

## Use of silver sulfadiazine 1% cream for the treatment and prevention of infected chronic leg ulcers

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### ABSTRACT

Treating skin lesions is complex due to the variety of aetiologies, the presentation of the wound, the course of the injury and the high number of associated comorbidities. The main aim of any treatment is to resolve any infection, as this is the essential condition for the lesion to subsequently heal. There is a lot of evidence in literature that a topical antibiotic treatment is better than a systemic antibiotic therapy for infected wounds. Silver sulfadiazine 1% cream (SSD Ag 1%), a topical chemotherapy antibiotic, has been proved to be effective for the prevention and cure of acute and chronic skin lesions that are infected or susceptible to superinfection. The purpose of this study is to confirm the efficacy of SSD Ag 1% in improving the quality of life of patients with lesions. The study was conducted at the Experimental Wound Treatment Outpatients Department of the Praia a Mare Local Healthcare Centre (Cosenza Health Authority, Italy); it involved 86 patients during a 4-month period, some of whom were treated in the outpatients department and some at home, with an average age of 69.6, for prophylaxis (50/86, 58%) or to treat ulcers, primarily leg ulcers (36/86, 42%). The results of using SSD Ag 1% cream showed that for patients on whom the product was used as treatment, pain perception fell in 18 out of 24 patients, with improved quality of life assessed using the Visual Analogue Scale-Quality of Life Scale. The efficacy of SSD Ag 1% was shown by 23 cases of healing in 12 weeks and 5 cases in 4 weeks and by 10 cases of resolution of the infection only. SSD Ag 1% was shown to be an excellent product both for prophylaxis (to prevent infections in high-risk ulcers) and for treating wound infections, combining efficacy and tolerability.

### INTRODUCTION

Treating skin lesions is complex due to the variety of aetiologies, the presentation of the wound, the course of

the injury and the high number of associated comorbidities. Wounds are usually contaminated with a wide variety of microorganisms. Antimicrobial treatment for the prevention and cure of acute and chronic skin lesions that are infected or susceptible to superinfection is therefore a very important issue for clinicians.

The main aim of any treatment is to resolve the infection, as this is the essential condition for the lesion to subsequently heal.<sup>1,2</sup>

All wounds contain microorganisms, but in most cases there is no infection. The interaction between microbial population and host can reach a point when the healing process is affected and the host is damaged. Predisposing factors that can affect the healing of a wound always to be considered include any immune system deficiencies and the locoregional perfusion of the tissue involved, which must be assessed. Reduced perfusion may be a consequence of the infection itself or be secondary to associated disorders (chronic obliterative arterial disease, diabetic foot, venous valve insufficiency, chronic ulcer, burns, surgical site infection). There is a lot of evidence in literature that a topical antibiotic treatment is better than a systemic antibiotic therapy for wounds, especially when the aforementioned risk factors are present.<sup>1-11</sup> It has been shown that silver sulfadiazine 1% cream (SSD Ag 1%) is also effective for preventing and treating methicillin-resistant *Staphylococcus aureus* infections.<sup>12-17</sup>

In any case, when such infections occur intervention is needed. The decision to intervene is made based on how

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fast a wound is healing and also on whether there are any subtle or obvious signs of infection.

There are four clinical stages of infection, and the appropriate therapy for treating the wound is chosen according to the stage. The first stage is marked by subtle signs of infection such as pain, bad smell, slight discharge near the wound. In the second stage, the subtle signs of infection become more marked and the healing process stops progressing. In both cases, a local antimicrobial therapy is used creating a moist environment that encourages the wound to heal. The third stage is marked by localised signs of infection such as pus, swelling, pain, rash, heat and involvement of the surrounding skin. The fourth and last stage has localised and general signs of infection (pyrexia, increase in white blood cells, *etc.*) which could develop into sepsis. In the last two stages, a systemic therapy is used for the infection.

On this basis, it is clear that it is essential to keep the wound, the surrounding tissue and the patient's general condition under continuous observation and assessment so that the right treatment can be given in time. Wound infections are always a subject of great debate as infection is undoubtedly the main enemy of wounds, as it delays healing, raising the likelihood of it becoming chronic and reducing the patient's quality of life; they therefore need to be prevented or, if already present, eliminated.

