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Research Article

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Anodyne therapy versus exercise therapy in improving the healing rates of venous leg ulcer

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ABSTRACT

Objective: The purpose of this study was to determine the best physical therapy program to increase wound healing rates in patients suffering from venous leg ulcer.
Methods: Forty patients who had venous leg ulcer for more than 4 weeks and not respondent well to medical treatment. Patients were classified into 4 equal groups 10 of each, Group (1): received 40 minute of monochromatic infrared energy (MIRE), Group (2): received 40 minutes of exercise program consisted of stretching and resisted exercise (RE), Group (3): received 20 minutes of exercise in addition to 20 minutes of resisted exercise (MIRE/RE), and group (4): control group which received conventional therapy of the ulcer. All groups received treatment 5days per week for 12days. Measurements of ulcer surface area and PUSH scale were conducted before treatment, post 6 days of treatment, and after 12 days of treatment.
Results: The one way analysis of variance was used to compare ulcer surface area and PUSH score which revealed that both treatment groups (MIRE and RE) had significant ($P< 0.05$) decrease in ulcer surface area and PUSH scale after 6 and 12days post application of treatment. On the other hand, the combination of MIRE and RE showed a highly significant decrease in ulcer surface area and PUSH score when compared with control or with individual treatment.
Conclusion: The results of this study suggest that combination of MIRE to RE is more effective than individual treatment to enhance the healing rate of venous ulcer of the leg.

Keywords: Venous ulcer, Monochromatic Infrared energy, Exercise

INTRODUCTION

Leg ulcers are a major health concern in the older population[1], affecting 1-3 % of the population aged over 60 years.[2,3] leg ulcers can take years to heal and profoundly impact the mental and social well being of the individual.[3] approximately 1 % of the total health care costs in the western world are likely to be used for management of chronic leg ulcers.[4]

A venous leg ulcer is the result of sustained venous hypertension associated with chronic venous insufficiency[5] which is believed to be caused by varying combinations of venous reflux, venous obstruction, and a poor functioning calf muscle pump.[6] Failure of the calf muscle pump to effectively promote venous return leads to abnormality high venous ankle pressures and produces evidence of chronic venous disease; leg ulcers are the end result of this process.[7]

Studies have found that the presence of venous insufficiency and subsequent venous hypertension may lead to calf muscle changes such as muscle fiber atrophy,[8] abnormal gait,[9] and reduced strength and functioning of the calf muscle.[10,11] There is evidence to suggest that exercise does improve calf muscle function in this patient population.[11,12] However, until very recently only one other study[12] has considered if improving the calf muscle pump function results in improved healing rates.

The Anodyne Professional Therapy System is a MIRE device that received marketing clearance from the U.S. Food and Drug Administration (FDA) in 1994 through the 510(k) process. The labeled indication is for "increasing circulation and decreasing pain." MIRE devices have been investigated as a treatment of multiple conditions including cutaneous ulcers, diabetic neuropathy, musculoskeletal and soft tissue injuries, including temporomandibular disorders, tendonitis, capsulitis, and myofascial pain. It delivers monochromatic near infrared energy through therapy arrays, each containing 60 superluminous diodes (890 nanometers, near infrared wave- length). These diode arrays are attached to a control unit that pulses MIRE at 292 times/second.[13]

The therapy arrays are placed in direct contact with the skin to temporarily increase local microcirculation. The ability of photo energy to increase microcirculation, possibly through the release of nitric oxide, has been documented in clinical literature.[14]

All light, visible or invisible, consists of photons. The size or mass of the photons is dependent on the specific wavelength of the light. Target tissues must first absorb light in order to have a biological effect. Additionally, absorption is best achieved when the light is 1) directed perpendicular to the skin, and 2) placed in direct contact with the skin. Moreover, photo energy emitted from a source that produces of a homogenous wavelength is often more effective therapeutically than light composed of several wavelengths.[15]

The purpose of the current study is to investigate the best treatment program in the enhancement of healing of chronic venous ulcer either MIRE or resistance exercise alone or in combination.

METHODS

Research design

A randomized controlled study was undertaken with participants randomly assigned to one of three intervention groups and control group.

