The Role of a Silver Releasing Lipido-colloid Contact Layer in Venous Leg Ulcers Presenting Inflammatory Signs Suggesting Heavy Bacterial Colonization: Results of a Randomized Controlled Study

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Abstract: Objective. Clinical interest of silver in the management of chronic wounds is not fully established. The main objective of this clinical study was to assess the ability of a new silver releasing lipido-colloid contact layer to promote the healing process of venous leg ulcers (VLU) presenting inflammatory signs suggesting a heavy bacteria colonization and then a delayed healing, in comparison to the same wound dressing not impregnated with silver salts. Methods. This was an open-labeled, randomized, controlled trial. VLU presenting at least 3 out of 5 clinical signs suggesting heavy bacterial colonization were recruited. Patients were treated with contact layer silver dressing ([CLS], Restore® Contact Layer, Silver* (Hollister Wound Care, Libertyville, Ill) or contact layer dressing ([CL] Restore® Contact Layer**, Hollister Wound Care, Libertyville, Ill) for 4 weeks, then all treated ulcers were treated with CL for the 4 additional weeks. Wound evaluation and area measurements were conducted weekly during the first 4 weeks and then at week 6 and 8. Main efficacy criterion was absolute wound area decrease (AD) at week 4 and week 8. Results. Patients (N = 102) were randomized and treated. Ulcers were present for nearly 11 months on average; 65% were recurrent and mean area was 20.0 ± 17.8 cm². Almost 80% of the treated VLU were stagnating/aggravating with their previous treatment. By week 4, mean surface area decreased by 6.5 ± 13.4 cm² (median: 4.2 cm²) and 1.3 ± 9.0 cm² (median: 1.1 cm²) in CLS and CL groups, respectively (P = 0.023). At week 8, median decrease was 5.9 cm² versus 0.8 cm² (P = 0.002) with a wound percentage decrease of 47.9% and 5.6% (P = 0.036). Median closure rate was 0.145 versus 0.044 cm²/day (P = 0.009) at week 4 and remained higher in the CLS group up to week 8 even after switching to CL dressing in these patients (P = 0.001). Odds ratio (multinomial logistic regression) of the chance to reach a ≥ 40% wound area reduction was 2.7 (95% CI: 1.1 to 6.7; P = 0.038) for silver treated ulcers. Dressing tolerance was good in both groups. Conclusion. A 4-week treatment with silver releasing lipido-colloid contact layer promotes a sustained increase of closure rate of venous leg ulcers presenting inflammatory signs suggesting a high bacterial load. Also marketed as *Urgotul® Silver and **Urgotul®, Laboratoires Urgo, (France).
Nearly all open wounds are contaminated by microorganisms, but this generally corresponds to a simple bacterial growth without leading to deleterious effects or compromising the progress of the healing process. If the probability of wound infection increases as the level of contamination does in acute wounds, it is more complex for chronic wounds which are able to content and tolerate without inducing local signs, large amounts of bacteria, many times higher than the usual threshold level ($\geq 10^6$ bacteria/g of tissue) defining infection in acute wounds. Nevertheless, many clinical and experimental studies indicate that the probability for chronic wounds to heal properly is limited when the bacterial load exceeds this level of contamination; even when body defenses are still able to prevent tissue invasion, bacteria can impair wound healing. Numerous mechanisms are involved in wound stagnation due to this bacterial growth: local release of endotoxins and exotoxins, of pro-inflammatory cytokines, local pH alteration, decrease in oxygen supply and increased MMPs/TIMPs (metalloproteinases/tissue inhibitor of metalloproteinases) ratio notably. This prolongs an inappropriate topical inflammatory reaction, which contributes to delay the wound healing process.

These considerations are theoretical grounds to support the use of silver in chronic wounds when a negative local impact of bacterial colonization is confirmed or suspected. Indeed, silver is a large spectrum antibacterial agent which covers virtually all the bacterial strains responsible for chronic wound colonization (including resistant species such as MRSA) with a weak toxicity against fibroblasts. Furthermore, this metallic ion has strong anti-inflammatory properties, inhibits MMP activity and promotes apoptosis of senescent cells. There is very little risk of seeing resistance develop to the silver ion because its mechanism of action involves many membrane- and nucleus-based sites.

Despite widespread use of silver ions in the management of chronic wounds, the clinical interest of silver in these wounds is not yet fully established. The main objective of this randomized clinical study was to evaluate the ability of a new silver releasing wound dressing to promote the healing process of venous leg ulcers presenting inflammatory signs suggesting a heavy bacteria colonization, when compared to the same wound dressing not impregnated with silver salts.

