

EFFECT OF AN INNOVATIVE PH LOWERING WOUND THERAPEUTIC ON MMP LEVELS AND BACTERIAL BIOFILM COLONIZATION OF CHRONIC NON-HEALING WOUNDS.

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BACKGROUND

Patients with chronic non-healing lower extremity wounds often are found to have chronic inflammation associated with biofilm bacterial colonization of the wound bed. Eradication of this biofilm and control of upregulated inflammation can be difficult to achieve without the use of long courses of systemic antibiotic administration. A novel wound therapy, Therworx Protect (TWX), has been developed that reduces the pH of skin and wound tissue, increasing their resistance to bacterial colonization. This product has been shown to be effective at reducing the incidence of catheter-associated UTIs and central line associated infections. In this study we have applied TWX to chronic non-healing leg ulcers and measured matrix metalloproteinase (MMP) levels in wound fluid and bacterial biofilm involvement of the wound bed before and after 4 weeks of TWX therapy.

OBJECTIVE

The primary study objective is to determine changes in MMP levels and biofilm involvement of chronic wounds treated with TWX over one month time and the correlation of these levels with wound healing.

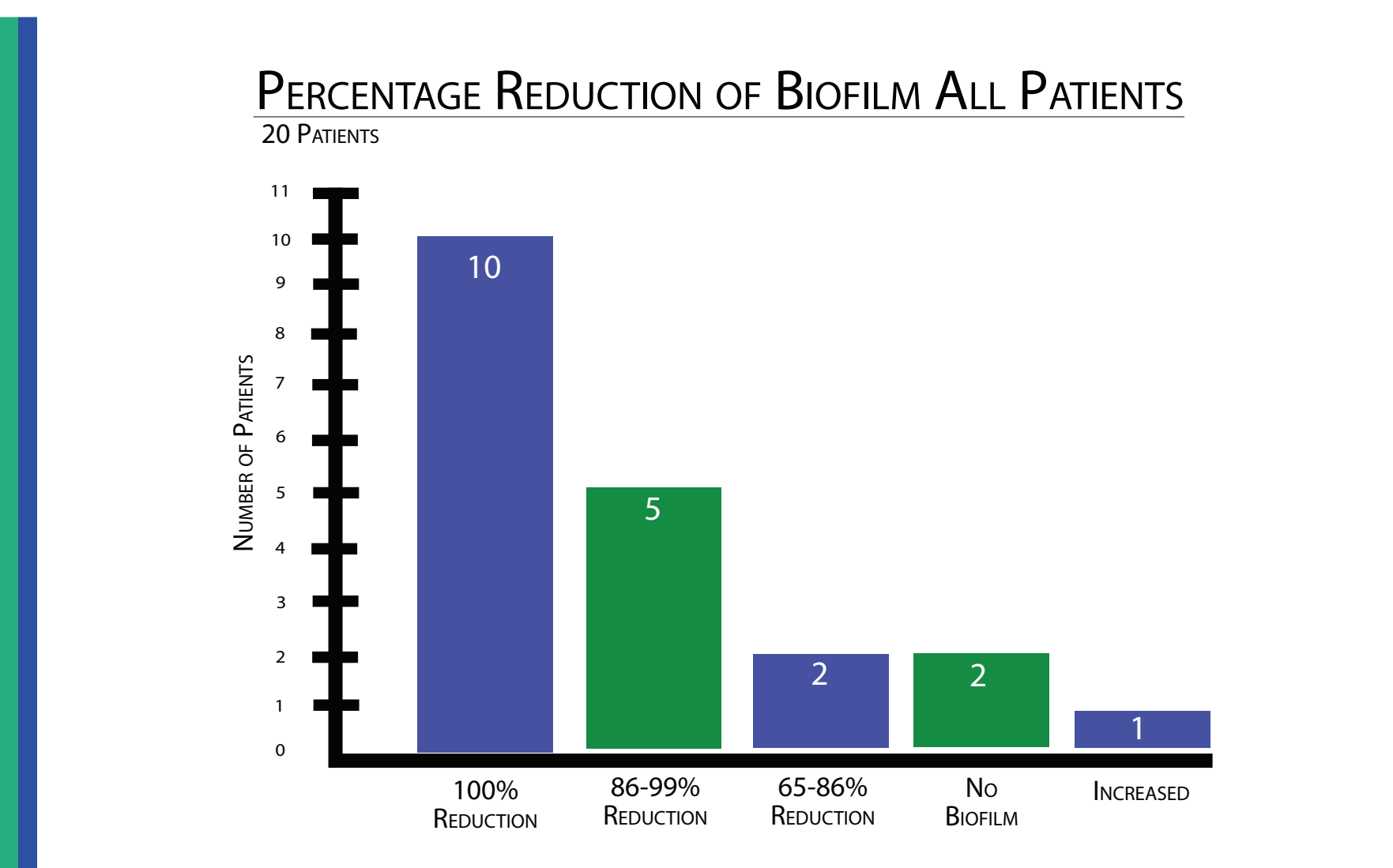
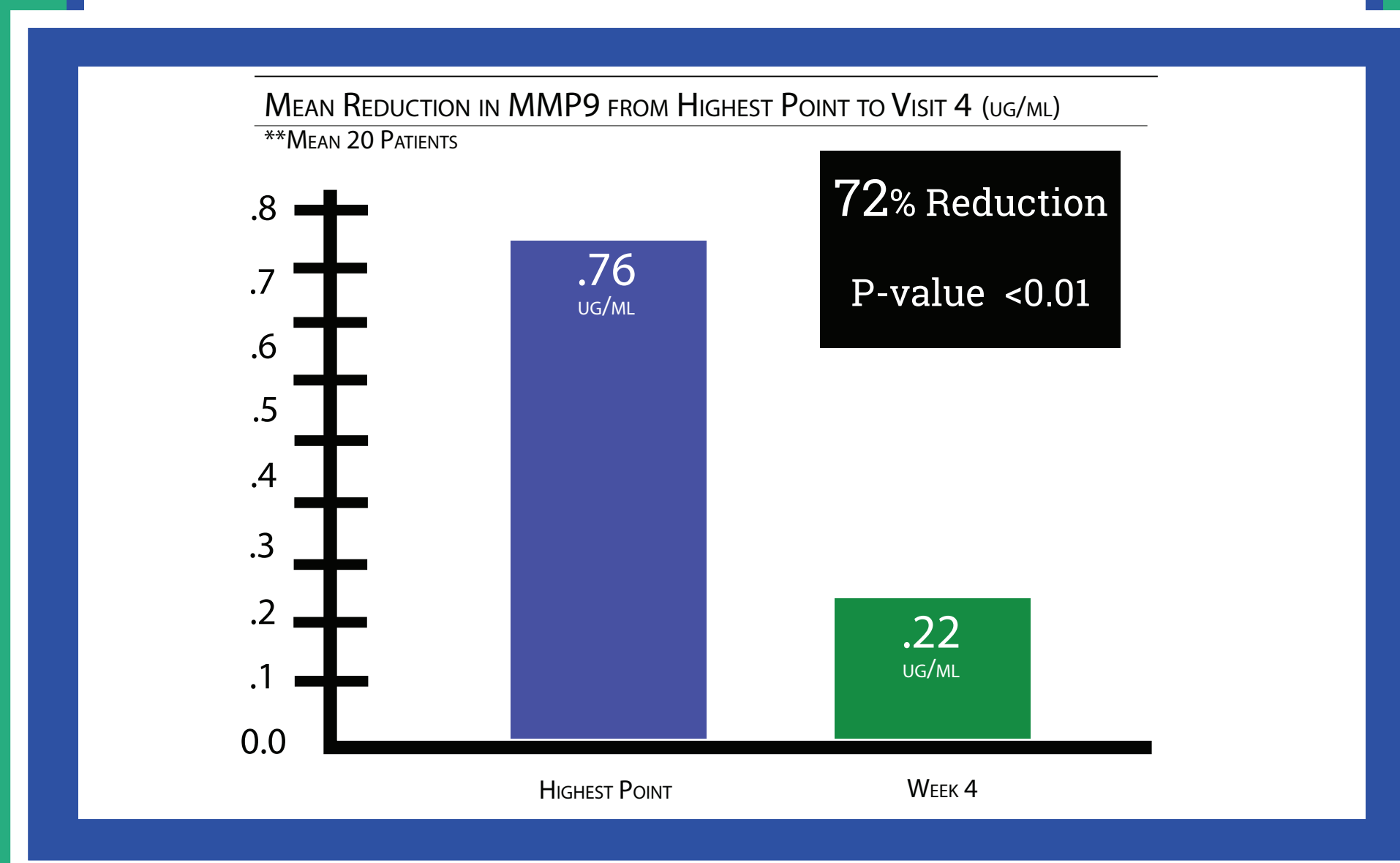
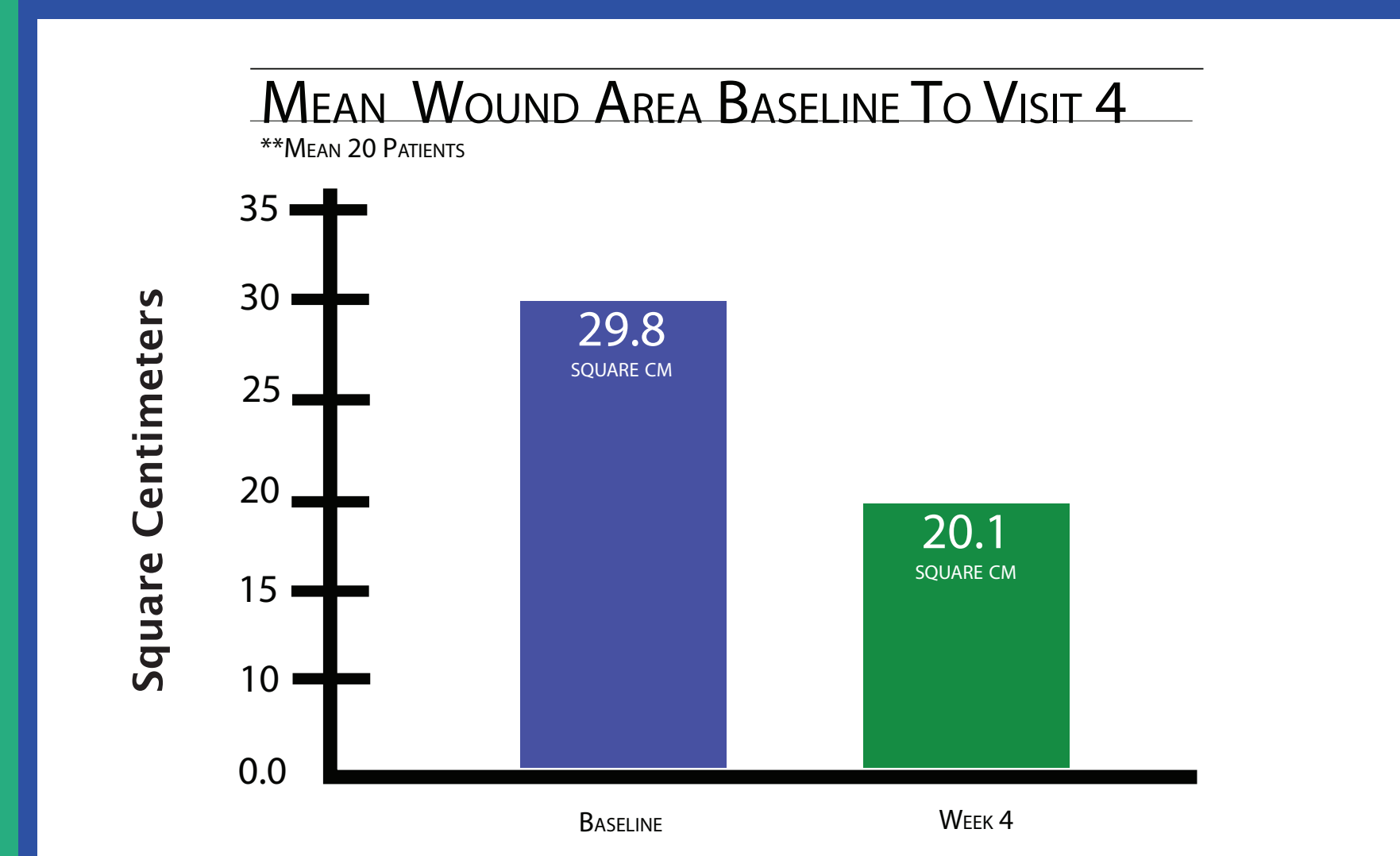
METHODS

