Part 2: Bacterial biofilm and the infection prevention "balancing act": the case for using a polyhexamethylene biguanide solution in chronic and complex wound management

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Prof Nurs Today 2016;20(2):42-45

Introduction

"Game changer" – an event, idea, or procedure that effects a significant shift in the current manner of doing or thinking about something.

This is the second in a two-part series in which the microbiome of chronic and septic wounds is examined, justifying the proactive clinical management of wound biofilm to control infection risk, improve patients' quality of life, reduce associated costs and promote better healing outcomes. The infection prevention practitioner has an important role to play in decision-making in complicated wound management, ensuring the selection and correct use of appropriate topical antiseptics, based upon local pathogen surveillance and insight into the prevalence of drug-resistant strains.

Biofilms are everywhere. Bacterial biofilm formation in wounds commences within hours of the initial contamination. This three-dimensional extracellular polymeric substance, embedded in a thick slimy blanket of sugar and protein, facilitates microbial adherence to the wound bed, and provides a medium for chemical signalling ("quorum sensing") and pathogenesis.

Moreover, the nature of subsequent colonisation, as well as the inherent "intelligence" of the microbial social structure, i.e. inter-species cooperation, mutual protection or competition, within a biofilm depends largely on the types of microbial species present.

Rapid advances in electron microscopy and clinical microbiology are challenging traditional approaches to the management of wounds and clinical wound infection, and suggest that the level of protection conferred by biofilm against the action of antibodies, neutrophils and antimicrobials has been grossly underestimated.

Therefore, the seamless integration of infection control, clinical pharmacology and an understanding of the dynamics of the wound bed microbiome are fundamental to the successful management of chronic and complicated wounds.

Predictable pathogens: bacterial biofilm formation as a precursor to infection?

The polymicrobial context of superficial and deep wound compartments is an entirely normal phenomenon, i.e. bacterial colonisation promotes a normal inflammatory response and is therefore a key component in the wound healing process.

However, it is now known that specific pathogens play an important role in wound colonisation, biofilm production and the risk of subsequent infection.

For example, acute, uncomplicated wounds are typically colonised with Gram-positive species representative of normal local skin flora. However, the microbiome evolves dramatically in complicated and non-healing wounds to include colonisation with Enterobacteriaceae and other Gram-negative species, such *as Klebsiella, Acinetobacter* and *Pseudomonas*, especially if exudate and debridement of non-viable tissue are poorly managed.

Systemic risk factors, e.g. diabetes mellitus, limb ischaemia, corticosteroid and/or broad-spectrum antibiotic therapy, may further influence the colonisation continuum with microbial species such as methicillin-resistant *S. aureus* and *Candida* spp.[4-6]

Therefore, the taking of superficial wound ("pus") swabs is controversial, and should only be considered as a tool which is available in the context of holistic assessment and care planning.

The presence of > 15 leucocytes/mm^3 on direct microscopy may be suggestive of an inflammatory process or possible infection. Semi-quantitative laboratory analysis, reported as a colony count >10^5 colony-forming units (CFUs)/g tissue, i.e. 100 000 CFUs, may be a predictor of critical colonisation or local wound infection, but the validity of the result is questionable at best, especially if the wound was not cleansed thoroughly beforehand, or if the sample was taken in the presence of slough or eschar. Certainly, prescribing antibiotic therapy based on culture results from superficial sampling alone is not recommended.[4-6]

Liaison with the medical microbiologist is advisable when there is a history of broad-spectrum antibiotic therapy or suspected drug resistance, especially extended-spectrum β-lactamase-positive and carbapenemase-producing isolates. PCR methods are able to detect most species of pathogens in a wound in a matter of hours, including antimicrobial resistance if the resources are available.

Rely on your eye!

The clinical wound assessment mnemonics "NERDS" (non-healing, increased exudate, red friable granulation, debris, and smell) and "STONEES" [increased size, increased temperature, os (probes to bone), new areas of breakdown, oedema or erythema, increased exudate, and smell] are useful tools that can be used to differentiate clinically between superficial and deep compartment wound infection, respectively.

