



Polyhexamethylene Biguanide Dressing – Another Promising Tool to Reduce Catheter-related Bloodstream Infection

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Purpose

This article provides a description of polyhexamethylene biguanide (PHMB), its current uses and clinical outcomes, and potential uses.

Review of Relevant Literature

PHMB is an antiseptic agent from the cationic biocide family, which also includes chlorhexidine. In vitro testing has found it to be effective against gram-positive and gram-negative bacteria including methicillin-resistant staphylococcus aureus, fungi and viruses. Its action is directed toward disruption of the cell wall, a mechanism not known for developing resistance. PHMB is currently used for many other products and industries for more than 50 years. Dressings impregnated with PHMB are now successfully being used to prevent surgical site infections.

Discussion

Elimination of catheter-related bloodstream infection (CR-BSI) is now the achievable goal for all healthcare settings. The use of PHMB provides another engineering tool targeting the skin as the source of these infections. Successful use with prevention of surgical site infections is now being reported. These wounds can become infected with the same organisms as those found in CRBSI.

Implications for Clinical Practice

This agent should be considered for clinical studies to determine the rates of CRBSI reduction resulting from its use.

Catheter-related bloodstream infection (CRBSI) continues to be a significant problem in our healthcare system. The current prevailing thought is that these infections are preventable when the insertion and care of catheters meet published guidelines. These documents use two approaches—work practice controls, which requires a change in human behavior, and engineering controls, which employs product and process changes.

The skin is a primary source of organisms producing CRBSI in percutaneously inserted central venous catheters, especially those used for a short period. One engineering control to reduce the burden of organisms on the skin is to place an antimicrobial dressing directly over and around the insertion site. The most common antimicrobial agent currently used is chlorhexidine gluconate. Recently a foam dressing with a new antimicrobial agent has been introduced for this purpose – polyhexamethylene biguanide or PHMB.

What is PHMB?

PHMB is a member of the family of cationic biocides, which are antiseptic agents. Quaternary ammonium compounds (e.g. benzalkonium chloride) and bisbiguanides (e.g., chlorhexidine) and polymeric biguanides (e.g., PHMB) are included in this family. For more than five decades, biguanides have been manufactured in a broad range of drugs including anti-malarial, anti-protozoal and blood glucose-reducing agents. Distinct anti-bacterial properties were found in this family with chlorhexidine being the first one to be synthesized. Early work with PHMB demonstrated that its antimicrobial effect was superior to other cationic biocides, however its chemical action could not be easily explained until recently. This limitation prevented the early use of PHMB in pharmaceutical products. (Gilbert & Moore, 2005)

Biguanides work by attacking the cell wall. Bacterial cell walls are composed of peptidoglycan, a mixture of hexose sugars and amino acids. Gram positive bacteria have a thick layer while gram negative bacteria have a thin layer that has an outer membrane containing lipopolysaccharides and lipoprotein. (Goering, et al., 2008) The external cell layer for both gram positive and

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negative organisms has a negative electrical charge, which attracts the positive charge of the biguanides. PHMB rapidly disrupts the cell by binding to the cell wall and displacing calcium, which acts as a stabilizing force. PHMB also concentrates in areas on the cell wall with maximum density of the electrical charge. This leads to changes in the phospholipid environment of the proteins in the cell wall. Once the cell wall is so disturbed, cellular components leak out, thus destroying the bacterial cell. PHMB is composed of longer polymer chain lengths allowing it to create larger areas on the cell wall and thus more disruption of the total cell. This mechanism differs from chlorhexidine, possibly making PHMB superior in its antimicrobial properties. (Gilbert & Moore, 2005)

PHMB has demonstrated effectiveness against both gram-positive and gram-negative bacteria, fungi, and viruses. One in vitro study demonstrated that PHMB can limit growth of methicillin-resistant staphylococcus aureus (MRSA) and pseudomonas aeruginosa, however it did not eradicate biofilm once it has formed. (Lipp, Kirker, Agostinho, James, & Stewart, 2010) Others have reported antimicrobial agents such as PHMB to be effective against biofilms. (Mulder, Cavorsi, & Lee, 2007) Another in vitro test created a "biocompatibility index" to rank various antiseptics for their cytotoxicity and microbiocidal effect. The tests, using *Escherichia coli* and *staphylococcus aureus*, ranked PHMB second for both organisms. Octenidine dihydrochloride ranked first for both organisms with various formulations of povidone-iodine, chlorhexidine, and silver ranked below PHMB. (Muller & Kramer, 2008) PHMB has also been found effective against micrococcus, pseudomonas, and klebsiella species. (W. Lee, Tobias, Bemis, & Rohrbach, 2004) Finally, it has shown amebicidal activity against *Acanthamoeba*. (J. Lee, Oum, Choi, Yu, & Lee, 2007)

