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Effects of vacuum-compression therapy on healing of diabetic foot ulcers: Randomized controlled trial

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Abstract—A single-blind, randomized controlled trial was conducted to evaluate vacuum-compression therapy (VCT) for the healing of diabetic foot ulcers. Eighteen diabetic patients with foot ulcers were recruited through simple nonprobability sampling. Subjects were randomly assigned to either an experimental or a control group. Before and after intervention, the foot ulcer surface area was estimated stereologically, based on Cavalieri's principle. The experimental group was treated with VCT in addition to conventional therapy for 10 sessions. The control group received only conventional therapy, including debridement, blood glucose control agents, systemic antibiotics, wound cleaning with normal saline, offloading (pressure relief), and daily wound dressings. The mean foot ulcer surface area decreased from 46.88 +/– 9.28 mm^2 to 35.09 +/– 4.09 mm^2 in the experimental group (p = 0.006) and from 46.62 +/– 10.03 mm^2 to 42.89 +/– 8.1 mm^2 in the control group (p = 0.01). After treatment, the experimental group significantly improved in measures of foot ulcer surface area compared with the control group (p = 0.024). VCT enhances diabetic foot ulcer healing when combined with appropriate wound care.

Clinical Trial Registration: ClinicalTrials.gov, NCT00477022, <http://www.diabetes.org>.

Key words: Cavalieri's principle, conventional therapy, diabetic foot ulcer, healing, randomized controlled trial, rehabilitation, stereology, ulcer area, vasotrain, VCT.

INTRODUCTION

Diabetic foot ulcers are common and serious complications of chronic diabetes mellitus [1]. The prevalence of foot ulcers among patients with diabetes is 15 percent [2]. Hospital stays are approximately 60 percent longer among patients with foot ulcers compared with those without ulcers [3].

Diabetic foot ulcers accounts for >50 percent of all nontraumatic lower-leg amputations [4]. Peripheral neuropathy and vascular insufficiency lead to foot ulceration. Diabetes also affects the flow of blood. Generally, poor circulation to the skin can lead to ulcers and infections. These wounds heal slowly or not at all, and amputation of the foot or part of the leg may be needed [3,5]. Effective prevention practices and appropriate interventions should decrease the incidence of foot complications and thereby reduce hospitalizations and lower-limb amputations among individuals with diabetes.

Abbreviations: CE = coefficient of error, IPC = intermittent pneumatic compression, VCT = vacuum-compression therapy.

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The effects of vacuum-compression therapy (VCT) on the healing of ischemic ulcers have been studied. This procedure involves the Vasotrain-447 (Enraf-Nonius, Rotterdam, the Netherlands), a machine with cycles of vacuum and subsequent compression to increase capillary filling. Use of the machine enhances the delivery of oxygen and nutrients to the wound, which, in turn, facilitates healing [6].

Although current preventive methods and treatment modalities effectively heal foot ulcers, statistics show a high incidence of foot ulcers and amputations in individuals with diabetes [2,4]. Closure of the wound is hampered by both physiological impairments in wound healing and an increased susceptibility to wound infection [3,5,7–8]. Therefore, if impairments are prevented and proper intervention achieved, healing should accelerate and the prevalence of amputations should decrease. On the other hand, only a few studies have examined the effects of the Vasotrain-447 in healing diabetic foot ulcers. Thus, we evaluated the impact of VCT with the Vasotrain-447 on diabetic foot ulcers using the stereological method based on Cavalieri's principle. We hypothesized that the diabetic foot ulcer surface area would decrease from the vacuum-compression effects of the Vasotrain-447.