According to the guidelines, the treatment used in the first two clinical stages of infection, as indicated above, is topical antimicrobials that can kill or inhibit the growth and division of the microorganisms. They include topical antibiotics that act on specific target areas of cells,<sup>1,2,14-16</sup> antiseptics and disinfectants. They are chosen to treat infected wounds based on their specific features and effectiveness against a pathogen, their cytotoxicity for human cells and their allergenicity. The most commonly used types are: chlorhexidine, iodine-based products and silver-based products.

SSD Ag 1% is a topical chemotherapy antibiotic, with selective toxicity, meaning that it acts on the germ causing the damage and not on eukaryotic cells.

The purpose of this study is to assess the efficacy of SSD Ag 1% in improving the quality of life of patients with lesions.

## MATERIALS AND METHODS

The pharmaceutical product involved in this study, used at the Praia a Mare Local Primary Health Care Centre (Cosenza Health Authority, Italy) in our Wound Care Clinic, is SSD 1% cream based on silver sulfadiazine, classified by the Health Ministry as an antibiotic and chemotherapy drug for topical use ATC: D06BA01. Because of its effectiveness and excellent benefit-cost ratio, it was reconfirmed in 2017 as one of approximately 200

essential drugs for adults and children.<sup>18,19</sup> It was also classified by the Agency for Healthcare Research and Quality (AHRQ) guidelines for treatment of infections in bed sore lesions as a level A drug for treatment of infections caused by Gram+, Gram- and anaerobic bacteria.<sup>12,13</sup> It is also one of the few antimicrobials not to create resistance, thanks to its double action mechanism (sulfadiazine and silver, which have a bacteriostatic and bactericidal action respectively).<sup>17</sup> It is also indicated for prophylaxis and as a local antibacterial treatment for second- and third-degree burns, ulcers of various aetiologies (including pressure ulcers) and, generally, skin conditions that are infected or susceptible to infection (Figure 1).

In our study, the SSD Ag 1% cream was used on 86 patients during a 4-month period, some of whom were treated in the outpatients department and some at home, with an average age of 69.6, for prophylaxis or to treat ulcers, primarily leg ulcers (malleolus, heel, sole and toes) of various aetiologies such as: venous, arterial, pressure (bedsores and traumatic), diabetic, dermo-rheumatological, post-surgical and, in one case, a third-degree burn. Before applying the cream, the wound bed was carefully cleaned with a saline solution and possibly antiseptics (based on silver ions, polyhexanide, *etc.*). The cream was then applied, using a sterile glove, directly on the wound in an even layer 2-3 mm thick. The secondary medication was usually absorbent materials such as alginate, polyurethane foam and/or a multicomponent multilayer bandage with four layers made from: a

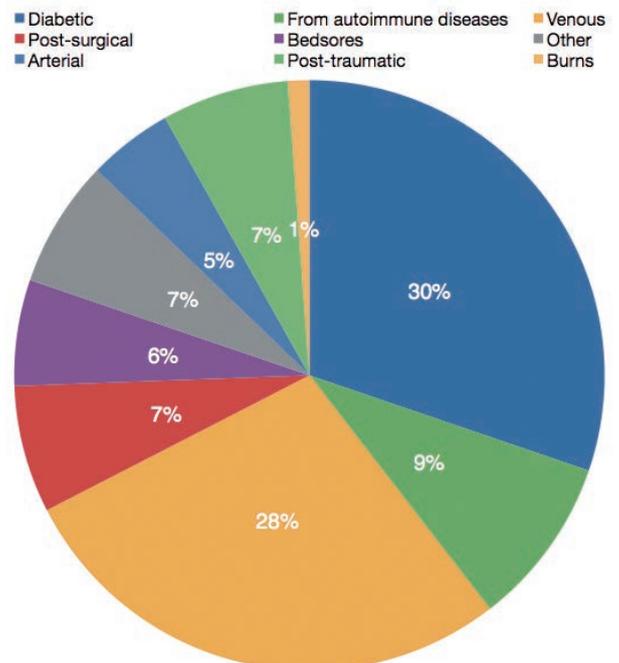


Figure 1. Types of ulcers.

medicated bandage (with zinc, zinc and coumarin, alginate, *etc.*), a cotton wadding bandage, a self-adhesive bandage and a short-stretch adhesive bandage. The medication was changed once, twice or three times a week according to the condition of the wound, the anatomical site and generally the patient concerned, therefore independently of the use of the SSD Ag 1%.

