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Low-level laser therapy on soft tissue healing after implantation: a randomized controlled trial

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Abstract

Background To explore the effect of low-level laser therapy (LLLT) on the healing of soft tissue around the implant after flap implantation and explore the possible mechanism.

Methods A total of 58 patients who underwent implant surgery were enrolled, with a total of 70 implants. They were randomly divided into the LLLT group and the control group. The LLLT group underwent LLLT with Nd:YAG (Fotona, 1064 nm) immediately after surgery and on the 2nd and 3rd day in the surgical area, while the control group did not receive any intervention. Pain assessment was performed in the first 3 days after surgery. The weight of peri-implant crevicular fluid (PICF), modified sulcus bleeding index (mSBI), gingival index (GI), and the expression levels of tumor necrosis factor-α (TNF-α), and vascular endothelial growth factor (VEGF) on the 7th and 14th days after surgery were evaluated.

Results On the first 3 days after surgery, the pain score of the LLLT group was significantly lower than that of the control group. On the 7th and 14th day after surgery, the PICF volume, mSBI, GI, and TNF-α levels of the LLLT group were lower than those of the control group. The VEGF levels in the LLLT group were significantly higher than that in the control group.

Conclusions LLLT can promote the healing of the soft tissue after implantation, effectively relieve postoperative pain, improve clinical indicators, reduce TNF-α, and increase the expression level of VEGF, which is worthy of clinical application.

Trial registration Retrospectively Registered Trials ChiCTR2400087562 (07/30/2024)

Keywords Low-level laser therapy, Soft tissue healing, Pain, TNF-α, VEGF

Introduction

With the advancement of dental implant technology and the implementation of China's centralized volume procurement policy for dental implant systems, an increasing number of individuals opt for dental implants to repair missing teeth within the oral cavity. The rise in the penetration rate of dental implants has also led to an increase in the incidence of postoperative complications, including early postoperative edema, postoperative wound infection, early dehiscence or perforation of the soft tissue flap, etc. [1]. The presence of these adverse complications can affect the healing of the soft tissues around the implant, thereby directly impacting the success of the implant. If the soft tissues around the implant can achieve good soft tissue attachment during the initial healing phase, a strong soft tissue seal can be formed to prevent bacteria and metabolic products from entering the deep tissues and colonizing the surface of the implant [2]. Since the oral environment is a constantly exposed

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microbial environment, the early healing of the soft tissues around the implant presents certain challenges [3]. Therefore, rapidly forming an effective soft tissue seal is crucial for establishing and maintaining the health of the peri-implant tissues. Seeking a method that can promote the healing of soft tissues around the implant and prevent early postoperative complications has become a significant challenge in the field of contemporary dental implantology.

LLLT, also referred to as photobiomodulation therapy, involves the utilization of infrared or near-infrared light to induce analgesic, anti-inflammatory, and biological stimulation effects [4, 5]. LLLT mainly exerts photobiological regulatory effects on the body, but its molecular mechanism is currently unclear. At the subcellular level, LLLT mainly acts on cellular mitochondria, among which cytochrome oxidase (CCO) plays an important role as the main photoreceptor and signaling site. LLLT enhances CCO activity, stimulates mitochondrial membrane potential changes, promotes adenosine triphosphate (ATP) production and cytochrome C transfer to molecular oxygen, thereby promoting cellular metabolism [6]. This study aimed to evaluate the effect of LLLT with Nd:YAG (Fotona, 1064 nm) on soft tissue healing after implantation and explore the possible mechanism.

Materials and methods

General information

Fifty-eight patients who underwent phase I implant surgery in the outpatient clinic of the Department of Stomatology of the First Affiliated Hospital of Nanchang University from April 2023 to January 2024 were enrolled in this study. Our study adheres to CONSORT guidelines. They were randomly divided into the low-level laser therapy (LLLT) group and the control group according to the randomized numeric table method.

