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Efficacy of a silver lipidocolloid dressing on heavily colonised wounds: a republished RCT

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Efficacy of a silver lipidocolloid dressing on heavily colonised wounds: a republished RCT

• **Objective:** To assess the ability of a silver lipidocolloid contact layer to promote the healing process of venous leg ulcers (VLUs) presenting inflammatory signs, suggesting a heavy bacteria colonisation, and then delayed healing, in comparison with the same wound dressing not impregnated with silver salts.
• **Method:** This was an open-labelled, randomised, controlled trial. VLU presenting at least 3 out of 5 clinical signs suggesting heavy bacterial colonisation were recruited. Patients were treated with contact-layer silver-dressing (CLS; Urgotul Silver [URGO Laboratories]) or contact-layer dressing (CL; Urgotul [URGO Laboratories]) for 4 weeks, then all treated ulcers were treated with CL for 4 additional weeks. Wound evaluation and area measurements were conducted weekly, during the first 4 weeks, and then at weeks 6 and 8. Main efficacy criterion was absolute wound area decrease (AD) at week 4 and week 8.
• **Results:** Patients (n=102) were randomised and treated. Ulcers were present for nearly 11 months on average; 65% were recurrent and mean area was 20.0 ± 17.8cm^2. Almost 80% of the treated VLU were stagnating/aggravating with their previous treatment. By week 4, mean surface area decreased by 6.5 ± 13.4cm^2 (median: 4.2cm^2) and 1.3 ± 9.0cm^2 (median: 1.1cm^2) in CLS and CL groups, respectively (p=0.023). At week 8, median decrease was 5.9cm^2 vs 0.8cm^2 (p=0.002), with a wound percentage decrease of 48% and 5.6% (p=0.036). Median closure rate was 0.145cm^2/day vs 0.044cm^2/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;6.7, p=0.038) for silver-treated ulcers. Dressing tolerance was good in both groups.
• **Conclusion:** A 4-week treatment with silver-releasing lipidocolloid contact layer promotes a sustained increase of closure rate of venous leg ulcers presenting inflammatory signs, suggesting a high bacterial load.
• **Declaration of interest:** This study was funded by a grant from URGO Laboratories. Dr Meaume and Dr Lazareth have served as paid speakers for URGO Laboratories. Dr Sauvadet and Dr Bohbot are employees of URGO Laboratories.

bacterial colonisation; silver lipidocolloid dressing; venous leg ulcer; republished study

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Nearly all open wounds are contaminated by microorganisms. This generally corresponds to simple bacterial growth, without leading to deleterious effects or compromising the progress of the healing process. In acute wounds, the probability of wound infection increases as the level of contamination does. However, it is more complex for chronic wounds, which are able to contain and tolerate large amounts of bacteria, many times higher than the usual threshold level (≥10^5 bacteria/g of tissue) defining infection in acute wounds,[1] without inducing local signs. 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 defences are still able to prevent tissue invasion, bacteria can impair wound healing.[2–11]

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.[10,12] 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 colonisation is confirmed or suspected. Indeed, silver is a large spectrum antibacterial agent which covers virtually all the bacterial strains responsible for chronic wound colonisation (including resistant species, such as MRSA) with a weak toxicity against fibroblasts.[13–15] Furthermore, this metallic ion has strong anti-inflammatory properties, inhibits MMP activity and promotes apoptosis of senescent cells.[16–18] 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.[19]

Despite widespread use of silver ions in the management of chronic wounds, the clinical benefit of silver in these wounds is not yet fully established.[20] The main objective of this randomised clinical study was to evaluate the ability of a silver wound dressing to promote the healing process of venous leg ulcers (VLUs) presenting inflammatory signs suggesting a heavy bacteria colonisation, when compared to the same wound dressing not impregnated with silver salts.

Methods

This multicentre, open-label, randomised, controlled clinical trial was conducted in two parallel groups, in 24 French investigating centres (hospital dermatology and vascular medicine departments).

Participants

Adult patients were included if they presented a VLU 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 5–40cm^2. Furthermore, selected VLUs were required to meet at least three of the five following clinical signs:

- Pain between dressing changes
- Perilesional skin erythema
- Oedema
- Foul odour
- 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 neoplasic lesion treated by radiotherapy or chemotherapy
- Ongoing treatment with immunosuppressive agents or high dose corticosteroids.

Study protocol

Patients who met the selection criteria gave 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 week 4, patients in the CLS group were treated with the CL and subjects in both groups were followed to complete healing or for a maximum of 4 additional weeks (8 weeks in total, for every included patient).

