Advanced Protocol of Shock Wave Therapy for Diabetic Foot Ulcer

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Abstract: Foot ulceration is one of the most common and severe complications of diabetes mellitus causing hospitalization and amputation of lower limb**.** Delivery of shock wave therapy stimulates the early expression of angiogenesis- related growth factors so it results in new vessel in-growth that improves blood supply, increases cell proliferation and accelerates tissue regeneration and healing. **Purpose of this study** was to evaluate the effectiveness of shock wave therapy in enhancing diabetic wound healing. **Material & methods** Forty diabetic patients with stage (II or III) lower limb ulcers were randomly divided into two groups (shock wave group and control group). Shock wave group received 3 sessions of unfocused shock wave (500 pulses/cm^2 at 0.1 mJ/mm^2) one session every week beside traditional wound care, the control group received traditional wound care. The methods of assessment were wound surface area and epithelialization rate. **Results** showed significant decrease in wound surface area and increase in the rate of epithelialization in shock wave group compared to the control group. **Conclusions** From the finding of the current study we concluded that shock wave with these parameters (500 pulses/cm^2 at 0.1 mJ/mm^2) is an effective, safe, relatively inexpensive, simple and available modality in enhancing and accelerating diabetic wound healing.

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Key Words: Diabetic Foot Ulcer, Shock Wave Therapy, Wound healing

1. Introduction:

Ischemia in diabetic patients had been shown to decrease granulation tissue formation, impair epithelialization and diminish biomechanical strength parameters in wounds. Decreased tissue oxygen tension also diminish collagen production in wounds, increase matrix metalloproteinase activity and cause abnormal expression of a variety of growth factors and cytokines within the wound **[1, 3]**. Fifteen per cent of people with diabetes will experience a chronic foot ulcer in their lifetime, and this can cause substantial emotional, physical, and financial losses **[1,2].**

Some specific physiotherapy modalities are used to enhance wound healing process such as LASER therapy, therapeutic ultrasound waves, electrical stimulation and ultraviolet rays. Other adjunct therapeutic modalities include the use of hyperbaric oxygen therapy, Ozone therapy, and the new method is shock wave **[4].** Shock waves are sound waves that are generated by a source that creates vibration which are then transported through tissue via fluid and solid particles interaction **[5].**

It has been used for the treatment of numerous musculoskeletal disorders, including calcified tendonitis of shoulder, chronic planter fasciitis, osteonecrosis of the femoral head, and delayed union and non union of fractures **[6].** Researchers have shown that the local delivery of shock wave therapy stimulates the early expression of angiogenesis-related growth factors, including endothelial nitric oxide synthesis, vascular endothelial growth factor and proliferating cell nuclear antigen. So new vessel will in-growth that improves blood supply, increases cell proliferation and accelerates tissue regeneration and healing [**4].**

2. Material and Methods:

Forty patients with lower limb ulcerations participated in this study. These patients had been divided randomly into two groups: one treated with shock wave therapy beside medications and traditional wound care methods (Group A) while the other treated with medical treatment and traditional wound care (Group B).

The inclusive criteria were

Diabetic patients with age ranged from 40 to 70 years suffering from diabetic foot ulcers for a period of at least 3 months, Area wider than 1 cm^2, and the ulcers had grade 2 or 3.

Exclusion Criteria included patients with any of the following:

Patients with malignancies, vascular insufficiency, renal failure, psychological problems, anemia, hyperthyroidism, favism, alcoholic drinkers, pregnant, or receiving radiotherapy, chemotherapy, immunosuppressant, or anticonvulsant drugs. Patients with Concurrent participation in another clinical study. Ulcers with surface area more than twenty cm², or Ulcers with grad 1(stage I, intact skin with impending ulceration) or grad 4 (stage IV, full thickness loss of soft tissue and extension into muscle, bone, tendon, joint capsule). Forty diabetic

patients matched with the previous inclusive and exclusive criteria had been selected randomly. These patients have been divided randomly into two groups: one treated with shock wave therapy beside medications and traditional wound care methods (Group A) while the other treated with medical treatment and traditional wound care (Group B).

