INTRODUCTION

The usefulness of silver for wound treatment has been known since 69 B.C. While silver metal (Ag) has no medicinal activity, silver ion (Ag⁺) has a broad antimicrobial spectrum, and is cytotoxic to bacteria, viruses, yeast, and fungi. Ag⁺ binds to DNA, RNA, and various proteins, leading to cell death via multiple mechanisms, such as protein and nucleic acid denaturation, increased membrane permeability, and poisoning of the respiratory chain. For this reason, resistance against the silver ion has only rarely been reported.

The past few decades have seen a renewed interest in silver as a topical antimicrobial agent. Silver sulfadiazine (SSD) is a very widely used silver formulation, especially in burns. More recently, dressing with nanocrystalline silver has been developed. These novel dressings release silver ions into the wound in a sustained fashion.

While the silver ion has great antimicrobial and bactericidal properties, it is also toxic to fibroblasts when present in high concentration. Silver sulfadiazine slows healing and should not be used. Instead, nanocrystalline silver, or alternatives such as octenidine and polyhexanide, lead to less infection and faster healing.

Our purpose in this study was to evaluate the existing evidence on the use of silver in wound care. The questions that we sought to answer were:

Background: Due to its strong antimicrobial activity, silver is a commonly used adjunct in wound care. However, it also has the potential to impair healing by exerting toxic effects on keratinocytes and fibroblasts. The published literature on the use of silver in wound care is very heterogeneous, making it difficult to generate useful treatment guidelines.

Methods: A search of high-quality studies on the use of silver in wound care was performed on PubMed. A detailed qualitative analysis of published articles was performed to evaluate the evidence for the use of silver in infected wounds, clean wounds, burns, and over closed surgical incisions.

Results: Fifty-nine studies were included in this qualitative analysis. We found that, overall, the quality of the published research on silver is poor. While there is some evidence for short-term use of dressings containing nanocrystalline silver in infected wounds, the use of silver-containing dressings in clean wounds and over closed surgical incisions is not indicated. Negative-pressure wound therapy accelerates the healing of contaminated wounds, especially when silver is used as an adjunct. For burns, silver sulfadiazine slows healing and should not be used. Instead, nanocrystalline silver, or alternatives such as octenidine and polyhexanide, lead to less infection and faster healing.

Conclusions: In infected wounds, silver is beneficial for the first few days/weeks, after which nonsilver dressings should be used instead. For clean wounds and closed surgical incisions, silver confers no benefit. The ideal silver formulations are nanocrystalline silver and silver-coated polyurethane sponge for negative-pressure wound therapy. Silver sulfadiazine impairs wound healing. Proper use of silver-containing dressings is essential to optimize wound healing. (Plast Reconstr Surg Glob Open 2019;7:e2390; doi: 10.1097/GOX.0000000000002390; Published online 9 August 2019.)

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1) What is the quality of the published studies on the use of silver in wound care?
2) What are the advantages and disadvantages of various silver delivery systems?
3) What is the evidence for the use of silver-containing dressings in infected and heavily contaminated wounds?
4) What is the evidence for the use of silver-containing dressings in clean and clean-contaminated wounds?
5) What is the evidence for the use of silver-containing dressings in burns?
6) What is the evidence for the use of silver-containing dressings over closed surgical incisions?
7) What is the optimal strategy for the use of silver-containing dressings?
8) How does silver compare to alternative, lesser known agents?

**METHODS**

A PubMed literature search was performed using the following search parameters: silver AND (antimicrobial OR antibacterial) AND wound AND randomized; Silver AND epithelialization AND randomized; Silver AND negative pressure. The results were screened manually to exclude articles that were not relevant to our study (not about wound care), not in English, or which did not compare a silver-containing product to another product. We also excluded clinical studies with fewer than 20 patients. The articles were manually screened and duplicates were excluded. The remaining articles were analyzed in detail qualitatively, to extract answers to our study questions. The articles analyzed in this study are shown in Table 1.

**RESULTS**

**Quality of the Evidence**

We found a total of 490 published studies using our PubMed searches. Four hundred and thirty-one articles were excluded for the following reasons: 149 were not relevant to our topic, 31 were not in English, 34 were duplicate articles across searches, and 196 did not have a nonsilver comparison group. We were thus left with 59 relevant studies. This included 8 basic science or animal studies (no level of evidence), 33 randomized-controlled trials (level 1 evidence), 1 retrospective study (level 3 evidence), 1 case series (level 4 evidence), 14 systematic reviews of randomized-controlled trials (level 1 evidence), and 2 qualitative review articles (no level of evidence).