Randomization was performed by a nonpractising physician. Control group: 35 implants (29 patients, 16 males, and 13 females, mean age 43.76 ± 16.346 years). LLLT group: 35 implants (29 patients, 12 males, and 17 females, mean age 44.83 ± 16 years). There was no statistical difference in the general information of the two groups of patients ($p > 0.05$). The patients were rendered to the groups.

Inclusion criteria: good health, no systemic diseases, no history of head and neck radiation therapy; periodontal health, no need for soft tissue augmentation; all delayed implants and no need for bone augmentation surgery; consecutive implants ≤ 2 teeth, and bone level implants; no history of allergy to chlorhexidine, penicillin antibiotics; over 18 years old; informed consent to the treatment method, good compliance can be followed up on time.

Exclusion criteria: uncontrolled periodontal disease; the number of consecutive implants > 2; the need for soft and hard tissue augmentation; the existence of systemic diseases and contraindications to implant surgery; smokers and alcoholics; poor compliance, oral hygiene can not be well controlled.

Methods

In the LLLT group, Nd:YAG (Fotona, 1064 nm) laser LLLT mode (MSP, power 1.5W, frequency 15 Hz, pulse width 100 μs) was used on the buccal and lingual sides of the implants on the immediate, 2nd and 3rd postoperative days, moving slowly in a "Z" pattern from the soft tissues at a distance of 0.5 cm to the soft tissues, uniformly irradiating the proximal and distal gingiva of the dental implants. The soft tissue between the gingival papillae of the near and far gingiva of the dental implants was irradiated for 2 min on both the buccolingual and lingual sides, avoiding prolonged stay of the laser in the same place and avoiding irradiation of the healing abutment. All LLLT were performed by the same operator, and both the operator and the study subjects wore goggles during irradiation. No postoperative interventions were performed in the control group. Study subjects in both groups were educated on oral hygiene and instructed to maintain good oral hygiene. The peri-implant crevicular fluid (PICF) samples on the 7th and 14th postoperative days were collected, and the pain index on the first 3 postoperative days and the clinical indexes including Modified Sulcus bleeding Index (mSBI) and Gingival Index (GI) on the 7th and 14th postoperative days were examined and recorded.

Clinical observation indexes

(1) Pain level score: Patients rated their discomfort/pain with a visual analog scale (VAS) on a scale from 0 (not at all satisfied) to 10 (totally satisfied) every day for 3 days after surgery. Specificly, draw a 10 cm horizontal line on the paper, divided into 10 segments on average, labeled as 0–10, Let the patient make a mark on the horizontal line to indicate the degree of pain according to self-feeling [7, 8].

(2) mSBI: A blunt-tipped periodontal probe was lightly probed (0.25N) into the proximal-middle, distal-middle, buccal, and lingual (palatal) gingival sulcus around the implant at a distance of 1 mm, and bleeding from the gingival margins was observed after 30 s. The grading of the 4 surfaces was recorded to take the average value for scoring. The scoring criteria were as follows: 0 = no bleeding along the gingival margins of the probing; 1 = iso-

lated punctate bleeding; 2 = bloating in the gingival sulcus as a line; 3 = severe or spontaneous bleeding.

(3) GI: Using a blunt-tipped periodontal probe, the proximal mesial labial (buccal) papilla, medial labial (buccal) margin, distal mesial labial (buccal) papilla, and lingual gingival margin of the peri-implant gingiva were examined. Each tooth was scored as an average of 4 point scores, and the scoring criteria were as follows: 0 = healthy gingiva; 1 = mild inflammation of the gingiva, mild change in gingival color, mild edema; 2 = moderate inflammation of the gingiva, red gingival color, shiny edema; and 3 = severe inflammation of the gingiva, with marked redness, swelling, or ulceration of the gingiva, and tendency to bleed spontaneously.

All the above operations were done by the same researcher.