**Methods**

This multicenter, open-label, randomized, controlled clinical trial was conducted in 2-arm parallel groups in 24 French investigating centers (hospital dermatology and vascular medicine departments).

**Patients.** Adult patients were included if they presented a venous leg ulcer with an ankle-brachial pressure index (ABPI) $> 0.8$. Ulcer duration had to be less than 24 months and baseline wound area had to range between $5 \text{cm}^2$–$40 \text{cm}^2$. Furthermore, selected leg ulcers were required to meet at least 3 of the 5 following clinical signs: pain between 2 dressing changes, perilesional skin erythema, edema, foul odor, and heavy exudation. Patients agreed to wear compression therapy daily in combination with the trial dressing. Exclusion criteria included: current local or systemic antibiotics in the week prior to inclusion, clinically infected wound or erysipelas, malignant wound, recent deep venous thrombosis or venous surgery, progressive neoplastic lesion treated by radiotherapy or chemotherapy, and on-going treatment with immunosuppressive agents or high dose corticosteroids.

**Design and procedures.** Patients who met the selection criteria gave their written consent to participate in the trial, and were randomly allocated to be treated either by a silver releasing contact layer dressing (CLS group) or by the same contact layer dressing without silver (CL group) for 4 weeks. After the fourth week, patients of the silver group were treated with the CL and subjects in both groups were followed to complete healing or to a maximum of 4 additional weeks (8 weeks in total, for every included patient).

At the inclusion visit, patient demographics, characteristics, leg ulcer history, and the number of pre-defined local signs were precisely recorded. The selection of compression therapy was left to the investigators’ discretion and the patient’s concordance was verified. An acetate tracer of wound surface area (planimetry) was conducted and a photograph of the ulcer was taken. Wounds were medically evaluated once a week during the first 4 weeks and then every 2 weeks until the eighth week. At each visit, wound status including colorimetric scale evaluation, perilesional skin appearance, number of local signs, acetate tracing and wound photograph were performed. In the silver group, blood samples (ancillary protocol) were taken at baseline and at week 4 (Pasteur Cerba Laboratories), to determine blood silver level (Electrothermal Atomic Absorption Spectrometry [ETAAS], Perkin Elmer model 4100 ZL).
Acceptability of the tested dressings was assessed by using open questions (to patients and healthcare professionals) and each patient’s concordance to compression therapy was documented at all physicians’ and nurses’ visits.

Concomitant local and general treatments, as well as local wound care, were documented during the study. Local use of antiseptics, but not antibiotics, was authorized. Investigators were allowed to withdraw patients from the study if unacceptable dressing-related adverse events occurred, or if they considered that the wound aggravation required a more appropriate treatment, such as systemic antibiotics.

**Endpoints.** Efficacy, which was the primary endpoint of the study, was assessed by the investigating physician at each weekly clinical evaluation (until week 4 and after, every 2 weeks until week 8), through the wound area measurement (judgment criteria).

As secondary endpoints, the wound closure, the clinical evolution (presence of each of the 5 selected clinical signs), the tolerance (occurrence of local adverse events), and the acceptability of the tested dressings were assessed during the 8 weeks follow-up. Photographs were also taken.

**Randomization.** A random list balanced by blocks of 4 patients was used. Each center received at least 4 sealed envelopes with a number corresponding to the chronologic order of patients’ inclusion. According to the center recruitment capacities, more than one block could be provided. No randomization error or deviation was detected by the on-site audits held during the study.

**Tested dressings and localized treatment.** The contact layer silver dressing (CLS) was presented as 10-cm x 10-cm dressings developed from a lipido-colloid technology. This sterile, nonadhesive, and nonocclusive dressing is composed of a polyester textile mesh impregnated with hydrocolloid particles and Vaseline®. Silver is incorporated within the structure as silver sulfate that gradually releases, over 7 days, and is released as silver ion when dressing enters in contact with wound fluids. The control contact layer dressing (CL) had similar characteristics to the test dressing, the only difference being the absence of silver content.

It was recommended that both dressings be changed every other day or less frequently, depending on the clinical condition of the wound and the volume of exudate. At each dressing change, wounds were inspected and cleaned exclusively with normal saline. If necessary, mechanical debridement was performed to remove slough and necrotic tissues. The ulcer was covered on its whole surface by the tested dressing followed by a secondary dressing (Ultrasorb®, Tetra Medical, France).

