Should antimicrobial dressings be classified according to their activity and be subject to stewardship like antibiotics?

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We are facing a huge future crisis regarding the treatment of infection caused by antimicrobial resistance (AMR) that has developed in many common bacterial pathogens. Although seen across the board in all microbes, antibiotic resistance in bacteria is, without doubt, the most alarming. We have become so accustomed to successfully treating bacterial infection with antibiotics that, over the past fifty years, they have been used sometimes inappropriately. Recent research has shown that 1 in 3 people will be given antibiotics in any one year and that at least 20% of these are given inappropriately (Smith et al, 2018). Since the introduction of antimicrobial stewardship in all healthcare facilities, we have seen the numbers of prescriptions for antibiotics drop overall by 4.5% between 2013 and 2017 (National Institute for Health and Care Excellence [NICE], 2018) and this is expected to continue. Whether this will have any major impact in stopping the further development of AMR or help reverse the trend for misuse of antibiotics has yet to be seen but it should have some effect.

In wound care, antibiotics are essential where there is evidence of infection and treatment is needed to prevent further spread into deep tissue and the development of sepsis. However, antibiotics are observed to be ineffective in some problematic wounds and patients can be prescribed several courses without eradicating the perceived infection in the wound. In the last 15 years, biofilm-based wound care has been encouraged and is now an accepted concept for current practice. Here the wound is debrided, cleaned and an antimicrobial dressing used topically to reduce bioburden and help wound healing. In health care, NICE guidelines have been introduced into a number of clinical settings (for example tissue viability, leg ulcer and diabetic foot clinics) for dealing with infected and problematic wounds and the prudent use of products available.

There are hundreds of products available for wound care and the numbers of products with demonstrable antimicrobial activity is increasing year on year to enable the practitioner to prevent, treat and heal infected wounds topically. Looking at antimicrobial dressings alone, there are over fifty different manufacturer's dressings listed on British National Formulary (BNF) where an antimicrobial agent is incorporated (BNF, 2019). The antimicrobial agents include honey, iodine, silver, polyhexamethylene biguanide (PHMB) and are incorporated into a variety of dressing types such as alginates, foams, hydrocolloids, among others.

Whereas this variety is to be applauded, it can be extremely confusing for the wound care practitioner when faced with treating a problematic wound. The physical nature of the carrier dressing is often the most important consideration. Does the wound necessitate a foam or alginate dressing for managing exudate? What about comfort for the patient? Is a hydrocolloid needed? The amount of choice can be overwhelming and having to make a decision on which antimicrobial agent to use can be confounding. Does the dressing need to release the antimicrobial agent into the wound? Do I want an antimicrobial dressing that will kill any microorganisms in the dressing? Do I want the microorganisms to be retained by the dressing? Do I want a dressing with high levels of antimicrobial activity to reduce bioburden and biofilm activity or do I want a dressing with moderate levels of activity to help keep organism at a manageable level that will continue to allow healing but prevent further biofilm formation? All these questions might go through the minds of the practitioner when choosing an appropriate dressing.

Topical antiseptics, e.g. silver, PHMB, iodine, are not under the same level of scrutiny as antibiotics and as such, their use is not regulated or enforced as strictly. Iodine has been used for many years in wound care and is certainly an excellent agent for skin antisepsis but is it appropriate for a chronic wound with a biofilm and high levels of organic matter? The use of antimicrobial agents in wound care is not governed by any stewardship and perhaps now is the time that they should be incorporated into local guidelines alongside antibiotics, to ensure that resistance does not develop to these antiseptics as we have seen with antibiotics.

