

Pain perception and management during chemical debridement with a topical desiccating agent: a case-series analysis

Objective: A new topical desiccating agent (TDA; DEBRICHEM, DEBx Medical BV, the Netherlands) based on methanesulfonic acid (MSA) and dimethyl sulfoxide (DMSO) has proved to be an effective biofilm- and necrosis-removing chemical debridement option. However, its application can be temporarily accompanied by sharp pain perception, depending on the individual patient. This study aimed to assess application-associated pain and two strategies to manage this.

Method: A single-centre, retrospective, case-series study design was used to assess pain associated with MSA/DMSO treatment. To lower pain sensation during the application, two different local anaesthetic procedures were applied using either an anaesthetic cream or a form of tumescent local anaesthesia (TLA). Pain was assessed using the visual analogue scale (VAS) before, during and at five minutes after treatment. Overall wound pain, pain during dressing change in general and during the last change, as well as during the last sharp debridement were assessed. Additionally, baseline pain medication, medication during treatment and local anaesthetic

management before MSA/DMSO application were recorded. Patients with peripheral neuropathy were excluded from the analyses.

Results: A total of 20 patients treated with TDA were identified. Application lasted 20 minutes before treatment. Chemical debridement was associated with individual pain during application (VAS range 0–10). However, using adequate management, pain could be effectively reduced with no significant difference between pain ratings for TDA and the usually applied sharp debridement.

Conclusion: Accompanying pain during (chemical) TDA debridement was well managed using ready-to-use anaesthetic approaches. It demonstrated no increased overall pain perception compared with sharp debridement and, in some individual cases, even lower pain ratings.

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chemical debridement • chronic wound • debridement • dessication • dimethyl sulfoxide • hard-to-heal • methane sulfonic acid • wound • wound care • wound dressing • wound healing

Biofilms play a major role in catheter-associated and hospital-acquired infections,¹ as well as in prolonged wound healing.^{2–7} They are defined as communities of microorganisms that adhere to a surface or to each other (microcolonies) and are encapsulated in a matrix of extracellular polymeric substance (EPS).^{8,9} According to Römmling and Balsalobre,¹⁰ biofilms contribute to >80% of postoperative wound healing disorders, and are found in both acute and most hard-to-heal (chronic) wounds.^{5,10–13}

The presence of a biofilm leads to a local, yet ineffective immune response, resulting in chronic inflammation and a delay in wound healing. Biofilms are especially challenging, as they often remain undiagnosed, especially in immunocompromised patients.⁹ They cannot be observed with the naked eye, revealing only subtle inflammatory signs. According to the consensus guidelines by Schultz et al.,⁵ the only broadly-approved diagnostic criterion for biofilms is treatment failure despite the use of antibiotics and antiseptics. If all other treatment options have been exhausted and nothing else explains the delayed wound healing, biofilms should be considered. Biopsies are recommended for diagnosis, since swabs frequently

lead to an underestimation of or complete failure to recognise the (often polymicrobial) microbiological spectrum.^{5,9,14} Since individual biopsies can miss biofilm infection,^{3,5,15,16} curettage samples, punch biopsies and samples from sharp debridement are recommended for diagnosis.^{17,18} Mature biofilms pose a particular therapeutic challenge because of their tolerance and even resistance to antibiotics.^{5–7,9} In particular, sessile bacteria are up to 1000-times more tolerant to antibiotics than planktonic bacteria,¹⁹ possibly due to their slow growth rate within the biofilm.²⁰

Following the consensus guidelines, antibiotics are valuable for local infection control and prevention of sepsis; however, they do not treat the biofilm itself.⁵ Therefore, the implementation of sharp debridement is recommended to reduce the microbial load of the

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biofilm, though this alone is also not sufficient.^{5,21} Aggressive mechanical/sharp debridement—especially near a vascular graft or an infected vascular anastomosis—can be problematic due to potential bleeding complications. When considering a suitable treatment option for biofilms, a special ‘mode of attack’ should be taken into account: mature biofilms mainly consist of fluid (>95%⁹). In vitro studies have shown that they harbour water channels that serve as a transport system for nutrients, oxygen and waste products.^{22,23} Therefore, chemical debridement by desiccation, for example with methane sulfonic acid/dimethyl sulfoxide (MSA/DMSO), can solve the problem of antibiotic resistance and vulnerable tissues by ‘drying out’ the metabolic supply of the bacteria within the biofilm.²⁴

