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Evaluation of a new silver foam dressing in patients with critically colonised venous leg ulcers

- **Objective:** To evaluate the performance (efficacy and safety) of an absorbent dressing impregnated with silver salts (UrgoCell Silver) in the management of leg ulcers with clinical signs of critical colonisation.
- **Method:** This was a prospective multicentre non-comparative phase III clinical trial. Patients were assessed weekly for up to four weeks. Assessment included clinical assessment of critical colonisation (severe spontaneous pain between dressing changes, erythema, oedema, malodour and heavy exudate), wound area tracing and photography. Acceptability was documented by the nursing staff when dressings were changed between two weekly evaluations.
- **Results:** Forty-five leg ulcers were included. At baseline the mean number of clinical signs of critical colonisation per ulcer was 3.6 ± 0.7 , which decreased to 1.2 ± 1.2 at the end of the fourth week of follow-up (an average reduction of 2.3 ± 1.3 , $p < 0.001$). Oedema, malodour, erythema and spontaneous pain disappeared at the fourth week in 80%, 70%, 69% and 65% of the treated ulcers respectively. Compared with baseline, the mean reduction in ulcer area was $35.0 \pm 58.0\%$ (median 33%, $p < 0.001$) after the four weeks treatment. Granulation tissue covered a mean 77% of the ulcer surface area at four weeks, compared with 41% at baseline. Only three local events were documented: contact dermatitis, a burning sensation and erythema.
- **Conclusion:** The results suggest that the test dressing had a favourable influence on the wound prognosis, and was well tolerated and accepted in the treatment of venous leg ulcers with clinical signs of critical colonisation.
- **Declaration of interest:** This study was sponsored by Laboratoires Urgo, Chenôve, France.

silver dressing; critical colonisation; venous leg ulcers

Recognising and managing chronic wounds at risk of developing infection is subject to intense debate.¹ There are difficulties in diagnosing infection,² with some studies supporting the concept of critical colonisation as an intermediate stage between simple colonisation and frank infection.³⁻⁶ Nevertheless, critical colonisation has yet to be clearly characterised.^{7,8}

At this stage, antiseptic agents for critical colonisation may control bacterial load and prevent the development of infection,^{9,10} although they may be toxic to fibroblasts and other viable cells.^{11,12} However, silver appears to have only a very weak toxic potential and only occasionally to induce microbial resistance,¹³⁻¹⁶ while *in vitro* studies have demonstrated the effectiveness of silver-based dressings against pathogenic bacteria.^{17,18} Thus, use of silver-releasing dressings with appropriate debridement on wounds at risk of developing infection is beneficial.^{9,19,20}

The purpose of this non-comparative study was to evaluate the efficacy and safety of a silver foam dressing (UrgoCell Silver, Laboratoires Urgo, Chenôve,

France) in the management of venous leg ulcers with clinical signs of critical colonisation.

Method

Patients

This was an open non-randomised multicentre study involving 12 sites including dermatology and vascular medicine hospital wards, private physicians, angiologists and dermatologists. It was conducted in adult outpatients treated for a venous leg ulcer or a leg ulcer of predominantly venous origin. Mixed ulcers were included if a venous aetiology was predominant.

Physicians selected critically colonised ulcers for inclusion. Ulcers were considered to be critically colonised if at least three of the five following signs were present:

- Severe spontaneous pain between two dressing changes
- Perilesional erythema
- Local oedema
- Malodour
- Heavy exudation.

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Table 1. Baseline patient and leg ulcer characteristics

Patient characteristics (n=45)	
Sex (M/F)	30/15 (67%/33%)
Age (years)	74.8 ± 11.2 (48-92)
Body weight (kg)	80.8 ± 20.3 (47-127)
Patient history and associated diseases*	
High blood pressure	31 (69%)
Heart disease	15 (33%)
Diabetes	10 (22%)
Cigarette smokers	10 (22%)
History of allergy	5 (11%)
Other history	16 (36%)
Venous history*	
Venous thrombosis	19 (42%)
Superficial venous surgery	15 (33%)
Sclerotherapy	20 (44%)
Family history of venous disease	34 (76%)
Target ulcer characteristics	
Leg ulcer duration	15.2 ± 18.5 (1-96)
Recurrent leg ulcer	24 (53%)
Surface area (cm ²)	12.6 ± 10.0 (2.6-48)
Altered perilesional skin	39 (87%)
ABPI	0.95 ± 0.12 (0.70-1.20)
Wound aspect (% of wound surface)	
Sloughy tissue	58.3 ± 29.4 (10-100) Median: 60
Granulation tissue	41.3 ± 29.4 (0-90) Median: 0
Necrotic tissue	0.4 ± 1.8 (0-10) Median: 40

* More than one pathology may be present
 ABPI = ankle brachial pressure index
 Results are presented as either numbers and percentages, or as mean ± standard deviation with the range in brackets

Selection of these signs was based on a EWMA position document⁸ and our own clinical experience.