All dressings on the formulary have to show evidence of their efficacy and there are some excellent European, Japanese

and American testing standards that do this. However, there is not one single standard that is suitable for all dressing types. In 2014, a draft British Standard (BS EN 16756) was proposed to assess the antimicrobial efficacy of wound dressings (British Standards Institution, 2014). This considers the log reduction of numbers of specific organisms over a 24 hr period in very defined parameters that would allow this method to be portable between laboratories but as yet it has not been fully adopted. This standard is based on challenge testing and log reduction of organisms compared either to a control dressing (same group of dressing, e.g. foam, but without antimicrobial agent) or the original inoculum. Different methods can help demonstrate different claims made by manufacturers. For example, if a claim states that the dressing reduces organism numbers within the dressing, then challenge testing and log reduction assays are important (Gallant-Behm et al, 2005; Thomas and McCubbin, 2003) but may be inappropriate if the claim is that the antimicrobial agent diffuses into the wound bed and reduces organism numbers there. Here, a zone of inhibition assay may be more appropriate (Thomas and McCubbin, 2003). The practitioner, when applying the dressing, should know what they are using the antimicrobial dressing for and if the claims made are appropriate.

My personal view is that it is now becoming important to be able to compare efficacy of all wound care products, especially dressings, against each other (irrespective of antimicrobial agent) in each product group (foams, alginates, hydrocolloids etc) and classify them as having high, moderate or low antimicrobial activity. This would give the practitioner more information when choosing the antimicrobial dressing. Using a standard log reduction assay or challenge test at 24 hrs compared to a control dressing against a wide range of organisms typically found in a wound could ascertain whether there was a high, moderate or low level of antimicrobial activity based on the log reduction. If this type of classification scheme was readily available, it would allow comparison of all the antimicrobial dressings, i.e. comparison of activity of silver versus PHMB versus honey in a particular carrier dressing.

It is important to mention that there are some modern dressings, for example, dialkylcarbamoyl chloride (DACC)-coated dressings, that do not incorporate an antimicrobial agent into the dressing but use properties of the dressing material to reduce microorganisms either through retention of the organism in the dressing away from the wound bed (thus removing organisms when the dressing is changed) or by killing microorganisms through a biochemical interaction within the dressing.

I think stewardship of antimicrobial dressings needs to be implemented at some point to help prevent resistance developing amongst the antiseptics and also a classification scheme would really help practitioners make more informed choices. *Valerie Edwards-Jones*

1. When should an antimicrobial dressing be used?

JT: Antimicrobial dressings should not be used routinely on wounds that are proceeding along the healing continuum. They should only be used when there are any signs/symptoms or indicators of local wound infection or spreading/systemic infection. Antimicrobial treatment should be implemented for 2 weeks and then reassessed and discontinued if no longer required.

EN: Antimicrobial dressings are indicated when a wound is displaying signs of local infection and alongside systemic antibiotics in cases of spreading infection. Antimicrobials also have a vital role to play in biofilm based wound management; regular debridement needs to be supported with topical antimicrobial dressings to help reduce biofilm reformation.

SW: Antimicrobial dressings should be considered when the clinician suspects that microbes within a wound are having a negative impact on the healing progression of the wound.

PS: It is recommended in most best practice guidelines and the instructions for use supplied by the manufacturers of antimicrobial dressings, that these products should be used when there are signs and/or symptoms of localised infection, or in conjunction with systemic antibiotics when spreading infection is present. This suggests that the clinician needs to be observant and responsive to patient concerns and changes in the wound which suggest that bacterial activity is increasing. This would enable them to apply the product at an early stage to suppress bacterial proliferation and prevent an infection developing.

2. What parameters should be considered when choosing which antimicrobial dressing to be used on a patient?

JT: Some of the many parameters that should be considered are:

- Depth/size location of wound
- Exudate volume and type
- Ability to conform wound bed and any dead space
- Any contraindications for the patient or the wound aetiology and site
- Any patient allergies
- Patient age, i.e. is it safe to be used on neonates or children
- Possible toxins released/effect on patient/wound
- Manufacturers guidelines to be followed
- Patients comorbidities and contraindications
- Patient choice — acceptance and comfort.

