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THERAPEUTIC POTENTIAL OF LASER THERAPY AND TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION IN CHRONICALLY INFECTED WOUNDS: A NARRATIVE REVIEW

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ABSTRACT

Chronic wounds such as diabetic foot ulcers, pressure ulcers, and venous leg ulcers pose a significant global health burden due to prolonged healing, recurrent infections, and high treatment costs. Traditional wound care often fails to adequately manage these complexities with chronic wounds, particularly when complicated by biofilm-forming, antibiotic-resistant pathogens.

This narrative review evaluates the therapeutic potential of two non-invasive biophysical modalities: Light Amplification by Stimulated Emission of Radiation (LASER) and Transcutaneous Electrical Nerve Stimulation (TENS) for chronically infected wounds. LASER therapy promotes healing through photo-biomodulation by enhancing mitochondrial activity, angiogenesis, collagen synthesis, and photodynamic bacterial destruction.

TENS facilitates healing via pain modulation, improved microcirculation, reduced inflammation, and fibroblast stimulation. Clinical and preclinical evidence highlights the efficacy of both modalities in accelerating wound closure, promoting tissue regeneration, and reducing infection. Furthermore, combining LASER and TENS may offer synergistic benefits by targeting multiple aspects of wound pathophysiology.

Although current evidence is promising, further randomized controlled trials are necessary to establish standardized protocols and evaluate long-term outcomes. Integrating LASER and TENS into multidisciplinary wound care could

significantly enhance healing in patients with chronic wound infections.

Keywords: LASER Therapy, Photo-biomodulation, Transcutaneous Electrical Nerve Stimulation, Wound Infection

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wound care strategies, especially in the event of concomitant factors such as impaired vascular supply, local pressure at the wound site, neuropathy, sustained inflammation, lack of angiogenesis, altered cell proliferation, overuse of antibiotics leading to bacteria resistance (antibiotic crisis), and factors associated with wound dressing, preparation and/or surgical debridement[1,14-16]. While the advancement in the treatment strategies of wound preparation, dressing, and debridement is quite promising[14-16], there appears to be neglect in the use and advancement of non-surgical strategies for chronically infected wounds.

Overview of Biophysical Agents in Wound Care

Over the years, novel therapeutic physical modalities have been advocated to enhance chronic wound healing. There are indications that Transcutaneous Electrical Nerve Stimulation (TENS), Ultraviolet Radiation (UVR), Light Amplification by Stimulated Emission of Radiation (LASER), Ultrasound therapy, and shortwave diathermy are capable of resolving chronically infected wounds[16,17]. These physical modalities, otherwise known as biophysical agents, appear to be effective in addressing both infection and the defective healing mechanisms in chronic wounds[16]. Given that tradition methods of wound management are often insufficient when dealing with persistent inflammation and infections seen in chronic wounds, it is imperative to consider these biophysical agents which, though non-pharmacological in application, have potential for activating endogenous therapeutic substances in the tissues of patients with chronically infected wounds. This narrative review explored the potential of LASER and TENS for the treatment of chronically infected wounds. The review discussed the rationale and mechanisms of action of each modality, present recent clinical and preclinical evidence supporting their use, and the methods of optimizing these therapies for chronically infected wounds.

METHODOLOGY

A search was conducted on Google Scholar, Scopus, Medline, and Web of Science using combined keywords such as LSAER and chronic wounds, TENS and chronic wounds, and Electrical stimulation and chronic wounds for articles and book titles. Relevant articles and book titles relating to the use of LASER therapy and TENS for chronic wounds were selected for this review.

LASER Therapy in Chronically Infected Wounds

LASER remains low-risk, cost-effective physical modality with promising outcomes in the treatment of chronic wound infections[18-20]. Generally, the literature revealed that LASER has a broad range of therapeutic effects in wound healing. LASER has been shown to activate mitochondrial activity by stimulating the mitochondria within cells, which increases adenosine triphosphate production that supports cellular functions necessary for tissue repair, such as protein synthesis, cell migration, and wound contraction[18-20]. There is evidence that LASER modulates inflammatory cytokines, thereby reducing

excessive inflammation in chronic wounds[18-20]. By reducing pro-inflammatory mediators, LASER helps to return the wound healing process to its normal pace, enhancing cell recruitment to the wound site[18-20]. Additionally, LASER enhances the formation of new blood vessels (angiogenesis) and promotes collagen synthesis, essential for wound closure[20,21]. These processes are especially beneficial in chronic wounds where vascularization and tissue regeneration are impaired.

