Using Lasers in Diabetic Wound Healing

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ABSTRACT
Lasers are a treatment choice that appeals to patients. Early research suggests that laser therapy may have a role in hastening wound healing. Attempts have been made to use helium neon, CO₂, and KTP lasers in encouraging wound healing in diabetics. We will review the English literature related to laser use in diabetic wound healing and discuss the concept of the use of nondestructive lasers for biostimulation. Further research is needed to assess effectiveness of biostimulation for diabetic wound healing.

INTRODUCTION
Patients with diabetes are well known to have an increased incidence of ulcers and wounds. Decreased sensation, increased blood glucose, and poor microcirculation all contribute to the increased number of nonhealing wounds in this group of patients. Physicians and patients find the process of caring for and healing diabetic wounds difficult and frustrating. Both are eager to find new ways to hasten the healing process. Lasers appeal to the public as cutting-edge tools for many dermatological problems not responsive to other modalities. Patients often come to our offices hoping lasers will cure whatever dermatological problem they may have, from acne to subcutaneous cysts. And, indeed, lasers are being studied as possible solutions for a wide range of health problems.

Lasers are commonly used in medicine to destroy tissue, and are currently used for treatments such as shaping corneas, resurfacing skin, coagulating vascular proliferations, and bloodless incisions.

Nondestructive lasers are frequently used in nonmedical settings, including entertainment laser shows, security boundaries in art museums, and laser pointers for presentations. They also are becoming more common in medical settings.

Laboratory studies suggest that nondestructive (or low-energy) lasers can improve wound healing in vitro. The results in vivo are less convincing, but encouraging enough that both patients and physicians seek more evidence that lasers can be used in wound healing. We first will describe in vitro and animal studies using nondestructive lasers. Next, we will review the English language literature related to the use of lasers in diabetic wound healing.

IN VITRO STUDIES
Experiments using nondestructive lasers reveal possible mechanisms of action on cellular function and wound healing. Helium-neon (HeNe) laser application increases collagen synthesis independent of cellular growth.
Other effects of lasers include: increased keratinocyte cell motility, growth factor release (TGF, PDGF, and bFGF), and keratinocyte interleukin-1α and interleukin-8 release. Conversely, the Nd-YAG laser suppressed collagen production. Finally, nondestructive laser treatment transforms fibroblasts to myofibroblasts. These cellular effects may be due to increased ascorbic acid uptake and hydroxyproline formation, stimulation of mitochondrial respiration, or increased adenosine triphosphate (ATP) synthesis in mitochondria.

**ANIMAL STUDIES**

In contrast to in vitro studies, animal studies using nondestructive lasers reveal conflicting results. Collagen synthesis increases after laser treatment in treated rats, but not in pigs. Treatment with HeNe laser does not consistently increase healing rates in animals. These studies are superior to most of the human studies in that they are well controlled. However, similar to the human studies, there is wide variation among studies in the dose and interval of laser treatment. This may account for some of the differences in study results.

**CLINICAL STUDIES USING LASERS FOR WOUND HEALING**

Low-powered lasers were first used in Europe in the 1970s to promote skin healing. The original studies were uncontrolled open studies that reported increased skin ulcer healing. Two later open studies using infrared lasers demonstrated improved healing of ulcers due to venous insufficiency. However, a case controlled study showed no difference in healing rates between control and treated patients. The Food and Drug Administration (FDA), citing the lack of convincing human studies, banned the sale of low-power laser systems as wound healing devices in 1983. Most recently, well-controlled studies have shown that HeNe laser increases healing in acute gingival incisions and prevents chemotherapy-induced oral mucositis.

