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Preventing Wound Infection:
Modern Silver Usage

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Introduction

The Centers for Disease Control and Prevention (CDC) call antibiotic resistance "one of the biggest public health challenges of our time," affecting at least 2.8 million patients each year in the United States alone.[1] The challenge now is to find antibiotic alternatives that can manage antibiotic-resistant microorganisms. Silver is one common alternative to topical antibiotics. It has a long history of use, both topically and systemically, with little evidence of harmful side effects. Silver can be used as silver nanoparticles, colloidal silver, and silver sulfadiazine.

History of Medical Silver

Silver has been used throughout history for various health benefits, from water purification to the precursors of modern wound dressings. Documentation of silver used for medicinal purposes dates back as early as 1850 BCE in Egypt, where it was applied directly to wounds.[2]

The use of silver in wound treatment specifically began around 1520 CE. Silver nitrate was used to chemically cauterize wounds, a treatment still used today. By the 1800s, this use of silver nitrate was the standard of care for skin ulcers and festering wounds.

In 1891, B.C. Crede started using colloidal silver for wound hygiene. It was used to disinfect hospitals, as well as to control infections through application to a wound,[3] eye drops, nose drops, and intravenous injection.[4] Then, in the early 1900s, colloidal silver was also ingested by or injected into tens of thousands of patients. Through this widespread use of silver, the phenomenon of argyria was discovered, where silver deposits develop in the skin and other tissues.

The long-term effects of argyria in humans are still unknown, but animal studies have shown no serious side effects. Regardless, silver is still more commonly used topically or in wound dressings today, to prevent argyria caused by ingestion.

Silver lost its popularity when penicillin was discovered in 1928 but has recently resurged as a practical antimicrobial for antibiotic-resistant infections and to reduce the development of antibiotic-resistant infections.[2]

Antibiotic-Resistant Infections

According to the CDC, at least 2.8 million people contract an antibiotic-resistant infection each year, thus making antibiotic resistance a major health concern for medical professionals.[1]

Even topical antibiotics can lead to antibiotic resistance, causing longer healing times from uncontrolled infections. Evidence shows that the negative effects of topical antibiotics may far outweigh the benefits, which are not as significant as many clinicians believe. Silver, iodine, and other nontoxic antiseptics have shown fewer side effects and similar efficacy to topical antibiotics, making them a preferable alternative.[5]

Additionally, the bacteria in biofilm show an increased affinity for developing antibiotic resistance. Biofilms decrease the penetrability of the microorganism and delay the effects of antimicrobials.[6] This is a serious problem because an individual bacterial cell can replicate as fast as every 4 to 20 minutes, and the reproductive rate grows exponentially.[7] The literature suggests that antibiotic efforts in wound care must be combined with antibiofilm tactics to ensure successful treatment, particularly in chronic infections.[8] Antibiofilm chemicals include silver, iodine, gallium, and ethylenediaminetetraacetic acid (EDTA).[9]

With the accelerating growth of antibiotic-resistant bacteria, wound care needs a new approach that considers not only immediate infection prevention, but also the long-term consequences of each treatment's approach. Multiple alternatives exist for topical antibiotics, each with its own unique benefits.

Table 1. Alternatives to Topical Antibiotics

Alternative	Benefits
Hydrogel-based wound dressings[10]	• Form natural polymers • Contain broad-spectrum antibacterial properties • Promote moist healing environment • Absorb exudate • Promote regeneration of lost tissue
Silver nanoparticles[11-13]	• Act as a bactericide • Interrupt microorganism replication • Prevent biofilm formation
Dialkylcarbamoyl chloride (DACC)–coated dressings[14]	• Bind bacteria that exhibit high cell surface hydrophobicity (CSH) • Remove bacteria from the wound bed without increasing inflammation
Polyhexamethylene biguanide (PHMB)[15,16]	• Has broad-spectrum antimicrobial activity • Promotes contraction and aids in wound closure
Gentian violet[17]	• Has antibacterial, antifungal, and immunotherapeutic properties • Is most effective against gram-positive microbes • When used with methylene blue, can improve exudate wicking, debridement, enhanced re-epithelialization, prevention of epibole, pain relief, and antimicrobial action without systemic absorption
Metal oxides (iron, zinc, etc.)[10]	• Contain antimicrobial agents • Induce proliferation of fibroblasts and angiogenesis
Medical-grade honey[16]	• Has antimicrobial, anti-inflammatory, and antioxidant effects • Acts as an alkaline medium to promote wound healing of chronic wounds • Stimulates an immune system response against infection
Methylene blue[18]	• Has antimicrobial effects • Can be used with enzymatic debriding agents, growth factors, or hydrogels without inhibition • Aids in autolytic debridement • Promotes re-epithelialization by flattening wound edges

Inclusion of Silver in Dressings

Silver has become the most commonly used alternative to topical antibiotics in wound dressings. Silver nanoparticles can be incorporated into dressings to decrease the risk of infection while allowing the dressing to continue facilitating a moist wound bed environment. In nanoparticle form, silver deconstructs the cell membrane of microbes in the dressing, passes into their cell body, and causes internal damage. There are various theories on how the silver nanoparticles precisely render the microbe inactive, but all agree that there is some level of intracellular damage.[2]

