

**EVALUATION OF THE EFFECT OF ONCE-WEEKLY TREATMENTS WITH THE
CERALAS D DIODE LASER ON WOUND HEALING**

FINAL REPORT

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PURPOSE

The purpose of this study was to evaluate the effect of the Ceralas D diode laser on healing ulcers of the foot and lower leg, when laser treatments were performed once a week and the ulcers were covered with only DuoDERM[®] hydroactive gel and sterile dressing.

MATERIALS AND METHODS

Materials

The Ceralas D diode laser was used to induce photostimulation. The laser energy was applied via a specially designed collimator.

Methods

Patients Selection:

The patients for this study were selected from individuals who presented to the Wade Park or Brecksville divisions of the Cleveland V.A. Medical Center with at least one ulcer on the foot or lower leg. Patients with all types of ulcers, including neurotrophic, venous stasis, traumatic and ischemic wounds, were eligible for the study. Patients with ulcers that penetrated the epidermis, dermis and deep fascia were included, while those with full thickness ulcers that involved deep abscess, osteomyelitis, or exposure of the tendon, capsule or bony structures were excluded from the study. In addition, patients were removed from the study if non-compliance interfered with the outcome of the treatments. All ulcers were classified as either chronic (>8 weeks) or acute (≤8 weeks). The study protocol was reviewed and approved by the Institutional Review Boards of the Ohio College of Podiatric Medicine and the Cleveland V.A. Medical Center to ensure that the rights and safety of the patients were protected.

Laser Treatments:

All subjects received laser treatment one time per week. At each visit, the ulcer was cleaned with sterile saline irrigation and, if necessary, mechanically debrided with a scalpel. Initial debridement was more effective with a scalpel, due to the excessive amounts of hyperkeratotic and fibrous tissues around the ulcer. The ulcer was then examined for changes in appearance from the previous visit. The laser power was set to 4 Watts, which is equivalent to applying 18 J/cm² of energy. The laser energy was applied to the ulcer in a criss-cross pattern to ensure complete exposure of the ulcerative area. After laser treatment, a digital photograph was taken of the ulcer for calculation of the area using imaging software. DuoDERM[®] hydroactive gel was then applied to the ulcer, and sterile dressing was placed over the gel. The patient was then re-appointed for follow-up in one week.

Analysis:

The primary outcome measured was the incidence of complete wound closure, as recommended by the FDA. A secondary outcome that was also measured was time to closure. In addition, the percent change in ulcer area, compared to the area at the initial visit, was calculated at the end of the treatment period for those ulcers that were non-healing.

RESULTS

All Patients

A total of 52 ulcers from 29 male patients were enrolled in the study. Of the 52 ulcers, 1 was removed due to the patient being in an auto accident, 1 was removed as a result of acute osteomyelitis, 4 from one patient were removed due to the development of acute ischemia, 2 from one patient were removed as a result of the patient being diagnosed with cancer, 4 were removed due to missed follow-up treatments, 6 from one patient were removed as a result of patient admission at a non-participating hospital, and 2 were removed due to general non-compliance. Thus, there were 32 ulcers from 20 male patients included in the analysis: 15 neurotrophic ulcers, 15 venous ulcers and 2 traumatic ulcers. Twenty-five of the 32 ulcers were classified as chronic, while 7 were acute (see Table 1).

Of the 32 ulcers, 23 (or 71.9%) were completely healed during laser treatment. This included 11 neurotrophic ulcers, 11 venous ulcers and 1 traumatic ulcer. Thus, 73.3% of the neurotrophic ulcers, 73.3% of the venous ulcers and 50.0% of the traumatic ulcers were completely healed.

Of the 23 healed ulcers, 16 were classified as chronic and 7 were acute. Thus, 64.0% of the chronic ulcers and 100% of the acute ulcers were completely healed. It should be noted that all chronic ulcers had been treated without success with some other modality prior to initiation of laser treatment. Other modalities included silvadine, accuzyme, panafil, regranex, betadine, bacitracin, bactroban, transorbant, xeroform, sorbsan, unna boots, apligraf and skin grafts.

The average time until wound closure was 7.5 weeks (1 to 29 weeks). On average, it took the neurotrophic ulcers 5.2 weeks (1 to 22 weeks) to completely heal. The average time to healing for venous ulcers was 9.1 weeks (2 to 29 weeks). The traumatic ulcer took 15 weeks to heal completely.

Diabetic Patients

A total of 18 ulcers from 12 diabetic patients were included in the analysis: 14 neurotrophic ulcers, 3 venous ulcers and 1 traumatic ulcer. Twelve of the 18 ulcers were classified as chronic, while 6 were acute (see Table 2).