The study was conducted at a dedicated clinic within Naser Hospital, Cairo, Egypt for 12 months commencing from June 2011. Patients were referred into the study by their general practitioners (GPs), practice/community nurses or consultants. To confirm eligibility, patients referred to the study underwent a specialist assessment in the vascular unit at the Naser Hospital, Cairo, Egypt. This assessment included a drawing photograph of ulcer, bacterial swab and pain assessment of the ulcer; ankle brachial pressure index (ABPI); blood pressure and mean arterial pressures.

Inclusion criteria specified that the ulcer was venous in origin with diagnosis by clinical examination and ankle brachial plexus index, ABPI $\geq$ 0.80; the current ulcer should not have been previously treated with high compression bandaging; ulcer size was between 1 cm^2 and 20 cm^2 and located between the knee and ankle. The patient's venous ulcer should have demonstrated unsatisfactory healing for at least the previous 4 weeks.

Patients were excluded if they were diabetic or had a co-existing mobility problem, e.g. major joint arthritis, had a body mass index (BMI) of $\geq$35 or ulcer size were greater than 20 cm^2. Ulcer patients who completed the study were age and gender matched.

Group Assignment

Forty patients was recruited into this study and was randomly assigned into four group: Group (1): consisted of 10 patients with venous leg ulcer and received MIRE treatment in addition to conventional venous leg ulcer treatment for 12 days, Group (2) consisted of 10 patients with venous leg ulcer and received resisted exercise (RE) in addition to conventional venous leg ulcer treatment for 12 days, Group (3) consisted of 10 Patients and received both MIRE and RE in addition to conventional venous leg ulcer treatment for 12 days, and lastly Group (4) which served as control group and received conventional venous leg ulcer treatment.

Instrumentations

For evaluation

Digitizer tablet with a stylus pen and cordless mouse (Genius Mouse Pen 8 x 6).

Figure 1: Digitizer stylus pen and cordless mouse (Genius Mouse Pen 8x6).

For treatment

Anodyne Therapy Model 120 for Professionals. Figure 2: Anodyne therapy system is a non invasive, drug – free device that delivers monochromatic infrared energy (MIRE) through infrared light emitting diodes, with a wave length of 890 nm, that are mounted in flexible therapy pads. When the therapy pads were placed in direct contact with the skin, the invasive infrared light, is absorbed by cells in the body and blood vessels begin to dilate, resulting in increased circulation in that area.

Figure 2: Anodyne therapy Model 120.

Procedures

For Evaluation

Measurement of wound surface area by using transparent films (Visitrak Digital Tracing Method) (Smith & Nephew Medical Limited, Hull, England) which enables the measurement of wound surface area and has been validated as a reliable measure of ulcer size with high intra-inter reliability:[16] The patient was positioned in a comfortable position with exposure of the foot. Double sterilized transparent plastic films (Tagaderm) was placed directly flat and attached to the skin around the wound area with avoiding any movement and distortion of the foot. Ulcer margins were traced by the same investigator to establish reliability of measurements. The tracing was taken before, and after two weeks of follow up. Then the traced ulcer margins was converted to a digitizer vector image by using a digitizer tablet and a stylus pen where the traced transparent film was placed flat on the digitizer tablet the stylus delineated the margins of traced wound. The digitized ulcer surface area was calculated by specialized software program (Autovue Professional, Cimmetry Systems, Inc).

Pressure Ulcer Scale (PUSH)

Progress in ulcer healing was also measured using the Pressure Ulcer Scale for Healing (PUSH). The PUSH scale was developed in 1997 and revised by Stotts et al.,[17] and includes three dimensions of ulcer healing, providing a more sensitive measure of healing than examining changes in ulcer area alone. The three subscales cover the area of the ulcer, the amount of exudates (i.e. light, medium and heavy) and the type of tissue (i.e. epithelial, granulating, slough or necrotic), giving a total score ranging from 17. Validation and reliability information has been reported in Stotts et al.[17] and Pompeo.[18]

Treatment Program

A. MIRE program: Each patient of group (1) received five sessions per week for a period of successive 2 weeks. The duration of each session was applied for 40 minutes. The treatment program was applied according to the following procedure: The patient was placed in a comfortable position such as long sitting on the bed. The places on which the electrodes were applied should be cleaned. The electrode pads were wrapped with a clear plastic wrapping to prevent contamination. The pads were placed with direct contact with the ulcer and the cables were connected to the base unit. The device was switched on after completing the treatment session of forty minutes the device was switched off and the pads were removed.