Most prior reviews found that the quality of the published data on the use of silver in wound care is poor. This is due to the fact that these studies use inconsistent, and sometimes subjective, outcomes measures, such as pain with dressing change, days until reepithelialization, number of dressing changes until reepithelialization, wound size reduction at various time points, presence of infection, etc. In addition, many of the published studies are funded, or even written, by manufacturers of silver-containing dressings.

**Silver Formulations, Effectiveness, and Toxicity**

While the silver ion is a very powerful bactericidal agent, it also has toxic systemic and local effects. The systemic toxic effects are due to silver absorption through the wound, leading to argyria, which manifests as irreversible gray skin discoloration and loss of night vision. However, systemic toxicity is rare because serum silver is rapidly excreted in urine and feces.

The local toxic effects of silver are more likely to occur, and are due to the cytotoxicity of the silver ion against keratinocytes and fibroblasts. Poon et al found that in monolayer cultures of keratinocytes and fibroblasts, silver became toxic to cells at a concentration of 33 ppm or greater. However, when fibroblasts were cultured in a collagen lattice, replicating more closely in vivo conditions, the toxic concentration increased to 60 ppm. On the other hand, for the silver ion to have effective bactericidal activity, a concentration of 30 to 40 ppm is needed.

Therefore, the ideal silver-containing dressing would maintain a sustained (several days), therapeutic (>30 ppm) silver ion concentration in the wound without causing systemic or local (<60 ppm) silver toxicity.

SSD contains silver, glycols, alcohols, and sulfadiazine (an antibiotic). SSD has been found to release an extremely high initial silver concentration into the wound (up to 3,176 ppm), which rapidly decreases to below therapeutic levels. SSD can therefore have high local toxicity, without providing the sustained silver levels necessary for microbicidal activity. In addition, propylene glycol, which is part of the SSD formulation, is known to cause bone marrow toxicity and leukopenia.

Newer dressings contain silver in a nanocrystalline state and elute silver into the wound in a sustained fashion, maintaining a concentration of up to 70 ppm for several days (slightly above the toxic threshold for keratinocytes and fibroblasts). These newer formulations include Silverlon (silver-coated nylon, Argentum Medical, Geneva, Ill.), Acticoat (silver-coated polyethylene, Smith & Nephew, London, UK), Mepilex Ag (silver-coated foam, Mölnlycke Healthcare, Norcross, Ga.), Mepitel Ag (silver-coated silicone, Mölnlycke Healthcare, Norcross, Ga.), Aquacel Ag (silver-coated cellulose hydrofiber, ConvaTec, Reading, UK), Promogran Prisma Ag (KCI, San Antonio, Tex.), and V.A.C. GranuFoam Silver (silver-coated polyurethane sponge, KCI, San Antonio, Tex.), amongst others. There are advantages and disadvantages to each of these formulations: Acticoat tends to adhere to the wound bed and can be painful upon removal, unlike Mepitel Ag and Mepilex Ag, both of which have a silicone interface, allowing them to adhere to the surrounding normal skin, but not to the wound itself (Table 2). Promogran Prisma contains collagen, which acts as a sacrificial substrate for matrix metalloproteinases, enhancing wound healing. The silver-coated polyurethane negative-pressure wound therapy (NPWT) sponge combines the advantages of NPWT with a sustained release of 20 to 40 ppm of silver, which is below the toxic threshold to keratinocytes and fibroblasts.
Table 1. Summary of the Articles Included in This Study