Twenty patients with chronic non-healing lower extremity ulcers of >4 weeks duration were identified and agreed to participate. Patients were included with diabetic foot ulcers, venous leg ulcers and ulcers associated with chronic arterial insufficiency. Baseline patient demographics and wound characteristics were recorded. Prior to treatment with TWX, samples of wound fluid and tissue samples were obtained for MMP and bacterial biofilm analysis. MMP activities were measured using a synthetic seven amino acid peptide with a fluorochrome-quencher pair that generates a fluorescent signal when the peptide is cut by MMPs.¹ Colony forming units (CFU) of viable bacteria in biofilm phenotype were measured by standard dilution plating technique following brief (10 minute) exposure of ultrasonically dispersed biofilm communities to dilute bleach (0.1%) followed by neutralization with 0.15% sodium metabisulfite.² The patients were treated for 4 weeks with standard treatment for the wound etiology plus application of TWX to the wound and peri-wound areas at all dressing changes. At weekly visits, wound characteristics were obtained and repeat wound fluid and tissue samples were obtained for MMP and bacterial analysis. At the completion of 4 weeks of treatment, wound size was re-measured to determine the percentage of wound healing over the 4 weeks of treatment. The study was approved and conducted under the guidelines of the University of North Carolina human studies sub-committee.