PICF collection and detection

Whatman No. III filter paper (Whatman Company, UK) was cut into 2.0 mm*10.0 mm filter paper strips, autoclaved and sterilized, and then dispensed into sterile EP tubes in a sterile ultra-clean table, 2 filter paper strips were placed into each tube, weighed 3 times with a microelectronic balance (Li-Chen Science and Technology Co. Ltd., Shanghai, China), and the average value was taken to record the weight as m1. Before clinical collection, the patients were First, gargle with 3% hydrogen peroxide solution for 1 min, then rinse the mouth with water, remove the soft dirt and plaque around the healing abutment, use a sterile cotton ball to isolate the wetness and blow the surface of the healing abutment with an air gun gently, after 30 s, insert the sterile filter paper strip into the buccolingual gingival sulcus of the healing abutment, and stop it when it meets with resistance, take out the strip of filter paper after 30 s, put it into the EP tube, and discard the strips of filter paper that were contaminated by the saliva or the blood in the gingival sulcus. The successfully collected gingival fluid specimens were weighed three times, and the average value was recorded as m2, and the actual weight of the gingival fluid was calculated as m2-m1. After the record was completed, the samples were put into the Human Genetic Resources Sample Bank of the First Affiliated Hospital of Nanchang University, and stored in the refrigerator at −80 ℃ for testing. When thawing the samples, 1 ml of PBS buffer (Wuhan Xavier Biotechnology Co., Ltd.) was added to the EP tubes and the samples were thawed for 1 h at room temperature, then the samples were centrifuged at 1200 r/min for 20 min at 4 °C, and the supernatants were taken to detect the expression levels of TNF-α and VEGF by enzyme-linked immunosorbent assay (ELISA). ELISA kits were purchased from Wuhan Bio-Tech Co. Ltd.

Table 1 Pain scores (VAS) in the two groups

Group	Day1	Day 2	Day 3
Control ($n=35$)	4.0(3.0, 5.0)	3.0(3.0, 4.0)	2.0(2.0, 3.0)
LLLT ($n=35$)	4.0(3.0, 4.0)	3.0(2.0, 3.0)	2.0(1.0, 2.0)
Z value	−2.135	−2.872	−2.962
p	0.033*	0.004**	0.003**

VAS visual analog scale, *LLLT* low-level laser therapy

* $p<0.05$

** $p<0.01$

Table 2 Clinical parameters in the two groups

Groups	Day 7		Day 14	
	mSBI	GI	mSBI	GI
Control (n = 35)	1.09 ± 0.34	1.32 ± 0.36	0.84 ± 0.35	0.89 ± 0.33
LLLT (n = 35)	0.91 ± 0.33	1.12 ± 0.31	0.63 ± 0.35	0.71 ± 0.31
p	0.036*	0.016*	0.016*	0.022*

mSBI modified sulcus bleeding index, *GI* gingival index, *LLLT* low-level laser therapy

* $p<0.05$

** $p<0.01$

Statistical processing

SPSS 27.0 statistical software package was used for statistical analysis. All data were subjected to a normality test, and measurements satisfying normal distribution were expressed as mean ± standard deviation and analyzed statistically using independent samples *t*-test, while data not satisfying normal distribution were statistically described by median (interquartile spacing) and analyzed using Wilcoxon rank sum test, and correlation between data was analyzed using Pearson analysis. The correlation was analyzed using Pearson analysis. $p<0.05$ was considered as statistically significant difference.

Results

Pain assessment

The VAS scores were lower in the LLLT group than in the control group on days 1, 2, and 3, the difference was statistically significant ($p<0.05$ or $p<0.01$) (Table 1).

Clinical parameters

The mSBI and GI of the LLLT group were significantly lower than those of the control group on both day 7 and day 14 after surgery ($p<0.05$ or $p<0.01$) (Table 2).