At the inclusion visit, patient demographics, characteristics, VLU history and the number of predefined local signs were 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 week 8. At each visit, wound status including colourimetric scale evaluation, perilesional skin appearance, number of local signs, acetate tracing and wound photograph were performed. In the CLS 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 using open questions (to patients and health 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 authorised. 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

The primary endpoint of the study was efficacy, assessed by the investigating physician at each weekly clinical evaluation (until week 4, then every 2 weeks until week 8), through the wound area measurement (judgment criteria).

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

Randomisation

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

Interventions

The CLS dressing (Urgotul Silver, URGO Laboratories) was presented as 10×10cm dressings, developed from a lipidocolloid 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

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Table 1. Reason for patient withdrawal

	CLS		CL	
	Week 0–4	Week 4–8	Week 0–4	Week 4–8
Consent withdrawn	1	0	0	0
Ulcer aggravation	2	0	4	5
Local adverse event	0	4	9	0
General intercurrent event	0	0	1	0
Other reason	0	1	0	1
Total	**3**	**5**	**14**	**6**

structure as silver sulphate that gradually releases, over 7 days, and is released as silver ions, when dressing enters in contact with wound fluids. The control CL dressing (Urgotul; URGO Laboratories) 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).

Sample size determination

A minimal sample size of 96 patients was determined a priori 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%).

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 (v6.12). If a patient withdrew before week 8 of the study, the efficacy analysis took into account the last evaluation available (last observation carried forward [LOCF]).

The groups were compared using Student's t-test or 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 randomised 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 (percentage decrease from baseline), the closure rate (AD/t where t is the number of days between two 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; $p<0.05$ 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 randomised. Three patients withdrew before the first ulcer evaluation at week 1 (one in the CLS group for consent withdrawal, and two 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). Considering the two treatment groups, this clinical trial involved 4796 cumulated days of treatment, 800 medical evaluations, and 2461 nursing care operations.

Baseline characteristics

Seventy-one per cent of the 102 patients were outpatients. The population was predominantly female with a mean age of 74.7±11.7 years (Table 2). Mean body mass index (BMI) was 28.8±7.3kg/m^2, 19% were diabetics, 32% had a history of venous thrombosis, and 40% of patients presented a history of superficial vein surgery. Eighty-six per cent of the patients were wearing compression bandage prior to randomisation.

At inclusion, necrotic tissue was absent from the wound bed, 51±28% of the wound surfaces were covered with sloughy tissue (yellow appearance on colourimetric scale) and 2.9% presented with healthy perilesional skin. Leg ulcers were present for almost 11 months on average (median 9.0 months) and 65% were recurrent. Mean surface area was 20.0±17.8cm^2 (median 14.6cm^2). Wound surface area in the CLS group was larger, but not significantly larger. At least three of the specified local signs were present in all ulcers.

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Overall, in the investigators' opinion, 79% of these ulcers were considered as stagnating or aggravating.

Wound area reduction

By week 4, ulcer area decreased by 6.5±13.4 cm^2 (median 4.2cm^2) in the CLS group and by 1.3±9.0cm^2 (median 1.1cm^2) in the CL group (Table 3 and Fig 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 5.9cm^2 and 0.8cm^2 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 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 (Fig 1). Closure rate was significantly higher by week 4 in the CLS group (median 0.145cm^2 vs 0.044cm^2/day; p=0.009). After switching to the non-silver containing dressing, this closure rate remained unchanged (0.135cm^2/day vs 0.023cm^2/day; p=0.01).

Percentage to reach 40% wound area reduction

By the end of the follow-up, 55% of the ulcers in the CLS group decreased by 40% or more, compared with 35% for wounds receiving only CL 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;6.7, p=0.038) in favour 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 colonisation

At week 4, no clinical signs were reported in 39.2% of ulcers in the CLS group, compared with 16.7% in the CL group (Fig 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 vs –1.0±1.4; p<0.001).

Local adverse events and dressing tolerance

Twenty-two local adverse events, possibly related to the tested dressings, were reported in 20 patients (Table 4). The types of adverse events reported were not different between the two groups. No infection occurred in the first period (day 0 to week 4) in the silver group treatment vs one infection in the control group. Four and five of the documented adverse events induced a discontinuation of the treatment in the CLS and CL groups, respectively. After the follow-up period, the perilesional skin was often considered

