A case series of twenty patients with Wagner III/IV diabetic foot ulcers: debridement with topical desiccation agent and subsequent healing by secondary intention.

Michel H.E. Hermans♦, M.D.

Introduction

Diabetic foot ulcers lead to serious morbidity[1] and have a significant socioeconomical impact[2 3]. An ulcer is typically covered with necrosis and a biofilm, and these two features add to the consistent inflammation, the underlying cause of skin ulceration in the first place[4]. Consequently, debridement (removal of infection, biofilm, and necrosis and, thus, their detrimental effects) is necessary[5]. After debridement, granulation tissue can start developing[6]: since most ulcers heal by secondary intention the presence of granulation tissue is essential[7].

Topical desiccation agent (TDA▲) is a compound that contains methanesulfonic acid. The acid, when in contact with water, works through a desiccating exothermic reaction that destroys most molecular bonds. The stratum corneum is protected from this reaction since it contains very little water, but necrosis, slough, and biofilm hold a lot of water and, thus, are strongly affected and quickly destroyed. The desiccation effect is virtually immediate; biological materials denature and coagulate together and tend to rapidly separate from the underlying tissues, "freeing" the lesion to develop granulation tissue[9].

TDA is designed as an alternative to surgical debridement and works effectively and rapidly. In contrast to surgical debridement, however, the use of TDA does not need the specific expertise or specialized setting (i.e., hospital) that are necessary for surgical debridement[8].

Inclusion/Exclusion criteria, Study Outcomes

A prospective, IRB-approved, non-comparative study was conducted to assess the overall response of diabetic foot ulcers to treatment with TDA. The main inclusion criterion for this study was the presence of a diabetic foot ulcer that had not responded to ambulatory treatment with advanced materials and methods for a period of at least 30 days, and had a Wagner classification of III or IV[10], indicating the seriousness of the lesions. Ulcers also had to have a culture-confirmed infection with multidrug-resistant *Pseudomonas Aeruginosa*. Sufficient distal perfusion was a *proviso* for study participation, as was the presence of impaired renal function.

The patient had to be a candidate for surgical debridement but, with patient consensus, the application of TDA was used as an alternative. Typical exclusion criteria included, but were not limited to, ischemia of the leg, the presence of osteomyelitis, and signs of systemic infection (i.e., septic shock).

Outcomes assessed were the overall status of the lesion (recurrence or continued post-interventional absence of necrosis and biofilm, development of granulation tissue, level of reepithelialization) at study end (scores: improved, unchanged, worsened; clinician's opinion), the development of intra- or post-intervention complications and/or pain, whether or not reinfection occurred clinically, size reduction of > 50%, and whether or not complete reepithelialisation had occurred.

♦ Hermans Medical Consulting. Hoorn, the Netherlands

▲ Debrichem, DEB^x Medical

This poster is supported by DEB^x Medical, Amsterdam, the Netherlands

Study protocol

The protocol for usage included cleaning of the wound and periwound skin, the use of a (local) anesthetic if necessary, and the subsequent application of TDA over the lesion.

After cleansing of the ulcer, it was cultured, TDA was applied for 60 seconds and removed by rinsing with saline. Modern dressings were applied and changed every 7 days. Cultures were taken on post-application-day 14 and 30. The end of study period was at day 40 post-intervention. No antibiotic use was allowed during the study.

Study population

Twenty patients, of which eight males, with 20 ulcers participated in the study. The average age of the patients was 74 +/- 12.2 years. The average ulcer size was 9.1 +/- 7.6 cm^2.

In 16/20 (80%) of all patients, revascularization had taken place prior to the application of TDA.

With regard to relevant comorbidities, two patients had undergone an organ transplanation (kidney: N=1, pancreas: N=1) and, accordingly, were taking immunosuppresive medication. 3/20 (15%) had suffered from a myocardial infarction within ≤ 12 months prior to the intervention. Five patients (25%) were undergoing dialysis while in the study and 6/20 patients (30%) were morbidly obese.

Results

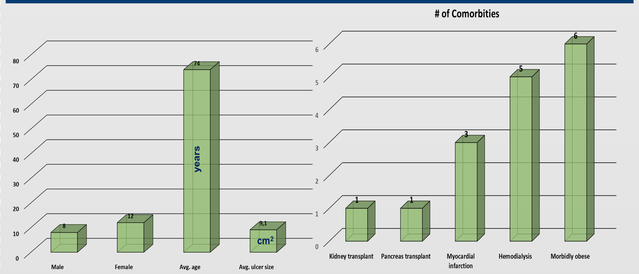
In 6/20 (30%) additional (sharp) debridement was necessary, primarily because of clinical reinfection. Five out of 20 (25%) suffered from some level of intra- or post-interventional pain, but pain had subsided in 95% of all patients at post-intervention day 3. Size reduction within 40 days occurred in 16/20 (80%) of the ulcers while complete reepithelialisation had happened in 6/20 (30%) of them.

The overall status of the ulcers at study end was improved/healed in 17 cases (85%), unchanged in two cases (10%) and worsened in one case (5%) (Clinician's opinion, Data courtesy of Dr. A.Bruttocao, M.D., Hospital University of Padua, Italy).

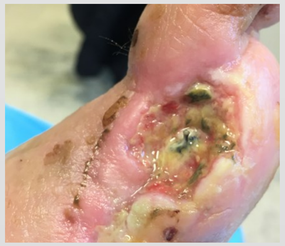
Discussion

The lesions assessed in this study were serious diabetic ulcers in patients with significant comorbidities. In addition, per the protocol, all lesions had to be clinically infected with *Pseudomonas Aeruginosa* to be allowed to enroll. Medications or comorbidities that have a negative influence on wound healing, typically exclusion criteria in most trials, were also allowed in this case series. It is, therefore, fair to say that the studied diabetic foot ulcers were hard to heal, although a formal in-study run-in period was not used to confirm this clinically.

