

The Benefit of Electrical Stimulation to Enhance Perfusion in Persons with Diabetes Mellitus

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The purpose of this study was to evaluate the effect of galvanic electrical stimulation on vascular perfusion in diabetic patients. Nineteen subjects with diabetes were enrolled. Eleven subjects (57.9%) were diagnosed with impaired peripheral perfusion based upon their initial transcutaneous oximetry values (<40 mm Hg). The subjects were studied over a 2-day period. On the 1st day, one foot was electrically stimulated for four 60-minute periods by an external electrical stimulation device. Vascular perfusion of both feet was assessed before and after the sessions of electrical stimulation. On the 2nd day, no electrical stimulation was applied and noninvasive vascular measurements were repeated. For the 1st hour, transcutaneous oxygen pressure was measured continuously during stimulation at the lateral aspect of the leg. Subsequently, perfusion between the periods of stimulation was measured on the dorsum of the foot with both transcutaneous oximetry and laser Doppler flowmetry after each stimulation period. In the group with impaired peripheral perfusion, a significant rise in tissue oxygenation as compared to the control measurements was measured during the first 5 minutes of stimulation ($p < .040$). For those without vascular disease ($T_c pO_2 > 40$ mm Hg) however, there was not a significant increase compared to baseline ($p = .280$). After the periods of stimulation, the stimulated feet did not show any higher perfusion levels than the control feet. Patterns in perfusion during the day, as measured by laser Doppler flowmetry, were similar in the tested feet and in the controls. These data suggest that external subsensory electrical stimulation induces a transient rise in skin perfusion in persons with diabetes and impaired peripheral perfusion. (The Journal of Foot & Ankle Surgery 37(5):396–400, 1998)

Key words: diabetes, electricity, perfusion, ulceration

Neuropathic foot ulcerations are common complications among patients with diabetes mellitus. Once wounds on the foot appear, they can easily lead to tissue necrosis and delayed wound healing (1). This situation is at least to some extent due to ischemia. Thus vascular disease can be an important contributor to faulty wound healing and eventual amputation (1–3). Under normal circumstances, the tissue of the foot is able to survive in the presence of very low oxygen tension levels. A wound, however, leads to increased oxygen demand because of the increased

metabolic requirements that are inherent in the process of wound healing (4). Therefore, it is reasonable to conclude that any intervention that might increase local tissue perfusion and oxygenation would be beneficial to heal chronic diabetic foot ulcers.

Several reports in medical literature have suggested that the application of electrical current enhances wound healing and surgical flap survival (5–11). Some authors suggest that these changes are due to increased tissue perfusion (7, 12, 13). Mohr and co-workers demonstrated altered perfusion after high-voltage pulsed stimulation of rat hind limbs (14), and Myrhage and Hudlicka showed that electrical stimulation facilitated an increase in capillary bed density in the muscular tissue of rats (15). Wakin found that increased blood flow was best achieved with low-frequency stimulation (16).

There are only a few studies in humans that have demonstrated that electrical stimulation enhances perfusion or enhances wound healing. In addition, in studies where human subjects were involved, there was considerable variation in the dose and type of the electric current used. Although patients suffering from peripheral vascular

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disease are probably the group most likely to benefit from electrical stimulation, several studies excluded patients with peripheral vascular disease from their studies (6, 13, 17). Additionally, inconsistent operational definitions have been used in the evaluation of the effect of electrical stimulation in humans and animals. Therefore, the objective of this study was to investigate the effect of electrical stimulation on tissue perfusion in the feet of human diabetic subjects, and to determine if electrical stimulation has a different effect on those with diabetes-related peripheral vascular disease compared to those without impaired lower extremity blood flow.

Methods

Nineteen subjects with diabetes mellitus were recruited to participate in this project. All subjects were diagnosed with diabetes mellitus according to WHO criteria (18). Demographic data for these subjects are summarized in Table 1. Besides having diabetes mellitus, subjects had to be willing to participate. Exclusion criteria were cardiac abnormality and malignity.

A baseline transcutaneous oximetry value taken on the lateral side of the left leg was used to determine whether or not each patient had lower extremity peripheral vascular disease. This was accomplished with the use of a Radiometer TCM3 transcutaneous oximeter.⁴ Eleven subjects (57.9%) with transcutaneous oxygen pressures ($T_c pO_2$) < 40 mm Hg were placed in the group with impaired lower extremity blood flow (PVD group). The remaining eight subjects (42.1%) were considered to have adequate perfusion (non-PVD group).