Mechanism of Action

Basically, LASER modalities are classified into two main types, namely, class IIIb or low-level laser therapy (LLLT), which has non-thermal effects and lesser tissue penetration, and class IV or high-intensity laser therapy (HILT), which has thermal effect and deeper tissue penetration[22]. The LLLT has photo-modulatory effects in biological tissues and is used to promote healing in chronic wounds such as diabetic ulcers, pressure sores, and venous leg ulcers[22]. In diabetic foot ulcers, LLLT was found to reduce wound size and improve re-epithelialization[22]. While in pressure ulcers, LLLT was found to aid faster wound closure and pain relief[22]. On the other hand, HILT was reported to have the ability to induce chemical, thermal, and mechanical and bio-stimulating actions capable of reaching the deeper tissues[22-24]. It has been shown to reduce musculoskeletal pain[23]. HILT is reported to deliver LASER energy faster than LLLT and is known to stimulate a larger surface tissue area than LLLT[20-22].

However, and more specifically, LASER finds application in chronically infected wounds as a photodynamic therapy (PDT) tool[25]. As a PDT tool, LASER combines the attributes of delivering light at a particular wavelength, a photosensitizer, and oxygen inducer that is capable of obliterating an infecting organism in chronic wounds[25]. The extent of penetration is dependent on the type of LASER used[21], although PDT tools differ in their means of delivering oxygen to the wound site[26]. The commonly used Type-II PDT generates oxygen through energy transfer within the wound site, which is limited by oxygen concentration in infected sites, unlike the Type-I PDT that is capable of generating oxygen via electron transfer when photons are absorb by the photosensitizer[26]. Overall, the use of LASER in chronically infected wounds is superior to antibiotics, especially in cases of antibiotics-resistant bacteria in chronic wounds[26].

Clinical Evidence

Several studies have demonstrated the effectiveness of LLLT in treating chronic wounds. Previous studies analysed the literature evidence in support of LLLT, including its ability to accelerate healing in chronic diabetic foot ulcer with a shorter time of complete healing compare to a control group[27,28]. A recent study found that LLLT demonstrated superior therapeutic outcomes compared to shockwave therapy[29]. There is consistent evidence that LLLT accelerates wound closure, promotes angiogenesis, and enhances fibroblast migration[18,30]. An animal model of chronic skin wounds demonstrated that LLLT significantly enhanced collagen deposition and re-epithelialization[18].

Optimization Parameters

Optimizing LASER Therapy: Wavelength, power density, and treatment duration are critical factors in optimizing LLLT[18]. For chronic wound healing, red (600–700 nm) and near-infrared (800–900 nm) wavelengths are most commonly used, as they penetrate deeper into tissues and stimulate the desired biological effects[18].

TENS Therapy in Chronically Infected Wound

Electrical stimulation (ES) of chronic wounds is the application of electric currents on the wound surface via electrodes placed directly on the wound. Wound healing by gentle electrical fields is a promising area of research that has shown significant potential in accelerating the healing process[31]. The use of ES was strongly recommended by the 2019 international guidelines for pressure ulcer to facilitate wound healing in recalcitrant Category/Stage II pressure ulcers, as well as any Category/Stage III and IV pressure ulcers[32]. In one study, ES of chronic wounds was shown to enhance cellular migration by inducing the migration of fibroblasts, keratinocytes, and macrophages to the wound site[31]. Also, ES of wounds induces angiogenesis, collagen synthesis, and anti-inflammatory effects by decreasing pro-inflammatory mediators[33,34]. Additionally, ES have bactericidal effects in chronically infected wounds[31,32,34]. Emerging studies revealed promising results in the management of chronic wounds by embedding ES in bandages through advanced technologies[33-36]. The studies demonstrated substantial evidence that ES of wounds accelerated wound closure by 30%, reduced scarring in mice and sped up wound closure[33-35].

There are different forms of ES, including the use of direct current (DC), alternating current (AC), pulsed current (PS), degenerative wave, high-voltage pulsed current (HVPC), microcurrent ES, and the transcutaneous electrical nerve stimulation (TENS)[31,34,37]. The DC is also known as galvanic current and is the use of continuous, unidirectional flow of charged particles from one pole to the other lasting 1 second or longer, while HVPC is the delivery of pulsed DC current via short monophasic pulses at an amplitude from 100 to 500 V [36]. Also, microcurrent ES is the use of pulsed monophasic low-voltage form of electrical stimulation, while TENS is the use of biphasic or modified AC currents[37]. However, the advantage using TENS in the management of chronic wounds over other forms of ES lies in its being inexpensive, portable, readily available, and easy to use for everyone with little precautions.

Mechanism of Action

Therapy involving TENS as a form of ES for chronic wounds uses low-voltage electrical currents applied through the skin around a wound surface or directly on the wound surface to stimulate cellular processes that support tissue repair and regeneration[38]. Originally, TENS was developed for pain relief, and studies have demonstrated that it aids pain relief, especially immediately after its application[39,40]. The only inadequacy in the use of TENS for pain relief is its inability to remove the root cause of the pain. TENS mediates its effect through the pain gate theory by inhibiting the transmission of

nociception at the substantia gelatinosa of the spinal cord[39,41]. Also, low frequency TENS is believed to stimulate the release of certain endogenous chemicals such as mu opioid, 5-HT2, and 5-HT3 receptors, while high frequency TENS mediates delta opioid receptors[39]. There are different forms of TENS in use, including conventional TENS (low intensity and high frequency, 50–100Hz), acupuncture-like TENS (high intensity and low frequency, 2–4Hz), and intense TENS (high intensity and high frequency, 200pps)[39-40].