Of the 18 ulcers, 13 (or 72.2%) were completely healed during laser treatment. This included 10 neurotrophic ulcers, 2 venous ulcers and 1 traumatic ulcer. Thus, 71.4% of the diabetic neurotrophic ulcers, 66.7% of the diabetic venous ulcers and 100.0% of the diabetic traumatic ulcers were completely healed.

Of the 13 healed ulcers, 7 were classified as chronic and 6 were acute. Thus, 58.3% of the chronic ulcers and 100% of the acute ulcers from diabetic patients were completely healed.

The average time until wound closure was 6.4 weeks (1 to 22 weeks). On average, it took the neurotrophic ulcers 5.6 weeks (1 to 22 weeks) to completely heal. The average time to healing for venous ulcers was 6.0 weeks (5 to 7 weeks). The traumatic ulcer took 15 weeks to heal completely.

Of the five diabetic ulcers that did not heal completely, four had shown healing potential but had either reached a plateau and failed to progress towards healing, or were healing at the time that the study was terminated. These included three neurotrophic ulcers that had obtained 15.28%, 77.86% and 91.12% closure, and one venous ulcer that was

45.08% smaller. One neurotrophic ulcer was 152.81% larger than the initial size of the ulcer at the time the patient was discharged from the study.

Non-Diabetic Patients

A total of 14 ulcers from 8 non-diabetic patients were included in the analysis: 1 neurotrophic ulcer, 12 venous ulcers and 1 traumatic ulcer. Thirteen of the 14 ulcers were classified as chronic, while 1 was acute (see Table 3).

Of the 14 ulcers, 10 (or 71.4%) were completely healed during laser treatment. This included 1 neurotrophic ulcer, 9 venous ulcers and 0 traumatic ulcers. Thus, 100% of the non-diabetic neurotrophic ulcers, 75% of the non-diabetic venous ulcers and 0% of the non-diabetic traumatic ulcers were completely healed.

Of the 10 healed ulcers, 9 were classified as chronic and 1 was acute. Thus, 69.2% of the chronic ulcers and 100% of the acute ulcers from non-diabetic patients were completely healed.

The average time until wound closure was 8.9 weeks (1 to 29 weeks). It took the neurotrophic ulcer 1 week to completely heal. The average time to healing for venous ulcers was 9.8 weeks (2 to 29 weeks).

Of the four non-diabetic ulcers that did not heal completely, two had shown healing potential but had either reached a plateau and failed to progress towards healing, or were healing at the time that the study was terminated. These included one venous ulcer that had obtained 53.55% closure and one traumatic ulcer that was 66.30% smaller. Two venous ulcers from one patient also did not completely heal: one ulcer was 72.91% larger and the other was 151.60% larger than the initial size of the ulcers at the time the patient was discharged from the study.

DISCUSSION

The results from this study were very encouraging, with 71.9% of all ulcers and 72.2% of ulcers from diabetic patients healing. These findings are better than those from the first two pilot studies. During the first study, which consisted of laser treatments once every two weeks in addition to standard care, 36.8% of all ulcers and 50% of ulcers from diabetic patients were completely healed. During the second study, which consisted of laser treatments twice weekly in addition to standard care, 52.9% of all ulcers and 61.5% of ulcers from diabetic patients were completely healed. It should be noted that in this study the original areas of the ulcers were, on average, less than half that of those in the first two studies.

There was no significant difference in number of ulcers healed between diabetic and non-diabetic ulcers, with 72.2% of diabetic ulcers and 71.4% of non-diabetic ulcers achieving complete closure. It should be noted, however, that the diabetic ulcers healed in an average of 6.4 weeks, while the non-diabetic ulcers healed in an average of 8.9 weeks. The original size of the ulcers does not appear to be a factor in time to healing between diabetic and non-diabetic ulcers, as the average initial size of the diabetic ulcers was 1.32 cm², and that of the non-diabetic ulcers was 1.66 cm².

While there was a high percentage of patients lost to the study, the majority was due to factors beyond the control of the investigators, as dictated by the protocol. Ten ulcers from four patients were removed as a result of unrelated medical complications and 6 ulcers

from five patients were removed due to non-compliance (including missed follow-up visits). This accounts for 16 of the 17 ulcers removed from the study. Only 1 ulcer from one patient was removed due to the development of osteomyelitis, which is listed as an exclusion criterion in the protocol.

It should be noted that there is a high factor of non-compliance in the veteran population. Those seeking treatment at a V.A. Medical Center typically do not have insurance or private doctors. As a result, many have to travel long distances to get to the hospital and often choose to skip or cancel an appointment. The incidence of non-compliance may not be typical of other wound care centers across the United States.

CONCLUSIONS

In conclusion, treatment with the Ceralas diode lasers once a week at 4 Watts with only DuoDERM[®] hydroactive gel and sterile dressing appears to enhance wound healing. It should be noted that this is based on comparative data, rather than controls within this study. The use of the collimator in place of the bare fiber does not appear to lessen the effect of the laser, and may even increase wound healing. The patients were highly satisfied with the use of the laser, and in general, had no discomfort during treatment. The physicians who used the laser also praised the ease of use and the effectiveness on wound healing.