| Article | Type of Study | Level of Evidence | No. Subjects (for Human Studies) | Purpose | Results |
|---------|---------------|-------------------|----------------------------------|---------|---------|
| Abarca-Buis, 2014 | Basic science | - | - | Evaluate silver ion elution from silver-coated polyurethane NPWT sponge | Silver ion concentration in wound exudate rises over several days |
| Ellenrieder, 2015 | Basic science | - | - | Evaluate effectiveness of polyurethane versus silver-coated polyurethane NPWT sponges at reducing MRSA colony counts | NPWT with silver-coated polyurethane sponge decreases MRSA colony counts more than NPWT with polyurethane sponge |
| Ngo, 2012 | Basic science | - | - | Compare biofilm formation with polyurethane NPWT sponge versus silver-coated polyurethane NPWT sponge | NPWT with polyurethane sponge reduces biofilm even more |
| Sachsenmaier, 2013 | Basic science | - | - | Compare activity of polyurethane NPWT sponge versus silver-coated polyurethane NPWT sponge against S. aureus and S. epidermidis | Silver-coated polyurethane NPWT sponge achieves a larger zone of bacterial inhibition than plain polyurethane sponge |
| Stinner, 2011 | RCT | 1 | 39 | Compare healing, pain, and cost with silver alginate versus gauze | The addition of a silver dressing to polyurethane sponge enhances the antimicrobial activity of NPWT |
| Vermeulen, 2007 | Systematic review | 1 | 847 | Compare healing and odor with silver-containing dressing versus plain foam | Silver alginate reduces pain compared to gauze, but does not accelerate healing or decrease cost |
| Gunal, 2015 | Retrospective | 3 | 21 | Compare polyurethane to silver-coated polyurethane sponges for NPWT for infected diabetic foot ulcers | Silver-containing dressing does not accelerate healing, but improves wound odor |
| Qian, 2017 | Basic science | - | - | Compare healing with SSD versus plain cream for chronic wounds | NPWT with polyurethane sponge accelerates the healing of diabetic foot ulcers |
| Applewhite, 2018 | Review | - | - | Evaluate healing with NPWT and promogran prisma in chronic wounds | NPWT with silver-coated polyurethane sponge accelerates healing even more. |
| Innes, 2001 | RCT | 1 | 17 | Compare epithelialization with Acticoat versus occlusive, silver-free dressing for skin graft donor sites | SSD slow epithelialization and increases hypertrophic scar formation |
| Krasowski, 2015 | RCT | 1 | 80 | Compare epithelialization with silver-containing dressing versus octenidine for lower-extremity ulcers | Promogran prisma accelerates healing due to its collagen component acting as a sacrificial substrate for proteases in the wound. |
| Michaels, 2009 | RCT | 1 | 213 | Compare healing with nanocrystalline silver versus non-silver-containing dressings for lower-extremity venous ulcers | NPWT promotes granulation tissue formation |
| Norman, 2016 | Systematic review | 1 | 576 | Compare healing with silver-containing dressings versus gauze for pressure ulcers | Oclusive, silver-free dressing leads to faster epithelialization and better scar than Acticoat. |
| O’Meara, 2014 | Systematic review | 1 | 4,486 | Compare healing with silver-containing dressings versus standard dressings for lower-extremity venous ulcers | Octenidine leads to faster healing and less pain than silver-containing dressing |
| Storm-Versloot, 2010 | Systematic review | 1 | 2,066 | Compare infection rates with silver-containing dressings versus non-silver-containing dressings for chronic wounds | Nanocrystalline silver does not accelerate healing of lower-extremity venous ulcers |
| Bergin, 2006 | Systematic review | 1 | 0 | Evaluate effectiveness of silver-containing dressings for diabetic foot ulcers | There are no good RCTs evaluating silver for diabetic foot ulcers |

(Continued)
| Article                      | Type of Study | Level of Evidence | No. Subjects (for Human Studies) | Purpose                                                                 | Results                                                                 |
|-----------------------------|---------------|-------------------|----------------------------------|--------------------------------------------------------------------------|--------------------------------------------------------------------------|
| PRS Global Open, 2019       |               |                   |                                  |                                                                          |                                                                          |

