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Case Study

Treatment of Chronic Wounds in Diabetic Patients with Low-Level Laser Therapy: A Case Series

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Abstract

Chronic wound management in diabetic patients presents a significant challenge due the multifactorial impairments in the wound healing process, including reduced angiogenesis, persistent inflammation, and delayed tissue regeneration. Low-Level Laser Therapy, through induction of the photobiomodulation effect in treated tissues, presents a promising additional treatment method to address these deficiencies. Research demonstrates that Low-Level Laser Therapy promotes angiogenesis and extracellular matrix formation and remodeling, and reduces oxidative stress and inflammation, all of which contributes to improved healing in diabetic wounds. While numerous studies have explored the effect of the mentioned treatment on wound healing, there is a lack of research on its effects on chronic diabetic wounds, with considerable variability in reported findings. The inconsistencies in the reported results led us to conduct our case study to better understand the direct potential benefits of Low-Level Laser Therapy on treatment outcomes of chronic wounds in diabetic patients. We used SkyPulse® laser (Fotona, Ljubljana, Slovenia) (1064 nm wavelength, 0.2 W/cm^2 irradiance) for treatment of chronic wounds in three diabetic patients. Our case study demonstrated significant improvements in wound healing, with observed increase in wound contraction, granulation tissue formation, and reduced inflammation, with no reported adverse effects of treatment. Our findings indicate that Low-Level Laser Therapy represents a valuable and cost-effective treatment for diabetic wounds. By integrating this treatment method in standard care, clinicians can address the underlying factors impairing wound healing, improve overall tissue regeneration, and increase the likelihood of a successful recovery.

Keywords: Wound Management; Low-Level Laser Therapy; Photobiomodulation; Diabetic Wounds; Chronic Wounds; Tissue Regeneration

Abbreviations

LLLT: Low-Level Laser Therapy; PBM: Photobiomodulation; ECM: Extracellular Matrix; VEGF: Vascular Endothelial Growth Factor; NO: Nitric Oxide; ER: Emergency Room

Introduction

Impaired wound healing in diabetic patients

Treatment of chronic wounds represents a significant challenge in modern healthcare, particularly due to their prolonged healing process and the complex nature of their pathogenesis. In patients with diabetes mellitus, impaired wound healing can be observed and is primarily a result of hyperglycemia. This leads to endothelial dysfunction, neuropathy, and immune dysregulation [1]. Hyperglycemia promotes the formation of advanced glycation end products and induces oxidative stress, leading to chronic inflammation that weakens the collagen structure and delays tissue repair [2]. In diabetic patients, the process of extracellular matrix (ECM) formation during wound healing is significantly impaired. Fibroblasts, which are responsible for synthesizing ECM components such as collagen and glycosaminoglycans, often exhibit reduced proliferation and an altered phenotype. This is partly due to the hyperglycemic environment, which disrupts the normal function of growth factors and cytokines essential for ECM production. Additionally, the accumulation of AGEs in diabetic wounds impairs the structure and function of the ECM, making it less stable and prone to degradation [3]. The altered ECM in diabetic wounds results in decreased collagen deposition and a disorganized matrix structure, which prevents cell migration and proliferation [4]. The dysfunction of neutrophils and macrophages weakens the immune defenses, prolonging the inflammation phase, and disrupting the transition to the proliferation phase of healing [5]. Additionally, impaired neoangiogenesis can be observed as a result of disruption in vascular endothelial growth factor (VEGF) signaling and reduction of nitric oxide (NO) production, which decreases sufficient blood flow to the wound site [6].

Effect of low-lever laser therapy (LLLT) on the formation of ECM

Low-level laser therapy (LLLT) is a non-invasive technique that utilizes specific wavelengths of light to induce the photobiomodulation (PBM) effect in treated tissues. This stimulates numerous cellular processes essential for normal wound healing [7]. PBM occurs when light photons are absorbed by mitochondrial chromophores, particularly cytochrome c oxidase, which triggers the production of adenosine triphosphate, reactive oxygen species, and NO. These molecules activate signaling pathways that are involved in cell proliferation, cell migration, collagen synthesis, and ECM formation and remodeling. PBM induced by LLLT also exhibits an anti-inflammatory effect by modulating the release of pro-inflammatory cytokines [8]. This reduces pain and swelling in the wound site and promotes the transition from the inflammatory to the proliferative phase of healing [9]. Furthermore, it stimulates neoangiogenesis by increasing the expression of VEGF and fibroblast growth factors, improving blood flow to the wound site [10,11].