B. RE program: Each patient of group (2) received five sessions per week for a period of successive 2 weeks. The duration of each session was applied for 40 minutes. The treatment program was applied according to the following procedure: The patient was placed in a comfortable position such as long sitting on the bed. Each session of exercise started and ended by passive stretching exercise of the calf muscle to the level of tension but not the level of pain. The total duration of stretching exercise is 20 minutes (10 minutes before resisted exercise, and 10 minutes after resisted exercise). The core exercise is isometric exercise for planter and dorsi- flexor of the ankle which last for 20 minutes.

C. MIRE-RE program: Each patient of group (3) received five sessions per week for a period of successive 2 weeks. The duration of each session was applied for 40 minutes. The treatment program was applied according to the following procedure: MIRE treatment was applied for 20 minutes followed by RE for another 20 minutes as described earlier.

D. Conventional Therapy: Conservative treatment consisted of cleaning the wound with normal saline and applying a paste bandage covered by an elastic diachylon bandage with a pressure of roughly 15-25 mmHg.

Data analysis

This study was a controlled post test experimental design with a control and a three treatment groups. Groups were compared for differences at different time interval,

ANOVA multiple comparisons followed by Tucky Kramer post hoc test was used for comparing differences between 3 treatment groups and control group. The level of significance was set at 0.05 for all statistical tests.

RESULTS

Patients were divided into four groups as described earlier in the material and methods section, there was no significant difference between them regarding age, and the duration of ulcer prior to treatments intervention as showed in Table 1.

Table 1: General characteristics of MIRE, RE, MRE/RE and Control groups.

Group	Sex (M/F)	Age (yr)*	Duration of ulcer (month)*
MIRE group	3/7	60.00±5.07	5.50±1.58
RE group	5/5	58.70±4.11	5.70± 2.35
MIRE/RE group	5/5	59.70±5.43	5.90±1.44
Control group	6/4	60.00±4.94	6.70±1.41

* Mean ± S.D.

Ulcer surface area was measured at specific day intervals as explained in the Table 2 which showed that all treatment interventions used significantly reduced ulcer surface area as compared to control group, similarly all intervention groups showed a significant reduction in ulcer surface area at day 6 and day 12 in comparison with base line measurement at day 1, on the other hand, there was no significant difference between MIRE group and RE group at day 6 and 12, but there was a significant difference between MIRE/RE group and Mire group, RE group, and control group either at day 6 or 12.

Table 2: Comparison of ulcer surface area of MIRE, RE, MRE/RE with Control groups.

Days	Treatment groups			
	Control	MIRE	RE	MIRE/RE
Day 1	11.61± 1.05	12.33± 1.02	11.65± 1.76	11.61± 1.77
Day 6	8.67± $0.60^{B,C,D,\dagger}$	6.59± $0.68^{A,C,D,\dagger}$	6.69± $0.62^{A,B,D,\dagger}$	6.46± $1.76^{A,B,C,\dagger}$
Day 12	7.43± $0.56^{B,C,D,\dagger}$	4.11± $0.96^{A,D,\dagger,\ddagger}$	4.55± $1.14^{A,D,\dagger,\ddagger}$	1.89± $1.72^{A,B,C,\dagger,\ddagger}$

Data were expressed as Means ± SD of 10 venous ulcer patients /group. C; Control group, MIRE; monochromatic infrared energy treated group, RE; resisted exercise treated group, MIRE/RE; monochromatic infrared plus resisted exercise treated group. [A]significantly different versus control group; [B]significantly different versus MIRE group; [C]significantly different versus RE group; [D] significantly different versus MIRE/RE group at $P \leq 0.05$. †significantly different versus Day 1; ‡significantly different versus Day 6; at $P \leq 0.05$. Significance was carried out by One-way ANOVA Tukey-Krammer test.

PUSH score was measured at specific day intervals as explained in the Table 3 which showed that all treatment interventions used significantly reduced in PUSH scale as compared to control group, similarly all intervention groups showed a significant reduction in PUSH scale at day 6 and day 12 in comparison with base line measurement at day 1, on the other hand, there was no significant difference between MIRE group and RE group at day 6 and 12, but there was a significant difference between MIRE/RE group and Mire group, RE group, and control group either at day 6 or 12.