The amount of PICF and the expression levels of TNF-α and VEGF

On both day 7 and day 14, the amount of PICF in the control group was significantly higher than that in the LLLT group ($p < 0.05$); the expression level of TNF-α in the control group was significantly higher than that in the LLLT group ($p < 0.05$) and the expression level of VEGF in the control group was significantly lower than that in the LLLT group ($p < 0.05$) (Table 3).

Correlation analysis

The results of Pearson analysis showed that the amount of PICF, the expression levels of TNF-α and VEGF were positively correlated with both mSBI and GI respectively (correlation coefficient $r > 0$, $p < 0.05$) (Table 4).

Discussion

Lasers have been extensively integrated into the field of clinical dentistry due to their demonstrated therapeutic advantages, such as anti-inflammation effects, and pain alleviation, as well as their ability to stimulate biological responses, including promotion of healing [9–11]. In recent years, there have been a lot of studies in this field. The mechanism by which LLLT works primarily involves augmenting the function of fibroblasts, keratinocytes, and immune cells, which leads to increased cell proliferation, enhanced collagen synthesis, and angiogenesis, as well as the induction of biostimulation and expedited wound healing through a cumulative and dose-dependent process [12]. In the early postoperative period, epithelial cells in the wound begin to migrate to the surface, fibroblasts proliferate, and cytokines and growth factors expressed by neutrophils and macrophages are involved in controlling and regulating the healing process [13], and the application of LLLT accelerates this by increasing keratinocyte motility (leading to faster epithelialization), fibroblast proliferation (leading to the accelerated synthesis of the extracellular matrix), and early angiogenesis process [14]. It has been observed that LLLT markedly diminishes swelling and enhances wound healing in the surgical site following implant surgery, in comparison to the control group [15]. Usumez et al. [16] found that using Nd: YAG (Fotona, 1064 nm, MSP, 0.25W, 8 J/cm2) can stimulate cell proliferation and fibroblast growth, accelerating wound healing. Laky et al. [17] showed significant efficacy in using Nd: YAG (Fotona, MSP, 2.5W, 20 Hz) combined with Er: YAG laser assisted treatment for periodontitis. This experiment is based on previous research and combined with the Fotona laser user manual. The laser irradiation process is set to pulse width MSP, power of 1.5W, and frequency of 1.5 Hz. At present, the research of LLLT in the field of implantation mostly focuses on the adjuvant treatment of peri-implant inflammation [18], and there are few clinical studies on the prospective promotion of soft tissue healing after implantation.

Pain after oral implant surgery is more common but is usually mild to moderate in the short term. The pain

Table 3 PICF, TNF-α and VEGF IN THE TWO GROUPS

Group	7d			14d		
	PICF(mg)	TNF-α(pg/ml)	VEGF(pg/ml)	PICF (mg)	TNF-α(pg/ml)	VEGF(pg/ml)
Control (n = 35)	4.02 ± 0.75	36.74 ± 5.65	30.85 ± 4.45	2.54 ± 0.47	22.61 ± 5.82	21.22 ± 0.68
LLLT (n = 35)	3.58 ± 0.73	31.29 ± 4.04	35.29 ± 4.96	1.72 ± 0.51	19.23 ± 3.17	24.26 ± 3.77
p	0.016*	< 0.001**	< 0.001**	< 0.001**	0.004**	0.002**

PICF peri-implant crevicular fluid, *TNF-α* tumor necrosis factor-α, *VEGF* vascular endothelial growth factor, LLLT, low-level laser therapy

* $p < 0.05$

** $p < 0.01$

Table 4 Correlation analysis

	PICF		TNF-α		VEGF	
	r	*p*	r	*p*	r	*p*
mSBI	0.344	< 0.001**	0.311	< 0.001**	0.192	0.023*
GI	0.475	< 0.001**	0.452	< 0.001**	0.354	< 0.001**

PICF peri-implant crevicular fluid, *TNF-α* tumor necrosis factor-α, *VEGF* vascular endothelial growth factor, *LLLT* low-level laser therapy

