

Review Article

Chronic wounds: treatments and relevant educational strategies



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Azevedo Maria-Manuel¹

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¹School D. Maria II, Rua da Alegria, Vila Nova de Famalicão 4760-067, Portugal.

Correspondence:

Azevedo Maria-Manuel. School D. Maria II, Rua da Alegria, Vila Nova de Famalicão 4760-067, Portugal.

E-mail: maria.manuel.azevedo2011@gmail.com

ABSTRACT

Introduction: Chronic wounds became a major public health problem leading to very high economic costs. They have a devastating impact upon patients, caregivers and the society in general, being a major source of patient morbidity. Even though all the advances, the role of antimicrobial agents is not clear.

Methods: We searched Medline/PubMed, Web of Science and Cochrane Database of Systemic Reviews, using the terms chronic wounds, patient morbidity, topic treatments, systemic treatments and education. Our focused was on the articles published since 2000.

Results: The rationale use of anti-infectious agents is crucial particularly in a context of a global emergence of microbial resistance. In this situation higher interest has been created in the use of topical therapies to manage wound infection. Concerning the utilization of systemic antibiotics, they are used as last resort when topical treatments are unsuccessful to the healing process. Data from the literature recognized scarcities in the wound care knowledge in several healthcare professionals.

Conclusion: Clinical assessment of patient wound is crucial to select the best wound treatment. In this context educational strategies are urgent to meet the needs of different professional groups and levels of expertise to maximize effectiveness.

Introduction

The terms acute and chronic wounds are frequently used in clinical practice however wound classification has received little attention. Acute wounds follow a healing process in an “orderly and timely reparative process”. Chronic wounds are defined as wounds that unsuccessful advance through a methodical and well-timed reparative process to produce anatomic and functional integrity over a period of 3 months (1). The process of wound healing must be checked with regularity and preferably by the same caregiver. This situation leads to very highly economic

costs being a major source of patient morbidity (2). The reduction of infection associated with wounds could result in significant overall health care cost savings. Every year, wound infections result in thousands of dollars in medical and hospital charges. Chronic wounds are linked with some features associated with conditions frequent in older people, such as continuous skin pressure, diabetes mellitus and arterial and venous insufficiency (3) (Figures 1 & 2).

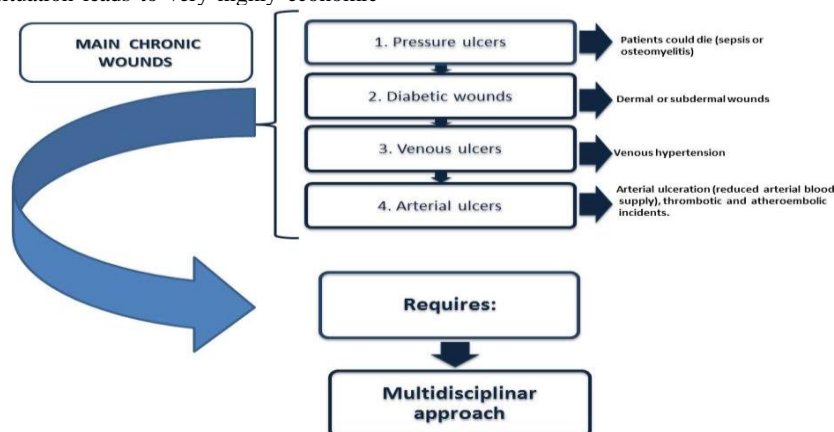


Figure 1. Main chronic wounds and multidisciplinary approach



Figure 2. Chronic wounds and wound healing

It is important to highlight that the treatment of chronic wounds includes many methodologies. In this approach topical and systemic treatments were considered and educational strategies were explored.

Methods

We searched Medline/PubMed, Web of Science and Cochrane Database of Systemic Reviews, using mainly the terms chronic wounds, patient morbidity, topic treatments, systemic treatments and education.

Results

Despite all the advances, the role of antimicrobial agents is not clear. This fact is related to the doubt around the issue of whether bacterial presence is an important factor in wound healing. Some investigations show a positive association between the bioburden, with higher bacterial counts, being associated with delayed wound healing (4, 5). However, others do not show such association.

Topical agents

As antibiotic resistance has become a major public health problem higher interest has been created in the use of topical therapies to manage wound infection. Concerning wound care dressings, they have evolved over time. In the last decade increase the interest in silver clinical application due to their antimicrobial and anti-inflammatory properties. A study performed by Kalan and collaborators, reveal that dressings with oxidized silver help the stalled wounds to change to a normal healing course. This study also hypothesises that the use of topical antimicrobial dressing targets the wound microbiome and reduces bioburden (6).