**CLINICAL STUDIES USING LASERS FOR WOUND HEALING IN DIABETICS**

**CO₂ laser debridement study**

One 5-year study used the CO₂ laser in both destructive and nondestructive modes, treating 63 ulcers, including 20 diabetic ulcers. The CO₂ laser was applied in a defocused range, at 8–10 W, with a 1–2 mm spot size. The ulcers were radiated weekly for up to 17 weeks. The investigators monitored microbial counts before beginning therapy and every 2 weeks during therapy. At the end of the study, they found that cultures of almost two thirds of the ulcers showed no bacterial growth, with 16 of 63 showing a few bacterial colonies and 3 of 63 showing “too many to count.” From this the authors concluded that the CO₂ laser helped to sterilize the ulcers. Thirty-three of 63 (52%) ulcers showed complete healing at the end of the study; 28 of 63 (44%) showed a partial response, while only 2 of 63 patients failed to respond to the laser therapy. Of note, 100% of the 20 diabetic ulcers showed complete response, with an average time to healing of 32 days. Based on these results, the investigators concluded that laser debridement resulted in reduced infections and faster healing. They noted that irritable dermatitis of surrounding skin, a common side effect of chemical debriding agents, is reduced with laser. Unfortunately, there were no nonlaser treated controls with which to compare the results.

**He-Ne laser irradiation effect on cutaneous circulation in diabetic feet**

To examine whether nondestructive laser irradiation increases blood flow in diabetics, an He-Ne laser was tested on 30 randomized, consecutive patients with diabetic ulcers or gangrene and elevated levels of glycosolated hemoglobin. Patients received one 50-minute treatment of either He-Ne laser irradiation or sham irradiation over both forefeet. It was determined prior to beginning the study that the He-Ne laser did not cause a rise in skin temperature. Treatment was followed by measurement of the temperature over the forefoot region by infrared thermography to assess skin blood circulation.
Skin temperature increased significantly after treatment with the He-Ne laser, while skin temperature in the sham-treated feet decreased. Skin temperature remained higher in the laser-treated subjects for at least 15 minutes after treatment, suggesting that blood flow increases are sustained after laser irradiation.

**Three case reports**

In 1988, Gogia et al.\(^{18}\) reported using a low-energy cold laser (Omniprobe, Omni International, Topeka, KS) at a frequency of 1,000 Hz. Laser irradiation was applied for 10 seconds to each approximately 3 mm\(^2\) of an imaginary grid over the ulcer. After whirlpool, this protocol was used to treat a traumatic tibial ulcer in a diabetic woman. The patient received 22 laser treatments and 25 whirlpool treatments. After 14 weeks, the tibial ulcer was reduced in size from 5.0 × 4.0 cm to a 0.25-mm defect. Because the laser and whirlpool therapies were applied together, there is no way to assess the laser therapy specifically.

Schindl and associates\(^{25}\) used He-Ne laser to treat a persistent radiation ulcer in a diabetic. This ulcer was on the plantar foot, had been present for over 45 years, and severely handicapped the patient. They treated the 375 mm\(^2\) ulcer twice a week with a 5-mm spot, 8 mW/cm\(^2\) for 35 minutes for a total energy density of 31.5 J/cm\(^2\). The ulcer was dressed with dry sterile dressings. After 4 treatments, the patient noted a significant decrease in pain. After 10 weeks, the ulcer healed.

The same authors reported similar success in a diabetic with a 440 mm\(^2\) radiation ulcer on her nose, which extended to the cartilage, present for 13 months.\(^{26}\) The patient was treated with an He-Ne laser, using a 5-mm spot, 2 mW/cm\(^2\) for 30 minutes, for a total energy density of 36 J/cm\(^2\). She received 3 treatments the first week, then 2 treatments per week for a total of 8 sessions. The ulcer was covered with sterile dry dressings between treatments. After 2 sessions, the patient experienced a significant reduction in pain. At the end of treatment, the ulcer was completely healed. During 18 months of follow-up, it did not recur nor were there any negative sequelae.

**CONCLUSION**

Nondestructive or low-energy lasers are an attractive but unproven modality to improve wound healing. *In vitro* and animal studies suggest that these lasers may hasten wound healing but the clinical utility of this therapy has not yet been defined in humans. Well-controlled trials are needed to determine whether this approach is effective, and if effective, the optimum patient populations and treatment schedules.

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