Value of combined exercise and ultrasound as an adjunct to compression therapy in chronic venous leg ulcers

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Introduction
Chronic venous leg ulcers are very difficult to treat and take very long time to heal. Compression therapy remains the mainstay of venous ulcer conservative treatment.
Aim
The aim of this study was to evaluate the effectiveness of combined therapeutic exercises and ultrasound as an adjunct to compression therapy for the treatment of chronic venous leg ulcers.
Settings and design
This study is a prospective randomized case-controlled one.
Patients and methods
Seventy-two patients with chronic venous leg ulcers were recruited from outpatient clinics. We allocated patients to four groups of 15 patients each. Group I was treated with therapeutic exercise program in addition to compression therapy. Group II was treated with underwater ultrasound and compression therapy. Group III was treated with therapeutic exercises as in group I and underwater ultrasound as in group II, in addition to compression therapy. Group IV was treated with compression therapy. The duration of follow-up was 12 weeks. Treatment outcome was assessed using the visual analogue scale for pain, ulcer size, the pressure ulcer scale for healing, maximum ankle dorsiflexion and plantar flexion using a plastic goniometer.
Results
Venous ulcer healing was greatest in patients receiving combined exercise and ultrasound in addition to compression therapy. Combined therapeutic exercises and ultrasound were well tolerated and no adverse reactions were noted. Patients receiving therapeutic exercises alone or ultrasound alone showed lesser degrees of improvements. No significant improvements were observed in any variable in patients who received compression therapy alone.
Conclusion
Combined prescription of exercises and ultrasound as an adjunct to compression therapy would be a more effective means of promoting chronic venous ulcer healing, when standard compression therapy have failed. It is safe, easy and well tolerated and should be considered as adjunctive therapy in patients with venous leg ulcers.

Keywords:
exercise, ultrasound, venous leg ulcers

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Introduction

Venous leg ulcers are the most common cause of leg ulcer, affecting 1% of the population [1,2]. This chronic condition represents the most prevalent form of difficult-to-heal ulcers [3,4].

At present, compression therapy remains the mainstay of venous ulcer conservative treatment [3,4]; however, up to 15–30% do not respond to treatment [5]. The duration of treatment may last a year or even decades [6,7], suggesting that adjunct treatments are necessary to speed healing of chronic venous ulcers.

Ankle joint mobility and calf muscle activity are the two components of calf muscle pump that promote venous return in adjacent veins [8]. Venous insufficiency impacts ankle mobility and lower limb musculature [9]. Limited ankle mobility has been associated with ineffective calf muscle pumping and venous ulceration [10–12]. Lower limb exercises have been shown to improve ankle mobility, calf muscle pump, lower limb haemodynamic and subsequently ulcer healing [11,13]. However, a recent review concluded that further study is required to determine the effect of therapeutic exercises on venous ulcer healing [14].

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Ultrasonic therapy is used for the treatment of chronic wounds, including venous leg ulcer [15,16]. Ultrasound delivered in a water bath has been used for ulcer debridement [16] and granulation tissue formation [17]. However, treatment of venous leg ulcers with therapeutic exercises or ultrasound has received mixed results [18–22].

In the light of this background evidence, we hypothesized that the synergistic effect of therapeutic exercises and ultrasound is possible and may facilitate healing of chronic venous ulcers. Studies using combined therapeutic exercises and ultrasound were not previously reported to our knowledge.

The aim of this study was to evaluate the effectiveness of combined therapeutic exercises and ultrasound as an adjunct to compression therapy for the treatment of chronic venous leg ulcers that had failed to respond to standard compression regimens.

Patients and methods

This study was designed as a randomized, prospective, controlled clinical trial to evaluate the additional value of therapeutic exercises and ultrasound as an adjunctive treatment for chronic venous leg ulcers. Between September 2013 and January 2015, 72 patients with chronic venous leg ulcers [23] were recruited from the outpatient clinics of Vascular Surgery Department and Physical Medicine, Rheumatology and Rehabilitation Department, Mansoura University Hospital, and enrolled in this study. Patient with ulcer that did not show signs of healing for at least the previous 12 weeks of compression therapy [24] and those who were able to tolerate compression and exercise therapy were included in the study. The exclusion criteria were as follows: bleeding disorders, thrombophlebitis, vasculitis, absence of pedal pulsations, cellulitis, arthritis, diabetes and sensory neuropathy.

To determine the sample size, the results from Escandon *et al.* [16] were used, in which more than 30% reduction in venous ulcer size was observed after 12 weeks of ultrasonic therapy. In the light of this study, 30% improvement was considered to be nonsignificant and was calculated with a sample size of 60 participants to detect improvement in healing at 90% power with an α value of 0.05 [25].

