Electromechanical therapy in diabetic foot ulcers: A systematic review and meta-analysis

Ayeshmanthe Rathnayake, Apoorva Saboo, Venkat Vangaveti, Usman Malabu.

Translational Research in Endocrinology and Diabetes, College of Medicine and Dentistry, James Cook University, Australia.

4

Introduction

Diabetic foot ulcer (DFU) is one of the most devastating and troublesome consequences of diabetes. Due to poor leukocyte chemotaxis and phagocytosis, diminished macrophage activity in the wound matrix, decreased collagen synthesis and deposition, and reduced growth factor release, wound recovery in diabetes patients is often slower than in healthy persons. The current therapies are not always effective because of the complicated aetiology and interactions of local and systemic components in DFU, and an optimal adjuvant therapy has yet to be established.

According to several earlier research, nonpharmacological treatments such electrical stimulation, low-level laser therapy, hyperbaric oxygen therapy, and foot off-loading may also be helpful in the healing of DFUs. Additionally, it has been proposed that the use of ultrasound, light therapy, and electrical stimulation will hasten the healing of DFUs by promoting the migration of different cell types and improving wound perfusion. However, an ideal adjuvant therapy has not yet been identified. Adjunctive therapy, such as electromechanical therapy, has become the latest modality in recent years, although there is a lack of significant research to support its utilization as a treatment standard.

Aim - Review the literature on the application of electromechanical therapies in the healing of DFUs.

We searched PubMed, Medline, EmBase, the Cochrane library, and Google Scholar for the most current research (1990–2022) on electromechanical treatments for DFUs.

The terms [Electromechanical therapy OR Laser therapy OR photo therapy OR Ultrasound therapy OR Shockwave therapy] AND [diabetic foot ulcers OR diabetes] were used as search criteria. Searches were restricted to English language articles only.

Methods – Systematic Review and Meta-analysis

The data was examined for the meta-analysis using Review Manager 5.4 and a 95% confidence interval. Using the random model, the heterogeneity between the studies was evaluated. To determine the entire cumulative impact, forest plots were curated.

Only studies that satisfied the inclusion criteria were deemed eligible after being located utilising the PRISMA technique and critical appraisal tools

Table 1. Inclusion and exclusion criteria for studies.

Inclusion criteria	Exclusion criteria
Studies on the electromechanical therapies in diabetic foot ulcers.	Anything not including the listed topics regarding electromechanical therapies in diabetic foot ulcers.
Peer reviewed research with all types of study designs (such as quantitative, qualitative, and mixed methods)	Anything other than peer-reviewed articles and literature such as reviews, blogs, books chapters, websites content, and more.
Published in KSA from 1990 to 2022	Published before 1990
Original article	Reviews
Randomized control trials	Meta-analysis/systemic reviews
English language research	Publications in languages other than English

Figure 1. The PRISMA flow chart.

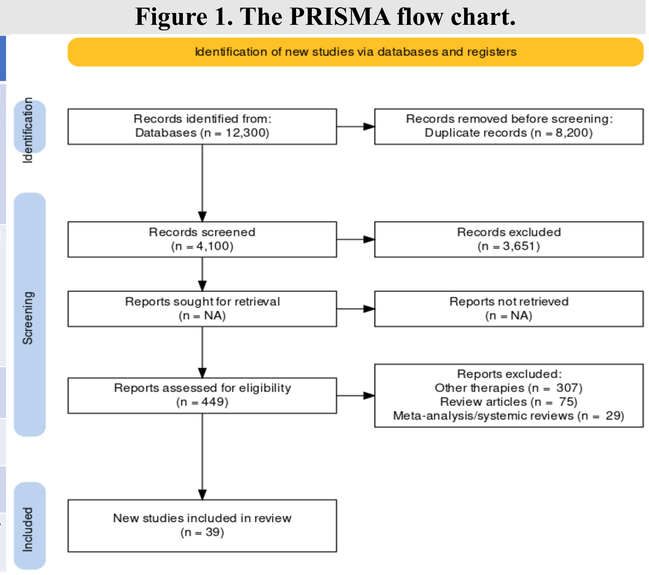


Figure 2. Forest plot showing mean effects for experimental (electromechanical therapies) and control/placebo groups of diabetic foot ulcer patients.

