Comparison of silver nylon wound dressing and silver sulfadiazine in partial burn wound therapy

Fereydoon Abedini1, Abdollah Ahmadi1, Akram Yavari1, Vahid Hosseini2* & Sarah Mousavi3

1 Department of Surgery, Imam Musa Kazem Hospital, Esfahan University of Medical Science, Esfahan, Iran
2 WPI-Advanced Institute for Materials Research, Tohoku University, Sendai, Japan
3 Clinical Pharmacy Department, Faculty of Pharmacy, Tehran University of Medical Sciences and Health Services, Research Center for Rational Use of Drugs, Tehran, Iran
* Present address: Laboratory for Biologically Oriented Materials, Department of Health, Science & Technology, ETH Zürich, Switzerland

Key words
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Correspondence to
S Mousavi, PhD, Clinical Pharmacy Department, Faculty of Pharmacy, Tehran University of Medical Sciences and Health Services, Research Center for Rational Use of Drugs, PO Box 14155-6451, Tehran, Iran
E-mail: smousavi@razi.tums.ac.ir
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Abstract
The study aims to perform a comparative assessment of two types of burn wound treatment. To do the assessment, patients with partial thickness burn wounds with total body surface area <40% were simple randomised to treat with nanocrystalline silver nylon wound dressing or silver sulfadiazine cream. Efficacy of treatment, use of analgesics, number of wound dressing change, wound infection and final hospitalisation cost were evaluated. The study showed silver nylon wound dressing significantly reduced length of hospital stay, analgesic use, wound infection and inflammation compared with silver sulfadiazine.

Introduction
Burn wounds need to be healed and reepithelialised as soon as possible in order to prevent infection, functional reduction, dysfunctions and cosmetic after-effects (1). Burn wounds have a higher chance of bacterial infection because of the accumulation of dead tissues, compromised immune system and blood supply, and infection is one of the major reasons of death after burn injuries (2). Silver sulfadiazine (AgSD) is one of the conventional therapeutics that has been used for a long time (3), but there are some reported adverse effects that increase the demand for new therapies and technologies in burn wound management (4).

Key Messages
- in this study, the efficacy of Agicoat® was evaluated and compared with the AgSD as a conventional protocol for burn wound treatment in most of Iranian burn clinics
- the study aims to evaluate the total hospitalisation cost, wound healing rate, analgesic use, fever as inflammatory index and total aerobic bacterial wound contamination for both therapies
- 185 patients with partial-thickness burn wounds who were treated at ‘Imam Musa Kazem’ burn hospital were reviewed for inclusion into the study
- sixty-nine burn wounds patients were included and randomised (the random number generator was used) into two groups and given burn wound treatment with 1% AgSD or Agicoat®
- 35 patients as subjects using silver nylon dressing and 34 patients as controls treated by AgSD
- long antimicrobial effectiveness of Agicoat® silver nylon dressing and others sustain the release of non crystalline silver wound dressings make them superior in wound healing
- they help activate regeneration and reepithelialisation of burn wounds, minimise patient’s pain, extra trauma during dressing changes, reduce healing time and hospitalisation period
- using of Agicoat® in moist environment which is a mandatory condition for administration of this silver nylon dressing improves wound recovery
- silver release from dressing could improve wound-healing progress by reducing infection rate which is one of the major factors for inflammation and retarding healing process
- it has been shown that total costs of both dressings are not significantly different, mostly because of higher initial cost (dressing cost) of Agicoat® although it
Silver has been known to have bactericidal properties and it has been at the core of many studies for several years (5). Silver recently gained renewed attention in the treatment of bacterial infection and prevention of wound sepsis in different presentation forms in conjunction with other materials such as wound dressings impregnated with silver salts or metal nanoparticles (6–8). One of the silver products that is increasingly being used to cover burn wounds, traumatic injuries, skin graft, diabetic ulcers, incisions, abrasions and minor cuts are silver dressings (9). Metallic and ionic silver was used in a variety of medicinal and medical devices such as topical creams, emulsions, catheters and medical prostheses (10–15). However, different methods have been used to impregnate wound dressings with silver compound, but coating a textile, fibre or polymer mesh with a layer of nanocrystalline silver resulted in sustained release and long-acting antibacterial wound dressings (9,16). In 1998, Tredget et al. (17) showed the safety and efficacy of a nanocrystalline silver-coated polyethylene mesh in preventing infection in burn wounds by reducing the bacterial burden. Although the anti-inflammatory mechanism of nanocrystalline silver is not clear (13), it might reduce inflammation by fighting the bacterial infection (18) – an important reason for persistent inflammation which leads to infiltration of neutrophils and elevated matrix metalloproteinases (MMPs) in infected wounds. MMPs play a role in the controlled degradation of the extracellular matrix. It has been shown that nanocrystalline silver and its derivative solution have anti-inflammatory effects; for instance, a study suggested that the level of MMPs is reduced in the presence of nanocrystalline silver dressings; elevated activities of these enzymes may lead to excessive extracellular matrix destruction. Also, nanocrystalline metallic silver dressings can suppress MMP-9 activity and reduce TNF-α levels in the wounds (19–21).