We allocated patients to four groups and had 60 envelopes, each containing a piece of paper marked with either group I, II, III or IV. Patients were randomized using the closed envelope method. All patients in the four groups were subjected to compression therapy using elastic multilayer dressing compression using a spiral technique from the base of the toe to just below the tibial plateau, to be changed every week. The bandage assists the calf muscle pumping action and increases the venous blood returning to the heart [3].

Group I included 15 patients (eight female and seven male). They were treated with therapeutic exercise program in addition to compression therapy. The exercise program was designed to improve ankle mobility and calf muscle pump to promote venous return. The program consisted of the following: warm-up with range of motion exercises and ankle circling, and plantar flexion of the ankle using elastic resistance bands with handle attachments. Patients completed this exercise in a seated position, with the knee straight. Holding the handles, the patients placed the band around the ball of the foot and stretched the band to achieve moderate resistance. They performed 15 plantar flexions, gradually increasing to 25. Dorsiflexion of the ankle was performed in seated and standing positions. Patients performed 30 dorsiflexion, gradually increasing to 75 [25,26]. Group II included 15 patients (eight female and seven male). They were treated with underwater ultrasound and compression therapy. The method of application was performed in water bath with a temperature of 34°C. The ultrasound beam was generated using Sonostat 733 (Siemens, Germany) apparatus. The ultrasound power density was 0.5 w/cm, the duty cycle 1 : 4 and frequency 1 MHz. The ultrasound transducer had an effective insonation area of 4 cm [2]. Both the transducer and the part to be treated were placed in a large glass vessel filled with degassed water. Any air bubbles clinging to or arising at the skin or transducer must be removed with the aid of a soft brush. The transducer was then moved over the ulcer in a circular motion, with a distance of 1 cm between the transducer and ulcer [27]. An ulcer of 5 cm^2 or less was exposed for 5 min. For every ulcer 1 cm^2 in excess, the time was increased by 1 min. The bath was emptied and cleaned after every treatment. The procedures were performed every other day. Dressing was removed for the duration of the procedure and reapplied immediately afterward [28]. Group III included 15 patients (seven female and eight male). They were treated with therapeutic exercises as in group I and underwater ultrasound as in group II, in addition to compression therapy. Group IV included 15 patients (nine female and six male). They were only treated with compression therapy. Therapeutic exercises and ultrasound were performed for 15 min, every other day for 12 weeks, for a total of 36 sessions. The 12-week duration was chosen on the basis of a mean ulcer healing time of 11 weeks for patients receiving venous ulcer therapy [29].

Patients were subjected to the following: complete history, physical examination and appropriate blood tests when indicated. Assessment of the treatment outcome was based on the parameters measured at the start and after 12 weeks of treatment. Pain was assessed using visual analogue scale: 0=no pain and 10=worst pain [16]. Ulcer size (in cm^2) was calculated by multiplying the maximum width and length of the ulcer (perpendicular to each other) [30]. The pressure ulcer scale for healing (PUSH) was used to assess venous ulcer healing using the following parameters: ulcer size, exudate and ulcer tissue type (necrotic tissue, slough, granulation tissue, epithelial tissue and closed). The final PUSH score ranges from 17 (most severe) to 0 (healed). It is an excellent, reliable, valid and practical tool for evaluating venous ulcer healing [31,32]. The ulcer was accepted as healed when all scabs were removed to reveal the intact underlying skin with no exudate [24]. Maximum ankle dorsiflexion and plantar flexion were assessed using a plastic goniometer [20].

Statistical analysis

Statistical tests were conducted with SPSS (version 10; SPSS Inc., Chicago, Illinois, USA), with significant level at P less than 0.05. The results were expressed as mean±SD and range. Analysis of variance combined with the post-hoc test was used to check comparability of the baseline characteristics of the four groups. The independent sample t-test was used to detect the degree of improvement after treatment.

Results

Demographic and ulcer characteristics as well as ankle dorsiflexion and plantar flexion of participants enrolled in this study were similar at baseline, with no statistical differences between groups in any of these variables (Table 1).

Venous ulcer healing was greatest in patients receiving combined exercise and ultrasound in addition to compression therapy. They demonstrated a highly significant reduction in ulcer size ($P<0.001$), a highly significant improvement in PUSH score (ulcer size, exudate, epithelial tissue, granulation tissue, slough and necrotic tissue) ($P<0.001$), a highly significant improvement in ankle dorsiflexion and plantar flexion ($P<0.001$), and a highly significant improvement in pain ($P<0.001$) (Table 2). Complete healing was observed in seven ulcers in the combined exercise and ultrasound group, whereas none of the ulcers in the other groups healed completely after 12 weeks of treatment.