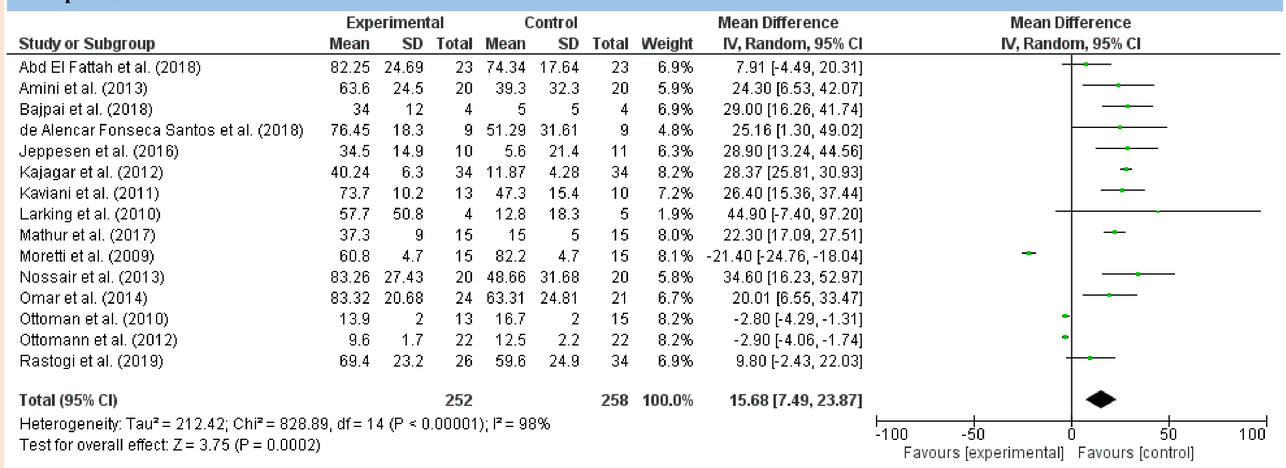
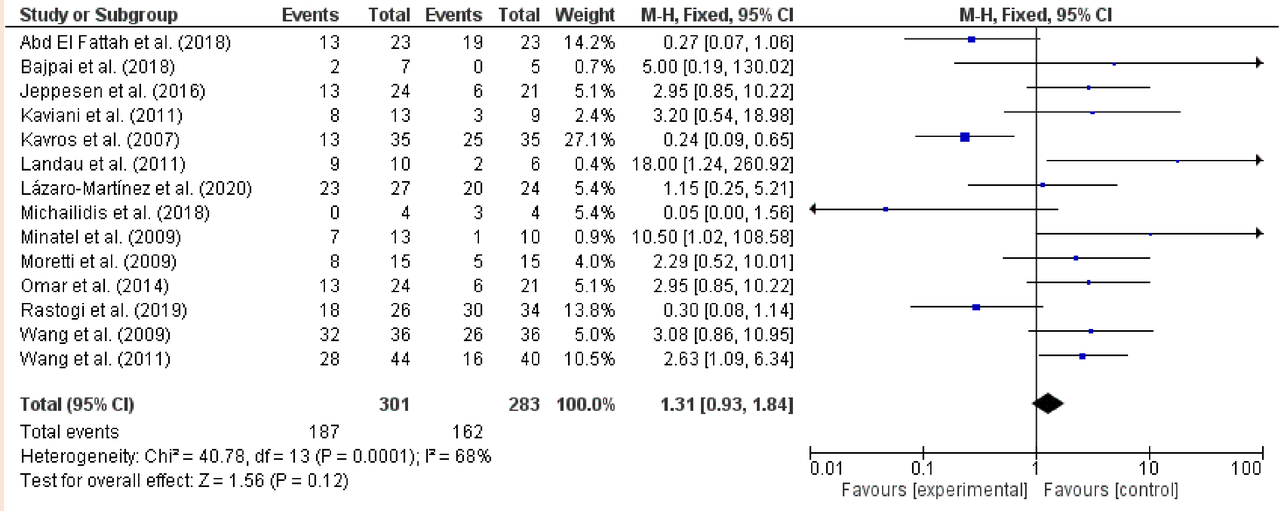


Figure 3. Forest plot showing main event of wound healing among experimental (electromechanical therapies) and control/placebo groups