* $p < 0.05$

** $p < 0.01$

begins a few hours after surgery, then gradually diminishes and fades away in about 2–3 days [19]. Some studies have shown that LLLT can also increase the levels of β-endorphin and 5-hydroxytryptamine in the blood, thus providing analgesia [20, 21]. Our experimental results showed that the pain VAS scores of the LLLT group that received LLLT in the first 3 postoperative days were significantly lower than those of the control group ($p < 0.05$), which suggests that LLLT can effectively improve the pain in the operative area after implantation, which is in line with the findings of previous studies.

Wound healing is a complex process, and this process includes an inflammatory phase, a proliferative phase, and a maturation phase [22]. The inflammatory response is the early stage of wound healing, both anti-inflammatory factor interleukin-10 (IL-10) and pro-inflammatory TNF-α, IL-1α, and IL-1β, play a very important role in the wound healing process, and they affect the wound healing through cellular stimulation, protein metabolism, chemoattractive effects, immune response regulation, and inflammatory regulation, so that the organism to achieve a balanced healing process [23]. Howerer, excessive inflammatory responses can disrupt normal tissue structure and function, leading to impaired wound healing. Safdari et al. [15] in their study on whether LLLT could reduce adverse reactions after implantation found that on postoperative day 7, the swelling of the operated area was significantly reduced in the laser group, and the degree of wound healing was better in the laser group on days 7 and 14. Berglundh et al. [24] found that the wound becomes filled with blood clots from the immediate postoperative period after implantation, and that the wound is infiltrated with a large number of neutrophils for the first 7 days after the operation, and that at the healing Early on, leukocytes accumulate in the fibrin network and begin to establish the initial mucosal closure. By postoperative day 14, epithelial tissue proliferates in the wound and peri-implant soft tissue attaches to the abutment surface via connective tissue. It has been shown that PICF free of blood contamination can be collected as early as 1 week after implant surgery [25]; therefore, in this study, we chose to collect PICF on postoperative days 7 and 14 to determine the expression levels of cytokines and growth factors contained, so as to assess the effect of LLLT on early wound healing. Meanwhile, at the 14th postoperative day, sutures were removed from the operated area in both groups.

TNF-α is a proinflammatory factor that upregulates the expression and protects the activity of matrix metalloproteinases (MMPs), which play an important role in tissue re-epithelialization, angiogenesis, and restoration of normal tissue structure [26]. Our results showed higher levels of TNF-α expression in the PICF at postoperative day 7 compared to postoperative day 14, which is consistent with the findings of Chien et al., who, in their study of cytokine expression levels in the PICF in the early healing phase of implantation, found that the TNF-α level decreased significantly from postoperative week 1 to week 2 [27]. It has been found that LLLT can downregulate the expression of TNF-α, IL-1β, and IL-6 in gingival tissues, effectively inhibit tissue inflammation, and promote early gingival wound healing [28]. Currently, numerous domestic and international studies indicate that LLLT has been successful in reducing the expression of TNF-α in the additional treatment of periodontitis and peri-implantitis [29]. The results of this study showed that the expression level of TNF-α in the control group was significantly higher than that in the LLLT group at the 7th and 14th postoperative days ($p < 0.05$), which indicates that LLLT can effectively reduce the degree of inflammation in the implant operated area, which is consistent with previous studies.

In the process of wound healing, VEGF is a major regulator of angiogenesis [30], which can improve microcirculation at the wound site by regulating cell proliferation, differentiation, and migration and promoting capillary formation, in addition to stimulating vasodilatation and extracellular matrix formation, which provides essential nutrients and oxygenation for wound healing and deposits the fibrin network required for wound healing [31, 32]. Several researchers discovered that LLLT could increase the levels of VEGF and its receptor in both human and rat mesenchymal stem cells [33]. Additionally, Hsu and colleagues observed a significant induction of VEGF expression during the early stages of orthodontic tooth movement through LLLT [34]. Our study showed that the VEGF expression in the control group was significantly lower than that in the LLLT group on the 7th and 14th postoperative days ($p < 0.05$), and the VEGF concentration in both groups decreased over time, which is consistent with the results of the previous study, suggesting that LLLT can effectively up-regulate the expression of VEGF during the initial stages after implantation, which can be beneficial in enhancing the healing process.