Combined therapeutic exercises and ultrasound were well tolerated and no adverse reactions were noted. Patients receiving therapeutic exercises alone or ultrasound alone showed lesser degrees of improvements (Table 2). No significant improvements were observed in any variable in patients who received compression therapy alone (Table 2) (Fig. 1).

Discussion

Venous leg ulcers are prone to complications and resistant to therapy [2,33]. In the last years, adjunctive therapy has been tested resulting in no improvements [11,18,28], promoting this study. Chuang and colleagues compared ultrasound therapy with standard care and standard care only. After 12 weeks, ultrasound provided no extra benefit and was more costly. Taradaj and colleagues compared

Table 1 Baseline demographic variables, ulcer characteristics, ankle dorsiflexion and plantar flexion (n=15)

Characteristics	Group I	Group II	Group III	Group IV
Sex (male/female)	7/8	7/8	8/7	6/9
Age (mean±SD)	51.2±6.5	52.1±6.9	50.9±7.1	51.3±6.8
Range (years)	42–63	40–64	40–63	41–62
BMI (mean±SD)	30.5±4.2	29.6±3.9	28.9±4.1	30.1±4.5
Range	27–32	28–31	26–33	29–30
Ulcer duration (mean±SD)	15.5±1.8	16.3±1.9	14.1±1.7	15.1±1.9
Range (months)	13–19	12–20	11–21	14–22
Ulcer size (cm^2) (mean±SD)	12.9±5.7	13.2±5.1	13.7±5.4	14.1±5.2
Range	5.9–23.4	6.5–21.3	6.1–20.6	5.9–23.2
PUSH score (mean±SD)	9.7±2.5	10.4±3.1	9.6±2.9	10.1±3.2
Range	8–14	7–15	9–13	7–13
ADF (mean±SD)	11.3±3.9	12.4±3.4	11.4±3.7	12.6±3.6
Range	7–19	8–21	9–20	10–20
APF (mean±SD)	15.6±5.6	16.1±5.8	15.9±5.7	15.8±5.9
Range	12–30	11–30	14–28	15–29
Pain score (mean±SD)	4.1±1.6	4.2±1.4	3.9±1.5	3.8±1.6
Range	2–6	3–6	2–5	3–5

ADF, degree of ankle dorsiflexion; APF, degree of ankle plantar flexion.

Table 2 Ulcer characteristics, ankle dorsiflexion and plantar flexion before and after treatment

	Group I	Group II	Group III	Group IV
Ulcer size (cm^2)				
Before treatment	12.9±5.7	13.2±5.1	13.7±5.4	14.1±5.2
After treatment	8.8±3.8	9.8±3.5	7.1±4.2	13.9±5.1
P	0.028	0.042	<0.001	0.916
PUSH score				
Before treatment	9.7±2.5	10.4±3.1	9.6±2.9	10.1±3.2
After treatment	7.8±1.7	7.9±1.9	6.5±1.3	9.8±3.1
P	0.022	0.013	<0.001	0.796
Ankle dorsiflexion (deg.)				
Before treatment	11.3±3.9	12.5±2.8	11.4±3.7	12.6±3.6
After treatment	14.1±2.1	14.4±1.9	15.5±1.9	12.9±3.5
P	0.025	0.038	<0.001	0.819
Ankle plantar flexion (deg.)				
Before treatment	15.6±5.6	16.1±5.8	15.9±5.7	15.8±5.9
After treatment	19.7±3.2	19.9±3.9	22.7±3.5	16.9±6.1
P	0.020	0.044	<0.001	0.620
Pain score				
Before treatment	4.1±1.6	4.2±1.4	3.9±1.5	3.8±1.6
After treatment	2.8±1.1	3.1±1.2	1.9±1.2	3.6±1.7
P	0.015	0.028	<0.001	0.743

ADF, degree of ankle dorsiflexion; APF; degree of ankle plantar flexion; PUSH score, pressure ulcer scale for healing score. Level of significance ($P<0.05$).

Figure 1

Pictures of ulcer before and after therapy.

many modalities: high-voltage stimulation and drug, ultrasound and drug, low-level laser therapy and drug, compression therapy and drug, and drug therapy alone. All studies were performed in operated and nonoperated patients. The results showed that compression therapy was the best, high-voltage stimulation and ultrasound were less effective, and laser therapy was useless. Jull and colleagues used progressive resistance exercise programme using heel raises for 12 weeks plus compression, whereas the control group used usual care plus compression. The parameters of assessment did not increase significantly in the exercise group.