MSA/DMSO is an innovative (hygroscopic) agent for chemical debridement.^{25,26} The solution should be applied directly to the wound and to an area of 1cm surrounding skin for 60 seconds and then washed off, removing devitalised tissue and bacteria-carrying biofilm.²⁴ Typically, only a single application is required.²⁷ MSA/DMSO contains methanesulfonic acid, which causes rapid dehydration. Contact with water in the wound bed causes an immediate reaction, releasing about 1500kJ/mol of energy, which destroys all biochemical bonds in infected or devitalised tissue, leading to dehydration and oxidation.²⁶ In the following days, the desiccated and denatured tissue coagulates and is separated from the wound bed, allowing granulation tissue to grow as an essential step in secondary healing.²⁸ Several case studies have shown the successful use of MSA/DMSO as a topical desiccant in hard-to-heal wounds, effectively removing devitalised tissue and biofilm.²⁴ Therefore, MSA/DMSO is considered as a potential alternative to surgical debridement.

Despite its efficacy, MSA/DMSO is an acidic therapeutic agent (pH 3–4) that causes a strong burning pain, thus necessitating effective pain management during application. Apart from systemic analgesia, local wound bed preparation using anaesthetic creams, gels, infiltration or tumescent anaesthesia can be considered.²⁴ To date, there is no consensus and virtually no research to assess the best approach for local anaesthesia during TDA use.

This study therefore aims to improve the analgesic management of topical MSA/DMSO application using topical local anaesthetic medications that are commonly used in a clinical setting. In an initial feasibility cohort, two methods were chosen to compare pain management strategies and to evaluate non-inferiority concerning individual pain ratings, when compared to frequently used sharp debridement.

Methods

Patients

In this single-centre, retrospective, case-series study patients were retrospectively recruited and selected

based on their treatment with the topical desiccating agent (TDA; DEBRICHEM, DEBx Medical BV, the Netherlands) within the last 12 months for a vascular ulcer of the lower extremity.

Patients with the diagnosis of a diabetic foot ulcer or known peripheral polyneuropathy were excluded, as were patients with insufficient data on pain from previous visits.

Data were obtained from standardised reporting during the wound treatment within the institution, either from electronic medical records or from paper-based documentation. (Demographic and wound data are available from the author upon request.)

Ethical approval and patient consent

Ethical approval for this monocentric retrospective study was obtained from the ethics committee of the medical faculty of the Heinrich-Heine-University Düsseldorf (approval number: 2025-3192).

As the study was based on retrospective data, patient consent was not required.

Local anaesthesia

For the study, two different forms of local anaesthesia were used prior to debridement with the MSA/DMSO:

- An anaesthetic cream (Emla; Aspen Germany GmbH, Germany): 2.5% lidocaine/2.5% prilocaine) (EMLA group)
- A variant of tumescent local anaesthesia (Xylonest; Aspen Germany GmbH, Germany): prilocaine hydrochloride: 1% solution diluted in 50ml sodium chloride) (TUM group).

Both groups, included an equal number of patients.

Treatment protocol

The local anaesthetic was applied 30 minutes before local MSA/DMSO treatment, and was used in both outpatient and inpatient settings. In addition, the basic analgesic medication, and the medication on demand for wound pain and dressing changes were regularly documented. (Data are available from the author upon request.) After 30 minutes, the anaesthetic cream was rinsed off with sodium chloride (EMLA group) and in the other group, the tumescent soaked compress was removed from the wound (TUM group). Afterwards, the MSA/DMSO agent was applied to the wound for 60 seconds as per the manufacturer instructions for use, and subsequently thoroughly washed off with sodium chloride after completion of the application time.

Pain ratings

Local wound pain, as well as pain arising during interventions and analgesic therapy, were regularly recorded in patients as part of the wound documentation (part of the mandatory documentation for obtaining a certification as a special wound centre), and served as the data basis for this retrospective analysis.