In recent times, TENS has been found useful in enhancing wound healing. It works by modulating pain signals to the brain, improving blood circulation to the wound, reducing inflammation, enhancing cellular functions necessary for tissue repair and potentially decreasing wound infection rates[38,42]. By stimulating sensory nerves, TENS inhibits pain transmission and induces the release of endorphins, which can significantly reduce pain at the wound site[38]. In the promotion of blood flow, TENS improves microcirculation at the wound site, which is critical for delivering nutrients and oxygen to the tissues and removing waste products. Enhanced blood flow accelerates the healing process by promoting cell proliferation and tissue repair[38]. Also, TENS stimulates fibroblasts and promotes collagen production, which is essential for wound healing[34,38]. Additionally, it can enhance cell migration and proliferation, particularly in diabetic wounds where these processes are often impaired[34,37].

Clinical Evidence

A study demonstrated that biphasic current or TENS therapy significantly improved healing rates by 70% in patients with diabetes by enhancing granulation tissue formation and reducing pain[43]. There are indications that TENS is effective in the treatment of leprous ulcer and chronically infected wounds[41,44-46]. In animal models, TENS has been shown to enhance collagen deposition, improve wound contraction, and reduce the inflammatory response[24]. Overall, the use of TENS in chronic wounds is premised in its ability to re-establish the natural state of the wound even when in a defective state. Preetam and colleagues asserted that the injury's existing state has a significant role in the start of repair and that the human skin that is not injured has a transcutaneous current potential of 20–50 mV and an endogenous electrical potential[41]. Hence, emphasizing the role of TENS in chronic wounds.

Application

To achieve optimal results, parameters such as frequency and intensity of TENS need to be adjusted to low or moderate frequency tolerable by patient. Also, it is essential to apply TENS after a proper wound dressing in which a clean moist gauze with normal saline is placed over the wound. The TENS electrodes of comparable size to the wound surface are placed on the gauge for stimulation. The gauze should remain in place after TENS stimulation until the next stimulation. The duration for application of TENS can be as 30 to 40 minutes or as much as 1 hour. The treatment should be repeated every other day. It is advisable to remove iodine from the wound surface or any other products that may slow the conductivity of electric currents in wounds during the use of TENS[37]. The United States food and drug

administration guidance document for electrical stimulation contradicts the use of ES for patients with demand-type cardiac pacemakers, cancerous lesions, pregnant uterus, and the carotid sinus region[47].

Combination Therapy

Given the potential of LASER and TENS in the management of chronically infected wounds, one underexplored approach to optimize treatment is to combine their treatments in order to effectively manage the wounds. For instance, it is advisable not to commence the use of ES, ultrasound, and pulsed radiofrequency stimulation in the first 48 to 72 hours after an injury[37]. Also, the subtle antimicrobial activity of LASER and TENS can be combined. LASER kills bacteria, while TENS prevents bacteria from entering the wound by maintaining a transcutaneous current around the wound that increases blood flow, thereby supplying oxygen and preventing the growth of bacteria. Hence, initial treatment for chronically infected wounds can begin with the use of LASER in the first week, continued with both LASER and TENS in the weeks ahead, and conclude with the use of TENS when there is substantial contraction of the wound. At all times, a standard wound dressing should precede the application of LASER and TENS.

Limitations and Future Directions

As a narrative review, this article lacks the methodological rigor of a systematic review. The literature selection process was not based on predefined inclusion or exclusion criteria, which may introduce selection bias and limit reproducibility. Although LASER and TENS have minimal adverse effects in comparison to other biophysical agents, the potential adverse effects associated with LASER and TENS discussed in this review are not exhaustive, hence should be checkmated in case of clinical adoption.

Given the increasing prevalence of chronic wounds and the challenges associated with their management, integrating these non-pharmacological strategies into wound care protocols could provide a more comprehensive and effective approach to wound healing. Further research, especially randomized controlled trials in optimizing treatment protocols, especially for combination therapy is needed to establish these therapies as mainstream clinical tools for chronic wound management.

CONCLUSION

The use of LASER and TENS as non-surgical treatments for chronic wound infections is a promising area of research. These modalities offer unique mechanisms of action that can address both the infection and the defective healing mechanisms seen in chronic wounds. Clinical and preclinical studies consistently show the efficacy of these therapies in improving wound healing outcomes, reducing infection, and enhancing tissue regeneration.

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