Treatment using LLLT has been proven to promote several biochemical processes involved in wound healing. However, the direct effect of PBM on the healing of chronic wounds has not yet been fully explored. The aim of this case study is to investigate the effect of LLLT on the healing process of chronic wounds in diabetic patients.

Case Study

In our case study, we present a series of 3 case reports following patients with diabetes mellitus admitted at the Department for Surgical Infections for the treatment of a chronic wound. The treatments were performed using SkyPulse® laser (Fotona, Ljubljana, Slovenia) with wavelenght set at 1064 nm and irradiance at 0,2 W/cm^2. A cluster head with a surface area of 14.5 cm^2 was used. The treatments consisted of local irradiation of the exposed wound for 30 seconds, 3 times a week for 3 to 4 weeks. In all cases, the patients received additional treatment of the accompanying morbidities.

Case report 1

34-year-old Caucasian female with diabetes mellitus type 1 presented in the Emergency room (ER) after sustaining a blunt injury to her right knee. At the initial examination, a wound was present above the patellar region. X-ray examination of the right knee showed no signs of recent fractures. Two days after the initial examination, she returned to the ER with fever (38°C) and chills. At the control examination redness and swelling of the right knee and upper third of the shin was visible. A fluctuation was palpable in the anteromedial part of the upper shin, right above the tibial tuberosity. Laboratory findings revealed elevated levels of C-reactive protein (360 mg/L), procalcitonine (5,61 µg/L) and leukocytes (8,3·10^9/L). Operative procedure was indicated and the patient was admitted at the Department for Surgical Infectons for further treatment. Incision and drainage were performed above the palpable fluctuation, which revealed a presence of a haematoma. Intraoperatively, swab samples were obtained and sent to microbiology for analysis. After the procedure we consulted the infectologists, and the patient was put on antibiotic therapy with flucloxacillin. During the hospitalisation, we observed delayed healing of the postoperative wound with a formation of a seroma on the lateral border of the wound. The microbiology analysis results later revealed a presence of a bacteria *Streptococcus pyogenes*. Infectologists were consulted again and recommended a switch of antibiotic therapy to piperacillin and tazobactam. A revision drainage of the newly formed seroma was indicated. However, the patient declined further surgical intervention and was subsequently discharged home after completing appropriate antibiotic treatment. The patient was then followed up after discharge through scheduled outpatient check-ups, where delayed healing of the wound was further observed. We opted for conservative treatment of the wound using LLLT.

Before undergoing treamtent with LLLT, the postoperative wound measured 2,5 cm in height and 1,5 cm in width (Figure 1). The wound bed was mostly covered in granulation tissue. Exudate

Figure 1: Status of the wound before starting treatment with LLLT.

production was low and the wound borders were slightly oedematous, with minimal epithelisation present. On palpation of the lateral border of the wound, a serous exudate was released, comfirming the presence of a seroma.

After 6 treatment sessions the wound measured 2 cm in height and 1 cm in width (Figure 2). Epithelisation was observed and the wound bed was completely covered in granulation tissue. Only minimal exudate was present, with observed resorption of the previously formed seroma.

Figure 2: Status of wound after 6 treatment sessions using LLLT.

Three weeks after beginning treatment with LLLT the wound was completely healed and the patient had no subjective complaints (Figure 3).

Case report 2

52-year-old Caucasian female with diabetes mellitus type 2 and arterial hypertension was referred to the Department for Surgical Infectons for the treatment of a chronic wound. The patient repor-

Figure 3: The wound was completely healed after 10 treatments with LLLT.

