



Shockwave Medicine and Leprosy The Ultimate Challenge for Skin Regeneration by Mechanotransduction

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Introduction

Leprosy, also known as Hansen's disease, is one of the oldest chronic infectious conditions known to mankind. It is caused by the *Mycobacterium Leprae*, a germ that attacks primarily the peripheral nerve system and may remain asymptomatic for years. The presence of skin granulomas, limb amputations, face and eye deformities have caused the largest historical social stigma in the world. The main problem of these patients, apart from the social stigma, is the presence of plantar perforating ulcers. These are chronic deep ulcerations of the anesthetic sole of the foot that are usually resistant to all treatments local or systemic. Plantar anesthesia, unprotective walking and poor quality of scars make these lesions usually recurrent. Unfocused Extracorporeal Shockwave Treatments (ESWT) has become a proven therapeutic tool in the treatment of diabetic foot. These patients suffer from similar chronic ulcers with a neuropathic, hypovascular, hyporegenerative infectious background, and has shown excellent results in the past decade. We hypothesize that the use of ESWT may have a similar result as in diabetic foot, improving plantar ulcer healing in patients with Leprosy.

Methods

We performed a blinded randomized clinical case control trial in forty patients with diagnosed Hansen's disease from the Sanatorio de Agua de Dios in Cundinamarca, Colombia. In order to standardize the outcomes, patients with plantar ulcers under 10mm² were chosen from the Hospital's database. Patients were randomized in two groups of 20. All patients were non reactive, and had previously completed more than one year of multidrug anti-leprosy therapy. All were informed of this experimental trial, of possible results and complications, and signed an informed consent. The ethics committee of the Sanatorio de Agua de Dios approved the study. The cases group received four sessions of unfocused electrohydraulic shockwaves at a bi-weekly interval. We used the ISMST approved protocol, applying 350 shockwaves x 10 times the size of the ulcer in square mm on each session, with a certified unfocused electrohydraulic ESWT device (Dermagold 100 – MTS-Germany). Both the cases and the control groups received the exact same regular treatment according to the Hospital Protocol, with wound lavage, debridement and local agents. All patients were evaluated by direct ulcer measurement in width and length, and a digital photography record was performed. The ulcers were described and recorded by our plastic surgeon. Patients were followed up and photographed every two weeks during treatment, and then at 3, 4 and 6 months. The digital photographs of the ulcers of cases and controls were measured at the end of the study by three blinded MD's who did not know if the patients were treated or not with ESWT. The clinical measurements were analyzed separately from the photographic measurements. We considered excellent results in a complete wound closure, good if healing was over 50% of the original size, fair if under 50% and poor if no change or increase in size was documented. We also measured subjectively the depth of the wound as *deep* or *superficial* if the edges of the ulcer were lower or higher than 3 mm. Any adverse effects were recorded. The study was done independently with no financial or material support from the manufacturers of ESWT devices or implants.

Results

We were able to follow up for six months a total of 16 cases and 15 controls, and there were no significant differences between the two groups in terms of demographics and clinical data. All ulcers under 1 mm² were excluded from the ESWT and control groups by the data analysis team. The average wound size in the ESWT group was 587mm² and the control group was 596mm². The proportions of ulcers that healed in six months in the ESWT and control groups were 63% and 12%, respectively. We had a complete closure in 6/16 patients of the ESWT group, and 1/15 patients with complete closure in the control group. Out of the patients with complete wound closure in the ESWT group, 34% healed after one month, 16% after two months and 50% after four months. The only patient with complete wound closure in the control group healed after 3 months. In the ESWT group we had 75% of good or excellent results after six months, while in the control group we had 20%. The depth of the ulcers, the aspect and vascularity of the wounds improved from deep to superficial in 65% of the ESWT group and 12% in the control group. All these results were statistically significant ($p > 0.05$). Subjectively, patients in the ESWT group reported increased sensitivity in the treated area, and pain control in the adjacent areas. Fluid wound drainage also decreased in the ESWT group, as reported by patients and nursing personnel. All patients reported the treatment as satisfactory in the ESWT group. We did not have any adverse effects or complications in either group.

Conclusion

The use of shockwave therapy in the treatment of chronic plantar ulcers in Leprosy patients showed excellent results in this case-controlled blinded RCT. There is a clear evidence of a positive influence of mechanotransduction stimulation in improving healing of these very complicated skin conditions. Some patients have these ulcers for more than 15 years and were surprised that finally something worked for them. Our results are very encouraging, especially this being the first study of ESWT for Leprosy patients. We found that the use of unfocused electrohydraulic ESWT improved significantly wound closure in chronic leprosy patients, with 51% better results than in controls. This was the only single different intervention in the treatment group. We did find also an improvement in wound drainage and the depth of the ulcers. Pain also improved in most of the patients. We believe that leprosy ulcers may need a larger number of sessions, as they are deeper than diabetic ulcers. All patients with ulcers under 1 mm² healed in the ESWT and control groups and were excluded from the study. We also treated 6 patients with larger ulcers and the results were similar. We expect to continue this research line with larger ulcers and in more patients. The general perception in our patients and the Agua de Dios community was extremely favorable, generating a social wave of demands for ESWT treatments. With this statistically solid results and subjective data, we are optimistic in being able to offer a non-invasive option with shockwave medicine for a large and suffered population of the world.