The baseline vascular assessment also included laser Doppler flowmetry. The laser Doppler perfusion imaging system⁵ consists of a low-power helium-neon laser beam, and an optical detector unit. The laser scans the tissue recording 4,096 measurement points, with a sampling depth in the order of 200–500 μ m. The area covered is 150 cm², located at the dorsum of the foot and toes. In the tissue, the laser light interacts with moving erythrocytes

and scatters and shifts according to the Doppler principle. A remotely positioned photo detector detects a fraction of the reflected light. After a scan is completed, all measurement values are compiled by a desktop computer and system software to form a color-coded image of the tissue perfusion.

The Micro-Z⁶ was used to deliver subsensory galvanic electrical stimulation. This system consists of a Dacron silver mesh sock and sleeve electrode connected to a battery-powered voltage delivery unit. An electrolyte fluid facilitated conduction of the current. A 50-volt current was delivered for 60 minutes at 100 twin-peak monophasic pulses per second. The current is subsensory and did not lead to any muscle contractions. The subjects put the sock and sleeve electrodes on and were allowed to adjust to the situation for about 20 minutes. After the acclimatization period, the baseline noninvasive vascular measurements were taken. The electrical stimulation device was turned on as soon as the first measurement was obtained. Every 5th minute of the first period of electrical stimulation, $T_c pO_2$ readings were repeated. The transcutaneous oximeter electrode was located between the sleeve and the sock on the lateral side of the lower leg to avoid any interference with either the electricity-conducting material or the electrical current itself. After the 1st hour, measurements identical to the baseline assessments were performed on both feet. These measurements were followed by three additional 60-minute periods of electrical stimulation followed by $T_c pO_2$ and laser Doppler perfusion measurements.

Data were collected over 2 consecutive days. On the 1st day, electrical stimulation was applied to one of the feet; on the 2nd day, no current was applied. However, the electrical sock, moistened by the conduction fluid, was still worn by the patient. This way, the 2nd day could also serve as a control for any changes in skin perfusion due to the warmth of the fabric or evaporation of conduction mist.

We used a general linear model to compare the perfusion of the tested foot and the contralateral foot on day 1 and day 2. A general linear model was also used to compare data collected during the 1st hour of stimulation and the 1st hour of the control day.

TABLE 1 Demographic characteristics of the subjects

Characteristic	Mean \pm S.D.	Minimum	Maximum
Age (yrs)	55.7 \pm 8.5	37	69
History of diabetes (yrs)	13.4 \pm 9.9	0.5	30
Ankle–Brachial Index	1.03 \pm 0.20	0.70	1.32
Initial $T_c pO_2$ (mm Hg)	47.8 \pm 9.2	30	63
Vibratory perception threshold (volts)	35.6 \pm 10.8	15	50

Female: male ratio = 6 : 13 (31.6%:68.4%).

⁴ Radiometer, Inc., Copenhagen, Denmark.

⁵ Lisca, Inc., Hewitt, NJ.

⁶ Prizm Medical, Inc., Deluth, GA.