### Study objectives

The purpose of our study is to check the quality of life of patients treated with SSD Ag 1%, quantifying the pain experienced because of the infection during the treatment, using the numerical Visual Analogue Scale (VAS) assessment scale and assessing Quality of Life (QOL) using the VAS-QOL9 scale, and to check reports of adverse effects during the treatment and the actual efficacy of the product on the infection. The study is also interested in checking the truth of objections made by some people to the use of this drug, such as: i) creation of drug resistance; ii) formation of a thick layer of cream that is hard to remove when replacing the medication; iii) high absorption at topical level (in the case of very extensive wounds); iv) doubts about preferences for using an antiseptic on its own rather than an antimicrobial; v) doubts about using SSD Ag 1% if there is necrotic tissue in conjunction with signs of infection.

## RESULTS

The results of using SSD Ag 1%, applied from the start of treatment to the end of the study on 86 patients, as prophylaxis (50 patients) and to treat infections (36 patients), showed that:

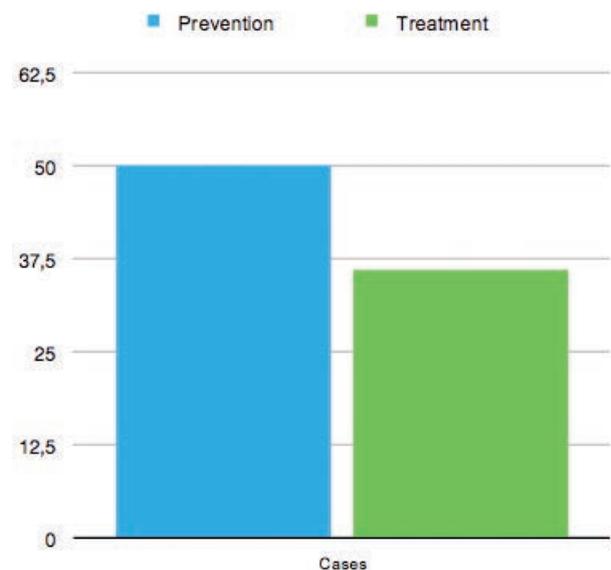
- For patients on whom the product was used as treatment, pain perception fell in 18 out of 24 patients with an infected wound and a score above 6 on the numerical VAS scale. As a result, the quality of life of each of these 18 patients increased from a score of 50 or less to a score of around 70 on the VAS-QOL scale (*i.e.* by around 15%), as the reduction in pain was associated partly with the wound healing and partly with the resolution of the infection.
- The actual efficacy of SSD Ag 1% was shown by 23 cases of healing in 12 weeks and 5 cases in 4 weeks (of which 19 in the prevention category and 9 in the treatment category) and by 10 cases of resolution of the infection only (out of 36 patients with an infected ulcer).
- During the study there were no adverse events connected to the drug in any of the cases, either after its first use or at the end of the study.
- With regard to the use of SSD Ag 1% for prophylaxis, none of the patients with an ulcer at risk of infection developed an infection at the end of the study.

The findings and objections of other users were proved wrong as follows:

- SSD Ag 1% did not create demonstrable resistance in any patients.
- No hard-to-remove paste was created if the cream was applied correctly (layer 2-3 mm thick on the wound bed).<sup>17</sup>
- The decision to use an antiseptic during the cleaning did not interfere with the use of the product in question. No adverse events were caused to patients by using both.
- The doubts about the frequency of changing the medication were proved wrong in our experience. The timing for changing the medication or the type of medication depends on the state/stage of the lesion to be treated in accordance with the correct care timing protocols, regardless of whether the drug is used.
- On the last objection, concerning the uncertainty of using SSD Ag 1% on a lesion with necrotic tissue, we can state that, with regard to the necrolytic capacity of the product in question, its use was shown to help remove the necrosis. The infection prevention effect was also useful and significant as infection of skin lesions with necrotic parts is greatly feared (Figures 2 and 3).

## DISCUSSION AND CONCLUSIONS

The results of this study showed that SSD Ag 1% is an excellent product both for prophylaxis (to prevent infections in high-risk ulcers) and for treating wound infections.



