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Current Issue

Effects of Silver on Wound Management

Robert H. Demling, MD;
Professor of Surgery, Harvard Medical School; Director, Burn-Wound Center, Brigham & Women's Hospital;
Leslie DeSanti, RN; Director, Burn and Wound Care Program, Health South Braintree Rehabilitation Hospital, Research Associate, Brigham & Women's Hospital, Boston, Massachussetts

Silver has been used for centuries to prevent and treat a variety of diseases, most notably infections. It has been well documented that silver was used in ancient Greece and Rome as a disinfectant for the storage of water and other liquids. For example, silver coins were placed in the jars of liquid to maintain sterility. The American settlers in the 1800s routinely placed silver dollars in barrels of liquids to avoid spoilage, and more recently, NASA used silver to maintain water purity on the space shuttle.

Free silver ions, or radicals, are known to be the active agents of antimicrobial silvers. Of interest are their extremely potent antimicrobial properties, as only one part per 100 million of elemental silver is an effective antimicrobial in a solution. Silver ions kill micro-organisms instantly by blocking the respiratory enzyme system (energy production), while having no negative effect on human cells.

In 1834, a German obstetrician, F. Crede, used a one-percent silver nitrate solution as eye drops in newborns, eliminating blindness caused by postpartum eye infections. Numerous studies in the early 1900s correlated low plasma silver levels with infections, suggesting silver to be an essential micromineral for people. Charged silver solutions (electrocolloidals) were approved in the 1920s by the US Food and Drug Administration (FDA) for use as antibacterial agents. Of significant importance is that no known bacterial

resistance has been reported to the silver ion, unlike current antibiotics.

In addition to its recognized antibacterial properties, silver solutions, especially those containing electrocolloidal elemental silver, were reported to improve the healing of indolent wounds and in the regeneration of damaged tissue. The description of decreased rubor in wounds indicates an anti-inflammatory property of silver. These silver solutions are still used in a number of prestigious wound care centers around the world today.

Virtually all of the reports on the use of the pure elemental silver to increase healing occurred prior to the 1940s after which a host of antibiotics became prevalent, decreasing the use of silver (except in burns). After 1940, the use of silver was in the form of salts and silver complexes in creams, which had antibacterial properties and were more shelf stable. However, the complexes, such as nitrate and sulfadiazine, retarded healing, and the beneficial effect of silver on wounds was no longer recognized.

Silver is not toxic to human tissue as has been demonstrated through centuries of use. Absorbed silver will interact with other metals and tissue proteins; however, these interactions do not appear to be harmful. One important side effect of silver to note, however, is argyria, which usually occurs after large oral intake of silver. Argyria is a process of silver granule deposition in the skin leading to a permanent blue/gray discoloration. When argyria is present, silver granules can be found in all organs, not just the skin; therefore, any form of silver, if given in large quantities, can be a causative factor in argyria (at least 10 grams needs to be absorbed). However, no tissue toxicity has been identified.

The most common causes of argyria are not from medicinal use of silver, but rather through constant environmental exposure. For example, silver miners or chemists who often work with silver may experience argyria. The constant use of silver plates and cups has also been noted to cause mild forms of argyria. In days past, European nobility, for example, were often noted as having bluish-colored skin; this was more than likely due to their constant use of silver place settings, silverware, and silver cups--hence the term blue blood.

Delivery of Silver to the Wound

Although silver itself has been shown to be harmless to normal human tissue, there has been toxicity noted from the salt or complexes used to deliver the silver. Silver nitrate solutions taken orally are noted to

produce severe intestinal damage.[5,6] The current antibacterial topical 0.5-percent silver nitrate solution used in burns and wounds is toxic to new cells on the wound surface. Nitrate is a potent oxidizing agent.[6] The sulfadiazine component of silver sulfadiazine produces local and systemic (bone marrow) damage and potent pro-inflammatory properties increasing wound surface exudates. Current data on silver products used in burns and wounds indicate that providing pure silver ions and radicals to the wounds produces the best antimicrobial results. How can the silver be delivered to the wound bed, however, without the related toxicity of the delivery systems? There have been and currently are several forms of silver used on wounds. The delivery of elemental or ionic silver (colloidal silver) without an added attached compound has historically produced the best wound healing and antibacterial results. Recently, a new silver delivery system that releases only the silver to the wound (Acticoat silver-coated antimicrobial barrier, Westaim Biomedical Inc., Exeter, New Hampshire) was introduced, and experiences to date suggest positive wound healing effects. As a result of Acticoat, new data is being obtained that verifies the historical concepts of silver benefiting wound healing properties.