Although there were no controls in this study, it is reasonable to assume that each patient served as her or his own control, as the mean duration of their respective venous leg was over 14 months. These patients failed to respond to compression therapy of at least 12 weeks and benefitted from combined exercise and ultrasound; therefore, it appears to be better than that achieved with compression therapy alone. This study demonstrated that combined exercise and ultrasound adjunctive therapy was the most effective treatment for chronic venous leg ulcers. It showed a highly significant improvement in ulcer size; PUSH score, in addition to complete healing of seven venous leg ulcers while there was no complete ulcer healing in the other groups.

A cornerstone of chronic venous ulcer management is the guidelines recommended by Wound Bed Advisory

Board Members, The Society for Vascular Surgery and the American Venous Forum. These guidelines include the following: debridement and removal of necrotic tissue and slough, moist wound environment and activation of epithelial tissue from the ulcer edge, and applying elastic compression therapy to promote venous return [34,35]. These guidelines are the base of our approach of adding therapeutic exercises and ultrasound to compression therapy for the treatment of chronic venous leg ulcer. The exercise program improves the following: microvascular endothelial function [36], haemodynamic performance [37], calf muscle pump and venous return to the heart [25], thereby promoting healing of chronic venous ulcers.

Furthermore, application of ultrasound produces a number of biological effects that stimulates the healing process of venous ulcers: fibroblast proliferation [38], fibrinolysis [39], protein synthesis [40], formation of granulation tissue and revascularization [24] and increased cell proliferation [21]. Ultrasonic therapy has been used for debriding and cleansing of ulcer's devitalized tissue, fibrin and bacteria with promising results [16,41,42]. The presence of devitalized tissue and fibrin has been reported to inhibit epithelial cell migration across the ulcer surface [43]. Many of the published articles demonstrated that therapeutic ultrasound significantly accelerates the healing process of venous leg ulcers [16,44,42].

The present study reported a highly significant reduction in pain in patients with venous ulcer treated with ultrasound. This reduction in pain is consistent with the finding of Escandon and colleagues [16,22,27,39]. In the combined therapeutic exercise and ultrasound group, patients reported zero or mild pain (1.9±1.2 visual analogue scale) after 12 weeks of treatment.

Patients with chronic leg ulcers had reduced ankle dorsiflexion and plantar flexion. Our study is in accordance with prior studies and led to the hypothesis that chronic leg ulcers are associated with poor range of ankle motion [8,45,46]. Ankle mobility is required to effectively pump the calf muscle to squeeze the veins and empty the vessels to return blood from the lower limbs to the heart [47]. Ankle mobility may be compromised by pain, oedema, muscle weakness, abnormal gait and compression bandaging [20,48]. As reduced ankle mobility leads to decreased activation of the calf muscle pump, this may attribute to venous insufficiency, ulcer formation and reduced healing outcomes in patients with chronic venous ulcers [9]. In the current study, patients who received combined exercises and ultrasound therapy showed a more significant improvement in ankle dorsiflexion and plantar flexion compared with the exercise or the ultrasound group, whereas there was no significant change in the group receiving compression therapy alone. Exercise training that targets on improvement in the ankle mobility and calf pump function was a useful adjunct therapy for enhancing chronic venous ulcer healing. Davis and colleagues and Yim and colleagues demonstrated a significant improvement in ankle mobility after 12 weeks of exercises.

The limitations of our study were as follows: no follow-up of the participants for additional period after completion of treatment and assessment of treatment outcomes for possible ulcer recurrence. The outcome of assessment was unblended. We did not examine factors that may affect vascularity and ulcer healing, such as cholesterol, smoking, oedema, quality of life and muscle power grading (due to pain and limited range of motion).

We recommend longer post-treatment patients' follow-up in further studies with larger sample size. Further studies need to be conducted on patients with different chronic wound aetiologies to determine the effect of these physical modalities on healing of these types of chronic wounds. We also suggest that combined exercise and ultrasound adjunctive therapy may not be reserved for the recalcitrant ulcer, but rather may be thought as valuable options early in the venous ulcer treatment strategy.

Conclusion

Combined prescription of exercises and ultrasound as an adjunct to compression therapy would be a more effective means of promoting chronic venous ulcer healing, when standard compression therapy has failed. It is safe, easy and well tolerated and should be considered as adjunctive therapy in patients with venous leg ulcers.

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Conflicts of interest

There are no conflicts of interest.

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