This concept was introduced by Sibbald et al in 2007, and validated in 2009.[2] Three or more of these signs should be sought for confirmation of the diagnosis. If increased exudate and odour are present, additional signs are needed to determine if the infection is superficial, deep, or both.

The responsible use of topical antimicrobial agents

Bacteria need to be metabolically active for antimicrobial agents to act, hence hibernating bacteria in biofilm may be unaffected by biocides that would normally kill active bacteria. In other words, standard doses of antibiotics, which effectively kill normally susceptible bacteria when grown in suspension in a clinical laboratory, may have little or no antimicrobial effect on the same type of bacteria protected within a biofilm structure. Therefore, the topical use of antibiotics in wound care is not recommended owing to the increased the risk of:

- Colonisation with drug-resistant species through selective pressure

- Allergic reactions
- Uncontrolled systemic absorption and potential toxicity.

However, the broad-spectrum microbicidal mechanism of action of antiseptics is considered to be a much safer alternative for both cleansing and topical therapy, provided that they can demonstrate an ability to penetrate biofilm and sustain activity in the presence of organic material and exudate.

Examples include cadexomer iodine and polyhexamethylene biguanide (PHMB).

Polyhexamethylene biguanide: a "game changer" for infection control and wound care

PHMB is a synthetic compound which has been in use for more than 60 years in various forms, i.e. contact lens cleansers and mouthwashes, and more recently to proactively manage acute wounds in high-risk patients, and to manage chronic wounds, such as postoperative fistulae, abscesses, lower limb and pressure ulcers and burns.

PHMB's bacteriocidal mode of action is via electrostatic interference with the microbial cell wall and metabolic processes. This prohibits the cells' ability to absorb any nutrients or dispose of waste products, effectively killing the bacteria without damaging the surrounding healthy cells.

The primary indication for using PHMB-based products is on wounds which meet either the "NERDS" or "STONEES" criteria to:

- Cleanse (by the combined action of a mild amphoteric alkaloid surfactant which attracts dirt and debris away from the wound bed)
- Aid autolytic debridement by supporting the action of macrophages and metalloproteases
- Damage or disrupt the biofilm structure, to allow penetration and microbicidal action
- Suppress the ongoing formation of biofilm
- Lower the microbial density or bioburden
- Reduce wound odour by default.

The impact of a chronic wound on a patient's psycho-social well-being

Controlling wound bioburden is likely to improve quality of life owing to a reduction in wound infection, wound pain and odour – all factors which are known to affect mobility, sleep and social interaction, and reduce quality of life in patients with chronic wounds.

The effect of chronic, unrelenting pain is very debilitating, and erodes the individual's quality of life while contributing significantly to stress and clinical depression. Increased levels of stress have also been demonstrated to further lower the pain threshold, decrease tolerance and delay wound healing.

Positive economic benefits

Wounds represent a significant financial burden to patients, medical insurance funders and national healthcare systems.[6,8,9,12] The European Wound Management Association Patient Outcome Group conducted a point prevalence survey in the UK in 2005 and 2006 on 1 644 patients with a total of 2 300 wounds in an attempt to produce an estimate of the total cost of wound care during that period.

Approximately 75% of these patients were cared for by district nurses, 21% were in hospital, and 4% were in the hospice setting. Measurement criteria for the survey were based on the following:

- Nursing time (minutes) per dressing change
- Travelling time (minutes)
- Documentation time (minutes)
- Total cost of nursing time
- Total cost of dressings
- Total cost of nursing time and dressings
- Total cost of wound-related hospitalisation.

The median duration of the wounds was 6-12 weeks. One in eight wounds was reported to show signs of infection, and a staggering 16% of patients had remained unhealed for ≥ 1 year. The overall cost of providing these resources was estimated to be £15-18 million, or £2.5-3.1 million per 100 000 population!