Silver dressings such as Acticoat® (Smith & Nephew, Largo, FL), a high-density polyethylene mesh coated with nanocrystalline silver and silver oxide using the physical vapour deposition technique (22), Silverlon® (Argentum LLC, Chicago, IL) or Agicoat® (Emad pharmaceuticals Co., Esfahan, Iran) – a woven silver-coated nylon fabrics in which silver is deposited on nylon fibres by autocatalytic electroless deposition techniques (23) – are among metallic silver dressings with sustained silver release. As their manufacturing methods are different from Acticoat® to Silverlon® and Agicoat®, the nanocrystalline structure and physical properties of silver crystals are distinctive in them. These morphological and chemical differences resulted in different silver-release profiles in Acticoat® and Silverlon® in terms of duration and net silver release rate; however, these wound dressings show acceptable antimicrobial properties in vitro. Agicoat®, a less-studied brand, also has a silver release-profile similar to its counterpart Silverlon® with approximately 600 mg/100 cm² of silver. It can release silver for a long time and show antimicrobial effectiveness.

In this study, the efficacy of Agicoat® was evaluated and compared with the AgSD as a conventional protocol for burn wound treatment in most of the Iranian burn clinics. Although using such a dressing in burn wounds is not new for some brands such as Acticoat®, the study investigates the efficacy of a brand new silver nylon wound dressing that was recently introduced to Iran and the international market. The study did not compare Agicoat® with Acticoat® which is less available in the Iran market due to its high prices; therefore, most burn clinics and patients prefer to use AgSD as a standard burn wound treatment protocol. The study aims to evaluate the total hospitalisation cost, wound healing rate, analgesic use, fever as inflammatory index and total aerobic bacterial wound contamination for both therapies.

Materials and methods

Patient population

Between April 2010 and July 2011, 185 patients with partial-thickness burn wounds who were treated at ‘Imam Musa Kazem’ Burn Hospital were reviewed for inclusion in the study; then 69 of them were treated with silver nylon wound dressing or AgSD cream until complete wound closure, which was defined by complete epithelialisation. The inclusion criteria were partial-thickness burn wounds, <24 hours post-burn injury and total body surface area (TBSA) between 10% and 40%. Exclusion criteria were full-thickness burns, pregnancy, immunocompromised patients, patients with known hypersensitivity to silver and its compounds, comorbidity (e.g. diabetes, and cardiac or renal disease), chemical or electrical burns, multiple trauma and age <5 and >60. Selected cases were categorised by age, sex, burn type and burn percentage. In all cases, informed consent was obtained from patients or their relatives. Both clinicians and patients or their relatives were aware of the treatment procedure (open label design). The study protocol was approved by the ethics committee of Imam Musa Kazem Hospital, Esfahan University of Medical Sciences, Esfahan, Iran.

The studied dressing

Agicoat® comprises a patented silver-coated woven textile that sustains released silver ion from the deposited nanocrystalline silver cluster on the textile fibres. This thin woven textile needs to be supported by an additional occlusive dressing on wound with cotton gauze or pads. According to the manufacturer information, the silver is deposited by autocatalytic electroless silver deposition onto the nylon fibres. It continuously releases silver ion and shows antimicrobial effectiveness up to 7 days, according to the data represented by the manufacturer and approved by Iran’s Food and Drug Organisation (unpublished data). Agicoat®, an approved wound dressing by the Iranian Food and Drug Organisation for use on all kinds of wounds, was used to provide an antimicrobial effectiveness...
and a barrier by lowering the risk of infection in contaminated, moist or high exudate burn wounds.

Wound dressing protocol

In the Agicoat\textsuperscript{®}-treated group, the treatment consisted of the application of a silver dressing. The Agicoat\textsuperscript{®} silver dressing was applied directly on wounds, and thereafter it was covered by cotton gauze and wetted regularly by sterile water. It must be wet, according to the manufacturer instruction. In case of high exudate wounds, just oversaturated cotton gauzes were changed. The Agicoat\textsuperscript{®} dressings were changed every 7 days until complete wound closure and healing. All patients were followed up in the hospital until the end of the study and the final examination. Wounds were assumed to heal when all areas of initial injury had fully reepithelialised. The other group received 1\% AgSD cream, which was covered with cotton gauze. AgSD dressings were changed every day until wound closure.

Study design and evaluation criteria

Sixty-nine patients with burn wounds were included and randomised (the random number generator was used) into two groups and given burn wound treatment with 1\% AgSD or Agicoat\textsuperscript{®}, 35 patients as subjects using silver nylon dressing and 34 patients as controls treated by AgSD. Two burn wound surgeons filled a demography form for incoming patients to the program. The surgeons recorded the type of burn wound, location of wound, size (length $\times$ width in centimetres), depth of wound and the amount of wound exudates. Both groups were compared with regard to the patient demographic data. The photographic records were performed for all the burn wounds. Efficacy of treatment was evaluated by the average number of analgesic doses, which was prescribed based on patient demands and assessed by visual analogue scale, number of wound dressing change, nursing time and time of burn wound healing between both groups. As fentanyl was the only analgesic medicine which was approved by the hospital regulatory for acute pains of burn patients, the number of its dose was considered to be a good measuring scale for comparison and assessment of the acute pain in both groups.