During the course of the three studies conducted by the OCPM Research Foundation, a treatment protocol for the use of the Ceralas D diode laser in wound healing has been developed and refined. The protocol that was developed for experimental study is inclusive of all parameters necessary to properly evaluate wound healing, and has shown the effectiveness of the laser in wound healing. Completion of the three studies has prepared the way for a multi-center study.

Table 1
Summary of All Ulcers Included in the Study

Type of Ulcer	Chronic or Acute?	Size of Ulcer (cm²)	Time to Healing (weeks)
Healed Ulcers			
Neurotrophic	Acute	5.28	3
Neurotrophic	Chronic	0.047	1
Neurotrophic	Chronic	0.10	1
Neurotrophic	Chronic	0.26	1
Neurotrophic	Chronic	0.13	1
Neurotrophic	Chronic	0.34	4
Neurotrophic	Acute	0.69	4
Neurotrophic	Acute	1.00	11
Neurotrophic	Chronic	0.0083	1
Neurotrophic	Chronic	0.96	22
Neurotrophic	Acute	0.85	8
Venous	Chronic	2.60	27
Venous	Chronic	7.88	29
Venous	Chronic	0.26	3
Venous	Chronic	0.17	2
Venous	Chronic	0.19	2
Venous	Chronic	0.33	2
Venous	Acute	2.80	5
Venous	Acute	1.84	8
Venous	Chronic	0.39	8
Venous	Chronic	2.95	7
Venous	Acute	2.62	7
Traumatic	Chronic	2.05	15
Non-Healed Ulcers			
Neurotrophic	Chronic	0.89	Treated for 36 weeks**
Neurotrophic	Chronic	0.89	Treated for 24 weeks**
Neurotrophic	Chronic	15.90	Treated for 28 weeks
Neurotrophic	Chronic	0.59	Treated for 3 weeks**
Venous	Chronic	19.30	Treated for 36 weeks**
Venous	Chronic	1.55	Treated for 16 weeks
Venous	Chronic	2.51	Treated for 16 weeks
Venous	Chronic	4.69	Treated for 16 weeks
Traumatic	Chronic	108.00	Treated for 44 weeks**

** Patient still active when study reached completion

Table 2
Summary of Diabetic Ulcers Included in the Study

Type of Ulcer	Chronic or Acute?	Size of Ulcer (cm²)	Time to Healing (weeks)
Healed Ulcers			
Neurotrophic	Acute	5.28	3
Neurotrophic	Chronic	0.047	1
Neurotrophic	Chronic	0.10	1
Neurotrophic	Chronic	0.26	1
Neurotrophic	Chronic	0.13	1
Neurotrophic	Chronic	0.34	4
Neurotrophic	Acute	0.69	4
Neurotrophic	Acute	1.00	11
Neurotrophic	Chronic	0.96	22
Neurotrophic	Acute	0.85	8
Venous	Acute	2.80	5
Venous	Acute	2.62	7
Traumatic	Chronic	2.05	15
Non-Healed Ulcers			
Neurotrophic	Chronic	0.89	Treated for 36 weeks** <i>152.81% larger</i>
Neurotrophic	Chronic	0.89	Treated for 24 weeks** <i>91.12% smaller</i>
Neurotrophic	Chronic	15.90	Treated for 28 weeks <i>77.86% smaller</i>
Neurotrophic	Chronic	0.59	Treated for 3 weeks** <i>15.28% smaller</i>
Venous	Chronic	19.30	Treated for 36 weeks** <i>45.08% smaller</i>

** Patient still active when study reached completion

Table 3
Summary of Non-Diabetic Ulcers Included in the Study

Type of Ulcer	Chronic or Acute?	Size of Ulcer (cm²)	Time to Healing (weeks)
Healed Ulcers			
Neurotrophic	Chronic	0.0083	1
Venous	Chronic	2.60	27
Venous	Chronic	7.88	29
Venous	Chronic	0.26	3
Venous	Chronic	0.17	2
Venous	Chronic	0.19	2
Venous	Chronic	0.33	2
Venous	Acute	1.84	8
Venous	Chronic	0.39	8
Venous	Chronic	2.95	7
Non-Healed Ulcers			
Venous	Chronic	1.55	Treated for 16 weeks <i>53.55% smaller</i>
Venous	Chronic	2.51	Treated for 16 weeks <i>72.91% larger</i>
Venous	Chronic	4.69	Treated for 16 weeks <i>151.60% larger</i>
Traumatic	Chronic	108.00	Treated for 44 weeks** <i>66.30% smaller</i>

** Patient still active when study reached completion