Pain was assessed using the visual analogue scale (VAS 0–10; where 0=no pain and 10=strongest imaginable

pain) during the MSA/DMSO application and at five minutes after. In addition, general wound pain (resting pain), general pain during dressing changes as well as pain during the last dressing change and the last sharp debridement were extracted from the records.

Pain assessments on the first day (the last dressing change without MSA/DMSO) and the second day (after MSA/DMSO application), compared to baseline, for general wound pain, general pain during dressing changes and pain during the last dressing change were evaluated. Also assessed were pain on the first (current pain) day and on the second day, the overall pain since the MSA/DMSO treatment.

Statistical analysis

Statistical analysis was performed using GraphPad Prism (Version 10.2.2, GraphPad Software LLC, US). Results are reported as median and range as well as mean \pm standard error of the mean (SEM). An alpha level of 5% ($p=0.05$) was assumed for statistical significance.

For the comparison of the EMLA and TUM pain ratings for the MSA/DMSO versus sharp debridement pain ratings, a Wilcoxon matched pairs test was performed. The Mann-Whitney U test was used to evaluate the comparison between pain levels when debrided with MSA/DMSO following application of TUM versus EMLA pre-treatment. As the mode of local anaesthetic pre-treatment did not lead to any significant difference, the data of the two groups were pooled and calculated against the intra-individual pain ratings for sharp debridement using a Wilcoxon test.

Results

A total of 20 patients were included in the study, 10 in each group. (Demographic and wound data are available from the author upon request.)

Anaesthetic cream pre TDA versus sharp debridement

Pain ratings for MSA/DMSO application after local anaesthetic treatment with EMLA cream ranged between VAS 0–9 (median: 6.5), while sharp debridement during wound dressing changes in the past was evaluated intra-individually with a VAS of 2–10 (median: 7.5) (Fig 1). Sharp debridement (SHARP) therefore showed a higher pain level than the TDA treatment under anaesthetic cream. The statistical comparison, however, did not reveal a significant difference (EMLA versus SHARP mean \pm SEM: 5.300 ± 1.033 versus 7.000 ± 0.7601 , respectively; $p=0.065$) between the groups. Nevertheless, a tendency for lower pain ratings for the EMLA-pre-treated MSA/DMSO application could be observed.

Tumescent anaesthesia pre TDA versus sharp debridement

Pain ratings for MSA/DMSO application after tumescent anaesthesia with Xylonest (TUM) ranged between VAS 0–10 (median: 7.5), while sharp debridement during wound dressing changes in the past was also evaluated

Fig 1. Comparison of pain ratings on a visual analogue scale (VAS) during methane sulfonic acid/dimethyl sulfoxide application after local anaesthetic pre-treatment with an anaesthetic cream (EMLA, $n=10$) and the individual pain sensation of sharp debridement during former wound treatment (SHARP, $n=10$)

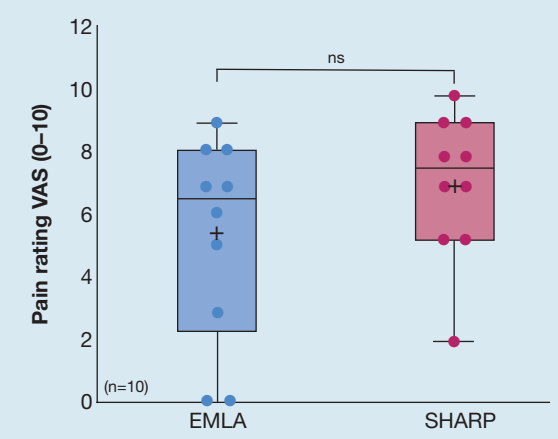
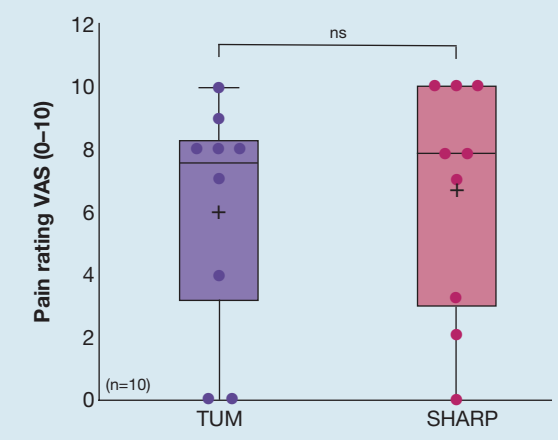