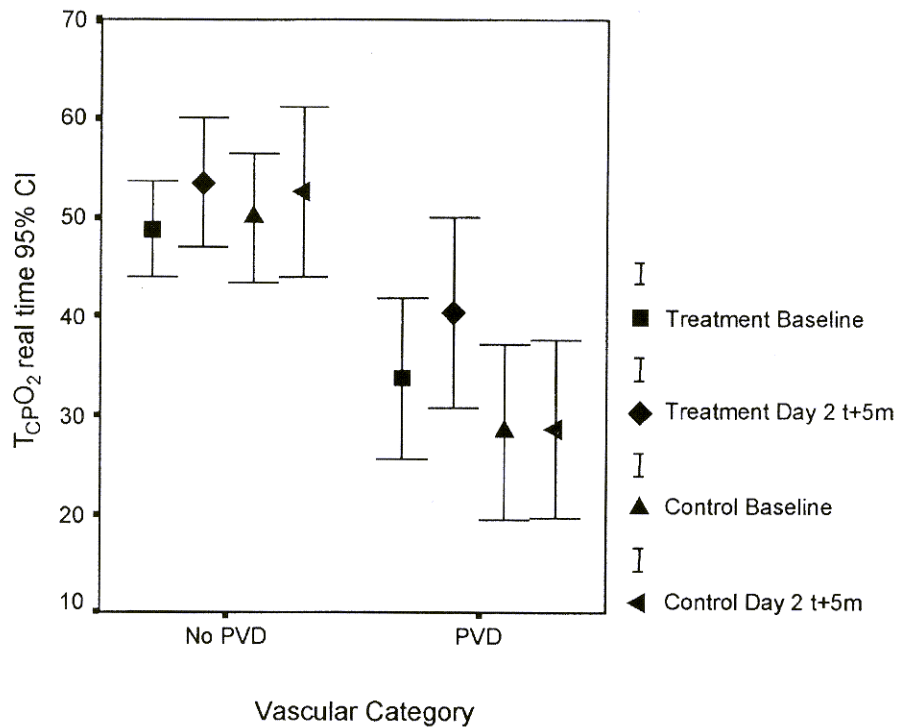


FIGURE 1 Average changes in real-time transcutaneous oxygen measurements taken on the lateral aspect of the leg after 5 minutes of electrical stimulation. There was a significant difference in patients with PVD ($T_c pO_2 < 40$ mm Hg) after 5 minutes of electrical stimulation. No other associations were significant.

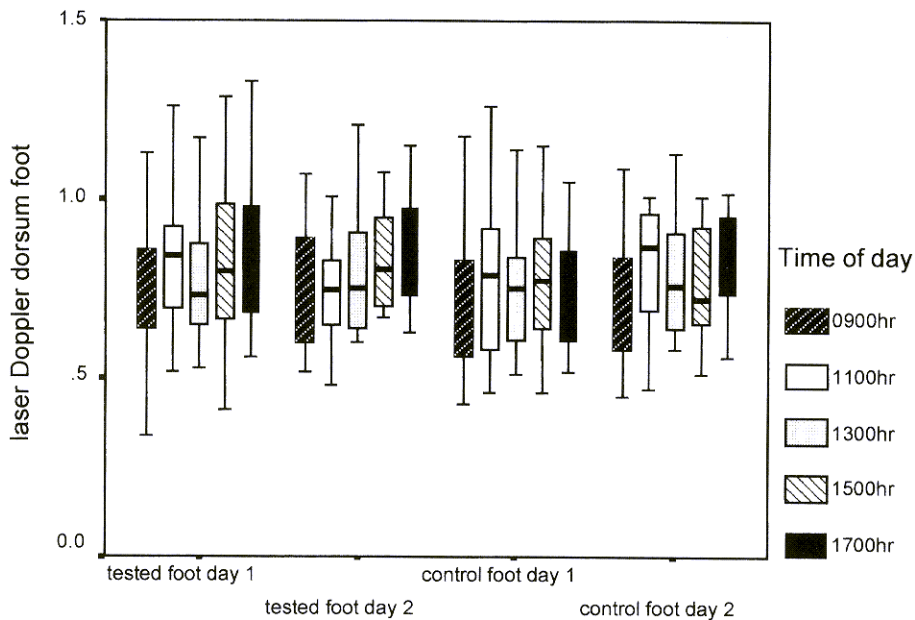


FIGURE 2 Box plot of the laser Doppler flowmetry. The data demonstrate a constant pattern throughout the day. The differences between the study foot and the control foot were not statistically significant nor were the differences between the study day and the control day.

electrical stimulation ($p = .040$) as compared to the control day. No constant pattern could be found during the rest of the 1st hour of stimulation.

Figure 2 shows the laser Doppler flowmetry results. General linear model analysis displayed a constant pattern

throughout the day. This pattern could be observed in both days and in both feet. However, the laser Doppler results did not show a significant difference between the electrically stimulated foot and the controls ($p = .27$). Analysis of the transcutaneous oximetry values suggested no

differences in oxygen pressure between the stimulated foot and either the control day or the control foot. Furthermore, no consistent pattern in transcutaneous oxygen pressure was observed over the course of the day.

Over the course of the entire day, no significant increase in perfusion in the stimulated foot was found between the group of subjects with peripheral vascular disease and the group with normal vascular perfusion. However, the feet still displayed the same constant pattern in the stimulated foot and the controls as measured with laser Doppler (PVD group, $p = .013$; non-PVD group, $p = .0001$). Transcutaneous oximetry showed no significant patterns throughout the day (PVD group, $p = .0564$; non-PVD group, $p = .1768$).