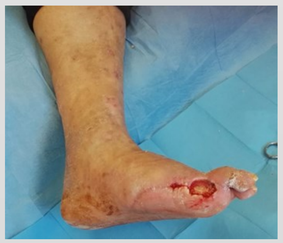
Demographics



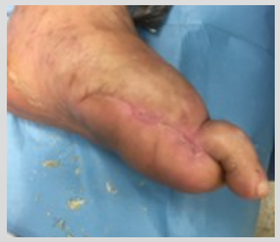
40-yr-old female, diabetic ulcer left foot
In existence for 4 months



Pre-application TDA

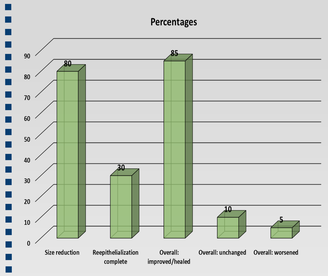


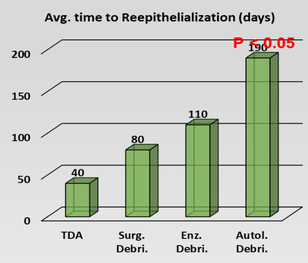
7 days post-application TDA



40 days post-application TDA

Results





In spite of these complicating factors, the overall healing results were quite satisfactory, with a large majority of the lesions showing improvement within only 40 days. Six out of 20 ulcers even completely reepithelialized, while there were no TDA-treatment associated complications and pain had subsided at three days post-intervention.

From a practical and health-economics point of view, it is an advantage that TDA-intervention does not need to be performed in the OR by highly specialized physicians. This may have been the primary reason for cost-reductions, associated with this type of treatment, at least in venous ulcers[11].

Limitations

This was a single centre, small, non-comparative case series with a number of patients with specific and very serious ulcers and a number of potentially healing-compromising circumstances. Also, the patients' sex was unequally divided in the study and the lesions were relatively small. Therefore, the results obtained cannot necessarily be extrapolated to other settings.

At the same time, biofilm and necrosis are virtually omnipresent in diabetic foot ulcers and there is no specific reason why their removal should not be one of the major objectives in wound healing in general: after all, healing per secondary intention, the way these lesions typically heal, cannot start without a wound bed filled with granulation tissue. Indeed, the primary purpose of assessing the TDA treatment, the removal of necrotic material or biofilm from ulcers, was proven successful, as reflected by the outcomes of the study.

Conclusion

A limited number of patients with very specific lesions underwent TDA treatment which was largely proven successful in removing biofilm and necrosis, allowing most ulcers to subsequently start improving and, for some, even reepithelialize completely within a period of only 40 days. Clinical implications include the fact that, within the proper indications for TDA, rapid debridement (as an alternative to surgical methods) can be achieved in simple ways and outside a hospital (OR) setting.

References:

1. McDermott K, Fang M, Boulton AJM, et al. Etiology, Epidemiology, and Disparities in the Burden of Diabetic Foot Ulcers. *Diabetes Care* 2023;46(1):209-21. doi: 10.2337/dci22-0043 [published Online First: 2022/12/23]
2. Armstrong DG, Swerdlow MA, Armstrong AA, et al. Five year mortality and direct costs of care for people with diabetic foot complications are comparable to cancer. *J Foot Ankle Res* 2020;13(1):16. doi: 10.1186/s13047-020 00383-2 [published Online First: 2020/03/27]
3. Driver VR, Fabbi M, Lavery LA, et al. The costs of diabetic foot: the economic case for the limb salvage team. *J Am Podiatr Med Assoc* 2010;100(5):335-41. [published Online First: 2010/09/18]
4. Omar A, Wright JB, Schultz G, et al. Microbial Biofilms and Chronic Wounds. *Microorganisms* 2017;5(1) doi: 10.3390/microorganisms5010009
5. Manna B, Morrison CA. Wound Debridement. StatPearls. Treasure Island (FL): DIME 2018.
6. Leaper DJ, Schultz G, Carville K, et al. Extending the TIME concept: what have we learned in the past 10 years? *Int Wound J* 2012;9 Suppl 2:1-19. doi: 10.1111/j.1742-481X.2012.01097.x [published Online First: 2013/01/05]
7. Schultz G, Bjarnsholt T, James GA, et al. Consensus guidelines for the identification and treatment of biofilms in chronic nonhealing wounds. *Wound Repair Regen* 2017;25(5):744-57. doi: 10.1111/wrr.12590 [published Online First: 2017/09/30]
8. Cogo A, Bignozzi AC, Hermans MH, et al. A desiccation compound as a biofilm- and necrosis-removing agent: a case series. *J Wound Care* 2022;31(10):816-22. doi: 10.12968/jowc.2022.31.10.816 [published Online First: 2022/10/15]
9. Ayello EA, Dowsett C, Schultz GS, et al. TIME heals all wounds. *Nursing* 2004;34(4):36-41; quiz, 41-2. [published Online First: 2004/07/13]
10. Wagner FW, Jr. The dysvascular foot: a system for diagnosis and treatment. *Foot Ankle* 1981;2(2):64-122. [published Online First: 1981/09/01]
11. Guest JF, Deanesi V, Segalla A. Cost-effectiveness of Debrichem in managing hard-to-heal venous leg ulcers in the UK. *J Wound Care* 2022;31(6):480-91. doi: 10.12968/jowc.2022.31.6.480 [published Online First: 2022/06/10]