Pearls for nursing practice

The following "pearls" for nursing practice apply:

- Appreciate the value of polymicrobial colonisation and its positive influence on healing
- Perform a risk assessment of the most likely microbial strains at wound bed level, which are usually representative of local flora and the patient's physical environment
- Understand that superficial sampling is of limited diagnostic value, i.e. the growth of bacteria from swabs is not synonymous with infection, and treatment based on culture results alone is not warranted.
- Use the "NERDS" versus "STONEES" assessment criteria in conjunction with other infection markers, e.g. a full blood count, procalcitonin and C-reactive protein, as well as patient co-morbid risk factors, to select appropriate topical antimicrobial products and/or justify the use of systemic antibiotics
- Use noncytotoxic, sustained-efficacy antiseptics, such as PHMB, proactively for wound bed cleansing, and the disruption and control of biofilm in chronic and complicated wound types
- Consider a stepwise and rational approach to the selection and use of topical antimicrobial dressings for non-healing and "maintenance" wounds (e.g. malignant, fungating

or critically ischaemic) where the long-term control of bioburden, exudate or odour, or the prevention of drug-resistant opportunistic infection, are the primary goals

- Treat the "whole patient" and not just "the hole" in the patient!

Conclusion

Both formal and anecdotal evidence appears to support the use of PHMB as a routine practice standard for chronic and complicated wound care. When critical colonisation or early infection is suspected in postoperative wounds and burns, the initiation of PHMB therapy can positively impact on the length of the patient's stay in hospital, the incidence of re-admission thereto, and the associated morbidity and mortality risks and overall treatment costs.

Conflict of interest

The author has received honoraria from B Braun Medical for generic continuing professional education seminars. No other potential conflict of interest exists relevant to this article.

Bibliography

1. "Game changer". Oxford Dictionaries [homepage on the Internet]. c2015. Available from: http://www.oxforddictionaries.com/us/definition/english/game-changer
2. World Union of Wound Healing Societies. Principles of best practice: wound infection in clinical practice. An international consensus. Wounds International [homepage on the Internet]. 2008. C2015. Available from: http://www.woundsinternational.com/media/issues/71/files/content_31.pdf
3. Best practice statement: the use of topical antiseptic/antimicrobial agents in wound management. Wounds UK [homepage on the Internet]. 2010. c2015. Available from: http://www.wounds-uk.com/pdf/content_9969.pdf
4. International consensus: appropriate use of silver dressings in wounds. An expert working group consensus. Wounds International [homepage on the Internet]. 2012. c2015. Available from: http://www.woundsinternational.com/media/issues/567/files/content_10381.pdf
5. Sibbald RG, Goodman L, Woo YK, et al. Special considerations in wound bed preparation: an update. Adv Skin Wound Care. 2011;24(9):415-436.
6. Andriessen A, Eberlein T. Assessment of a wound cleansing solution in the treatment of problem wounds. Wounds. 2008;20(6):171-175.
7. Horrocks A. Prontosan wound irrigation and gel: management of chronic wounds. Br J Nurs. 2006;15(22):1222-1228.
8. Moore Z. The important role of debridement in wound bed preparation. Wounds International [homepage on the Internet]. 2012. c2015. Available from: http://www.woundsinternational.com/media/journals/_/574/files/19-23-23.pdf
9. Mulder GD, Cavorsi JP, Lee D. Polyhexamethylene biguanide (PHMB): an addendum to current topical antimicrobials. Wounds. 2007;19(7):173-182.
10. Moore K, Gray D. Using PHMB antimicrobial to prevent wound infection. Wounds UK. 2007;3(2):96-102.
11. Romanelli M, Dini V, Barbanera S, et al. Evaluation of the efficacy and tolerability of a solution containing propyl betaine and polihexanide. Skin Pharmacol Physiol. 2010;23 Suppl:41-44.
12. Drew P, Posnett J, Rusling L. The cost of wound care for a local population in England. Int Wound J. 2007,4(2):149-155.
13. Bradbury S, Fletcher J. Prontosan® made easy. B Braun Medical [homepage on the Internet]. 2011. c2015. Available from: http://www.bbraun.com/documents/Nanosites/Content_Prontosan_Made_Easy.pdf
14. Wolcott RD, Rhoads DD, Bennett ME, et al. Chronic wounds and the medical biofilm paradigm. J Wound Care. 2010;19(2):45-46. c2015.