Discussion

The real-time transcutaneous oximetry measurements taken on subjects with peripheral vascular disease in the 1st hour of electrical stimulation suggest an improvement in skin perfusion during electrical stimulation. However, they failed to show enhanced perfusion in subjects without impaired vascular disease (Fig. 1). The small sample size could have influenced the analysis of the measurements on the subjects without peripheral vascular disease. It is unlikely that just the heat of the sock could have caused the increase in perfusion, since the perfusion of the contralateral foot without the sock was not different. Stoner and co-workers stated that increase in temperature has no influence on the perfusion of the skin of the calf (19). However, we have found nothing in the medical literature to address a difference in responsiveness to heat in subjects with peripheral vascular disease or diabetes mellitus. The other measurements in the 1st hour did not show any consistent pattern.

Analysis of the measurements that were taken between the periods of electrical stimulation did not suggest augmented perfusion after electrical stimulation. However, the measurements taken with the laser Doppler flowmeter suggested a consistent pattern throughout the day. This pattern was not significantly influenced by electrical stimulation. This could imply that the effect of electrical stimulation does not persist after the stimulation is stopped. Therefore, electrical stimulation might only have a temporary effect on perfusion. Transcutaneous oxygen measurements did not suggest a diurnal pattern, in contrast to the laser Doppler flowmetry values. The consistent diurnal pattern measured with laser Doppler would also imply that this method should be precise enough to detect any changes in perfusion caused by electrical stimulation.

The real-time transcutaneous oxygen measurements taken on the lower leg of patients with diabetes are probably not comparable to those taken at the dorsum of the foot. The influence of electrical stimulation might

be different at these two locations. Kjartansson and co-workers, however, stated that electrical stimulation acts through "nerval vasodilatation" (20). The high frequency and the twin-peak properties of the current make the electricity penetrate deep into the tissue. Since the nerves that would cause the vasodilatation are present in both places, it is likely that the effect occurs in both places.

The mechanism of action of electrical stimulation is poorly understood. There are very few studies that describe its mechanism of action or its potential benefit. Kjartansson and co-workers hypothesized that electrical stimulation may improve flap survival through two mechanisms. The first mechanism involved electrical activation of large-diameter sensory nerves, which would inhibit sympathetic vasoconstrictory neuron activity. The other proposed mechanism was an activation of small- to medium-sized sensory neurons to release vasodilatory neurotransmitters (20). Currier reported increased circulation within 1 minute of stimulation. The perfusion remained at a steady level throughout the remainder of the study treatment (21, 22) Lui et al. suggested that the associated vascular changes should be considered systemic events (23).

The characteristics of the current are important parameters of electrical stimulation. Indenbom et al. found that the impedance of the skin for currents under 30 volts is determined by macropores of skin appendages like hair follicles and sweat glands. The impedance of the skin with currents over 30 volts, however, was found to be dependent on the electroporation of the lipid-corneocyte matrix of the outermost layer of the skin (stratum corneum) (24). The voltage used in our study was 50 volts. This could lead to the conclusion that the impedance of the skin was not dependent on the adnexa of the skin, but on the lipid membranes of the stratum corneum. Other factors that affect the resistance of the skin are position of the subject and electrode placement. Supine position of the subject and a greater distance between the electrode increases the impedance (25). Eating a large meal and cleaning the skin with alcohol also increases the impedance of the skin (25). Since there are many factors that have influence on the skin resistance, it was not possible for us to accurately assess the current.

The current applied in this study was subsensory and did not lead to any muscle contractions. Loubser et al. used electrical stimulation of nerves to produce muscle contractions (26). They found that the stimulation caused increased photoplethysmographic waveform amplitude and pedal skin temperature. Since the current used in our study did not lead to muscle contractions, it is uncertain if the results Loubser et al. reported are comparable to ours.

Diabetics with poor skin perfusion seem to benefit most from electrical stimulation. Patients with foot ulcers would

benefit most from the possibility to increase the perfusion of the foot. We conclude that electrical stimulation might serve as a valuable adjunct in the prevention of both ulceration and limb loss. These preliminary data suggest a rationale for further clinical trials to evaluate the effect of different levels of electrical stimulation on both peripheral perfusion and wound healing.

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