Results

The mean difference for these studies also showed significant difference among experimental and control groups (15.68; 95% CI, 7.49, 23.87). The overall effect was significant (P= 0.0002) that indicates experimental groups have improvement in the DFUs healing compared to control group. Fifteen studies in the forest plot compared the electromechanical therapies vs placebo/control groups that showed significant difference (P<0.00001) in heterogeneity among the groups with 98% I^2 value (*Figure 2*). Similarly, data from fourteen studies compared the number of healed wounds among experimental and control groups. The overall effect was non-significant (P=0.12) with mean difference (1.31; 95% CI, 0.93, 1.84) for these studies showing better healing among experimental groups compared to control group. There was also a moderate degree of heterogeneity among these studies (I^2=68%, P=0.00001) (*Figure 3*).

Discussion

Extracorporeal shockwave treatment (ESWT) - Accelerates the production of angiogenesis-related growth and proliferation factors, shorten the inflammatory phase, and reduce the risk of wound infection. ESWT significantly lessens pain in the vicinity of the wound via modifying substance P and calcitonin gene-related peptides. ESWT has emerged as a viable first-line treatment for DFU. Figure 2 and 3 compare electromechanical treatments with the placebo/control group. The mean difference for these studies revealed a significant difference between the experimental and control groups, although, the analysis revealed heterogeneity across the groups with a 98% I^2 value. Overall, there was a significant difference between the experimental and control groups in how quickly DFUs healed. Our findings support those of earlier research by Butterworth *et al.*, Dymarek *et al.* and Omar *et al.*, which prove the effectiveness of ESWT on chronic wounds. Histopathologic analysis show that ESWT can have both a direct and indirect impact. ESWT might encourage collagen production, fibroblastic growth, and angiogenesis by increasing cellular ATP production, which then activates purinergic receptors and Erk1/2 signalling [67, 70, 93]. EWST is therefore believed to have the ability to speed up the healing process.

Low-level laser therapy (LLLT) - has been identified as a viable mechanism of treatment to hasten the healing of ulcers with studies showing a considerable decrease in the size of the ulcer and DFU pain. The LLLT parameters used in our study were based on the RCTs showing wavelength: 400–904 nm, power density: 30–180 mW/cm^2, and fluence: 2–10 J/cm^2. Most of these variables complied with the suggested LLLT settings. The impacts of LLLT on numerous cellular processes and molecular pathways, such as promoting expression of regulators for cell proliferation, migration, survival, and granulation, were part of the mechanism of LLLT in hastening the healing process of chronic DFU. Additionally, it was discovered that the LLLT group's ulcers had more granulation tissue than the control group. LLLT can increase the expression of essential fibroblast growth factors and induce collagen production in damaged fibroblasts of diabetic mice. Transforming growth factor beta, interleukin-1 and interleukin-8, platelet-derived growth factor (PDGF) increased macrophage phagocytic activity. The synthesis of collagen and extracellular matrix may be increased, the above-mentioned key cytokines and growth factors may be attracted, and the migration, proliferation, and differentiation of various cell types may all be encouraged by LLLT. Furthermore, increase the expression of heat shock proteins 70 and 1 in injured tissues can increase the synthesis of growth factors like transforming growth factor-beta and aid in wound healing. All these factors may collectively play significant roles in the healing of DFUs.

Safety - Electromechanical therapies are acceptable as non-invasive adjuvant treatments. Electromechanical treatments can have adverse effects during treatment, including temporary skin reddening, mild discomfort, and tiny hematomas. Rarely are serious adverse effects and consequences such as bleeding, thrombosis, muscle injury, and wound infections.

Limitations

- The results may only be applicable to people with diabetes and foot ulcers as this meta-analysis only included patients with DFU.
- Cost-effectiveness was not investigated based on the data available.
- Heterogeneity observed in the meta- analysis.

Conclusion

According to the findings of the systematic review and meta-analysis, electromechanical treatments are viable and secure choices for individuals with DFUs. Electromechanical therapy can considerably reduce treatment ineffectiveness, speed up healing, and minimize the time it takes for DFUs to heal.

Rathnayake, A., Saboo, A., Vangaveti, V. et al. Electromechanical therapy in diabetic foot ulcers patients: A systematic review and meta-analysis. J Diabetes Metab Disord (2023). https://doi.org/10.1007/s40200-023-01240-2