**Figure 2.** Use of silver sulfadiazine 1% cream for the treatment and prevention of infections.

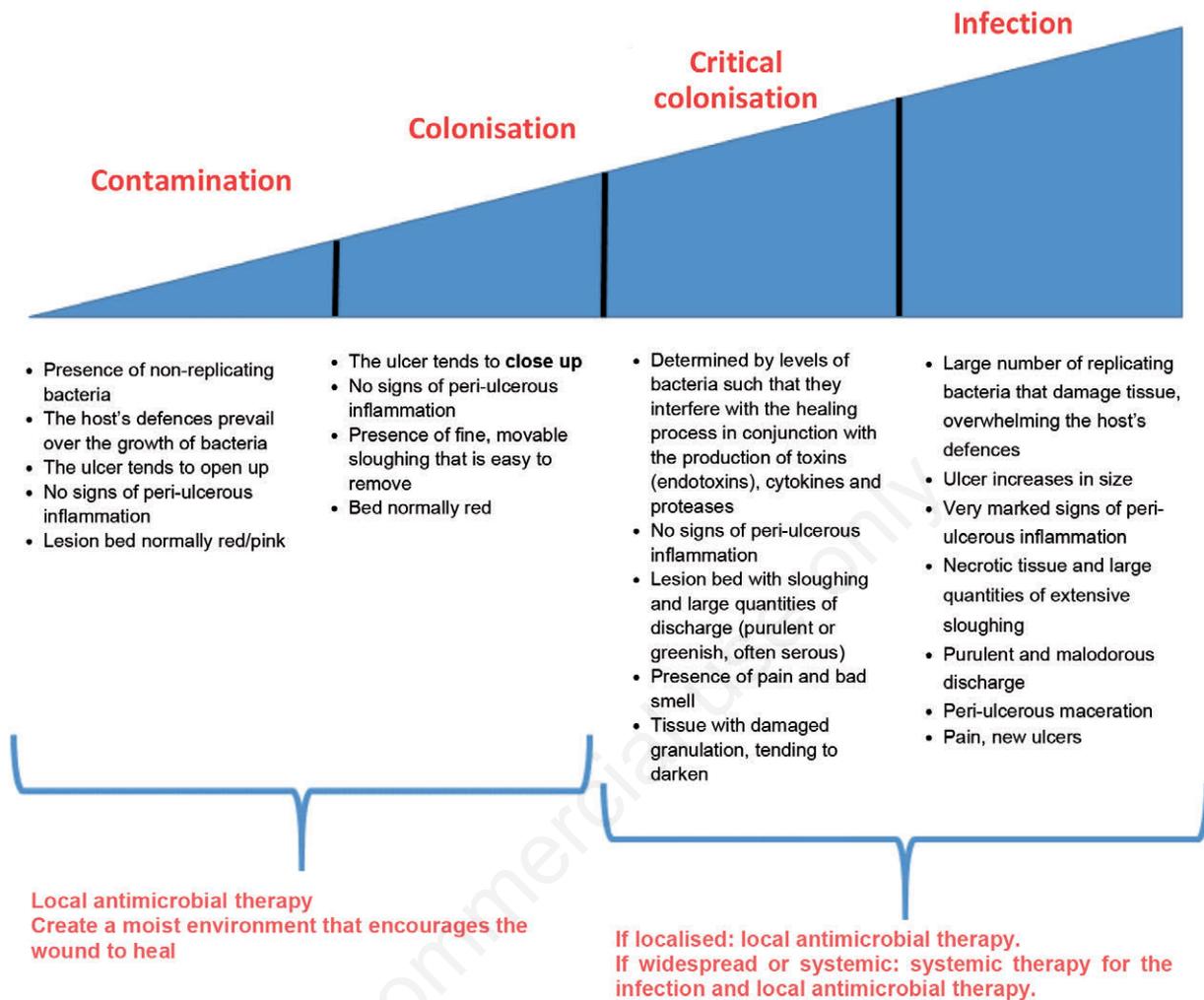


Figure 3. Microbial count level.