METHODS

Participants

We recruited 18 subjects with diabetic foot ulcers by performing simple nonprobability sampling and approaching the consultant physician. Patients were selected based on the following inclusion criteria: a diabetic foot ulcer corresponding to grade 2 of the University of Texas Diabetic Foot Wound Classification System (wound penetrating to tendon or capsule, not involving bone or joint) [9–10], no history of deep venous thrombosis, and no hemorrhage in ulcer. Subjects were excluded if they had significant loss of protective sensation, hemorrhage, or vertigo or had not completed their treatment. We assessed sensory status using a biothesiometer (Bio-Medical Instrument Company, Newbury, Ohio) and by applying a Semmes-Weinstein 10 g monofilament (Touch-Test Sensory Evaluator, North Coast Medical, Inc, Morgan Hill, California) to the plantar surface of the foot. Subjects who were unable to detect the monofilament on the plantar surface of the foot or who had a vibrator perception threshold of more than 25 V as measured with a biothesiometer were considered to have a significant loss of protective sensation [10–11]. This single-blind randomized controlled trial was conducted at the Department of Physiotherapy, Razmejo-Moghadam Outpatient Clinic, Zahedan University of Medical Sciences, Zahedan, Iran, in 2006. The purpose of the study and the testing protocol to be used were explained to the subjects. The local ethical committee approved the study, and all patients gave their written voluntary informed consent before participation.

Procedures

We administered a brief questionnaire to obtain each subject's medical history. Subjects were questioned regarding the history of their disease, type of diabetes, duration of diabetes, and site of ulcer. Patients were randomly assigned through a computerized randomization schedule to either an experimental or a control group. Patients were randomized and assigned to their groups after the initial screening. Neither participants nor research staff administrating the interventions or assessing the outcomes were blinded to group assignment. However, to avoid bias, a technician blinded to the group allocation performed all tracings and area determinations in both pretreatment and posttreatment stages.

Ulcer Surface Area Measurements

Ulcer surface area can be estimated by either (1) point grid overlays or (2) boundary contour tracings. Contour tracing obviously appears more accurate because it provides a direct measurement of the area, while point counting provides an estimate of the area. The advantage of point counting is that it does not require much time. Several studies have shown that point-counting techniques are a more reliable and efficient than planimetric techniques for obtaining the required surface area of ulcers [12–13]. Point counting is very commonly used in stereology for unbiased area and volume estimation [14], where counts are made of randomly overlaid lattice points that fall within a closed area. An unbiased estimator of surface area (A) is

$$A = P \times A(p) \ , \qquad (1)$$

where $A(p)$ is the area associated with one point in the grid and P is the number of test points hitting the ulcer shape on the transparent sheet [14–15].

In this research, we estimated before and after treatment the foot ulcer surface area stereologically using the regular point-counting grid method based on Cavalieri's principle [14–15]. The outer margins of the ulcers were traced on a transparent sheet and the ulcers were cleaned with normal saline and debrided when necessary. We used the point-counting grid with some point sets at distinct densities on a transparent sheet to estimate the surface area of the ulcers [16–19]. A test point is two intersecting lines (+) that is said to hit the object if the quadrant of space in the upper right-hand corner of the intersecting lines lies inside the object. We used this square grid test system with 0.5 cm between test points—i.e., $A/p = 0.25$ cm^2 representing area per point—to estimate the surface area of the ulcer. We superimposed the test system on the samples of ulcer shapes and counted the number of points hitting the ulcer shape. Superimposing of the test system was performed one time for each ulcer shape.

Gundersen and Jensen developed a well-known coefficient of error (CE) prediction formula for the Cavalieri estimation method [14]. The new formula not only provides the CE of the test system but also gives information on the density of the point-counting grid. We estimated the CE using Gundersen and Jensen's consecutive formula [14]:

$$\mathrm{CE} = \sqrt{[3(A - \sum P_i) + C - 4B/12]/\sum P_i} \ , \quad (2)$$

where

$$A = \sum P_i^2 \ ,$$

$$B = \sum (P_i \cdot P_i + 1) \ , \text{ and}$$

$$C = \sum (P_i \cdot P_i + 2) \ .$$

P_i is the number of points that hit the ulcer shape on the transparent sheet. If the CE was less than 10 percent, it was used as a reference for all samples [14].