Biologic Properties of Silver Related to Wound Healing

There appear to be three properties of silver that positively affect wound healing, which, though likely having separate mechanisms of action, are difficult to separate when assessing changes in wound healing. These include antimicrobial, pro-healing, and anti-inflammatory properties.

Antimicrobial properties.

The antimicrobial activity of silver ions is well defined. Silver ions rapidly kill microbes by blocking the cell respiration pathway. The speed of action is almost instantaneous once the silver reaches the microbe. The efficacy of microbe killing is based not only on the amount of silver ion present, but likely also the presence of other silver radicals generated by a silver-releasing product.

Because of the mechanism of action, microbial resistance to silver itself has not been reported. In addition, silver has repeatedly been shown to be nontoxic to human cells. As mentioned before, toxicity occurs from the complexes used to deliver silver, such as nitrate and sulfadiazine. Acticoat releases 30 times less silver than other topical silver products, but the release of silver in Acticoat is over a longer period of time; the nanocrystalline structure used in Acticoat allows for a greater surface area for silver release.

The rate and degree of microbial killing is significantly faster with the Acticoat silver delivery than other silver products. One explanation is that only silver is released from the complexes, while silver and a number of potent silver radicals are released from the silver nanocrystals on the membrane. These radicals may have more potent antimicrobial properties than silver alone. Therefore, not all silver products are alike relative to antimicrobial properties. These same findings were reported for all other significant bacteria and fungi.

Prohealing effects. Past observations and some recent studies using a pure silver delivery system have demonstrated an increased re-epithelialization rate of noninfected partial-thickness acute wounds. Therefore, in addition to antibacterial properties, there appears to be a prohealing property to silver. The studies were done on noninflammed acute wounds that were either donor sites or had been grafted. The studies demonstrated more rapid rates of re-epithelialization compared to standard moist healing methods. The mechanism of the prohealing properties has yet to be defined, which is understandable given the fact that elemental silver delivery to a wound has only been recently re-introduced. Silver salts and complexes, especially silver nitrate and silver sulfadiazine, on the other hand, have been shown to impede re-epithelialization.

Anti-inflammatory properties of silver. Defining anti-inflammatory properties of silver, which can improve healing, is difficult because of silver's potent antimicrobial activity. For example, silver has been reported to decrease surface zinc, which is required for metalloproteinase activity (MMP) activity. The decrease in MMP activity would be advantageous in a burn wound or a chronic wound; an excess MMP activity may retard healing. However, it remains difficult to determine the role of the antibacterial effect of the silver on this process as bacteria also increase MMP activity. Silver blocks MMP activity in an in-vitro model. Silver has also been reported to increase wound surface calcium. Calcium, in turn, has been reported to increase re-epithelialization rate. Current studies are again more observational in nature, and controlled studies are warranted; however, this data at least allows one to develop a hypothesis of action.

Biochemical effects of silver. Several important biochemical effects of silver on the wound were documented decades ago. However, only recently with the new concepts on wound healing and healing impairment, can a mechanism of action be presented. The major focus of wound healing has been on the

relationship between tissue destruction by excess inflammation and tissue synthesis stimulated by a prohealing environment. The effects of silver are varied and many more effects have likely not yet been defined. Since excess inflammation retards healing, an anti-inflammatory effect would be of benefit. A prohealing effect may also be found unrelated to inflammation. More formal studies need to be done.

Summary

Elemental silver and its radicals have been known for centuries to have potent antimicrobial properties, which can certainly benefit a wound if infected. History also strongly suggests a direct healing effect of silver unrelated to infection control. However, the topical use of pure silver in a colloidal solution was abandoned for the use of more stable silver complexes and topical creams. This switch occurred before current wound healing concepts were developed, and the effect of silver on wound biology was not pursued until recently.

There are two reasons for this lack of research interest. The first reason is the inhibitory response of wounds to the currently used silver salts and creams, which reportedly have been shown to retard various phases of healing.[26–29] Unfortunately all silver products were assumed to have the same negative effect. Recent evidence clearly indicates that the salt or complex attached to the silver retards healing, not the silver itself.

The second reason was the lack of an effective pure silver delivery system so that the silver response could be tested. The availability of a stable pure silver delivery system for wounds, such as is found in Acticoat silver-coated microbial barrier, and the initial clinical observations of a positive wound response has renewed interest in an this old remedy. The results of the anticipated studies on silver and wound biology should of considerable interest to all wound care professionals.

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