**Table 1. (Continued)**

| Article                      | Type of Study | Level of Evidence | No. Subjects (for Human Studies) | Purpose                                                                 | Results                                                                 |
|-----------------------------|---------------|-------------------|----------------------------------|--------------------------------------------------------------------------|--------------------------------------------------------------------------|
| Chambers, 2007              | Systematic review | 1                | 1,108                            | Evaluate effectiveness of silver-containing dressings for lower-extremity ulcers | Silver-containing dressings do not accelerate lower-extremity ulcer healing |
| Dumville, 2015              | Systematic Review | 1                | 336                              | Evaluate effectiveness of silver alginate for pressure ulcers             | Silver alginate does not accelerate pressure ulcer healing               |
| Karr, 2013                  | Case series    | 4                 | 20                               | Compare healing with polyurethane NPWT sponge versus Silverlon + polyurethane NPWT sponge for chronic wounds | Quality of evidence for silver is poor                                   |
| Toussaint, 2015             | Basic science  | -                 | -                                | Compare epithelialization with Mepilex Ag versus triple antibiotic ointment | Triple antibiotic ointment achieves faster epithelialization and less scarring than Mepilex Ag |
| Selcuk, 2012                | Basic science  | -                 | -                                | Compare activity of SSD, mupirocin, Acticoat, and octenidine against Acinetobacter baumannii | Highest antimicrobial activity is achieved by Acticoat, followed by octenidine, then mupirocin, then SSD |
| Khorasani, 2009             | RCT            | 1                 | 30                               | Compare epithelialization with SSD versus aloe vera                      | SSD leads to slower epithelialization                                   |
| Shahsdad, 2013              | RCT            | 1                 | 50                               | Compare epithelialization and pain with SSD versus aloe vera             | SSD leads to more pain and slower epithelialization                     |
| Baghel, 2009                | RCT            | 1                 | 78                               | Compare epithelialization and infection with SSD versus honey            | SSD leads to more infections and slower epithelialization               |
| Shah, 2013                  | RCT            | 1                 | 78                               | Compare epithelialization and infection with SSD versus honey            | SSD leads to more infections and slower epithelialization               |
| Sami, 2011                  | RCT            | 1                 | 50                               | Compare epithelialization and infection with SSD versus honey            | SSD leads to more infections and slower epithelialization               |
| Mujalde, 2014               | RCT            | 1                 | 110                              | Compare epithelialization, cost and infection with SSD versus honey      | SSD leads to more infections, higher cost, and slower epithelialization  |
| Maslihood, 2006             | RCT            | 1                 | 50                               | Compare epithelialization, pain and infection with SSD versus honey      | SSD leads to more infections, more pain, and slower epithelialization    |
| Varas, 2005                 | RCT            | 1                 | 47                               | Compare pain with SSD versus Acticoat                                   | SSD leads to more pain                                                  |
| Muangman, 2006              | RCT            | 1                 | 50                               | Compare pain with SSD versus Acticoat                                   | SSD leads to more pain                                                  |
| Huang, 2007                 | RCT            | 1                 | 98                               | Compare epithelialization with SSD versus Acticoat                      | SSD leads to slower epithelialization                                   |
| Caruso, 2006                | RCT            | 1                 | 84                               | Compare epithelialization and cost with SSD versus Aquacel Ag           | SSD leads to slower epithelialization and higher cost                   |
| Muangman, 2010              | RCT            | 1                 | 70                               | Compare epithelialization and cost with SSD versus Aquacel Ag           | SSD leads to slower epithelialization and higher cost                   |
| Barret, 2000                | RCT            | 1                 | 20                               | Compare epithelialization, hospital length of stay and cost with SSD versus Biobrane | SSD leads to slower epithelialization, longer hospital stay, and higher cost |
| Gerling, 1988               | RCT            | 1                 | 30                               | Compare epithelialization, number of dressing changes and cost with SSD versus Biobrane | SSD leads to slower epithelialization, more dressing changes, and higher cost |
| Bugmann, 1998               | RCT            | 1                 | 76                               | Compare epithelialization and number of dressing changes SSD versus Mepitel | SSD leads to slower epithelialization and more dressing changes         |
| Subrahmanyam, 1998          | RCT            | 1                 | 50                               | Compare epithelialization with honey versus SSD                         | Honey achieves faster epithelialization than SSD                        |
| Shahzad, 2013               | RCT            | 1                 | 50                               | Compare epithelialization and pain with aloe vera versus SSD             | Aloe vera achieves faster epithelialization and less pain than SSD      |
| Silverstein, 2011           | RCT            | 1                 | 101                              | Compare epithelialization, pain and cost with Mepilex Ag versus SSD     | Mepilex Ag achieves faster epithelialization, less pain, and less cost than SSD |
| Yarboro, 2013               | RCT            | 1                 | 24                               | Compare epithelialization with Aquacel Ag versus SSD                    | Aquacel Ag achieves less pain and requires fewer dressing changes       |
| Adhya, 2015                 | RCT            | 1                 | 54                               | Compare epithelialization with nanocrystalline silver-containing hydrogel versus SSD | Burn epithelialization is faster with nanocrystalline silver-containing hydrogel than with SSD |

