Effect of Low-level Light Therapy on Post-operative Healing of Secondary Chronic Osteomyelitis of the Jaws - A Prospective Study

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Abstract

Introduction: Osteomyelitis of the jaws is a common disease of the maxillofacial region. The goal of treatment is to alleviate pain, reduce infection, inhibit the progression of the disease and induce bone and mucosal healing. In addition to surgical management and antibiotic and oxygen hyperbaric therapy, new therapeutic strategies for the treatment of osteomyelitis are developed. One of the novel approaches is photobiomodulation therapy or low-level light therapy (LLLT). **Materials and Methods:** After surgical treatment, experimental group patients (n = 4) were treated with LLLT for five sessions with an extraoral pulsed 635-nm LED lamp (Repuls7, Repuls Lichtmedizintechnik GmbH, Austria), maximum output power: 140 mW/cm^2, frequency: 2.5 Hz, duty cycle: 50%. Clinical achievement and patient pain perception (through Visual Analogue Scale score) were evaluated at 1-, 3- and 6-month follow-up appointments and compared with control group (n = 4) patients, treated with standard therapy. **Results:** At three and six months, clinical achievement was better in patients treated with LLLT. Pain and discomfort resolution was significantly greater in the experimental group. **Discussion:** Taking into consideration the results of this study, it can be concluded that LLLT shows potential for improving clinical outcome of surgical and medical treatment of secondary chronic osteomyelitis of the jaws. Furthermore, pain and discomfort were significantly reduced in patients treated with LLLT. Further research with a larger sample size is needed to obtain a more accurate insight into this promising field.

Keywords: Healing, infection, low-level light therapy, osteomyelitis, regeneration

Introduction

Osteomyelitis of the jaws is still a fairly common disease in maxillofacial clinics and offices.[1] The word ‘osteomyelitis’ originates from the ancient Greek words osteon (bone) and muelinos (marrow) and means infection of the medullary portion of the bone. Common medical literature extends the definition to an inflammation process of the entire bone including the cortex and the periosteum, recognising that the pathological process is rarely confined to the endosteum. The infection becomes established in the calcified portion of the bone when pus and oedema in the medullary cavity and beneath the periosteum compromise or obstruct the local blood supply. Following ischaemia, the infected bone becomes necrotic and leads to sequester formation, which is considered a classical sign of osteomyelitis.[2] Although other aetiological factors can cause inflammation and subsequently ischaemia of bone, such as trauma, radiation or chemical agents, the term ‘osteomyelitis’ is used in the medical literature to describe a true infection of the bone induced by pyogenic microorganisms.[3] Osteomyelitis of the jaws differs from osteomyelitis of long bones due to the specific oral environment. This plays a major role in the aetiology and pathogenesis of the disease and has a direct impact on the modality of treatment. To optimise diagnosis

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and treatment, many classification systems of osteomyelitis occurred in the literature, and amongst them, the Zurich classification system is considered the most reliable.[4]

Therapy of osteomyelitis of the jaws is currently controversial. The goal of treatment is to alleviate pain, reduce infection, inhibit the progression of the disease and induce bone and mucosal healing. One of the novel treatments is photobiomodulation (PBM) therapy or low-level light therapy (LLLT). PBM therapy is an application of light, usually with lasers or LEDs, for the therapeutic purpose of improving tissue regeneration, reducing inflammation or inducing analgesia.[5] One of the major features of LLLT is the promotion of angiogenesis and tissue perfusion, which has significant implications in the treatment of jaw osteomyelitis.[6] Its bio-stimulatory effect on bone repair was documented in a systematic review by Escudero *et al*., who also stated that acceleration of this process was present regardless of different light parameters or graft materials used in studies.[7] The aim of this study is to evaluate the effect of 635-nm pulsing LLLT on secondary chronic osteomyelitis post-operative healing.