Ethics

The protocol of this study approved by the ethical committees of the faculty of physical therapy (Cairo University. Egypt). Every patient applied informed consent before starting the study. All participants were informed about the nature and the effect of the treatment and measurement devices. The patients were also instructed to report any side effects during the treatment sessions.

Measurements

1-Assessment of wound surface area:

It was calculated according to planimeter method by placing a piece of sterilized transparency film over the wound and tracing the wound perimeter on the film with fine tipped transparency marker. A separate transparency was used for each wound. The traced transparency film placed over carbon paper with a white paper in between and transcribed the tracing into metric graph paper and the numbers of square millimeters on the graph paper within the ulcer surface area was counted (only full1millimetre squares inside the perimeter was counted) and the area was converted to square centimeters. The tracing process was repeated three times to establish measurement reliability. The mean of the three trials calculated and considered as the ulcer surface area . This assessment was done before and after 12 weeks of treatment **[7].**

2- Epithelialization rate:

The area traced measured. The healed area, given by the expression 1-A1/A0 x100 was calculated from the original wound area (A0) and the unhealed area (A1).

Treatment procedures:

Group A (Experimental, Shock wave group).

This group was treated with the essentials of foot ulcer care and medical treatment beside shock wave therapy. After the disinfection of the wound, the shock wave applicator head was placed over the wound, the cleaned wound was covered with sterile ultrasound gel and a sterile drape, over which further coupling was spread to provide an air-free contact for extracorporeal shock wave therapy head (ESWT). The head was then moved directly on the wound and the edges. The protocol consist of a course of three sessions (a session every 1 week), with 500 pulses per 1 cm^2 of wound delivered at each session at a flux density of 0.1 mJ/mm^2. unfocused ESWT used as it is more suitable and specific for superficial wound healing, as compared with focused ESWT **[8].**

BTL-5000 SWT power device is an extracorporeal shockwave delivery system that is approved for distribution and use in the United States by the Food and Drug Administration (FDA). Following the procedure, the type of dressing previously used by the patient was used to dress the wound. The patient was instructed to report any side effects during or after the treatment sessions. The treatment session lasted about 2 or three minutes. The protocol consisted of three sessions, one session every week. The patient was followed up every week to see the progression of the case and the healing. After the end of each session, the probe was cleaned with disinfectant material (alcohol) to avoid infection.

Group B (control group):

Patients in the control group were treated with the essentials of foot ulcer care, namely debridement, adequate pressure relief and treatment of infection, as required by current international guidelines.

Statistical procedures:,

Data of the study recorded as the means ±SD. The data analyzed by using SPSS 18 (SPSS inc. USA). Compare between both groups of the study performed by (ANOVA).

3. Results

All the patients involved in the study have been continued the study until the end of it. None refused or withdrawn. The demographic data for the patients showed that there is no significant difference between both groups (As reported in table1).Shock wave group composed of 20 patients (15 males and 5 females) their ages ranged from 44 to 68 with a mean ±SD (56.6±7.51 years), While the control group consisted also from 20 patients (14 males, 6 females), with age ranged from 42 to 64 with a mean ±SD (55.15± 6.36 years).The statistical analysis showed that there was no significant difference in wound surface area for both groups at the beginning of the study, the means ±SD of wound surface area for shockwave group and control group were (8.86±3.41) and (8.32±3.88) respectively. After 12 weeks there was significant decrease in the surface area of both group, they become (1.92±3.28) and (4.65±3.43) for shock wave and control group respectively. A significant difference was observed in the wound surface area between both groups after 12 weeks (*P*-value <0.01). The results also showed that there was significant difference in the rate of epithelialization between both groups after 12 weeks. The rate of epithelialization for shock wave and control group were (83.26 ± ±27.43) % and (48.66 ±31.68) % respectively (*P*-value < 0.001). Both the decrease in wound surface area and increased epithelialization

rate in shock wave group, in compare to control group, were statistically significant.