**Sample size determination.** A minimal sample size of 96 patients was a priori determined to have 80% power to detect, at 8 weeks, a 15% superiority of CLS if relative wound area regression in the CL group was within a 20%–25% range with an expected standard deviation of 26% (bilateral approach, alpha risk fixed at 5%).

**Data processing and statistical analysis.** Statistical analysis was conducted by a company independent of the sponsor, in concordance with the statistical analysis plan drawn up and approved by the different parties involved in the trial. Data analysis was conducted with SAS/FSP (version 6.12) under Windows 2000 software. If a patient withdrew before the eighth week of the study, the efficacy analysis took into account the last evaluation available (last observation carried forward [LOCF]).

The treated groups were compared using the Student’s \( t \)-test or the nonparametric Wilcoxon test for continuous variables and chi-squared test for categorical variables.

All analyses were conducted on the intent-to-treat population defined as all randomized patients with at least one follow-up planimetry value.

The main efficacy parameter was the absolute wound area decrease (AD, cm\(^2\)) from baseline at week 4 and week 8. Secondary endpoints were the relative wound area regression (% decrease from baseline), the closure rate (AD/t where \( t \) is the number of days between 2 planimetric measurements), and the number of predefined local signs at weeks 4 and 8. Comparisons were performed with the nonparametric Wilcoxon test. The number of ulcers reaching a ≥ 40% area regression was evaluated by multinominal logistic regression including age, body mass index, ulcer duration, and baseline area, as covariates; \( P < 5\% \) was considered significant.

Study protocol was submitted and approved by the Medical Ethics Committee of Versailles, France. This clinical trial was conducted in compliance with Good Clinical Practice and with the principles in the Declaration of Helsinki. All patients gave written consent to participate after having received full written information regarding the study objectives and conduct.

**Results**

Between May 2004 and August 2006, 102 patients were included and randomized. Three patients withdrew before the first ulcer evaluation at week 1 (1 in the CLS
group for consent withdrawal, and 2 in the control group for ulcer aggravation and intercurrent event). Therefore, the efficacy analysis on the ITT population included 99 subjects (51 patients treated with the silver sequential strategy [CLS] and 48 patients with the continuous strategy with the control dressing [CL]).

In total, 8 and 20 patients dropped out from the study before week 8 in CLS and CL, respectively (Table 1).

If considering the 2 treatment groups, this clinical trial involved 4796 cumulated days of treatment, 800 medical evaluations, and 2461 nursing care operations.

**Baseline characteristics.** Seventy-one percent of the 102 patients were outpatients. The population was predominantly women with a mean age of 74.7 ± 11.7 years (Table 2). Mean body mass index (BMI) was 28.8 kg/m² ± 7.3 kg/m², 18.6% were diabetics, 32.4% had a history of venous thrombosis, and 40.2% of patients presented a history of superficial vein surgery. Eighty-six percent of the patients were wearing compression bandage before randomization.

At inclusion, necrotic tissue was absent from the wound bed, 50.8% ± 27.6% of the wound surfaces were covered with sloughy tissue (yellow appearance on colorimetric scale), and 2.9% of the treated wounds presented with a healthy perilesional skin. Leg ulcers were present for almost 11 months on average (median 9.0) and 65% were recurrent. Mean surface area was 20.0 cm² ± 17.8 cm² (median 14.6 cm²). Wound surface area in the CLS group was larger, but not significantly larger. At least 3 of the pre-specified local signs were present in all ulcers.

Overall, in the investigators’ opinion, 79.4% of these ulcers were considered as stagnating or aggravating.

**Wound area reduction.** By week 4, ulcer area decreased on average by 6.5 ± 13.4 cm² (median 4.2 cm²) in the CLS group and by 1.3 ± 9.0 cm² (median 1.1 cm²) in the CL group (Table 3 and Figure 1; P = 0.023). After week 4, when all patients in the CLS group switched to the non silver-containing contact layer, their ulcer area continued to decrease while no clinically relevant change was observed in the CL group. At week 8, the median absolute wound surface reduction was 5.9 cm² and 0.8 cm² in the CLS and CL groups, respectively (P = 0.002). The same trends were observed when surface area evolutions were expressed as percentage reduction from baseline. By week 8, median ulcer area regression was 47.9% in the CLS group and was 5.6% in the CL group (P = 0.036).

