating microscope can offer clearer and magnified images of the surgical area during surgery by using its amplification and illumination characteristics so that clinicians can have a more detailed understanding of the surgical site and characteristics, thereby improving the accuracy and perfection of surgical operation [15,16].

At present, laser microsurgery has been widely used in the dental field, which is a highly precise minimally invasive

surgical technique combining laser and microscopic techniques. During surgery, the fine structure at the end of the root canal can be observed, and the diseased tissue and the periapical situation can be clearly identified using the magnification and illumination characteristics of the microscope [17]. Laser is used for cutting and disinfection, which can precisely remove periapical pathological tissue and achieve tight isolation [18]. However, laser microsurgery alone has some limitations in the treatment of chronic periapical periodontitis. In this study, ultrasonic oscillation was applied, which generated pressure waves in the root canal by ultrasonic waves with high frequency vibration, thus generating bubble and hydrodynamics effect [19]. With this hydrodynamics effect, the bacteria in the root canal and the dirt on the root canal wall can be effectively removed, thereby reducing the inflammatory response and infection in the root canal. Moreover, it can promote the healing of the periapical tissue and the regeneration of the bone tissue, thereby contributing to the cure of periapical periodontitis.

The levels of TNF-α, IL-6, and CRP in GCF have a close relationship with chronic periapical periodontitis, and these biochemical indicators have important clinical significance in the diagnosis and treatment of chronic periapical periodontitis [20,21]. In particular, TNF-α and IL-6 are important regulators in the inflammatory process and are involved in immune

response, cell proliferation, and phagocytosis of inflammatory cells. Meanwhile, systemic inflammatory response may also lead to an elevated CRP level [22]. Georgiou et al. found among 53 subjects from the immunological characteristics and healing characteristics of chronic periapical periodontitis in a single tooth that systemic low-grade inflammation caused by compensatory immunosuppression resulted in loss of homeostasis [23]. In this study, the total effective rate in the treatment group was significantly higher than that in the control group (98% vs. 82%), suggesting the significant efficacy of ultrasonic oscillation plus laser microsurgery in the treatment of chronic periapical periodontitis. After treatment, the levels of TNF- α , IL-6, and CRP in the treatment group significantly declined, and they were significantly lower than those in the control group, suggesting that ultrasonic oscillation plus laser microsurgery can effectively reduce the inflammatory response and ameliorate the inflammatory state of periapical tissues. The inflammatory pathogenesis in GCF is as follows. Bacterial infection causes inflammation, and chronic periapical periodontitis usually results from root canal infection. Then bacteria trigger an inflammatory response in the periapical tissue, activating immune cells and releasing inflammatory factors such as TNF- α and IL-6, which promote the migration and proliferation of inflammatory cells, enhance the immune response, and activate other inflammatory mediators, thus worsening the inflammatory response. Chronic periapical periodontitis is not restricted to periapical tissue, and the inflammatory factors released may also lead to systemic inflammatory responses. As a result, the level of CRP, an acute-phase protein, rises, which reflects inflammation in the body.

Ultrasonic oscillation plus laser microsurgery works in the following way. Comprehensive clearance: Ultrasonic oscillation can remove the bacteria and dirt in the root canal and reduce the inflammatory response caused by bacterial infection. Laser microsurgery can accurately remove the periapical lesions and reduce the production of inflammatory factors. Therefore, ultrasonic oscillation plus laser microsurgery can eliminate the lesions more comprehensively, accelerate the healing of periapical tissues, and reduce pain and complications. Accelerated healing: Ultrasonic oscillation can facilitate the healing of periapical tissue and the regeneration of bone tissue, and minimally invasive and accurate laser microsurgery contributes to the rapid healing of postoperative wounds. Therefore, the combined treatment can accelerate the rehabilitation process. Precise treatment: Laser microsurgery is characterized by precise operation around the root apex, which can avoid damage to the surrounding normal tissues, and ultrasonic oscillation can help clean the root canal, making the treatment more precise and reducing pain. Mild complications: The combined treatment can reduce complications, such as postoperative infection and inflammatory response, and thus improve the safety of treatment.

Horhat et al. found among 60 patients with chronic periapical periodontitis that oligomeric epoxy resin-based sealants significantly improved the periapical index, tooth mobility, and post-treatment tooth healing [24]. In this study, MTA was used for retrograde filling in the control group, and it was found that MTA had good biocompatibility and could promote the regeneration of hard tissue. The levels of Ca, P, and ALP in the treatment group were higher than those in the control group after treatment, suggesting that the combined treatment can contribute to the repair and regeneration of bone tissue. The possible reason is that ultrasonic oscillation and laser microsurgery exert a synergistic effect to accelerate the healing process of bone tissue. In addition, there were no significant differences in the preoperative pain score and MGVI between the control group and treatment group, indicating that the two treatment methods are similar in terms of preoperative pain and periapical imaging results. However, postoperative pain score and MGVI were superior in treatment group. O-PAI in the treatment group was better than that in the control group after treatment. The above results demonstrated that ultrasonic oscillation plus laser microsurgery can significantly relieve pain and improve the periapical imaging result. The O-PAI system can reflect the pathological changes and degree of chronic periapical periodontitis by evaluating the periapical bone and root surface. The more serious the condition, the higher the O-PAI and the worse the bone destruction and periodontal tissue inflammation. The authors believe that the combined treatment can more thoroughly eliminate the periapical lesion and bacteria, and reduce inflammatory response and nerve excitation, thereby relieving pain and enhancing clinical efficacy.

4.1. Limitations of the study

This is a single-center study with a small sample size, so it is crucial to enlarge the sample size based on the experience of more medical centers.

5. Conclusions

Ultrasonic oscillation plus laser microsurgery has significant efficacy and safety in the treatment of chronic periapical periodontitis. It can reduce pain and inflammatory response and contribute to rapid repair of bone tissues without increasing adverse reactions.

Authors' contribution

Hongling Si: study design and performance, data analysis and collection, manuscript drafting; Ruidi Wang: study design, supervision, significant manuscript revision. Both authors have approved the submission and publication of this manuscript.

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Conflict of interest

The authors declare no conflict of interest.

Ethics approval

This study was approved by the ethics committee of Xi' an Jiaotong University (approval No. XJU202001004), and conducted in accordance with the 1964 Helsinki declaration and its later amendments.

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