By helping to reduce infection by managing bioburden, using silver as part of the wound management plan can aid in healing and reduce the costs associated with wound infection. The less time patients spend tending to and managing the wound, the more they can engage in their daily and desired activities. Similarly, the faster a wound heals, the less time the medical staff must dedicate to managing the wound and the fewer resources are required.[19]

Contraindications to Silver Dressings

Can we revise this to read: Despite their wide range of benefits, silver nanoparticles are not appropriate for use in certain wounds, most notably in surgical wounds that are closed and clean.[20] The primary benefits of silver—wound closure and antimicrobial actions—are not needed in these wounds.

Additionally, silver should not be used in combination with enzymic debridement agents. Silver inactivates enzymatic debriding agents and so should not be used in conjunction.

Increasing the Efficiency and Effectiveness of Silver in Dressings

The effects of silver nanoparticles in wound healing can also be improved through the use of additional elements. These elements include surfactants, chelators, calcium, gelling fibers, sulfates, and nylon.

Surfactants

Surfactants act to combine two otherwise repellent substances. In the case of silver nanoparticles, surfactants promote the combination of silver and hydrogel dressings.[21] In addition to the facilitation of loading silver onto the dressing, the surfactant improves the antimicrobial activity of the silver nanoparticles by disrupting the biofilms present in the wound.[22] The most notable surfactant used for loading silver onto hydrogels is rarasaponin.[21] Surfactants allow the addition of silver into dressings to combine the antimicrobial properties of silver with the moisture-balancing properties of the dressing.

Chelators

With increases in nanotechnology, silver particles can be made smaller and smaller. However, recent literature suggests that there is a threshold at which silver nanoparticles become too small and may begin to become toxic to mammals at high levels of absorption.[23] More research is still needed on human subjects, but until guidelines are established it is important to control the release of smaller silver nanoparticles. This is where chelators are of assistance.

Chelators bind the silver to other particles in the dressing to combine the effects of silver and the additional particle. For example, the chelation of silver nanoparticles to polydopamine has been shown to stabilize the release of silver.[24] Additionally, chelators have been shown to improve silver's antimicrobial properties within biofilm.[25] These effects demonstrated by chelators are especially important in burn wound healing, given the small amount of viable tissue that needs to be maintained.

Additionally, chelators have been shown to improve silver's antimicrobial properties within biofilm.

Calcium Pectinate

Calcium is regularly taken up by cells through the cellular membrane. When combined with silver in wound dressings (for example, calcium pectinate wound dressings), the calcium increases biocompatibility with human cells. Typically, pectinate dressings increase exudate absorption from the wound bed, but they do not have antibacterial properties on their own. By augmenting silver's biocompatibility with human cells, calcium pectinate amplifies silver's antibacterial properties while decreasing potential side effects such as argyria within the wound. It also combines the exudate absorption benefits of the calcium pectinate with the antimicrobial properties of silver to better meet the needs of the wound.[26]

Gelling Fibers

In biofilm-forming bacteria, especially those that are gram-negative, the inclusion of silver into gelling fibers provides antibiofilm effects. The silver breaks down and circumvents the biofilm to separate the biofilm from the wound bed. Meanwhile, the gelling fiber promotes granulation tissue formation. These outcomes in combination outperform gelling fibers alone, as well as other dressings that include silver, especially when there is a large amount of uncontrolled biofilm present in the wound bed.[27] Recent literature stresses the importance of a combined antimicrobial and antibiofilm strategy to promote wound healing, and both components of this strategy are present in gelling fiber and silver dressings.[28]

The silver breaks down and circumvents the biofilm to separate the biofilm from the wound bed.

Sulfates

Silver sulfadiazine is the primary combination of sulfates that integrate silver in wound healing. Unlike silver nitrate, this substance has an improved ability to degrade biofilms by killing bacteria directly. In vitro experimentation showed that sulfadiazine binds to biofilm and allows the silver to circumvent the biofilm's exclusionary properties.[29] However, the literature is conflicted on whether silver sulfadiazine promotes or impairs wound healing, and this may depend on the amount of biofilm present.[20,29] At this time, more research is needed.

Nylon

Nylon is a flexible and permeable dressing that can be made transparent to view the wound easily without disrupting the wound bed. In recent studies, nylon-silver dressings have been primarily used for partial- or full-thickness burns. Nylon does not manage exudate well but does decrease the need for analgesics because the dressing is not removed as frequently for inspection. Therefore, nylon allows for the inclusion of silver into burn wound care while reducing pain associated with dressing changes and adhesives.[30]

Conclusions

The use of silver in wound care has a long history of efficacy, with few to no side effects. When faced with the ever-growing problem of antibiotic resistance, health care professionals turn to alternatives to manage microbes in the wound. Silver offers a cost-effective and practical solution to antibiotic resistance in wound care. Health care professionals can consider the use of silver for appropriate wounds to decrease healing times and improve the quality of life of their patients.

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