Materials and Methods

Following approval by the Ethical Committee of the Faculty of Dentistry, University of Belgrade (approval number & date: 36/7, 15 April 2021), a clinical study was conducted at the Clinic for Maxillofacial Surgery, Faculty of Dentistry, University of Belgrade, from May 2021 to February 2023. Patients were treated according to the principles established in the Helsinki Declaration. Signed informed consent was obtained from each patient before treatment. Osteomyelitis in patients was confirmed by biopsy and histopathological verification. At the same time, tissue microorganism cultures were obtained in order to determine if another antibiotic therapy is indicated besides empirical. Correlation was made with medical history, clinical presentation and radiological findings, after which patients diagnosed with secondary chronic osteomyelitis, according to the Zurich classification system,[4] were included in this study. Accordingly, all patients included in this study presented with infections of the mandible which were not resolved after one month of proper care, characterised by the presence of pus, bone sequestra and fistula formation [Figure 1]. Exclusion criteria were previous radiation therapy in the head & neck region, metastatic or recurrent malignant disease of the jaw, use of bisphosphonates, ongoing tobacco use or pregnancy. The study prospectively included eight patients, of which four patients were treated with standard therapy and assigned to the control group and four patients were treated additionally with LLLT and assigned to the test group (four women, mean age: 55 ± 8; four men, mean age: 58 ± 4). In all patients, the mandible was involved. In this study, patients were randomly allocated to groups using a randomisation procedure to ensure unbiased assignment. In addition, the experienced examiner responsible for the patient assessments remained blinded throughout the study.

A mucoperiosteal flap of minimal disturbance to surrounding tissues was reflected. An extraoral approach was also established for patients with extraoral fistulas [Figure 2a]. Sequestra [Figure 2b], necrotic bone [Figure 2c] and overlying granulation tissue were removed. Symptomatic neighbouring teeth were extracted and sharp bony edges were removed. Specimens were sent for histopathological evaluation [Figure 2b and c]. All patients received intravenous empiric wide-spectrum antibiotic therapy, which was changed to culture-guided antibiotic therapy if indicated, based on cultures obtained at the time of biopsy. Following discharge, patients were prescribed a mouth rinse for 7 days (chlorhexidine gluconate 0.12%). Sutures were removed 7 or 10 days after surgery. Extraoral LLLT application was performed postoperatively on days 3, 5, 7, 10 and 14 [Figure 3]. In all test group patients, a pulsed 635-nm LED lamp (Repuls7, Repuls Lichtmedizintechnik GmbH, Austria) was used (maximum output power: 140 mW/cm^2, frequency: 2.5 Hz, duty cycle: 50%). Patients were positioned in an upright position in a dental chair and the lamp had an extraoral position, perpendicular to the area to be illuminated at a distance of 30 cm from the skin. The treatment surface irradiance was measured at the given distance and was 27.2 mW/cm^2. The most important beam parameters are summarised in Table 1.

Patients were clinically evaluated preoperatively and postoperatively at follow-ups. Follow-up examinations were scheduled at one, three and six months after completion of treatment. The presence of oedema, pain, pus and fistulas was evaluated. The severity of patient pain perception was assessed using a Visual Analogue Scale (VAS). The VAS consisted of a 10-cm horizontal line marked from 0 (no pain) to 10 (most severe experienced). Complete resolution of the symptoms (no symptoms) was defined as the absence of any discomfort, corresponding to a zero VAS score.

Evolution of the disease was detailed as follows: Partial clinical achievement (PA) – partial covering of the previously exposed bone with re-epithelisation and no signs of oral or cutaneous draining fistulas; complete clinical achievement (CA) – complete coverage of the previously exposed bone with re-epithelisation, with no signs of oral or cutaneous draining fistulas; Suboptimal clinical achievement (SOA) – the absence of soft-tissue closure or other additional complications (e.g. pathological fracture and oral or cutaneous draining fistulas).

Statistical analysis

The results are presented as mean ± standard deviation, median (interquartile range) or count (per cent) depending on data type and distribution. Due to small sample size and lack of power, exact testing is performed, Fisher's exact test for nominal data and Mann–Whitney U for numerical data. Graphics for plotting individual-level data were created using an interactive graph tool according to guidelines for basic science data visualisation.