Table 2. Patient and ulcer baseline characteristics

	CLS (n=52)	CL (n=50)	p-value
Sex (F/M) (n)	36/16	35/15	0.9327
Age (years)	76.6±10.2	72.8±12.9	0.2632
Weight (kg)	81.7±24.0	77.6±21.2	0.3450
Height (cm)	165.8±8.7	166.4±10.9	0.7302
BMI (kg/m^2)	29.6±8.2	27.8±6.2	0.3334
Diabetes n (%)	9 (17%)	10 (20%)	0.7270
History of venous thrombosis n (%)	16 (31%)	17 (34%)	0.7273
Compression bandage prior inclusion n(%)	43 (83%)	45 (90%)	0.2836
Ulcer characteristics*			
Recurrent ulcer n (%)	34 (65%)	32 (64%)	0.8837
Duration (months)	11±8 (9.5)	10 ± 8 (9.0)	0.8428
Wound area (cm^2)	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 perilesional skin			
Healthy	1 (1.9%)	2 (4.0%)	0.6139
Erythematous	45 (87%)	44 (88%)	0.8249
Oedematous	32 (62%)	25 (50%)	0.2407
Eczematous	9 (17%)	9 (18%)	0.9269
Other	17 (33%)	20 (40%)	—
Local signs n (%)			
Pain between two dressing changes	46 (89%)	40 (80%)	0.2401
Periwound erythema	44 (85%)	42 (84%)	0.9319
Oedema	39 (75%)	31 (62%)	0.1572
Foul odour	31 (60%)	18 (36%)	0.0170
Heavy exudation	39 (75%)	40 (80%)	0.5458
Number of local signs n (%)			
3 signs	21 (40%)	31 (62%)	—
4 signs	19 (37%)	17 (34%)	0.0041
5 signs	12 (23%)	2 (4.0%)	—
Ulcer status			
Moderate improvement	10 (19.2%)	11 (22%)	—
Stagnation	16 (30.8%)	21 (42%)	0.3078
Aggravation	26 (50.0%)	18 (36%)	—

* Results presented as mean±SD (median), unless otherwise specified

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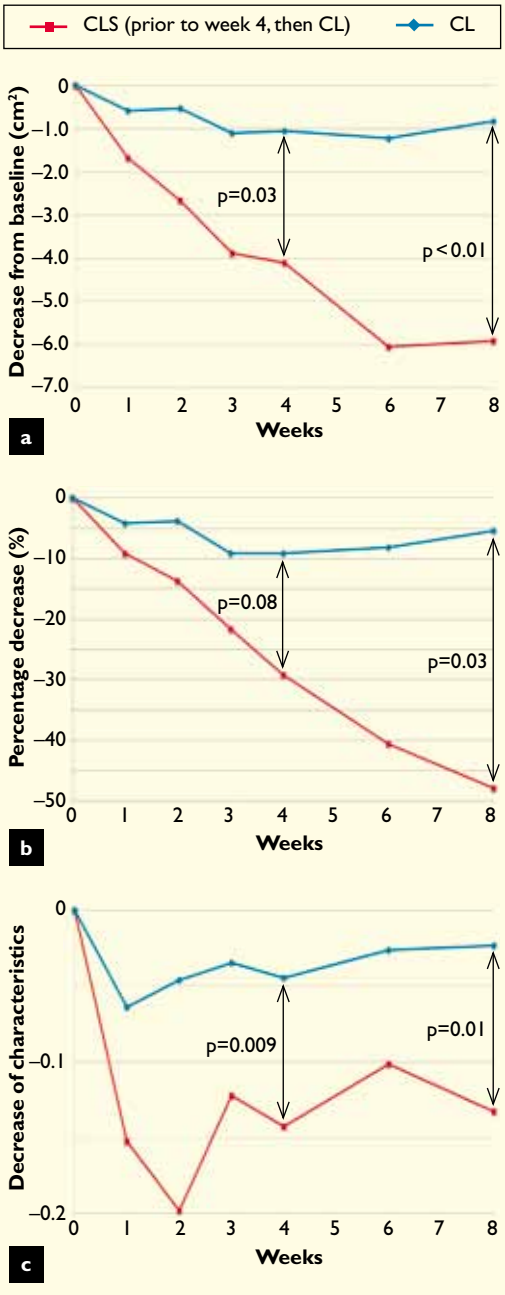
Fig 1. Absolute and relative ulcer area regression and closure rates. Showing median of absolute, (a), and percentage, (b) wound area decrease from baseline, and median of characteristics, (c)



'healthy' in more cases in the CLS group than in the CL group (39% vs 19%), compared with 1.9% and 4%, respectively, at baseline. No skin staining was detected at the weekly investigating evaluations.

The dressing acceptability was similar in the two treatment groups and the interval between two dressing changes was a little bit longer in the CLS group than in the CL group (2.12 days vs 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 1.62µg/l (limit of detection of blood silver with the selected method) in seven cases and was <3.7µg/l in the other three patients.

Discussion

This open-label, randomised, controlled study evaluated the efficacy of a therapeutic option including the use of a silver dressing over 4 weeks, followed by the application of the same dressing not containing silver for 4 additional weeks. The control group (CL) was treated without silver during entire trial. The studied dressings were derived from a lipidocolloid technology, which has been largely evaluated in clinical situations.[21–24] 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 VLUs 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% in the CLS group compared with 5.6% in the CL 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 5.9cm² (median value) in the CLS group versus 0.8cm² 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 CLS group. In addition, no secondary infection was noted during the silver treatment period (the first

4 weeks of treatment) versus two local infections in the control group at the same time.