	Before LLLT (Day 1)	After LLLT (Day 21)
Wound size	2,5 cm x 1,5 cm	Healed
Exudate	Low	None
Wound bed	Granulation tissue with areas of hypergranulation	/
Wound edge	Oedematous	/
Periwound-skin	Erythematous	Normal

Table 1: Case report 1: Wound status of the patient before and after treatment with LLLT.

ted sustaining a blister 3 months prior to the examination, which failed to heal successfuly. The wound was present in the plantar region of the left foot, above the VI. and V. metatarsophalangeal joint. At the initial examination, necrotic tissue was visible in the wound borders, without clinical signs of infection present. Initially, dressing changes were performed every 2 to 3 days during which we applied hydrogel and polyurethane foam to the wound to facilitate the removal of necrotic tissue. After a month, the necrotic tissue was absent and the wound bed was covered in granulation tissue with some fibrine layer present. The wound measured 3 cm in height and 3 cm in width (Figure 4). There was hyperkeratosis visible on the edges of the wound, while surrounding skin showed signs of maceration. There were no clinical signs of infection present. After a careful examination, we decided to begin treatment with LLLT.

After 6 treatments with LLLT the wound measured 2 cm in height and 2 cm in width. The wound bed was covered in granulation tissue and the surrounding skin showed no signs of maceration (Figure 5). Four weeks after beginning treatment the wound was completely healed and the patient reported no side effects (Figure 6).

Case report 3

52-year-old Caucasian male with diabetes mellitus type 2, arterial hypertension and hyperlipidemia was referred to the Department for Surgical Infections for treatment of a non-healing postoperative wound. Six months prior to the referral, the patient underwent a transphalangeal amputation of the right hallux due to the presence of osteitis in the distal phalanx. At the initial examination, the wound measured 1 cm in height and 2 cm in width (Figure 7). The wound bed was covered mostly in fibrine layer with some granulation tissue visible in the superior edge of the wound. Hyperkeratosis was present in the borders of the wound and the surrounding skin showed signs of maceration. The wound presented without clinical signs of bacterial infection. We opted for conservative treatment with LLLT.

Figure 4: Status of the wound before starting treatment with LLLT.

Figure 5: Status of the wound after 6 treatment sessions using LLLT.

	Before LLLT (Day 1)	After LLLT (Day 30)
Wound size	3 cm x 3 cm	Healed
Exudate	Moderate	None
Wound bed	Granulation tissue (70%), Fibrine layer (30%)	/
Wound edge	Hyperkeratosis	/
Periwound-skin	Slight maceration	Normal

Table 2: Case report 2: Wound status of the patient before and after treatment with LLLT.

Figure 6: Status of the wound after completing 13 treatments with LLLT.

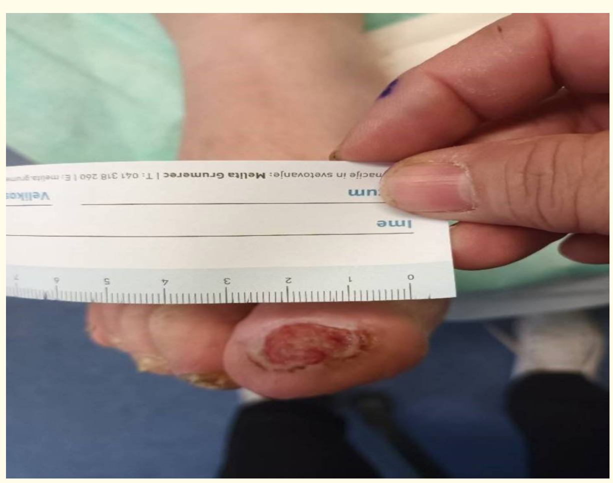

Figure 7: Status of the wound before treatment with LLLT.

After 8 treatments with LLLT the wound showed signs of healing, measuring 0,5 cm in height and 1 cm in width. Granulation tissue was present in the wound bed and the surrounding skin showed no signs of inflammation or maceration (Figure 8). Minimal hyperkeratosis was still present in the borders.

After 14 treatment sessions with LLLT the wound was completely healed. The patient had no subjective complaints during and after treatment (Figure 9).

Figure 8: Status of the wound after 8 treatment sessions with LLLT.

Figure 9: The wound healed after 14 treatments with LLLT.

	Before LLLT (Day 1)	After LLLT (Day 32)
Wound size	2 cm x 1 cm	Healed
Exudate	Moderate	None
Wound bed	Granulation tissue (60%), Fibrine layer (40%)	/
Wound edge	Slight maceration	/
Periwound-skin	Normal	Normal

Table 3: Case report 3: Wound status of the patient before and after treatment with LLLT.