Concerning iodine, reduces bacterial bioburden in the wound bed, however can be cytotoxic. Nevertheless, an *in vitro* study using cadexomer iodine showed no toxicity for human cells at concentrations of 0.45% (7). This compound was been reported to exhibited higher efficacy comparatively to other wound dressings against bacterial wound biofilms (8).

Activated carbon is also incorporated in several available dressings mainly for malodorous wounds (9). Relatively to metronidazole concentrated gel, can be used as a topical agent for wound management (10). Relatively to honey since ancient times has been used in wound care (11), evidence from experimental works and some trials has proposed that honey may accelerate wound healing. Honey is a viscous, supersaturated sugar solution derived from nectar gathered and modified by the honeybee, *Apis mellifera*. It contains around 30% glucose, 40% fructose, 5% sucrose and 20% water among many other constituents, such as amino acids, vitamins, minerals and enzymes. A reduction in the overall risk of adverse events with honey relative to silver sulfadiazine was also reported (12).

Mechanisms of action

Silver, charged nanoparticles could adhere to the cell wall affecting key proteins and enzymes leading to an increase in cell permeability causing its damage (13, 14). On the other hand, silver products lead to reactive oxygen species (ROS) production (15). Relatively to iodide, its action is not completely understood (16), however can disrupts bacterial cell wall, disturb proteins, enzymes and nucleotides leading to cell death (17, 18). Metronidazole can lead to ROS production inducing DNA damage inhibiting their replication (19, 20).

Systemic agents

Concerning the utilization of systemic antibiotics, they are used as last resort when topical treatments are unsuccessful to the healing process (21). The wound type could influence the prescription mainly when the consequences of infection are potentially serious (22). Systemic agents include four main groups: penicillins, cephalosporins, aminoglycosides and quinolones, nevertheless, there are numerous other antimicrobials agents in routine practice such as clindamycin, metronidazole and trimethoprim. The main problem with the use of systemic agents is that antimicrobials must have not only intrinsic activity against pathogens, but also the ability to distribute to infected tissues. Poor tissue penetration, leading to inadequate drug concentrations and treatment failure, may be caused by vascular

insufficiency with disruption of normal blood and lymphatic flow to devitalized tissue (23, 24).

Mechanisms of action

The mechanism of action of Penicillin involves the interference with the development of bacterial cell walls and crosslinkages. The work developed by Bild and co-workers, revealed activity of ampicillin and amoxicillin against certain Gram-positive and Gram-negative organisms; however, there are inactivated by penicillinases produced by *S. aureus* and *E. coli* (25). Concerning cephalosporin's the mechanism is analogous to penicillin's and present a wide range of activity against both Gram-negative and Gram-positive organisms (25). Regarding aminoglycosides, are active against the more resilient Gram-negative organisms and act by interfering with the protein synthesis. Despite their wide range of activity, aminoglycosides can be nephrotoxic and ototoxic, consequently serum levels should be monitored (25). In respect to quinolones, they are active against Gram-positive and Gram-negative organisms and act preventing the formation of DNA within the cell nucleus. Concerning ciprofloxacin, it is approved for skin and soft-tissue infections; however, a high incidence of staphylococcal resistance may occur. According this element is recommended that its use is avoided in methicillin resistant *S. aureus* (25). Regarding clindamycin, is active against Gram-positive cocci including penicillin-resistant staphylococci and many anaerobes organisms. Metronidazole, could be used against anaerobic organisms (25) and sometimes used in combination with other agents, such as ampicillin (26).