EN: There is a range of different antimicrobial agents, e.g. silver, honey, PHMB, all of which can be incorporated into a number of different carrier dressings, e.g. alginates, hydrofibres, hydrocolloids and

hydrogels. The dressing type is of primary importance and this should be selected after careful wound assessment. Ensuring the wound exudate is contained effectively to avoid periwound maceration, or donating moisture to promote a moist wound healing environment will determine the choice of dressing type before selecting the antimicrobial agent. Other considerations should include any known allergies, for example to silver or bee products. Frequency of dressing change should also be considered. Some silver dressings are indicated to be changed every 3 or 7 days. If changed sooner, they become costly to use; so if there are other reasons why a wound needs more frequent reviewing, then this would not be a cost-effective choice of product.

SW: Please see my answer to question 3. In addition, the constituent microorganisms should also be considered. Many dressings have proven data against bacteria but not yeast and fungi thus if fungal infection is suspected, a dressing with an antimicrobial (not just antibacterial) claim should be selected.

PS: The choice of agent is dependent on individual patient requirements such as age, sensitivity to the antimicrobial and/or carrier dressing or wound pain. The selection of carrier dressing should be made following a wound assessment which factors the site and size of the wound, the level of exudate etc. Before applying any antimicrobial dressing a full patient assessment should be undertaken.

3. Can all antimicrobial dressings be used in the same way?

JT: Antimicrobial dressings all have different physical properties, such as the level of antimicrobial activity they release, the duration of effectiveness, their mode of action, for example, hydrophobicity, as well as the possibility of the release of toxins. Therefore, specific products should be chosen to reflect the overall treatment aim and objectives, and decisions made, following a holistic patient and wound assessment.

EN: If silver is released into the wound, it will be absorbed systemically and, therefore, risks of toxicity and resistance are greater. For this reason, silver products are generally recommended for a maximum of 2-weeks use. Iodine also has contraindications and limited dosages. Other dressings pose less risk because they do not release agents into the wound bed. Regardless of which antimicrobial is chosen, all wounds should be reassessed regularly and used for the shortest time possible. There are occasions when sometimes it might be necessary to use an antimicrobial for longer, for example as part of biofilm management when stopping early may allow the biofilm to re-form.

SW: I don't think so. No two wounds are the same thus some dressings are more appropriate for some wounds than others. For example, some dressings have been tested and proven to maintain antimicrobial activity over an extended duration whilst others may only claim effective activity for a much shorter (<72) duration. This means that the choice of dressing could be impacted by the treatment regime. The level and constituents of wound exudate can have a significant impact on the antimicrobial activity of a dressing and the topography of the wound can also impact on the efficacy of the antimicrobial dressing thus these factors should be considered when selecting the appropriate dressing.

PS: It would be helpful to have data which would support the use of the different dressings in terms of antimicrobial efficacy. However, at this time clinicians are limited to information produced by the manufacturer and guidance produced from agencies such as NICE. The important consideration when using any antimicrobial dressing is that it is used when early signs of infection are detected, and prolonged use is avoided. The most commonly used antimicrobial agents (honey, silver, iodine and PHMB) all have a broad spectrum of activity but are available in different concentrations which may influence the effectiveness. The role of the carrier dressing is then to manage the local conditions at the wound interface and the surrounding skin, ensuring that the antimicrobial agent is in intimate contact with the tissues and can work effectively. It may also have a protective layer to protect the wound from external contamination, and prevent cross infection occurring.

4. Are there any circumstances when an antimicrobial dressing should be used on a non-infected wound?

JT: Antimicrobials may be used for some patients with non-infected wounds. The use of an antimicrobial dressing can assist in reducing the wound bacterial burden, thus aiding the prevention of spreading/systemic infection. For patients who are considered at high risk of infection, e.g. patients with autoimmune disease or taking immunosuppressants, I would, therefore, consider the use of an antimicrobial dressing. I would also consider using antimicrobial dressings for chronic non-healing wounds where clinical assessment may indicate the presence of biofilms. This, alongside effective debridement, can reduce the bioburden of the wound and encourage the wound to move along the wound healing continuum.