Discussion

Our case study was designed to investigate the effect and potential clinical implications using LLLT in the treatment of chronic wounds in diabetic patients. When designing the case study, we anticipated to observe accelerated wound healing due to the effect of PBM on cellular mechanisms involved in the healing process. With the expected transition from the inflammatory to the proliferative phase of healing, we anticipated an increase in granulation tissue formation in the wound bed following treatment. Furthermore, an increased rate of epithelisation was expected, accompanied by decreased maceration of the surrounding skin. Based on our hypothesis, we also anticipated the use of LLLT to demonstrate cost-effectiveness, since the increased healing rate diminishes the need for further dressing changes, which are often required in the management of chronic wounds. By conducting this case study, we aimed to provide evidence supporting the clinical and economical benefits of implementing the use of LLLT for treatment of chronic wound in diabetic patients in standard practice.

Multiple studies have been conducted to assess the effectiveness of LLLT on wound healing, involving human and animal subjects. However, the results reported in these studies are inconsistent, with some showing significant improvements in the healing process, while others report minimal or no effect. This variability can be attributed to differences in wound types and variations in the treatment protocols used across studies. A study by Hopkins., *et al*. including 22 healthy subjects with induced wounds assessed the potential effects of LLLT on wound healing. The results revealed that LLLT enhanced healing, as evidenced by increased wound contraction in the treatment group compared to the control group. Moreover, indirect healing effect on the surrounding tissue was described [12].

A meta-analysis by Mosca., *et al*. based on 218 articles, including 11 *in vivo* studies aimed to provide background and examine the evidence for therapeutic applications of light energy treatments in wound healing. The study described observed therapeutic benefits in treatment of chronic wounds of different ethiologies after exposure to various doses ranging from 0.1 to 10 J/cm^2, and wavelengths from 405 to 1,000 nm [13].

A meta-analysis by Beckerman., *et al*. evaluated the efficacy of LLLT for musculoskeletal and skin disorders based on 36 randomized clinical trials involving 1,704 patients. The analysis showed that LLLT had a positive effect on wound healing in only a limited number of studies. However, it proved to be effective in conditions such as rheumatoid arthritis, post-traumatic joint disorders, and myofascial pain [14].

A study by Kheiri., *et al*. demonstrated the effectiveness of LLLT in promoting osteogenesis in critical-size bone defects. Meta-analysis based on 18 clinical studies was performed and revealed that LLLT stimulates neovascularization, proliferation of osteoblasts and fibroblasts, and supports the formation of callus [15].

In our case study, by utilizing treatment with LLLT, we confirmed the beneficial effects of PBM on the healing process, with observed closure of the chronic wound in all 3 patients. By implementing this treatment method, accelerated wound healing was observed, with no reported side effects during and after treatment. In all 3 cases we observed an increase in granulation tissue formation and epithelisation rate after beginning treatment with LLLT. The observed improvement in the wound healing process can be partly attributed to the concurrent management of the patients' comorbidities. Nevertheless, treatment with LLLT proved to be a clinically effective and also a cost-efficient solution, since the positive treatment outcome diminished the need for further dressing changes. Based on the results of the conducted study supported by the evidence of existing literature, we conclude that utilizing LLLT in everyday practice is an effective, patient-friendly and cost-efficient solution in the treatment of chronic wounds in diabetic patients. Nonetheless, additional studies are required for further and more precise evaluation of the direct impact LLLT has on treatment outcomes.

Conclusion

Our case study demonstrated that LLLT is highly effective in promoting the healing process in chronic wounds in diabetic patients. The findings revealed that LLLT significantly accelerated wound closure, by enhancing granulation tissue formation and increasing epithelialization rate. These outcomes indicate that LLLT facilitates an optimal healing environment while improving patients' comfort and quality of life. Moreover, the therapy proved not only to be clinically effective but also a cost-efficient method, as the improved healing outcomes reduced the need for further dressing changes, minimizing both material usage and overall treatment costs. Our case study, supported by existing literature, highlights the clinical effectiveness of LLLT as a practical and cost-efficient solution for enhancing the wound healing process. The evidence provided supports the integration of LLLT into routine clinical practice for the effective management of chronic wounds in diabetic patients.

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