Wound contamination for aerobic micro-organisms was assessed according to the described methods (24,25) every 3 days. Briefly, swabs were immersed in 0.5 ml sterile normal saline and after wound swabbing they were cultured on soybean casein digest agar plates immediately by the surface culture method and were incubated for 48 hours. Visible colonies on plates were counted and reported as total count. Also, body temperature was registered three times per day. The anaerobic micro-organisms did not count due to the technical limitation.

The final hospitalisation cost was evaluated according to the cost of antibiotics, analgesics, dressings and hoteling costs and included nursing and visiting costs.

Statistical analysis

All data were expressed as mean $\pm$ SD. For parametric data, Student’s independent $t$-test was used to compare data; for nonparametric data, Mann–Whitney test was used. Chi-square test was performed to determine the relationship between parameters. Significance was defined as a $P$ value of $<0.05$.

Results

Sixty-nine patients were recruited: 24 males and 11 females in the Agicoat\textsuperscript{®} treatment group, and 23 males and 11 females in the 1\% AgSD treatment group ($P=0.99$), respectively, with approximately 119 000 and 112 000 cm$^2$ total treated burn area. The TBSA burn percent was not significantly different in both groups ($P=0.8$). Age distributions were between 5 and 52 in both the study groups and the mean age of patients was 26.2 $\pm$ 1.7 in Agicoat\textsuperscript{®} group, while it was 27.9 $\pm$ 1.7 ($P=0.99$) in the 1\% AgSD group. Burn wounds were also classified by the cause of burns which included hot liquids, fire and others, which was the same in both groups ($P=0.51$). Demographic data of the patients in both groups are shown in Table 1. All patients remained in the study till complete wound healing and nobody left before end of the study because of unwanted reaction, death or the adverse effects of dressing.

The Agicoat\textsuperscript{®} treatment group had manifested significantly lower analgesic doses scores than the 1\% AgSD-treated group ($P=0.001$). The average number of days with fever (2.9 for Agicoat\textsuperscript{®} and 6.3 for AgSD) to the total number of body temperature registration (34 for Agicoat\textsuperscript{®} and 59.2 for AgSD) also was significantly less for the Agicoat\textsuperscript{®} group ($P=0.046$). Also, positive cultures regarding micro-organisms were less for Agicoat\textsuperscript{®} (82 positive cultures out of 200) compared to 1\% AgSD treatment group (142 positive cultures out of 200, $P=0.001$). The data are summarised in Figure 1. Finally,
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Figure 1 (A) Average healing time (days) in Agicoat® and silver sulfadiazine group ($P = 0.007$). (B) Average administrated narcotic analgesic doses in Agicoat® and AgSD group ($P = 0.001$). (C) Fever index (fever registration to total body temperature registration) for both groups ($P = 0.046$). (D) Average positive contaminated culture to total microbiological culture ($P = 0.001$).

Discussion
Partial-thickness burn wounds are difficult to manage. Wound infections, elevated levels of pain and delayed wound healing are the main problems to deal with.

In previous studies, AgSD, an inexpensive medicine, had shown its efficiency in reducing the risk of infection (26). AgSD was a broad-spectrum topical antimicrobial agent active against Gram-positive cocci such as *Staphylococcus aureus* and Gram-negative bacilli, particularly *Pseudomonas aeruginosa*. It has been used as the standard treatment protocol in partial-thickness burn wounds for several years. Therefore, it is compared as the standard protocol to an available, rather low price nanocrystalline silver nylon wound dressing, Agicoat®.

Partial-thickness burn wounds are challenging because of the long healing time and periodical wound dressing changes which hurt and slow down the wound healing. Therefore, daily changes of AgSD dressing with associated pain and risk of nosocomial infections are higher than Agicoat® which needs longer time to change. As a result of the fewer dressing changes in the Agicoat® treatment group, less pain accompanies the use of Agicoat® dressing which favoured the patients. This directly results in fewer analgesic doses compared to the AgSD treatment group. However, previous studies have shown that nanocrystalline silver dressings have analgesic properties (27,28), but this study did not evaluate pain as an independent value and compare the specific pain reduction of the studied dressing to AgSD; for instance, our evaluation
that Agicoat® although it decreases the frequency of dressing changes and nursing cost.

Conclusion

Agicoat® advanced antimicrobial silver nylon wound dressing is an effective barrier against microbial penetration in partial-thickness burn wounds. The study results suggest that it significantly decreases the analgesic use, risk of infection, fever as inflammatory index and the healing time compared with the 1% AgSD treatment group. The presented data show that Agicoat® could be used as an effective dressing to manage partial-thickness burn wounds.

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