Intervention

In addition to the conventional therapy to be described later, the experimental group received VCT 1 hour a day, 4 times a week, for 10 sessions (a total of 12 sessions during 3 weeks; the first and last sessions were considered for evaluation only). The VCT was produced with the Vasotrain-447, which can produce both positive and negative pressure. Both negative and positive pressures have been intermittently used in vascular reeducations [20]. However, because of the circulation impairments in diabetic foot ulcers, both parameters of the negative phase—i.e., pressure and duration—were set higher than the parameters of the positive phase [21]. The involved lower limb was placed into the Vasotrain-447, which is cylindrically shaped. The proximal part of the cylinder was fixed around the midpart of the thigh with a rubber balloon. The machine was set for vascular disease. Treatment was performed with the following parameters: –0.10 bar (–75 mmHg) of negative pressure for 60 s, followed by 0.05 bar (38.5 mmHg) of positive pressure for 30 s. Importantly, the positive pressure of 38.5 mmHg is the minimum pressure. The parameters just mentioned were determined according to disease, patient tolerance and comfort, and factory-recommended settings for the Vasotrain-447. The control group received only the conventional therapy, which included debridement, blood glucose control agents, systemic antibiotics, wound cleaning with normal saline, offloading (pressure relief), and daily wound dressings. All patients were instructed to use an ankle-foot cast splint for pressure redistribution at all times during ambulation.

Statistics

Data were analyzed statistically using SPSS 11 (SPSS Inc, Chicago, Illinois). Kolmogorov-Smirnov test for normality was performed for all outcome variables. Levene's test was used for equality of variances. Independent and paired *t*-tests were used for comparison between pretreatment and posttreatment test results between groups and within groups, respectively. A *p*-value >0.05 was accepted as being statistically different. All data are presented as mean ± standard deviation.

RESULTS

A total of 20 patients met the inclusion/exclusion criteria, but only 18 were actually enrolled in the study. Nine patients (nonsmokers, seven females and two males) received VCT in addition to conventional therapy and nine patients (nonsmokers, eight females and one male) received conventional treatment. Two patients (one in each group) did not complete their treatment sessions. The mean age of the experimental group was 58.2 ± 8.07 and that of the control group was 57.6 ± 8.02. Mean ulcer duration was 45 ± 6.7 days for the two groups. The body mass index in both groups was 23.44 ± 3.7. Both groups received their protocol for 10 treatment sessions, and the measurements were repeated. No adverse events or side effects were reported in either intervention group during the study.

The mean ulcer surface area was compared between and within the two groups to determine the effects of both treatment protocols, VCT and conventional therapy. The interventions decreased foot ulcer surface areas from 46.88 ± 9.28 mm^2 to 35.09 ± 4.09 mm^2 in the experimental group (p = 0.006) and from 46.62 ± 10.03 mm^2 to 42.89 ± 8.1 mm^2 in the control group (p = 0.01). The frequency of foot ulcer improvement in the experimental and control groups was 5/9 and 1/9, respectively ($p < 0.05$).

The differences between pretreatment and posttreatment measurements were calculated as the improvement ratio in both groups. The improvement ratio between two groups was then compared. These ratios in the experimental and control groups were –11.79 ± 9.54 mm^2 and –3.73 ± 3.14 mm^2, respectively. Therefore, the mean foot ulcer surface area significantly decreased in the experimental group compared with the control group (p = 0. 03).

Before treatment, the mean foot ulcer surface areas in the experimental and control groups were 46.88 ± 9.28 mm^2 and 46.62 ± 10.03 mm^2, respectively. An independent-samples *t*-test identified the difference between the experimental and control groups as not significant (p = 0.95). Therefore, both groups were matched in terms of foot ulcer surface area. However, after treatment, the mean foot ulcer surface area significantly decreased in the experimental group compared with the control group (p = 0.024). Surface areas after treatment were 35.09 ± 4.09 mm^2 and 42.89 ± 8.1 mm^2 in the experimental and control groups, respectively.

Subject age was not significantly correlated with improvement ratio in either the experimental (p = 0.80) or control group (p = 0.42).

DISCUSSION

The findings showed that foot ulcer surface area decreased after 10 VCT sessions with the Vasotrain-447. Foot ulcer surface area also decreased following 10 sessions of conventional therapy. Comparisons of the improvement ratio and the mean ulcer surface area after treatment showed a significant decrease in surface area in the experimental group compared with the control group. The major finding was that adding alternating VCT to conventional therapy increased the healing effects of conventional therapy. The improvement ratio of foot ulcer surface area in the experimental VCT group was greater than the improvement ratio in the conventional therapy control group.