Results

The duration of follow-up was six months. A total of eight patients took part in the study, of which 4 (50%) were women (patients' mean age: 56.5 ± 6). Patient healing and pain perception were examined. At one month, in all patients, complete healing was observed and maintained; at three months in two patients treated with standard therapy, complete clinical achievement was not maintained while it was maintained in all four patients of the experimental group; at six months, also in two patients, partial clinical achievement remained, while in the experimental group, all patients maintained complete clinical achievement [Table 2]. Patient pain perception at one month was significantly lower in the experimental group compared to the control group, while at three and six months in the experimental group, there was no pain perception ($x = 0$). The VAS scores are shown in Table 3 and Graph 1.

Discussion

According to the Zurich classification system, secondary chronic osteomyelitis of the jaws is considered the same disease as acute osteomyelitis but at a different stage.[8] Acute osteomyelitis of the jaws becomes secondary chronic after 1 month of infection persistence. Both are considered true bone infections and are accompanied by more or less extensive suppuration. Complications of secondary chronic osteomyelitis predominantly include the formation as well as the development of bone sequestra.[9] The final common pathway in all treatments of acute and secondary chronic osteomyelitis of the jaws is to achieve a shift in the disturbed balance between the responsible pathogen(s) and host defences to the latter, allowing the body to overcome the infection. Improvement of local vascularisation is further accomplished by surgical decortication, exceeding conventional surgical debridement, which not only removes the poorly vascularised (infected) bone but also brings well-vascularised tissue to the affected bone, thus facilitating the healing process and allowing antibiotics to reach the target area.[10] Another modality of treatment that can be utilised in osteomyelitis therapy is hyperbaric oxygen therapy (HBO).[11-13] However, patients who undergo HBO therapy need more resources, which cannot be provided by all centres, and careful monitoring.[14] HBO therapy has an acceptable rate of complications,[14] but complications occur.[15-17] PBM has no reported adverse effects when used in different treatment modalities such as treatment of oral mucositis due to radiation therapy,[18,19] third molar surgery complications,[20] crown-lengthening complications[21] and COVID-19 in a patient with comorbidities.[22] Wadee *et al*., compared LLLT and HBO therapy in patients with chronic diabetic foot ulcers and showed more favourable results with the use of LLLT.[23] Vescovi *et al*., showed the most favourable results with surgical approach and laser therapy combined in terms of clinical improvement and complete healing of bisphosphonate-related osteonecrosis of the jaws.[24] In another study, the same group showed significantly higher success rates with a combined approach based on medical, surgical and LLLT therapy.[25] Pain control was also shown to be supported by the utilisation of LLLT in patients with osteonecrosis[26] as well as in other fields and treatment modalities.[27,28] A study by Scoletta *et al*., showed improved symptoms and decreased size of lesions in patients with bisphosphonate-related osteonecrosis of the jaws treated with only LLLT.[29] These significant results are indicative of the possible important role of LLLT in the treatment of osteomyelitis in the future. Aside from osteomyelitis research, the effect of LLLT on bone repair was thoroughly

Figure 1: Extraoral fistula assessment

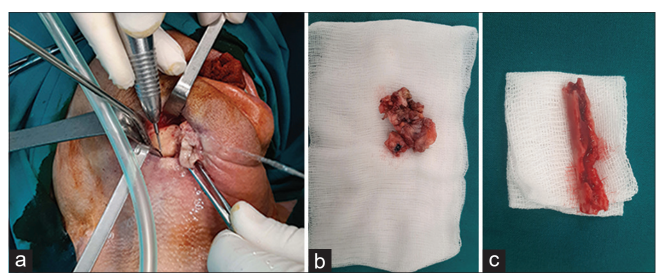
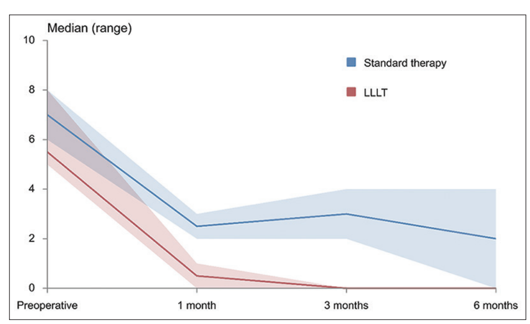