**Wound closure rate.** By the end of the first 2 weeks,
a strong increase in closure rate was evident in the CLS group, whereas a weak acceleration was noted in the CL group (Figure 1). Closure rate was significantly higher by week 4 in the CLS group (median 0.145 cm² versus 0.044 cm²/day; \( P = 0.009 \)). After switching to the non-silver containing dressing, this closure rate remained unchanged (0.135 cm² versus 0.023 cm²/day; \( P = 0.001 \)).

**Chances to reach a 40% wound area reduction.**
By the end of the follow-up, 55% of the ulcers in the CLS group decreased by 40% or more as compared to 35% for wounds receiving only the non silver releasing dressing throughout the study period (\( P = 0.051 \)). Odds ratio (multinominal logistic regression) of the chances to reach this endpoint was 2.7 (95% CI: 1.1 to 6.7; \( P = 0.038 \)) in favor of the CLS group.

In this model, influence of included covariates (age, BMI, ulcer duration and baseline area) was not significant, only the “treatment factor” proved to be significant (\( P = 0.034 \)).

**Local signs of heavy bacterial colonization.**
At week 4, no clinical signs were reported in 39.2% of ulcers in the CLS group, compared to 16.7% in the CL group (Figure 2). At the last medical evaluation, the medians of the number of pre-specified local signs were of 1.0 and of 2.5 in the CLS and CL groups, respectively. On average, as compared to baseline, the number of clinical signs decreased significantly more in ulcers treated with the silver dressing during the initial 4 weeks of the study (-2.5 ± 1.5 versus -1.0 ± 1.4; \( P < 0.001 \)).

**Local adverse events and dressing acceptability.** Twenty-two local adverse events, possibly related to the tested dressings, were reported

**Table 1. Reasons why patients dropped from the study.**

<table>
<thead>
<tr>
<th></th>
<th>CLS Before W4</th>
<th>Between W4-8</th>
<th>CL Before W4</th>
<th>Between W4-8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consent withdrawal</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Ulcer aggravation</td>
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<td>0</td>
<td>4</td>
<td>5</td>
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<tr>
<td>Local adverse event</td>
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<td>9</td>
<td>0</td>
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<td>General intercurrent event</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Other reason</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>3</td>
<td>5</td>
<td>14</td>
<td>6</td>
</tr>
</tbody>
</table>

**Table 2. Patient and ulcer characteristics at baseline.**

<table>
<thead>
<tr>
<th></th>
<th>CLS (n = 52)</th>
<th>CL (n = 50)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (F/M) (n)</td>
<td>36/16</td>
<td>35/15</td>
<td>0.9327</td>
</tr>
<tr>
<td>Age (years)</td>
<td>76.6 ± 10.2</td>
<td>72.8 ± 12.9</td>
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</tr>
<tr>
<td>Weight (kg)</td>
<td>81.67 ± 23.97</td>
<td>77.55 ± 21.18</td>
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<tr>
<td>Height (cm)</td>
<td>165.77 ± 8.65</td>
<td>166.44 ± 10.86</td>
<td>0.7302</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>29.6 ± 8.2</td>
<td>27.8 ± 6.2</td>
<td>0.3334</td>
</tr>
<tr>
<td>Diabetes n (%)</td>
<td>9 (17.3%)</td>
<td>10 (20%)</td>
<td>0.7270</td>
</tr>
<tr>
<td>History of venous thrombosis n (%)</td>
<td>16 (30.8%)</td>
<td>17 (34%)</td>
<td>0.7273</td>
</tr>
<tr>
<td>Compression bandage prior inclusion n (%)</td>
<td>43 (82.7%)</td>
<td>45 (90%)</td>
<td>0.2836</td>
</tr>
</tbody>
</table>

**Ulcer characteristics**

| Recurrent ulcer n (%) | 34 (65.4%) | 32 (64.0%) | 0.8837  |
| Duration (months)     | 11 ± 8 (9.5) | 10 ± 8 (9.0) | 0.8428  |
| Wound area (cm²)      | 22.3 ± 20.4 (16.3) | 17.5 ± 14.4 (12.6) | 0.1142  |
| % surface covered with slough (median) | 50 | 45 | 0.2877  |

**Condition of the perilesional skin**

| Healthy | 1 (1.9%) | 2 (4.0%) | 0.6139  |
| Erythematous | 45 (86.5%) | 44 (88.0%) | 0.8249  |
| Oedematous | 32 (61.5%) | 25 (50.0%) | 0.2407  |
| Eczematous | 9 (17.3%) | 9 (18.0%) | 0.9269  |
| Other | 17 (32.7%) | 20 (40%) | 0.1142  |