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Table 1. (Continued)

| Article                  | Type of Study | Level of Evidence | No. Subjects (for Human Studies) | Purpose                                                                 | Results                                                                 |
|--------------------------|---------------|-------------------|----------------------------------|--------------------------------------------------------------------------|--------------------------------------------------------------------------|
| Gee Kee, 2015            | RCT           | 1                 | 96                               | Compare epithelialization with Mepilex Ag versus Acticoat                | Acticoat has slower healing and more pain compared to Mepilex Ag         |
| Godhi, 2017              | RCT           | 1                 | 60                               | Compare epithelialization with SSD versus silver                        | Petrolatum leads to faster epithelialization than SSD                    |
| Brown, 2016              | RCT           | 1                 | 89                               | Compare epithelialization with Aquacel Ag versus Acticoat               | No difference in epithelialization or infection between Aquacel Ag and   |
| Vloemans, 2014           | Systematic review | 1            | 266                              | Compare epithelialization, pain and length of hospital stay with SSD     | Biobrane achieves faster epithelialization, shorter length of stay, and   |
| Wasiak, 2013             | Systematic review | 1            | 1,307                            | Compare epithelialization and infection with various burn dressings     | less pain than SSD                                                      |
| Heyneman, 2016           | Systematic review | 1            | -                                | Compare epithelialization with SSD versus nanocrystalline silver        | Nanocrystalline silver dressings lead to faster epithelialization than   |
| Gravante, 2009           | Systematic review | 1            | 285                              | Compare infection and pain with SSD versus nanocrystalline silver       | Nanocrystalline silver leads to less infection and pain than SSD         |
| Aziz, 2017               | Systematic review | 1            | 717                              | Compare epithelialization and infection with honey versus SSD           | Honey results in faster epithelialization and less infection than SSD    |
| Vicira, 2018             | Review        | -                 | -                                | Evaluate the effectiveness of incisional NPWT in high-risk incisions    | Incisional NPWT improves wound outcomes                                  |
| Abboud, 2016             | RCT           | 1                 | 110                              | Compare pain with Silverlon versus Gauze                                | Silverlon reduces pain                                                  |
| Biffi, 2014              | RCT           | 1                 | 112                              | Compare infection with Aquacel Ag versus Gauze                         | Aquacel Ag does not decrease infection compared to gauze                |
| Newman, 2019             | RCT           | 1                 | 160                              | Compare wound complications with incisional NPWT versus silver dressing  | Incisional NPWT decreases wound complications compared to silver dressings |
| Ozaki, 2015              | RCT           | 1                 | 500                              | Compare infection with Acticoat versus Gauze                           | Acticoat does not reduce infection rates                                |
| Ruiz-Tovar, 2015         | RCT           | 1                 | 147                              | Compare infection with silver-containing dressing versus mupirocin versus | Silver-containing dressings have more infections than mupirocin ointment  |
| Dumville, 2016           | Systematic Review | 1            | 5,718                            | Compare infection with silver-containing dressings versus standard       | Silver-containing dressings do not reduce infection rates               |
| Li, 2017                 | Systematic review | 1            | 2,196                            | Compare infection with silver-containing dressings versus standard       | Silver-containing dressings do not reduce infection rates               |

Abbreviations: MRSA, Methicillin-resistant Staphylococcus aureus; NPWT, Negative-pressure wound therapy; RCT, Randomized control trial; SSD, Silver sulfadiazine
**Table 2. Commonly Used Dressings Containing Nanocrystalline Silver**

| Product          | Manufacturer                  | Composition                          | Properties                        |
|------------------|-------------------------------|--------------------------------------|-----------------------------------|
| Silverlon        | Argentum Medical, Geneva, Ill. | Silver-coated nylon                  | Highest silver concentration      |
| Acticoat         | Smith & Nephew, London, UK    | Silver-coated polyethylene           | Can adhere to the wound bed, causing pain with removal |
| Mepilex Ag       | Mölnlycke Healthcare, Norcross, Ga. | Silver-coated foam with silicone interface | Adheres to normal skin and not wound bed |
| Mepitel Ag       | Mölnlycke Healthcare, Norcross, Ga. | Silver-coated silicone                | Adheres to normal skin and not wound bed |
| Aquacel Ag       | ConvaTec, Reading, UK         | Silver-coated cellulose hydrofiber    | Absorbs exudate                   |
| Promogran Prisma Ag | KCI, San Antonio, Tx.       | Oxidized regenerated cellulose, collagen, and silver | Contains collage, which acts as a sacrificial substrate |
| V.A.C. GranuFoam Silver | KCI, San Antonio, Tex.     | Silver-coated polyurethane sponge    | Combines advantages of NPWT and silver |

**Infected Open Wounds**

Wound infection in the form of planktonic organisms or biofilm is known to impair wound healing. Foreign microorganisms in an open wound deplete local micronutrients and oxygen, and produce toxins that impair healing mechanisms. Therefore, eradicating infection is a prerequisite to obtaining a healed wound.