Fig 2. Comparison of pain ratings on a visual analogue scale (VAS) during methane sulfonic acid/dimethyl sulfoxide application after tumescent anaesthesia (TUM, $n=10$) and the individual pain sensation of sharp debridement during former wound treatment (SHARP, $n=10$)

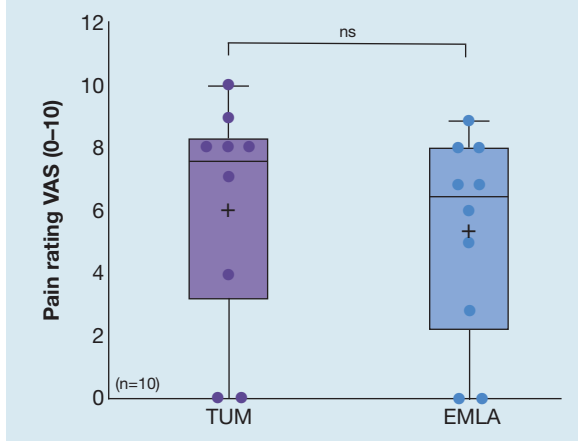


intra-individually with a VAS of 0–10 (median: 8.0) (Fig 2). Again, the TDA under TUM demonstrated lower pain ratings; however, without a statistically significant difference (TUM versus SHARP mean \pm SEM: 6.000 ± 1.125 versus 6.700 ± 1.165 , respectively; $p=0.516$).

Tumescent anaesthesia versus anaesthetic cream

Direct comparison between the two groups (TUM versus EMLA) revealed no significant difference in pain ratings for MSA/DMSO application after local anaesthetic pre-treatment (TUM versus EMLA mean \pm SEM: 6.000 ± 1.125 versus 5.300 ± 1.033 , respectively; $p=0.511$). The TUM-treated group generally demonstrated higher VAS scores (median: 7.5, range: 0–10) than the EMLA-treated group (median: 6.5, range: 0–9) (Fig 3).

Fig 3. Comparison of pain ratings on a visual analogue scale (VAS) during methane sulfonic acid/dimethyl sulfoxide application after tumescent anaesthesia (TUM, n=10) and local application of an anaesthetic cream (EMLA, n=10)



MSA/DMSO versus sharp debridement

As the type of local anaesthetic pre-treatment before TDA application did not reveal any significant difference, patient data were pooled, and intra-individual pain ratings were compared to pain ratings for sharp debridement from dressing changes in the past (Fig 4a,b). Again, the pain ratings during the application of a TDA with any form of anaesthetic pre-treatment demonstrated lower pain ratings than sharp debridement. The comparison did not show a statistically significant difference (MSA/DMSO versus SHARP mean±SEM: 5.650±0.7479 versus 6.850±0.6777, respectively; $p=0.071$).