EN: Antimicrobial agents should generally be reserved for infected or critically colonised wounds and used for the shortest possible time period. However, there may be certain exceptional situations when they may be indicated for a non-infected wound. This may include high-risk wounds or patients, e.g. immune-compromised patients, wounds with exposed bone, some diabetic foot ulcers. These decisions would be made on an individual basis and usually under specialist advice and review. Some podiatrists/diabetic foot clinics will recommend prophylactic antimicrobials as the implications for

developing a wound infection in this cohort of patients are serious. Local guidelines should be consulted.

SW: I am not aware of situations where this is likely to provide a patient benefit. Typically if the wound is not infected then a dressing that supports healing and wound closure is likely to be more beneficial.

PS: The preventative role of antimicrobial dressings has not been fully investigated in high risk patients where a wound infection can significantly increase morbidity or mortality such as those with diabetes. In these circumstances the clinician may risk assess and use clinical judgement to make an informed decision of how to treat the wound. There is some published data to suggest that dressings containing silver and PHMB can be effective in reducing overgranulation tissue, particularly around exit site wounds such as PEG sites.

5. Would a classification scheme of efficacy of topical antimicrobial dressings help the clinician to choose the most appropriate dressing?

JT: Most definitely this would help with antimicrobial selection and appropriate use as for many clinicians, this can be difficult due to the many different types of antimicrobial dressings and different mode of actions.

EN: Classifying antimicrobial dressings into low, medium and high levels of antimicrobial activity might be useful when comparing dressings against each other, where there are a number of suitable carrier choices for a particular wound. However, it still requires the clinician to decide whether the wound requires a low, medium or high level, and this may not be straightforward to determine. In practice, the choice of antimicrobial is usually made based on the carrier properties as described above. In general, the principle behind using an antimicrobial is to use it for the shortest time possible until signs of infection have resolved.

SW: I think this could be useful. The claims made based on specific laboratory tests are not always clearly translated to label claims. For example, it is not always very clear which dressings have achieved an antimicrobial claim, compared to those that were not effective enough against yeast and fungi to receive approval as an antimicrobial dressing. If the wrong dressing is selected, it can lead to high expense and low patient benefit.

PS: Absolutely, as long as this was simple and easy to understand and based on independent evidence. Factors such as levels of antimicrobial activity, and whether or not the agent is active in the dressing or in the wound would be very useful for all known dressings. It would also be interesting to explore the concept of using different antimicrobial dressings intermittently for short periods on a wound, rather than the current practice which is to use for a defined time period, e.g. 2 weeks.

6. Do you think the use of antimicrobial dressings should be more closely monitored to prevent antimicrobial resistance developing?

JT: Yes I do. As a Tissue Viability Specialist I am concerned about the inappropriate and long term use of antimicrobial dressings, therefore I feel we need close stewardship of their use to prevent future possible antimicrobial resistance developing.

EN: Potential resistance should always be a concern for anyone in wound care. The rise in antibiotic resistance is probably a key driver for the increased development and use of topical antimicrobial dressings and these play a pivotal role in reducing the risks of wound-related sepsis as well as the burden of chronic non-healing wounds. For these reasons we need to ensure continued access to effective agents for the future. There is always room for improvement in local monitoring of prescribing of antimicrobial dressings, alongside a greater emphasis on education and training to ensure appropriate and judicious use of these important resources.

SW: Where there is a true risk of antimicrobial resistance this could be of benefit, but often terms relating to resistance are confused and can lead to inappropriate choices. Genotypic 'resistance' is often confused with a phenotypic 'reduction in susceptibility' and antibiotic resistance can be confused with antimicrobial resistence. The presence of biofilm infections can also reduce susceptibility to antibiotics and antimicrobials. Monitoring is always beneficial as data gives us the power to make decisions. However, the cost of effective, meaningful monitoring may make this challenging.

PS: Antimicrobial resistance is a real concern and it would be the responsible course of action to do this. However, in order to apply an antimicrobial dressing when the early signs of infection are observed suggests that these products need to be readily accessible. At the present time, there is no readily available method for detecting the bacterial susceptibility to these agents. Perhaps this should become common place and something for future consideration.

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