Probing bleeding is an important diagnostic method to monitor the health of peri-implant soft tissues, and it is more pronounced in the presence of peri-implant inflammation, and mSBI increases with the degree of inflammation, while healthy peri-implant tissues are free of probing bleeding [35]. GI responds to the health of the gingiva by probing the bleeding and by observing the gingival texture and color visually. PLI can reflect peri-implant plaque attachment, which is the initiator of peri-implant inflammation, and plaque accumulation may lead to lymphocyte and plasma cell-based inflammatory infiltration, which in turn causes peri-implant mucositis

or peri-implantitis [36]. Gingival sulcus fluid is not simply a leakage, but rather a secretion from the connective tissue of the gingiva into the sulcus. It is an exudate that comes from the capillaries in the tissue, containing inflammatory cells, electrolytes, and immune factors. Recent research suggests that alterations in the quantity of this fluid around dental implants can indicate the level of inflammation in the surrounding soft tissues and bone loss near the implant site. [37]. The results of this study showed that the amounts of mSBI, GI, PLI, and PICF in the control group were significantly higher than those in the LLLT group at the 7th and 14th postoperative days ($p < 0.05$), which suggests that LLLT has a positive effect on soft tissue healing and anti-inflammation in the initial postoperative period after implant surgery.

Apse's study showed that using LLLT in treating periodontitis led to significant improvements in gingival index, bleeding on probing, and plaque index. They also found a positive correlation between the amount of gingival sulcus fluid secretion and these clinical indicators, which can effectively reflect the inflammation level in periodontal and peri-implant tissues [38]. This study also found a positive correlation between the amount of peri-implant crevicular fluid (PICF) and the clinical assessments mSBI, GI, and PLI ($p < 0.05$), consistent with previous research. Additionally, it showed that the levels of TNF-α and VEGF in PICF were linked to mSBI and GI ($p < 0.05$), suggesting that these markers could serve as reliable indicators of soft tissue recovery in the early stages post-implant surgery. Moreover, all participants in the study actively participated in the entire process, and no adverse effects such as delayed wound healing, infections, or tissue damage were noted, indicating that the use of LLLT is both safe and beneficial following implant surgery.

As a limitation of our study, it should be noted that this study was a single-center randomized controlled trial with a relatively modest sample size, potentially leading to selection bias. Future research could involve a longitudinal cohort study with a larger patient to validate our findings.

Conclusions

The administration of LLLT following implant surgery can enhance the early healing of the peri-implant soft tissues, which is worthy of further investigation.

Abbreviations

LLLT	Low-level laser therapy
VAS	Visual Analog Scale
PICF	Peri-implant crevicular fluid
mSBI	Modified sulcus bleeding index
GI	Gingival index
TNF-α	Tumor necrosis factor-α
VEGF	Vascular endothelial growth factor

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12903-024-05258-7.

Supplementary Material 1

Authors' contributions

Q.Z. and S.Z: Methodology, writing-original draf, and writing-review and editing; C.W.J. and S.X.: investigation, formal analysis, and data curation; Y.W.: validation; B. W.: project administration and supervision.All the authors approved the final version of this article.

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Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the First Affiliated Hospital of Nanchang University (IIT [2023] Linlun Shen No. 214). Informed consent was acquired from all the patients involved in the study and patients confidentiality was strictly respected.

Consent for publication

Not Applicable.

Competing interests

The authors declare no competing interests.

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