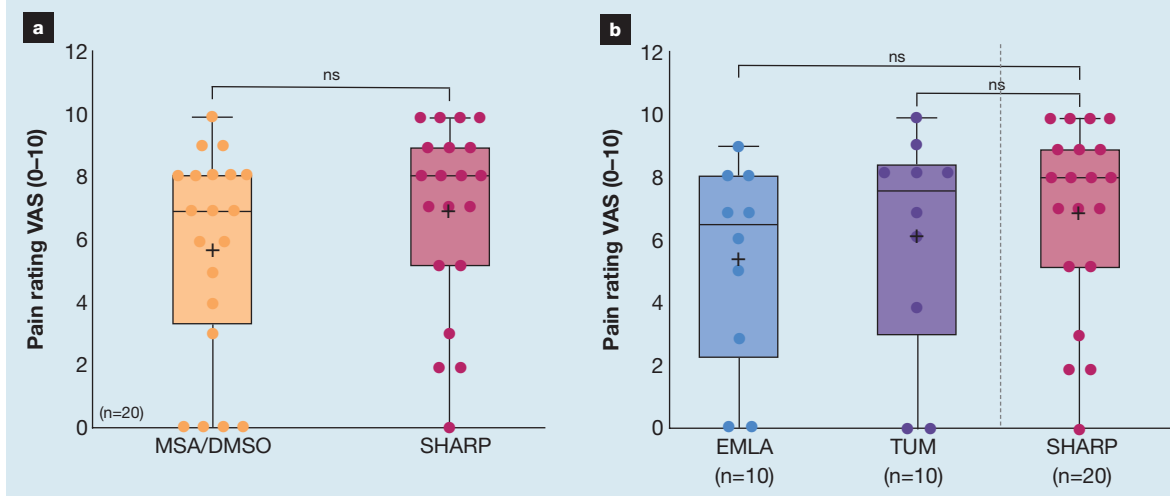
Discussion

Wound bed preparation by removal of necrotic tissue and slough, which support biofilm formation, is a central element to support angiogenesis, granulation and proliferation.^{5,24} To achieve this, regular sharp debridement is a commonly recommended procedure.^{5,9} Biofilms play a central role in hard-to-heal wounds⁹ as well as vascular graft infections. However, surgical or sharp debridement, perhaps even mechanical debridement, is not always possible—for example, in the vicinity of anastomoses in vascular prosthesis infections—due to patient pain or lack of training of the healthcare professional. Pain especially can be a limiting factor when considering different forms of debridement in patients with high pain scores.²⁹

The MSA/DMSO agent used in this retrospective single-centre study is an innovative desiccating (hygroscopic) agent for chemical debridement.^{25,30} From the experience of various healthcare practitioners and in exchanges with the manufacturer, it is recommended that the wound be prepared with a local anaesthetic, such as lidocaine or prilocaine, before application of the MSA/DMSO agent, as chemical debridement has been reported to be painful.²⁴ However, to date and to the authors' knowledge, no comparison on pain levels between different local anaesthetic pre-treatments and comparison to sharp debridement has been performed to evaluate best practice approaches. Specifically, the question posed by this present study was whether chemical debridement could be considered more or less painful than sharp debridement under the same forms of local anaesthesia.

The patients in this study did not show any significant differences in individual pain ratings for treatment with chemical debridement following local anaesthetic pre-treatment when compared with the pain caused by

Fig 4. Comparison of pain ratings on a visual analogue scale (VAS) between methane sulfonic acid/dimethyl sulfoxide (MSA/DMSO) application independent of the local anaesthetic (LA) pre-treatment (MSA/DMSO (including LA)) and sharp debridement (SHARP) (a). Individual comparison of the grouped pain ratings for MSA/DMSO application after pre-treatment with either anaesthetic cream (EMLA) or tumescent anaesthetic (TUM) versus pain ratings for sharp debridement (b)



sharp debridement.³¹ Therefore, the results show a non-inferiority in relation to the painfulness of the treatment, eliminating concerns of healthcare practitioners regarding a more intense pain perception during TDA treatment than during sharp debridement. The results of this study even demonstrated a tendency towards lower pain ratings for the TDA compared with sharp debridement under proper analgetic management for both types of analgesic (1 score lower on VAS for TDA; Fig 4).

An important advantage of chemical debridement with MSA/DMSO is that, in most cases, it only requires a single application.²⁷ This is in contrast to selective sharp debridement which, ideally, is conducted frequently but which results in a painful procedure at each dressing change.³² Thus, due to its painfulness and the necessary extent of tissue removal, surgical debridement is usually conducted in the operation room (OR), while sharp debridement is usually performed during wound dressing changes at the bedside.³¹ Both, however, necessitate repeated application, specific skills and time resources (additional to the local anaesthetic pre-treatment which is necessary for both sharp and chemical debridement).

As MSA/DMSO is easily applied and, as the findings of this study indicate, results in mainly moderate pain ratings (if pre-treated with local anaesthetics) slightly lower than that of sharp debridement, the application of the TDA can save OR capacity and time; not having to perform sharp or surgical debridement under OR conditions but applying a chemical debridement at the bedside further frees up anaesthesiological and surgical personnel and has been shown to shorten treatment costs and hospitalisation time due to more efficient wound management.^{27,31,33} Furthermore, there is consensus that mechanical/sharp debridement is a central instrument of biofilm management; however, it is not sufficient on its own due to the rapidity of biofilm reformation.^{5,21,29,31} In addition, a too rigorous application of mechanical/sharp debridement can cause excessive bleeding or damage fragile granulation tissue, which would be a setback in the wound healing process.³¹