Figure 2: (a) Surgical procedure; (b) Sequestra; (c) Necrotic bone removal

Figure 3: Low-level light therapy session



Graph 1: VAS scores

Table 1: Report parameters in experimental and clinical photobiomodulation papers

Description	Data
Manufacturer	Repuls Lichtmedizintechnik GmbH
Model identifier	Repuls 7
Year produced	2017
Number and type of emitters (laser or LED)	LED, 7
Wavelength and bandwidth (nm)	635
Pulse mode (CW or Hz, duty cycle)	2.5 Hz, 50%
Beam spot size at target (cm^2)	200,96
Irradiance at target (mW/cm^2)	27.2
If pulsed peak irradiance (mW/cm^2)	27.2
Exposure duration (min)	6
Number of treatments	5
Radiant exposure (J/cm^2)	0.2
Number of points irradiated	1

LED: Light-emitting diode

Table 2: Healing during the course of the study

	Standard therapy (n=4)	LLLT (n=4)	P
1 month	4 (100)	4 (100)	1.000
3 months	2 (50)	4 (100)	0.429
6 months	2 (50)	4 (100)	0.429

Results are presented as count (%). Testing is performed using Fisher's exact test. LLLT: Low-level light therapy

Table 3: Visual Analogue Scale during the course of the study

	Standard therapy (n=4)	LLLT (n=4)	P
Pre-operative	7 (2)	5.5 (2)	0.400
1 month	2.5 (1)	0.5 (1)	0.029
3 months	3 (2)	0	0.029
6 months	2 (4)	0	0.429
Δ 6M-pre-operative	−5 (4)	−5.5 (2)	0.629

Results are presented as median (IQR). Testing is performed using Mann–Whitney U-test (exact test). IQR: Interquartile range, LLLT: Low-level light therapy

carried out and showed stimulation of bone production;[30-32] therefore, the positive effect of this treatment modality can be postulated. A stimulating effect was recorded in terms of blood and lymph neovascularisation,[33,34] synthesis of RNA, DNA, collagen and its precursors, as well as positive effects on the levels of prostaglandin, phagocyte cytoplasmic granules, cell proliferation and production of adenosine-5'-triphosphate.[35,36] Furthermore, an existent penetration of LED 635-nm low-level light through the soft and hard tissues of the jaws was demonstrated[37] which implies that the complete jaw bone thickness receives therapeutic doses.

In this study, patients diagnosed with secondary chronic osteomyelitis according to Zurich's classification[4] were included. In all patients, the mandible was involved and tooth extraction performed before onset of symptoms was identified as the most significant predisposing local factor. Results showed significantly better clinical achievement after 3 and 6 months in the group treated with LLLT, as well as better pain and discomfort resolution. These results support the postulation that LLLT improves blood and lymph flow and therefore improves medical therapy in the affected area by providing antibiotics with the possibility of reaching more affected tissue. With regard to the findings of this study, it can be postulated that with the use of LLLT, it is possible to reduce the period of antibiotic therapy use in the future in patients with secondary chronic osteomyelitis.

Conclusions

It can be concluded that LLLT is a promising modality for improvement of clinical outcomes of surgical and medical treatment of secondary chronic osteomyelitis of the jaws. Furthermore, pain and discomfort were reduced in patients treated with LLLT. LLLT improves tissue perfusion, as well as bone and soft tissue healing and analgesia. This study shows preliminary results, and due to a small sample size, further inclusion and treatment of patients are indicated and will demonstrate more information on the exact benefits of adjuvant LLLT in treating patients with secondary chronic osteomyelitis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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