Additional inclusion criteria were:

- Ulcer area between 5cm² and 40cm²
- Ulcer duration between three and 24 months
- Ankle brachial pressure index greater than 0.7
- Ability to wear compression therapy and the test dressing.

The main exclusion criteria were:

- Patients receiving systemic antibiotics at the time of enrolment or in the previous week
- Patients who had had deep venous thrombosis in the three previous months
- Ulcers with clinical signs of infection or erysipelas of the lower limb such as cellulitis, green exudate and inflammation of the surrounding skin and that required systemic antibiotics, according to the investigating physician.

Method

Efficacy — the primary study endpoint — was judged by the physician at each weekly visit based on an assessment of each of the five selected signs of critical colonisation. The dressing was considered effective if there was a significant reduction in these signs and in the wound surface area.

Secondary endpoints — tolerance (occurrence of local adverse events) and acceptability of the dressing — were also assessed.

At baseline, after gaining the patients' written consent to participate, the patient's general characteristics were recorded, the test leg ulcer was fully described, wound-area tracing and photography were performed, and the dressing was applied.

Participants were seen weekly for four weeks by the investigating physician. Full study documentation and recommendations for dressing use were provided, along with a nurse case-report form to document the dressing-change characteristics at each dressing removal.

The nurse in charge of the patient performed dressing changes in the patient's home between the weekly clinical evaluations. Wounds were cleansed with normal saline only. The frequency of dressing change was at the investigating physician's discretion, based on the state of the wound.

All study participants were offered compression therapy in combination with the test dressing.

The test dressing

UrgoCell Silver is composed of three layers:

- A lipidocolloid dressing (Urgotul) impregnated with silver salts (contact)
- A highly absorbent polyurethane foam (intermediate)
- A polyurethane film (outer).

This silver dressing is indicated for moderately to highly exudating chronic wounds that are at high

risk of clinical infection. The manufacturer recommends that the dressing be changed every two to three days.²¹⁻²⁴

Statistical analysis

Data analyses were performed with the SAS 9.0 for Windows. A descriptive statistical analysis was performed on all patients included in the trial. The statistical analysis was performed on the basis of intention-to-treat (ITT) for all endpoints, and all patients who received at least one care operation with the test dressing after their inclusion were included in the efficacy and tolerance analyses. No patients were withdrawn before the first week of treatment. If a patient withdrew before the end of the treatment period, the analysis took account of the last evaluation (last observation carried forward, LOCF).

Continuous data were described by sample size, mean, standard deviation, median and range.

The following statistical methods were used for changes with respect to inclusion:

- MacNemar test for binary variables
- Signed ranks test (Wilcoxon) for the clinical score
- Student's paired t-test for continuous variables.

Ethics

The study protocol was approved by the Medical Ethics Committee of Versailles (France), and the clinical trial was then conducted in compliance with good clinical practice and the principles of the Declaration of Helsinki.

All patients gave written consent to participate after having received full written information about the study objectives and conduct.

Results

Baseline characteristics: patients and leg ulcers

Forty-five patients were included in the study between February and September 2005 by the 12 investigating centres. Table 1 outlines the baseline patient and ulcer characteristics. Perilesional skin was documented as 'healthy' in only six of the 45 patients (13%).

Table 2 outlines the clinical indicators of critical colonisation, as defined for the purposes of this study, and the number of patients who demonstrated one or more of them at baseline. All ulcers had at least three clinical signs at baseline, and 44% (n=20) had four to five signs.

Study participants had previously been treated by the investigating physicians. Treatments had included paraffin gauze, foam or alginate. At baseline, 73% (n=32) of the study ulcers were considered to be stagnant or deteriorating.

Forty-one patients (91%) had received compression before inclusion in the study: 62% monolayer bandaging, 22% multilayer bandaging and 16% compression hosiery.

Table 2. Clinical indicators of critical colonisation and clinical score

Clinical indicators	Baseline No. of patients (%)	Week 4 No. of patients (%)
Pain between two dressing changes	31 (69)	11 (24)
Perilesional erythema	38 (84)	12 (27)
Oedema	24 (53)	5 (11)
Malodour	28 (62)	8 (18)
Heavy exudate	40 (89)	19 (42)
Clinical score*		
Score 0	—	16 (36)
Score 1	—	12 (27)
Score 2	—	7 (16)
Score 3	25 (56)	6 (13)
Score 4	14 (31)	4 (9)
Score 5	6 (13)	—
Mean clinical score		
Mean ± SD (range)	3.6 ± 0.7 (3-5)	1.2 ± 1.2 (0-14)

* Number of clinical indicators of critical colonisation present
SD = standard deviation

Nine patients (20%) did not wear their compression therapy on each day of the four-week follow-up period; the remainder (80%) were concordant throughout.