**Local signs n (%)**

| Pain between 2 dressing changes | 46 (88.5%) | 40 (80.0%) | 0.2401  |
| Periwound erythema | 44 (84.6%) | 42 (84.0%) | 0.9319  |
| Edema | 39 (75.0%) | 31 (62.0%) | 0.1572  |
| Foul odor | 31 (59.6%) | 18 (36.0%) | 0.0170  |
| Heavy exudation | 39 (75.0%) | 40 (80.0%) | 0.5458  |

**Number of local signs n (%)**

| 3 signs | 21 (40.4%) | 31 (62.0%) | 0.0041  |
| 4 signs | 19 (36.5%) | 17 (34.0%) | 0.0041  |
| 5 signs | 12 (23.1%) | 2 (4.0%) | 0.3078  |

**Ulcer status**

| Moderate improvement | 10 (19.2%) | 11 (22.0%) | 0.3078  |
| Stagnation | 16 (30.8%) | 21 (42.0%) | 0.3078  |
| Aggravation | 26 (50.0%) | 18 (36.0%) | 0.3078  |

Results presented as mean ± SD and (median) unless otherwise specified.
in 20 patients (Table 4). The types of adverse events reported were not different between the 2 groups. No infection occurred in the first period (day 0–week 4) in the silver group treatment versus one infection in the control group (9.2% versus 19.8%), compared to 1.9% and 4%, respectively, at baseline. No skin staining was detected at the weekly investigating evaluations.

The dressing acceptability was similar in the 2 treatment groups and the interval between 2 dressing changes was a little bit longer in the CLS group than in the CL group (2.12 days versus 1.84 days, respectively).

Blood silver was determined at baseline and at week 4 in 10 patients in the silver treated group and remained lower than 1.62 µg/mL (limit of detection of blood silver with the selected method) in 7 cases and was < 3.7 µg/mL in the last 3 patients.

### Discussion

This open-label, randomized, controlled study evaluated the efficacy of a therapeutic option including the use of a silver-releasing dressing over 4 weeks followed by the application of the same device not containing silver for 4 additional weeks. The control group (CL) was treated without silver during the entire trial. The studied dressings were derived from a lipidic-colloid technology, which has been largely evaluated in clinical situations. A clear and unambiguous superior efficacy of the studied option was documented. The introduction of a 4-week silver based local treatment...
was followed by a clinically relevant promotion of the healing process in leg ulcers presenting inflammatory signs, suggesting high bacterial load.

At the end of the follow-up period, the wound areas had decreased by a median of 47.9% of the silver group compared with 5.6% in the control group. This constitutes a significant difference (P = 0.036), even after adjusting for the number of topical signs at inclusion.

In terms of absolute regression after 8 weeks of treatment, the surface area decreased by 5.9 cm² (median value) in the silver group versus 0.8 cm² with the control (P = 0.002). This difference was observed in the first 2 weeks of treatment since the closure rate was significantly faster in the tested group at all time points over the first 4 weeks. The principal gain occurred in the first 2 weeks, and this was then maintained throughout the entire follow-up period.

At the end of the follow-up period, 82.4% of the ulcers of the CLS group showed a regression of their baseline surface area, while 17.6% increased their surface. In the control group, these percentages were similar (54.2% of the ulcers regressed and 45.8% increased their surface area).

Regression analysis, which included in their model ulcer outcome prognosis factors (age, BMI, ulcer duration, area at inclusion, recurrence of the ulcer), showed that the likelihood of obtaining an area regression of 40% in 8 weeks was 2.7 times greater with the silver sequential strategy than with continuous treatment in the control group (OR: 2.7; 95% CI: 1.1; 6.7; P = 0.038). None of the other factors in the model were significant.

In association with the effect on the surface area, a clinical improvement based on the number of clinical signs after 8 weeks of treatment was documented in the silver group. In addition, no secondary infection was noted during the silver treatment period (the first 4 weeks of treatment) versus 2 local infections in the control group at the same time.