Biofilm is especially difficult to treat, because it enhances bacterial recalcitrance to antimicrobials. This is due to molecules within the extracellular polymeric substance of the biofilm that interfere with antibiotic function or physically shield the bacteria. One strategy to combat biofilm and jumpstart healing is by disrupting the biofilm and displacing the bacteria into a planktonic (rather than sessile) state, where they are more susceptible to systemic antibiotics. This can be achieved with sharp debridement of the wound. However, even with adequate debridement, even a few remaining bacteria can recreate the biofilm within 48 hours.

A combination of surgical debridement and long-acting topical antimicrobials has been used as an effective method to combat biofilm. The ideal topical antimicrobial agent should be nontoxic to host tissue, have a broad antimicrobial spectrum, and maintain sustained levels in the wound until all infection is eradicated.

Nanocrystalline silver satisfies the above requirements. Several randomized-controlled trials and systematic reviews have demonstrated that dressings that contain nanocrystalline silver are beneficial for wounds that have high bacterial counts and bad odor. Silver-containing dressings also have the advantage of requiring less frequent dressing changes than non-silver-containing dressings, leading to lower pain levels.

NPWT has been shown to decrease bacterial counts and accelerate healing in contaminated wounds. The addition of silver to the sponge plays a synergistic role with NPWT. The use of silver-coated polyurethane sponges has been shown to reduce bacterial counts of biofilm-causing organisms, such as *Pseudomonas aeruginosa* and *Staphylococcus aureus*, including MRSA, more than plain polyurethane sponges, leading to faster healing in infected diabetic foot ulcers. The synergistic effects of silver and NPWT can be achieved by using a silver-coated polyurethane sponge or by adding a silver layer under a plain polyurethane sponge.

**Noninfected Open Wounds**

In contrast, there is very little evidence in favor of silver for noninfected wounds. Multiple meta-analyses and randomized-controlled trials found that nanocrystalline silver-containing dressings were no more effective than gauze for lower-extremity ulcers, chronic noninfected wounds, and pressure ulcers. In fact, for noninfected, open wounds, silver-containing dressings have been found to increase cost and delay epithelialization. In an animal study of clean burns, Mepilex Ag had slower healing than triple antibiotic ointment. For skin graft donor sites, Acticoat has been found to delay epithelialization by more than 50% when compared to occlusive dressings. As mentioned above, dressings containing nanocrystalline silver lead to silver ion concentrations in the wound of up to 70 ppm, which is above the toxic threshold for keratinocytes and fibroblasts.

**Burns**

Even though SSD is widely used for the treatment of second-degree burns, it has been shown to have some of the worst outcomes in burn treatment, in terms of infection and epithelialization. It is less effective than aloe vera, sucrose, petrolatum gel, honey, sucralfate, petrolatum gauze for lower-extremity ulcers, chronic noninfected wounds, and pressure ulcers. In an animal study examining several dressings for burns, Selcuk et al found that the most effective dressing against *Acinetobacter baumannii* was Acticoat, followed by octenidine, then mupirocin, with SSD being the least effective dressing. In an animal study examining several dressings for burns, Selcuk et al found that the most effective dressing against *Acinetobacter baumannii* was Acticoat, followed by octenidine, then mupirocin, with SSD being the least effective dressing. In an animal study examining several dressings for burns, Selcuk et al found that the most effective dressing against *Acinetobacter baumannii* was Acticoat, followed by octenidine, then mupirocin, with SSD being the least effective dressing. Brown et al found that Aquacel Ag and Acticoat were equivalent for burn healing.