Educational strategies and chronic wounds

The main causes of chronic wounds are related with advanced age, overweight problems and comorbidities associated (1). By tradition wound care has been principally responsibility of the nurse. It is estimated that community-based nurses spend 25–50% of their time treating wounds (27). However, a work by Caroline McIntosh drew attention to the fact that 70% of the nurses certify that during their basic nurse training they did not receive satisfactory education on chronic wounds (28). Furthermore, data from the literature recognized scarcities in the wound care knowledge in several healthcare professionals (29). Educational strategies need to be specifically targeted to meet the needs of different professional groups and levels of expertise to maximize effectiveness. It is of extreme importance the formation of clinical leaders, which possess the adequate skills, knowledge and attitudes in order to spread and implement evidence based wound care locally. Actually, educators work in partnership with physicians, industry and wound organizations to offer further effective educational initiatives an opportunity to network (30). A study conducted by Guyatt and co-workers revealed that the best path to deal with chronic wounds is the acquisition of specific skills during educational initiatives that concentrate on information retrieval, research design and systematic reviewing (31). A study by Frank and colleagues, underlines the need of changes in medical students' curricula to intensify wound education and awareness in order to enhanced communication, permanence of care, reduced hospital stays and costs (32). Teledermatology is one appreciated instrument for bedridden patients living in rural and urban areas when there is lack of easy access to specialty care providers. Wound consultations ought to be a practice for all bedridden patients who have a wound, since they have a huge potential to prevent the worsening of ulcers (33).

Conclusion

Concluding, to decide the best treatment for optimal wound care is crucial to assess globally the patient and the wound. Furthermore, operational care for chronic wounds requires a multimodal approach, supplementary partnerships are needed. It is essential transdisciplinary collaboration between clinicians and scientists in order to facilitate improvement models that strictly mimic human wound closure.

Ethical disclosure

No potential conflict of interest was reported.

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Nothing to declare.

Author contributions

MM Azevedo designed the study and wrote the manuscript.

Conflict of interest

No conflict of interest

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References

1. Mustoe TA, O'Shaughnessy K, Kloeters O. Chronic wound pathogenesis and current treatment strategies: a unifying hypothesis. *Plast Reconstr Surg.* 2006; 117(7 Suppl):35S-41S. doi: 10.1097/01.prs.0000225431.63010.1b
2. Gupta S, Gabriel A, Lantis J, Téot L. Clinical recommendations and practical guide for negative pressure wound therapy with instillation. *Int Wound J.* 2016; 13(2):159-74. doi:10.1111/iwj.12452
3. Gould L, Abadir P, Brem H, Carter M, Conner-Kerr T, Davidson J, et al. Chronic wound repair and healing in older adults: current status and future research. *Wound Repair Regen.* 2015; 23(1):1–13. doi:10.1111/wrr.12245
4. Halbert AR, Stacey MC, Rohr JB, Jopp-McKay A. The effect of bacterial colonization on venous ulcer healing. *Australas J Dermatol.* 1992; 33(2):75–80. doi:10.1111/j.1440-0960.1992.tb00083.x
5. Lookingbill DP, Miller SH, Knowles RC. Bacteriology of chronic leg ulcers. *Arch Dermatol.* 1978; 114(12):1765–8. doi:10.1001/archderm.1978.01640240007002
6. Kalan L, Zhou M, Labbie M, Wiling B. Measuring the microbiome of chronic wounds with the use of a topical antimicrobial dressing- A feasibility study. *Plos One.* 2017; 12(11):e0187728. doi:10.1371/journal.pone.0187728
7. Zhou LH, Nahm WK, Badiavas E, Yufit T, Falanga V. Slow release iodine preparation and wound healing: in vitro effects consistente with lack of in vivo toxicity in human chronic wounds. *Br J Dermatol.* 2002; 146(3): 365-374. doi:10.1046/j.1365-2133.2002.04605.x
8. Fitzgerald DJ, Renick PJ, Forrest EC, Tetens SP, Earnest DN, McMillan J, et al. Cadexomer iodine provides superior efficacy against bacterial wound biofilms in vitro and in vivo. *Wound Repair Regen.* 2017; 25(1): 13-24. doi:10.1111/wrr.12497
9. Roop Chang Bansai MG. Activated carbon and its surface structure. In: *Activated Carbon Adsorption*. 1 ed. Boca Raton, FL: CRC Press; 2005: 1-65.