Table 3: Comparison of PUSH score of MIRE, RE, MRE/RE with Control groups.

Days	Treatment groups			
	Control	MIRE	RE	MIRE/RE
Day 1	13.70± 1.16	13.20± 1.22	12.70± 1.25	12.60± 0.84
Day 6	8.67± $0.60^{B,C,D,\dagger}$	6.59± $0.68^{A,C,D,\dagger}$	6.69± $0.62^{A,B,D,\dagger}$	6.46± $1.76^{A,B,C,\dagger}$
Day 12	7.43± $0.56^{B,C,D,\dagger}$	4.11± $0.96^{A,D,\dagger,\ddagger}$	4.55± $1.14^{A,D,\dagger,\ddagger}$	1.89± $1.72^{A,B,C,\dagger,\ddagger}$

Data were expressed as Means ± SD of 10 venous ulcer patients /group. C; Control group, MIRE; monochromatic infrared energy treated group, RE; resisted exercise treated group, MIRE/RE; monochromatic infrared plus resisted exercise treated group. [A]significantly different versus control group; [B]significantly different versus MIRE group; [C]significantly different versus RE group; [D] significantly different versus MIRE/RE group at $P \leq 0.05$. †significantly different versus Day 1; ‡significantly different versus Day 6; at $P \leq 0.05$. Significance was carried out by One-way ANOVA Tukey-Krammer test.

DISCUSSION

Leg ulceration is a debilitating condition characterized by long periods of ulceration and a high incidence of recurrence.[19] Venous ulcers cause significant social and economic impact due to their recurrent nature and long lasting course between onset and healing. When they are not properly managed, about 30% of the healed venous ulcers relapse within the first year, and that increases to 78% after two years. Thus, due to prolonged treatment, patients with venous ulcer need frequent health care delivered by physicians and other professionals, therefore,[20] The purpose of the current study is to elucidate a new physical therapy treatment program for the enhancement of venous leg ulcer healing.

The current study showed the 3 treatment group and control showed no significant difference regarding the ulcer size, duration of ulcer, and age of the patients, which indicate that the outcome measures either ulcer size or PUSH score are only in response of treatment interventions.

The result of the current study showed that there was a significant improvement in healing in the MIRE group compared to the control group, as measured by a reduction in ulcer area and PUSH scores. Possible reasons for improved healing rates in the MIRE group may be due to that MIRE technique had been shown to increase blood circulation by 400% over the baseline circulation after 30 minutes of application, as opposed to elevation of skin temperature to the same degree with heat therapy, which increases blood flow by only 40%.[13] Increased circulation possibly accounts for the reported increased healing rates after 12 weeks of MIRE application.

Another possible reason is that mono chromatic infrared energy modality increases nitric oxide (NO) in the blood and plasmas of normal adult subjects.[21] An elevation in nitric oxide (NO) has been suggested to be the basis of improved rates and quality of healing during L-arginine or nitroglycerin therapy in patients with wounds.[22] It has been proposed that through this NO-mediated process, MIRE might prove beneficial in patients with venous and diabetic ulcers and in patients who exhibits low rates of post amputation wound closure.[21]

On the other hand, the result of the current study showed that there was a significant improvement in healing in the RE group compared to the control group, as measured by a reduction in ulcer area and PUSH scores. Possible reasons for improved healing rates in the RE group may be due to that venous hemodynamic is maintained for up to 30 minutes after cessation of exercise.[23] Similarly, structured exercise programs are associated with improvements in calf muscle pump function.[11,12,24,25]

Based on the result of the current study, the third group which combined the beneficial effect of both MIRE and RE showed a significant decrease in the ulcer size and PUSH score when compared to control group or even to each treatment modality alone, which is quit logical.

CONCLUSION

It was concluded that the combination of MIRE and RE was highly effective in the enhancement of venous leg ulcer wound healing.

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Ethical approval: We certify that this study involving human subjects is in accordance with Helsinki declaration of 1975 as revised in 2000 and that it has been approved by the relevant ethical committee.

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