In contrast, MSA/DMSO 'differentiates' between biofilm-infected tissues and debris, and the 'healthy' vital tissue underneath using two components—the water concentration of the wound tissue and the length of the application time.^{24,25,30} MSA/DMSO reacts on contact with water in an exothermic reaction thus drying up the wound bed through rapid desiccation.³⁰ In this process, around 1500kJ/mol of energy are released, thus destroying all biochemical bonds in infected or devitalised tissue.³⁰ The more water the tissue contains, the faster the reaction will take place. Therefore, as biofilms mostly consist of water (>95%),^{9,22,23} they will react faster with the MSA/DMSO agent and will dry out completely with the recommended application time of 60 seconds.^{24,25,30} The healthy tissue underneath does not contain

enough water to kickstart such a reaction with MSA/DMSO in the same amount of time, and thus will be 'spared'. Therefore, when using MSA/DMSO, it is important to adhere to the recommended application time to protect the vital tissue. When applied correctly, the aspect of protecting the vital tissue underneath the biofilm is another advantage of chemical debridement when compared to the more invasive method of mechanical/sharp debridement.

Another important aspect is that the presence of biofilms can keep a wound stuck in a non-healing state and remain as an 'undefined tissue type' or 'unhealthy granulation tissue', when a wound usually should progress towards granulation and re-epithelialisation. Therefore, complete biofilm removal is crucial to allow the wound to progress along its healing trajectory.²⁹ While mechanical/sharp debridement is only able to reduce the microbial load⁵ and leaves behind biofilm remnants which rapidly reform within hours.²⁹ Chemical debridement with MSA/DMSO devitalises the biofilm and gives the wound milieu a 'kickstart', from an inert state to an active healing process, which has been shown to be especially successful in hard-to-heal wounds.^{29,31}

Over the following days to weeks after MSA/DMSO application, the desiccated and denatured tissue coagulates together and becomes separated from the wound bed, allowing the latter to grow granulation tissue as an essential step in secondary healing or wound closure.²⁸ Furthermore, the MSA/DMSO agent is not just applied to the wound bed, but also to the periwound skin (1cm in diameter), which prevents bacteria from migrating into the wound and thus reduces the risk of reinfection.^{29,31}

Nonetheless, singular costs for the use of a TDA need to be considered and weighed against other forms of debridement, as well as its availability and the individual preferences of the patient and healthcare professional.

Another challenge was the notion of a sharp pain during application, which had restricted treatment with a TDA.²⁴ A perception of excessive pain during the TDA treatment was not observed in the present study. However, the findings of this study could demonstrate a non-inferiority of the TDA treatment in terms of pain and even a tendency towards less pain than during sharp debridement. The results of the analysis showed pain levels to be manageable using local anaesthetic approaches, such as anaesthetic creams and tumescent anaesthesia.

Limitations

The nature of this preliminary investigation, which represents a small observational cohort, should be considered a limitation. To gain a better understanding of the pain dynamics and best practices for local anaesthesia, larger studies will be necessary. Also, using higher concentrations in the local tumescent anaesthetic approach may be able to reduce treatment-related pain even further and should be explored in the future.

Conclusions

The MSA/DMSO agent should be considered as an adjunct or even potential alternative to mechanical/sharp debridement, as the findings of this study could demonstrate that the painful sensation caused by the MSA/DMSO treatment is manageable with a combination of local anaesthetics and the usual individual pain medication, taken by the patients during wound dressing changes. (Data are available from the author upon request.) No significant difference between pain ratings for chemical and sharp

debridement were demonstrated by the results of the study, thus demonstrating a non-inferiority in relation to patients' individual pain sensation. A future initiative would be to further lower individual pain ratings during MSA/DMSO application, for example, by using higher concentrations of local tumescent anaesthetic agents. **JWC**

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Reflective questions

- What alternative debridement strategies can be used in wound management in general?
- How can pain be effectively managed during chemical debridement with a topical desiccating agent?
- What are the benefits, if any, of using chemical debridement as an adjunct or even alternative to mechanical/sharp debridement?