10. Paul JC, Pieper BA. Topical metronidazole for the treatment of wound odor: a review of the literature. *Ostomy Wound Manage.* 2008; 54(3): 18-27. PMID: 18382045
11. Sato T, Miyata G. The nutraceutical benefit, part III: honey. *Nutr Pharmaceut.* 2000; 16 (6):468-9.
12. Jull AB, Cullum N, Dumville JC, Westby MJ, Deshpand, S, Walker N. Honey as a topical treatment for wounds. *Cochrane Database Syst Rev.* 2015; 6(3):CD005083. doi:10.1002/14651858.CD005083.pub4
13. Xu H, Qu F, Xu H, Lai W, Wang YA, Aguilar ZP, et al. Role of reactive oxygen species in the antibacterial mechanism of silver nanoparticles on *Escherichia coli* O157: H7. *Biometals.* 2012; 25(1):45-53. doi:10.1007/s10534-011-9482-x
14. Cho KP, Park JE, Osaka T, Park SG. The study of antimicrobial activity and preservative effects of nanosilver ingredient. *Electrochim Acta.* 2005; 51(5):956-60. doi:10.1016/j.electacta.2005.04.071
15. Percival SL, Bowler PG, Russel D. Bacterial resistance to silver in wound care. *J Hosp Infect.* 2005; 60(1): 1-7. doi:10.1016/j.jhin.2004.11.014
16. Lipsky BA, Hoey C. Topical antimicrobial therapy for treating chronic wounds. *Clin Infect Dis.* 2009; 49(10): 1541-9. doi:10.1086/644732
17. Cooper R. A review of the evidence for the use of topical antimicrobial agents in wound care. *World wide wounds.* 2004; 1:1-8.
18. Sibbald RG, Leaper D, Queen D. Iodine made easy. *Wounds Int.* 2011; 2(2):1-4.
19. Trend MA, Jorgensen MA, Hazell SL, Mendz GL. Oxidases and reductases are involved in metronidazole sensitivity in *Helicobacter pylori*. *Int J Biochem Cell Biol.* 2001; 33(2): 143-53. doi:10.1016/S1357-2725(00)00085-6
20. Sigeti JS, Guiney Jr DJ, Davis CE. Mechanism of action of metronidazole on *Bacteroides fragilis*. *J Infect Dis.* 1983; 148(6):1083-9. doi:10.1093/infdis/148.6.1083
21. Edmond M, Roberts V, Watkins PJ. Blood flow in the diabetic neuropathic foot. *Diabetologia.* 1982, 22(1):9-15. doi:10.1007/BF00253862
22. O'Meara S, Cullum N, Majid M, Sheldon T. Systematic reviews of wound care management: (3) antimicrobial agents for chronic wounds; (4) diabetic foot ulceration. *Health Technol Assess.* 2000; 4 (21):1-237. PMID: 11074391
23. Morgan M. Treatment of MRSA soft tissue infections: an overview. *Injury.* 2011; 42 (suppl 5): S11-S17. doi:10.1016/S0020-1383(11)70127-9
24. Bassetti M, Baguneid M, Bouza E, Dryden M, Nathwani D, Wilcox M. European perspective and update on the management of complicated skin and soft tissue infections due to methicillin-resistant *Staphylococcus aureus* after more than 10 years of experience with linezolid. *Clin Microbiol Infect.* 2014; 20(Suppl4):3-18. doi:10.1111/1469-0691.12463
25. Bild D, Selby J, Sinnock P. Lower extremity amputation in people with diabetes: epidemiology and prevention. *Diabetes Care.* 1989; 12(1):24-31. doi:10.2337/diacare.12.1.24
26. Brand P, Coleman W. The diabetic foot. In: Rifkin E, Porte D, editors. *Diabetes mellitus: theory and practice*, 4th edition, 1990, New York: Elsevier: 792-811.
27. Bale S. Using different designs in wound healing research. *Nurse Res.* 2004; 11(4):42-53. doi:10.7748/nr2004.07.11.4.42.c6214
28. McIntosh C, Ousey K. A survey of nurses' and podiatrists' attitudes, skills and knowledge of lower extremity wound care. *Clin Educ.* 2008. 4(1): 59-68.
29. Lloyd-Jones M, Young T. The role of the health care assistant in tissue viability. *J Tissue Viability.* 2005; 15(3): 6-10. doi:10.1016/S0965-206X(05)53002-X
30. Flanagan M. Barriers to the implementation of best practice in wound care. *Clin Educ.* 2005; 1(3):74-82.
31. Guyatt GH, Meade MO, Jaeschke RZ, Cook DJ, Haynes RB. Practitioners of evidence based care: Not all clinicians need to appraise evidence from scratch but all need some skills. *Br Med J.* 2000; 320 (7240): 954-5. doi:10.1136/bmj.320.7240.954
32. Frank Werdin, Mayer Tennenhaus, Hans-Eberhardt Schaller, Hans-Oliver Rennekampff. Evidence-based Management Strategies for Treatment of Chronic Wounds. *Eplasty.* 2009; 9: e19. PMID: 19578487
33. Hayashida K, Fujioka M, Senju C. Teledermatology may play a role in reducing severity of pressure ulcers in both rural and urban settings. *Wounds.* 2014; 26(4): 83-8.