There have been no reports found in the literature of resistance developing to PHMB in more than 50 years of its use. The mechanism of action on cell wall degradation indicates that there are no methods for organisms to circumvent this action to create resistance to PHMB. (Gilbert & Moore, 2005)

How is PHMB Currently Used?

Early use of PHMB for clinical application was hindered by difficulties in understanding its chemical action. Its early use for consumer products proved it to be very successful as a broad-spectrum antibacterial agent. Examples include water treatment for swimming pools, prevention of salmonella infection in hatching eggs, impregnation into fabric to reduce microbial growth, and general environmental cleaning. It is used as the disinfectant for contact lens solution and oral mouthwashes. (Allen, White, & Morby, 2006)

Clinical use of PHMB currently extends to wound care. The bioburden of wounds, especially chronic wounds, is well known to impair tissue healing. Biofilm from *pseudomonas aeruginosa*, *klebsiella pneumoniae*, *staphylococcus aureus*, and *Escherichia coli* are known to form inside wounds, dramatically increasing the amount of antibiotics required for complete closure. Several in vitro studies have reported various types of dressing material impregnated with PHMB to have positive impact on killing the microorganisms. (Lipp, et al., 2010; Shah,

2007) A narrative literature review of wound care reviewed the bacterial bioburden in chronic wounds and the antimicrobial agents used in the care of these wounds. A small trial of 12 patients with 26 wounds reported that 8 patients had organisms cultured before and after the use of a 0.3% PHMB gauze dressing. These patients had been unresponsive to dressings containing silver and iodine. Among these 8 patients, there was an average reduction in wound size by 2.2 cm² with the use of PHMB dressings (Mulder, et al., 2007).

What are the Clinical Outcomes with PHMB?

Single site clinical studies with PHMB have identified favorable trends. PHMB 0.2% is added to many types of surgical site dressing material. At the 2010 conference of the Association for Practitioners in Infection Control, two posters provided details of process improvement projects at hospitals of varying sizes. Both of these projects involved comparing the rate of surgical site infections (SSI) during a period using standard gauze dressings to a period using dressings containing PHMB. During the standard gauze period, Keller reported 30 SSI in 5309 procedures for a rate of 0.56 per 100 surgical cases. During the period using PHMB-impregnated gauze dressings, there were 19 SSIs in 5591 surgical cases for a rate of 0.34 per 100 surgical cases. This represents a decrease of SSIs by 40% (Kehler, 2010). Milliken reported 7 SSIs in 218 procedures for a rate of 3.21% during the standard gauze period. During the period using the PHMB gauze dressing, the SSI rate was 1.5% or 3 out of 200 procedures, a 53% reduction (Milliken, 2010).

Another published study assessed the rates of SSI, with specific attention to MRSA infections, during two 11-month periods. During the first period, plain sterile gauze dressings were used on all surgical sites. During the second 11-month period, sterile gauze dressings with 0.2% PHMB were used on all surgical sites. The data showed a rate reduction of 24% for all SSIs and the MRSA-SSIs were reduced by 47.6%. (Mueller & Krebsbach, 2008)

Conclusion

CR-BSI and SSI are part of the group of healthcare-acquired conditions with restricted reimbursement for treating these complications. Both are considered to be preventable complications. The available data on PHMB-impregnated dressing is currently limited to SSIs, however these wounds are at risk for infection from the same organisms as catheter insertion sites. In vitro and early clinical data on PHMB shows promise that it could be of benefit in addressing the risk of CR-BSI. It would seem appropriate to move forward with clinical studies on the use of PHMB-impregnated dressings for central venous catheter insertion sites, creating one more engineering control to eliminate the skin organisms as a cause of CR-BSI.

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