It reduces pain perception and improves the quality of life of patients with chronic skin lesions as much as possible. SSD Ag 1% is a very tolerable drug, is tolerated well on the wound bed and does not create drug-resistance (average of 57 mg eliminated in urine in 24 hours). It is a cheap, effective, safe and manageable drug. It keeps the environment moist and acts as a barrier for the wound bed. It does not alter the frequency of changing the medication or the use of materials usually used as secondary medication. It is also indicated for self-medication as it is easy to use.

Treatment with SSD Ag 1%, in accordance with efficacy, effectiveness and efficiency standards, ensures that the treatment is provided in compliance with the most appropriate prescribing practices and good clinical practice, combining the effectiveness of the drug with good tolerability and affordable costs for the National Health Service.

## REFERENCES

1. Heal CF, van Driel ML, Lepper PD, et al. Topical antibiotics for preventing surgical site infection in wounds healing by primary intention. *Cochrane Database Syst Rev* 2014;12.
2. Edwards R, Harding KG. Bacteria and wound healing. *Curr Opin Infect Dis* 2004;17:91-6.
3. Hoffmann S. Silver Sulfadiazine: an antibacterial agent for topical use in burns. *Scand J Plast Reconstr Surg* 1984;18: 119-26.
4. Fakry SM, Alexander J, Smith D. Regional and institutional variations in burn care. *J Burn Care Rehab* 1995;16:86-90.
5. Klasen HJ. A historical review of the use of silver in burns. *Burns* 2002;26:117-30.
6. Buckley SC, Scott K, Das K. Late review of the use of Silver Sulphadiazine dressings for the treatment of fingertip injuries. *Injury* 2000;31:301-4.

7. Bishop J, Phillips LG, Mustoc TA, et al. A prospective randomized evaluator blinded trial of two potential wound healing agents for the treatment of venous stasis ulcers. *J Vasc Surg* 1992;16:251-7.
8. Blair SD, Backhouse CM, Wright DD. Do dressings influence the healing of chronic leg ulcers? *Phlebology* 1988;3: 129-34.
9. Van Den Hoogenband HM. Treatment of leg ulcers with split-thickness skin grafts. *J Dermatol Surg Oncol* 1984;10: 605-8.
10. Ouvry PA. A trial of Silver Sulfadiazine in the local treatment of venous ulcers. *Phlebologie* 1989;42:673-9.
11. O'Meara SM, Cullum MA, Majid M, et al. Systematic review of antimicrobial agents used for chronic wounds. *Br J Surg* 2001;88:4-21.
12. AHCPR Clinical Practice Guidelines. Treatment of pressure ulcers. Managing bacterial colonisation and infection. Rockville, MD: Agency for Health Care Policy and Research (AHCPR); 1994. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK17932/>
13. Calosso A, Zanetti E. Prevenzione e trattamento delle lesioni da decubito. Linee guida integrali della AHCPR (Italian version). [Prevention and Treatment of Bedsore Lesions, AHCPR Integral Guidelines]. Pavia, Italy: Ed. AISLeC News; 2002.
14. Castellano JJ, Shafii SM, Ko F, et al. Comparative evaluation of silver-containing antimicrobial dressings and drugs. *Int Wound J* 2007;4:114-22.
15. Marone P, Monzillo V, Perversi L, et al. Comparative in vitro activity of silver sulfadiazine, alone and in combination with cerium nitrate, against staphylococci and gram-negative bacteria. *J Chemother* 1998;10:17-21.
16. Tehrani R. Silver Sulfadiazine for MRSA infections. *Indian J Dermatol Venereol Leprol* 2004;70:186.
17. Giraldi E, Zorzi L. Razionale di impiego dell'argento sulfadiazina nelle lesioni cutanee croniche infette [Rationale for the use of Silver Sulfadiazine in infected chronic skin wounds]. *Acta Vulnol* 2013;11:83-9.
18. World Health Organization (WHO). WHO Model List of Essential Medicines. 20th List, ed. March 2017 (amended August 2017). Geneva, Switzerland: World Health Organization; 2017. Available from: <http://apps.who.int/iris/bitstream/handle/10665/273826/EML-20-eng.pdf>
19. World Health Organization (WHO). WHO model list of essential medicines for children. 6th List, ed. March 2017 (amended August 2017). Geneva, Switzerland: World Health Organization; 2017. Available from: <http://apps.who.int/iris/bitstream/handle/10665/273825/EMLc-6-eng.pdf>