**Closed Surgical Incisions**

One study found that the use of Silverlon as a dressing over closed surgical incisions resulted in less pain. However, there is no evidence that the use of a silver-containing dressing to cover a closed surgical incision reduces infection or accelerates healing. This has been demonstrated in numerous randomized-controlled trials examining both clean and clean-contaminated operations.
surgical dressing that has been shown to reduce infection, wound healing complications, and reoperation is incisional NPWT, such as Prevena (Silver-impregnated foam, KCI, San Antonio, Tex.) or plain polyurethane foam with an NPWT machine. Multiple studies have demonstrated the effectiveness of incisional NPWT in high-risk incisions. Incisional NPWT is effective regardless of whether a plain polyurethane sponge or a silver-coated polyurethane sponge is used.

Alternatives to Silver

There are several silver-free antimicrobial topical wound treatments that have been shown to be effective. Some of these dressings are widely used in Europe, but not in the United States.

Octenidine dihydrochloride (OCT) is a surfactant that can be used as a topical antimicrobial with a very broad spectrum. It has been shown to be less toxic to keratinocytes and fibroblasts than silver, leading to faster wound healing. Polihexanide (PHMB) is also an antimicrobial with a very broad spectrum, which has been shown to have superior efficacy as a wound washing agent when compared to normal saline. There is no resistance to either OCT or PHMB, and both have strong activity against MRSA, VRE, and Candida albicans. Both OCT and PHMB have been used successfully as instillation solutions for NPWT in heavily contaminated wounds.

Finally, medical-grade honey has been shown to be a valuable option for wound management. Honey has a low pH and generates a low, sustained concentration of hydrogen peroxide, which gives it broad antimicrobial activity against both Gram-positive and Gram-negative organisms, without toxic effects on tissue. Honey leads to faster burn epithelialization than SSD.

DISCUSSION

Our qualitative literature review on silver has limitations: it is not a quantitative systematic review. This is due to the heterogeneity of the outcome measures in the published literature, which makes it difficult to pool data and generate meaningful conclusions. However, from our qualitative analysis, we can provide the following strategies for the proper use of silver in wound care:

1) SSD slows healing, and should be avoided in wound care, including in burn treatment. In addition, it should not be used as the gold standard for burn research.

2) In infected wounds, dressings containing nanocrystalline silver are helpful in the early treatment phase (first 2–3 weeks) to reduce bacterial counts and mitigate wound odor. It is best used as an adjunct to surgical debridement. As the wound becomes cleaner, silver-free dressings should be used to minimize toxicity towards keratinocytes and fibroblasts. Silver-containing dressings should not be used long-term.

3) During the early phase of treatment, NPWT with a silver sponge is especially useful, because it combines the advantages of NPWT with the antimicrobial properties of silver. In addition, the silver ion concentration produced is in the wound is 20 to 40 ppm, which is bactericidal, but lower than the toxic threshold to keratinocytes and fibroblasts.

4) In clean wounds, there is no role for the use of silver-containing dressings, as these can delay epithelialization. As discussed above, these dressings elute silver ion up to a concentration of 70 ppm, which is within the toxic range for keratinocytes and fibroblasts.

5) Silver-containing dressings have not been shown to decrease the risk of infection when used over closed surgical incisions. One study found decreased pain when silver-containing dressings were used over a closed incision. For high-risk closed surgical incisions (in patients who smoke, who have diabetes, etc.), the use of incisional NPWT with a plain polyurethane sponge lowers the risk of wound healing complications.

6) Alternatively, lesser known topical wound treatments, such octenidine and polyhexanide, may produce good outcomes, especially when used as instillation solutions for NPWT.

CONCLUSIONS

The judicious and selective use of silver in wound care in the correct situation can help accelerate healing, primarily as an adjunct to surgical debridement in infected wounds. Silver-containing dressings, especially nanocrystalline silver, are most useful in infected wounds, but do not provide added benefit in clean, noninfected wounds, and may slow the healing of those wounds. Moreover, silver-containing dressings do not confer an added advantage when applied over closed surgical incisions. In burns, dressings containing nanocrystalline silver are beneficial, but SSD leads to slower epithelialization, higher cost, more infections, and more pain. Plastic surgeons must be familiar with these nuances to optimize patient outcomes.

Jeffrey E. Janis, MD, FACS
Department of Plastic and Reconstructive Surgery
The Ohio State University Wexner Medical Center
915 Olentangy River Rd, Columbus, OH 43212
Phone: (614) 366-1242
Fax: (614) 293-9024
E-mail: jeffrey.janis@osumc.edu

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