Finally, dressing acceptability and local tolerance were similar in the 2 treatment groups. Included wounds were venous leg ulcers presenting at least 3 of 5 predefined local signs (pain between 2 dressing changes, perilesional skin, erythema, edema, foul odor, or strong exudation). Even if none of these signs taken in isolation is specific, their combination might suggest strong bacterial contamination, a factor known to delay the healing process. Baseline aspect of the selected ulcers confirmed the relevance of this criterion. In addition to possible strong bacterial load, these wounds were present for almost 11 months on average, their mean area was greater than to 10 cm², and 65% of the ulcers were chronic. All these parameters are identified as a poor healing prognosis. Experienced physicians confirmed this and observed that about 80% of these ulcers were considered as stagnating or aggravating at inclusion, despite best applied standard of care that included efficient compression therapy. Overall, these ulcers can be regarded as “stuck” in the inflammatory phase, and that high bacterial load was probably the predominant responsible factor.

This hypothesis supports the use of adding silver releasing dressing to localize treatment in these situations. The large antibacterial spectrum of this metallic ion combines to its direct anti-inflammatory properties will participate in reducing the inappropriate inflammation of chronic wounds and will help to switch ulcers from stagnation to a more favorable healing trajectory. The results of this study confirm the relevance of this strategy. When comparing dressings that differed only by the capacity of one of them to release silver, ulcers treated with this latter device quickly increased their closure rate whereas, in the control group, limited changes were observed.

Other studies in the treatment of leg ulcers support this view. However, these trials suffered from some limitations to be strongly convincing. The CONTOP trial used a pragmatic design, and variations between centers in localized treatment might be a confounding factor that renders results difficult to interpret. Meaume et al compared an alginate dressing to a silver releasing hydroalginate dressing. Both leg and pressure ulcers were included if they presented 2 local signs suggesting high bacterial load. The main efficacy parameter was the 2-week global mASEPSIS score to evaluate risk of developing infection. Reduction of this score did not differ between groups, but closure rate, which was a secondary endpoint, was significantly superior in the silver-treated wounds. The study design used by Jorgensen et al is closer to the present study’s design. Leg ulcers, characterized by a documented delayed healing during a 4-week run-in period were selected if they presented at least 1 sign suggesting “critical colonization.” Wounds were treated either with silver-releasing foam or non-silver foam for 4 weeks. In that trial, the relative median wound area decrease was significantly higher in the silver treated group as compared to the control treated group (45% versus 25%; P = 0.034).

The present study differs from these trials in at least 3
major aspects. First, this study compared strictly similar dressings in both groups differing only by their ability to release silver. Therefore, any observed difference could be more reliably related to silver rather than to another possible difference between dressings. Secondly, the selected wounds had to meet at least 3 out of 5 signs supporting high bacterial load. Finally, the strategy used in this study is quite different from those previously employed in published studies testing the alginate silver\textsuperscript{34} and the foam silver dressing\textsuperscript{35} where patients were followed up for 4 weeks. This period of silver treatment was selected empirically, based solely on the fact that many clinicians consider this period sufficient when determining whether or not the selected treatment is able to re-start the healing process. Although the study with the foam silver dressing suggested that these 4 weeks of treatment can shorten wound-closure time in comparison with the control group, it could not be ruled out that the effect is only transient in nature. Therefore, the study investigating silver strategy (CLS) included an additional follow-up phase used to confirm that the re-started healing process induced by treating the wound with a silver dressing was sufficient to guarantee a sustained acceleration in wound closure.

While the results of the present study cannot explain precisely how silver stimulates healing in stagnating leg ulcers, this observation supports that silver ions have a “starter” effect.

A limitation of this study is that it was open-label, like all other studies in wound care management. The wound area tracings were measured by an independent person who was unaware of the test dressings. Furthermore, a blind review of the planimetric and photographic data was performed at the end of the study to validate the investigators’ evaluations, by 2 independent and experienced physicians. These reviewers did not know the received dressings and classified the final target ulcer status according to a 7-point scale (from “leg ulcer strongly improved” or “healed,” to leg ulcer “strongly aggravated”). This review detected no difference between investigators and reviewers evaluations and confirmed that the decision rules followed by the investigators when the treatment was prematurely discontinued were not different for patients treated with the silver releasing dressing or the control. Therefore, this blind review fully corroborates the evaluations made by the investigators.

Conclusion

This clinical study reports on the efficacy and good tolerance of a silver releasing contact layer with lipido-colloid technology in the management of stagnate, chronic wounds with inflammatory signs that suggest high bacterial load. Treatment with CLS rapidly induces an increase in the closure rate protecting these wounds from becoming “stuck” in the inflammatory stage due to heavy bacterial load, and creates a more favorable microenvironment that increases the probability of achieving complete wound closure.

Acknowledgments

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References

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