The majority of recent research has shown that one of the most common problems in diabetic patients is delayed wound repair due to vascular insufficiency and decreased blood flow [7–8,22]. Some researchers state that healing of a diabetic foot ulcer may be delayed or prevented for many reasons, including chronic inflammation, infection, sensory neuropathy, motor disorders of the foot, edema, and high levels of glucose in the ulcer area in addition to vascular insufficiency [3,7–8,22]. In other words, the same significant inhibitors of diabetic foot wound healing were identified in different studies. In spite of the many different methods used in these studies, the common finding on diabetic foot ulcer treatment is that establishing appropriate circulation in limb and regional tissues is critical. Therefore, any factor that improves blood flow in the limb helps repair the ulcer [2,5,23]. Researchers believe that VCT systems do improve total tissue blood flow and oxygenation. These systems increase periwound perfusion and consequently accelerate wound healing by producing alternating positive and negative pressure [6,24–29].

Many researchers have focused on alternating positive and negative pressure to accelerate the healing process in a diabetic foot ulcer. Different methods, such as negative pressure wound dressings [25–26], VCT [6], intermittent pneumatic compression (IPC) [27], and high-voltage pulsed current [30], have been recommended. In recent decades, the role of vacuum systems in improving tissue circulation and wound healing has been emphasized and the use of negative-pressure wound dressings for treatment of ischemic ulcers has been highly recommended. Eginton et al. reported that vacuum-assisted closure dressings decreased wound depth and volume more effectively than moist gauze dressings. Negative-pressure wound treatment may accelerate closure of large foot wounds in the diabetic patient [25]. Carson et al. also found that vacuum-assisted closure in addition to a protocol of general supportive and local wound care resulted in a high rate of closure [31]. However, Herscovici et al. showed that while vacuum-assisted closure did not eliminate the need for formal debridement of necrotic tissue, it might help avoid free tissue transfer in some patients with large traumatic wounds [26].

Our study was based on recent research evidence that increasing limb and ulcer area blood flow was possible through the application of negative pressure. Our findings were similar to some studies [6,28] and in contrast with others [24,29]. We showed that the VCT (with the parameters mentioned previously) is an important factor in diabetic foot ulcer repair. In accordance with our results, McCulloch and Kemper showed that VCT effectively promotes capillary filling [6]. Increased capillary filling is a primary factor in improved healing. Traditional teaching assumes that the distal arterial tree is maximally dilated in patients with critical limb ischemia. Endovascular or arterial bypass procedures are commonly used to increase distal perfusion. However, treatment such as spinal cord stimulation or IPC has been shown to improve limb salvage rates [27]. IPC increases blood flow in patients with critical limb ischemia and may benefit those who are not candidates for revascularization. Abu-Own et al. reported that the venous pump of the foot helps blood return to the heart [32]. They found that intermittent pneumatic compression of the foot in the sitting position increases the laser Doppler flux and transcutaneous oxygen tension. Unlike other physiotherapy modalities, the Vasotrain-447 can apply both positive and negative pressure, with cycles of vacuum and subsequent compression to increase capillary filling. The durations of the positive and negative pressures are set according to the type of lesion. In our study, we used a long-duration negative pressure, since negative pressure, with its vacuum property in vascular disorders, is one of the most effective treatments [21]. The results showed that the vacuum effects produced with the Vasotrain-447 facilitated wound healing, presumably by enhancing the delivery of oxygen and nutrients to the area.

The result of our study was in line with other research that produced the negative pressure with different methods. Ours was the second study to use negative and positive pressure of the Vasotrain-447, emphasizing the negative pressure, for diabetic foot ulcer treatment. In any case, our study differed from prior studies in the duration of the negative pressure phase [6].

CONCLUSIONS

Our results showed that VCT with conventional therapy more effectively healed diabetic foot ulcers than conventional therapy alone. VCT effectively prompted capillary filling and therefore helped patients with arterial circulation problems. Thus, for wound healing and limb preservation, we recommend VCT, in addition to conventional therapy, for patients with diabetic foot ulcers and nonhealing wounds.

However, further studies are necessary for evaluation of the effects of VCT on other variables, such as hemoglobin A1c. Hemoglobin A1c, a measure of the amount of glucose bound to the hemoglobin A molecule, is probably the most readily recognized example of hyperglycosylation in diabetes. Hemoglobin A1c is used to measure blood glucose control during an extended period (e.g., several weeks). The higher the blood glucose level, the higher the bound glucose and the hemoglobin A1c value.

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