Finally, dressing acceptability and local tolerance were similar in the two treatment groups. Included wounds were VLUs presenting at least three of five predefined local signs (pain between two dressing changes, perilesional skin, erythema, oedema, foul odour, or strong exudation). Even if none of these signs taken in isolation is specific, their combination might suggest strong bacterial contamination,[25,26] a factor known to delay the healing process.[9–12,27,28] 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 10cm^2, and 65% of the ulcers were chronic. All these parameters are identified as a poor healing prognosis.[29–31] 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,[32,33] and that high bacterial load was probably the predominant responsible factor.

This supports the use of silver dressings in localised treatment in these situations. The large antibacterial spectrum of the silver ion, combined with its direct anti-inflammatory properties, could help to reduce inflammation of chronic wounds and help to switch ulcers from stagnation to a more favourable healing trajectory.[13–18] The results of this study support the relevance of this strategy; comparing dressings that differed only by the addition of silver, ulcers treated with CLS quickly increased their closure rate whereas, limited changes were observed in the control group.

Other studies on the treatment of VLUs support this view.[34–36] However, these trials suffered from some limitations to be strongly convincing. The CONTOP trial[36] used a pragmatic design and variations between centres in localised treatment might be a confounding factor that renders results difficult to interpret. Meaume et al.[35] compared an alginate dressing with a silver-releasing hydroalginate dressing. Both leg and pressure ulcers were included if they presented two 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 Jørgensen et al.[34] is closer to the present study's design. VLUs, characterised by a documented delayed healing during a 4-week run-in period were selected if they presented at least one sign suggesting 'critical colonisation'. 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% vs 25%; p=0.03).

The present study differs from these trials in at least three 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. The selected wounds also had to meet at least three out of five 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[34] and the foam silver dressing[35] where patients were followed

Fig 2. Percentage of ulcers with no local, specified signs at each medical evaluation

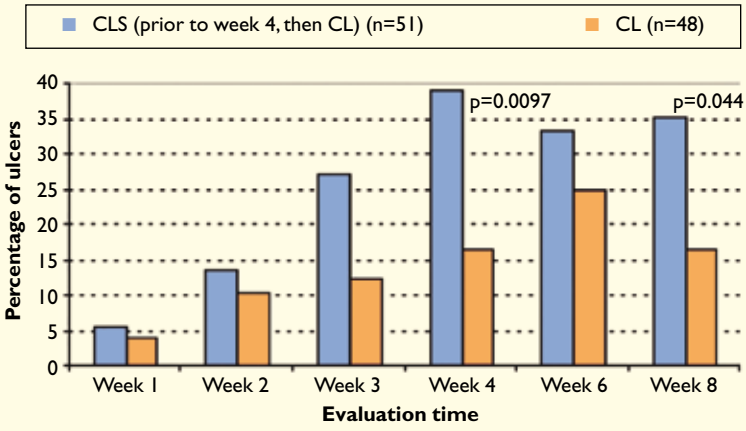


Table 3. Wound area reductions and closure rates

	CLS (n=51)	CL (n=48)	p-value*
Endpoint week 4			
Absolute reduction (cm^2)	–6.5 ± 13.4 (–4.2)	–1.3 ± 9.0 (–1.1)	—
Relative reduction (%)	–28.1 ± 36.7 (–29.1)	–8.6 ± 54.6 (–9.5)	—
Closure rate (cm^2/day)	0.20 ± 0.42 (0.15)	0.08 ± 0.56 (0.04)	—
Endpoint week 8			
Absolute reduction (cm^2)	–8.1 ± 16.3 (–5.9)	–1.0 ± 12.0 (–0.8)	0.002
Relative reduction (%)	–36.6 ± 48.8 (–47.9)	–6.2 ± 80.2 (–5.6)	0.036
Closure rate (cm^2/day)	0.14 ± 0.27 (0.14)	0.10 ± 0.54 (0.02)	0.001

Results presented as mean ± SD (median);
*Wilcoxon test

Table 4. Local tolerance

	CLS	CL
Nature of adverse events (n)	n=11	n=11
• Erythema/oedema	1	2
• Infection	2	1
• Periwound skin irritation	4	4
• Pain	2	1
• Overgranulation	0	1
• Other	2	2
Definitive discontinuation of treatment	4	5

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 restarted 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.

Limitations

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 two 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 lipidocolloid 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 favourable micro-environment that increases the probability of achieving complete wound closure. ■

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