RESULTS

Sixty-seven percent of patients healed >30% over the 4-week treatment phase. The mean wound size decreased significantly from 29.8 ± 27.2 cm² at baseline to 20.1 ± 20.5 cm² after 4 weeks (P = .01). The mean MMP-9 at peak level was 0.76 ug/ml. After 4 weeks of TWX treatment, this level decreased to 0.22 ± 0.1 ug/ml (P < 0.01). At baseline, 15 of 20 patients had detectable levels of biofilm activity with a mean of 207,144 CFU/ml of homogenate. Among the 18 patients with detectable biofilm during the study, 10 had elimination of all detectable biofilm activity after 4 weeks of TWX treatment. Five patients experienced reduction of biofilm activity by > 86%. The total mean activity after 4 weeks of TWX treatment was 3109 CFU/ml of homogenate (P = 0.10).

RESULTS



Patient 004 Visit Baseline



Patient 004 Week 4



Patient 018 Visit Baseline



Patient 018 Week 4

DISCUSSION

These data are strongly suggestive of a trend towards a reduction in MMP activity and are statistically significant, but biofilms and total bacteria levels are not statistically significant due to the sample size. Additional patients are being entered into the study.

CONCLUSION

Treatment of chronic non-healing wounds with standard treatment protocol plus TWX therapy resulted in reduction in the incidence of biofilm and total bacteria wound involvement and statistically significant reduction in MMP-9 levels. Most wounds, despite lack of response to standard therapy prior to study enrollment, achieved >30% closure during the 4-week treatment phase. Study in additional patients will further define the beneficial effects of TWX on chronic non-healing wounds.

REFERENCES

- 1 US Patent 8,058,024B2
- 2 P.L. Phillips, Q. Yang, G.S. Schultz. The Effect of Negative Pressure Wound Therapy with Periodic Instillation Using Antimicrobial Solutions on Pseudomonas Aeruginosa Biofilm on Porcine Skin Explants. International Wound J, 10 (suppl. 1) 48-55, 2013.