Table (1) show the results of WSA and epithelialization rate pre and after treatment for both groups

	Age(mean±SD)	WSA pre (mean±SD) cm2	WSA post (mean±SD) cm2	Epithelialization rate
SW group	56.6±7.51	**8.86±3.41**	**1.92±3.28**	83.26 ±27.43 %
Control group	55.15±6.36	**8.32±3.88**	**4.65±3.43**	48.66±31.68 %
t-value	**0.65**	**0.46**	**2.57**	3.69
p-value	**0.51**	**0.64**	**0.0001**	0.001
S	**NS**	**NS**	**S**	S

*SD: standard deviation, S: significance, NS: non significant, S: significant. SW: Shock Wave
WSA: wound surface area

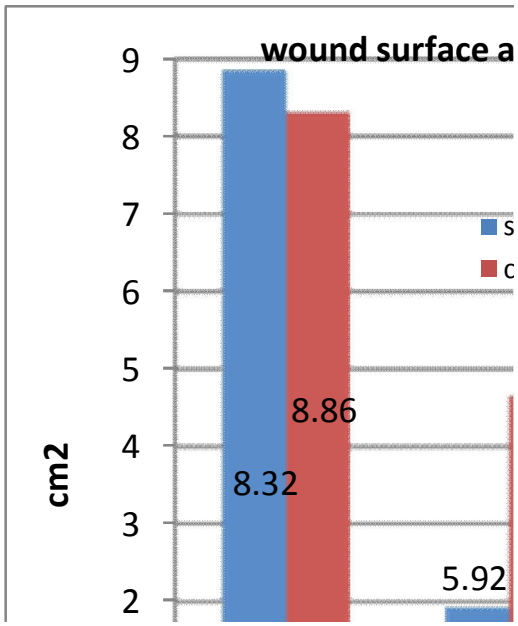

Fig (1) show the statistical difference pre and post treatment for both groups.

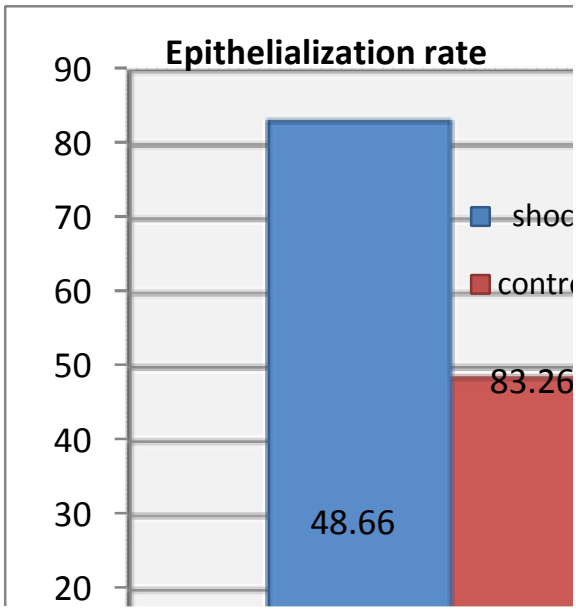

Fig (2) show statistical difference for epithelialization rate after 12 weeks for both groups

Fig (3.a) (diabetic male patient (60 y) with 4 months unhealed wound due to un-proper fit prosthesis after below-knee amputation) before the treatment with ESWT.

Fig (3.b) the same case, 6 weeks after application of shock wave therapy.

Fig (3.c) the same case,10 weeks after application of shock wave therapy.

Fig (4.a) diabetic male patient (57y) with 3 months right lateral foot pressure ulcer before the treatment with shock wave therapy.

Fig (4.b) the same case after 12 weeks of shock wave application.

4. Discussion:

The mechanism of tissue healing is a complex biological process that involves a perfect and coordinated cascade of cellular and molecular events promoting tissue reconstitution. This process arises as a response of the tissue to injuries induced by trauma or by surgical procedures. The process of wound healing is characterized by three phases that overlap and present a characteristic profile: inflammatory phase, proliferative phase and remodeling phase **[9].** Despite some recent advances in the understanding of these basic processes, wound healing disorders continue to cause diseases and even death. A wide variety of therapies has arisen with the advances in technological applications **[10].**

The results of this study revealed that there was a significant difference in wound surface area after 12 weeks (post-treatment) of the treatment between in shock wave group and the control group (*P* value = 0.0001) although there was no significant difference between the two group at the beginning of the study (pre-treatment). That could prove the efficacy of ESWT in acceleration of wound healing in lower limb ulcers in diabetic patients. Also, it was found that application of shock waves on lower limb ulcers 3 times showed a statistically significant increase in the epithelialization rate after 12 weeks by (83.26±27.43) % (*p* value = 0.0001). In comparison, the control group showed a rate of epithelialzation after 12 weeks of (48.66±31.68)%.

According to our reviewing of the previous studies there was no specific or recommended protocol of shock wave therapy for diabetic patients so we create a special program depend on the previous pre-clinical studies or general recommendation for using shock wave to similar cases. So our protocol of the shock wave group consisted of a course of three sessions of unfocused ESWT (a session every 1 week), with 500 pulses per 1 cm^2 of wound delivered at each session at a flux density of 0.1 mJ/mm^2. We chose, in this protocol, to administrate the shock waves every 1 week for 3 sessions on the basis of the "new guidelines of the international society for medical shock wave treatment" which suggested the application of 1 to 6 sessions, with an interval of 1 week.

We also chose the unfocused shock wave as the preclinical studies suggest that unfocused shock wave therapy is superior for the treatment of superficial soft tissue defects **[11],** and selected 500 impulses at 0.1mj/mm^2 according to a study by **Kamelger., et al [12]** who assessed a dose dependent effect of shock wave therapy of varying impulses (200, 500, 1500, 2500, 5000 and, 0) at 0.1 mj/mm^2, with an optimum enhancement at 500 impulses. This study showed non-significant increase at 1500 impulses and increased necrosis at 5000 impulses.

So shock wave therapy provides acceleration in wound healing in diabetic foot ulcers and this come in agree with**(Meirer *et al.,*)[13,14,] & (Wang *et al.,*)[2] who stated that** The mechanism of shock wave in acceleration of wound healing still unclear but the previous studies found many physiological changes in the tissue after application of shock wave which lead to accelerate the wound healing, one of the reported effect of shock wave application was the increasing the release of growth factors as endothelial growth factor (VGEF), transforming growth-factor pl (TGF-p 1) and insulin growth fact-I (1GH-I) which may lead to improve the wound healing specially the chronic one. Also (**Mittermayer *et al.,* ; Reichenberger *et al.,*; Wang *et al.,*2002; Wang *et al.,*; Hsu *et al.,*)[15,16,17,2,18] stated that** the enhancement in vascularity and blood perfusion in the tissue in response to shock wave application due to increase neovascularization and angiogenesis which have an essential a role to improve blood supply and tissue regeneration that accelerate the closure of chronic wound.

(Wang *et al.,* ; Arno *et al.,*; Kuo *et al.,*;Goertz *et al.,*; Davis *et al.,* [19,20,21,22,23] stated that One of The other expected causes which lead to accelerate the wound healing is the anti-inflammatory effect of shock wave, as there are many studies suggested that the shock wave produce an adequate amount of energy that can produce controlled inflammation of the designated tissue. This inflammation has been shown to stimulate many mediators such as transforming growth factor beta 1 (TGF-B1) and insulin-like growth factor 1 (CGF-I) and initiates the healing process also decrease leukocyte infiltration, tissue apoptosis and Increased recruitment of skin fibroblasts, was found due to down-regulation of oxygen radical synthesis expression.

Conclusion

From the previous discussion of these results and according to reports of researches in the field related to the present study, it could be concluded that application of shock wave therapy on the lower limb ulcer in diabetic patient can improve and accelerate the closure of wound and decrease the time of healing, leading to decrease the physical, psychological and financial complications for these patients and decrease the costs. The results of the current study would introduce a scientific applicable protocol for an effective and safe modality that can help physical therapists, physicians and clinicians in their dealing with diabetic patients who suffer from lower limb ulceration to overcome this problem and improve the quality of life.

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