Efficacy

All patients included were included in the efficacy analysis, and none were lost to follow-up despite the outpatient nature of this clinical trial.

At baseline, as stated above, all wounds had between three and five of the indicators for critical colonisation. By week 4, 36% (n=16) ulcers had no indicators remaining, while 22% (n=10) still had three to four. No study ulcers had all five indicators by the study end compared with 13% at baseline.

Table 2 shows the mean number of indicators from study start to completion. The reduction in number was highly significant (p<0.001).

Clinical-indicator percentages at baseline and study end are shown in Fig 1. The physicians documented the perilesional skin as 'healthy' in 17 patients (38% versus 13% at baseline). By the fourth week of treatment, mean ulcer surface area of granu-

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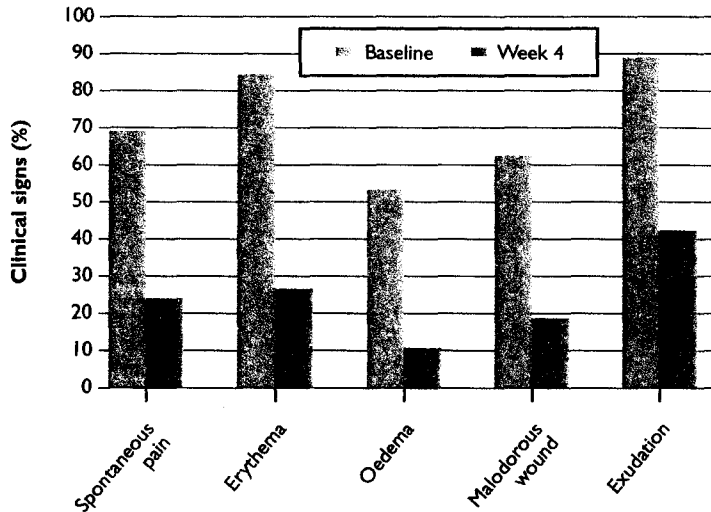
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Fig 1. Percentage reduction in ulcer surface area over the four weeks of treatment



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lution tissue was 77% (versus 41% at baseline), slough was 23% (versus 58% at baseline) and necrosis 0.1% (versus 0.4% at baseline). Mean ulcer area reduction was $35 \pm 58\%$ (median 33%; $p < 0.001$) after four weeks' treatment.

In the investigators' opinion:

- 11% of the ulcers healed ($n=5$) in a mean time of 22.4 ± 9.13 days
- 67% ($n=30$) improved
- 16% ($n=7$) were stagnating
- 7% ($n=3$) worsened.

Local tolerance (safety)

Three local adverse events, considered to be dressing related, were reported by the investigators:

- One patient developed 'moderate' contact dermatitis during the fourth week of treatment and was withdrawn from the study. This patient had a lesion at inclusion
- One patient experienced a burning sensation on the wound on the first day of treatment. The test dressing was discontinued and an alginate dressing applied. However, he was included in the analysis as it took account of the last evaluation available (LOCF)
- One patient experienced 'moderate' erythema beneath the test dressing after one week of treatment. However, use of the dressing continued and the erythema disappeared after a few days.

Dressing changes

In all, 470 care episodes were documented, representing 1250 cumulated days of treatment.

The studied dressing was removed every 2.66 ± 1.93

days (range 1-13). It was left in place for two days or more in 76% of cases. The nurses considered it easy to use and apply, and that it conformed well to the wound bed.

Discussion

The aim of this study was to evaluate the efficacy and safety of UrgoCell Silver in the management of venous or mixed leg ulcers with indicators of critical colonisation. The indicators studied are congruent with heavy bacterial colonisation.²

The total number of indicators significantly decreased during the four-week treatment period with the test dressing. This simple clinical score was shown to be sensitive to wound evolution, with an apparently limited inter-observer variability as reflected by the low variance of its distribution: the score decreased with the disappearance of the local clinical signs.

Indicators that appeared to be particularly responsive to the test dressing were malodour, wound pain and erythema, which is in line with other silver-dressing studies.^{9,25}

Wound surface area reduction was noted in 35% of ulcers after four weeks of treatment. As this was not a controlled trial, it is difficult to compare these efficacy results with those of other silver dressings, as the leg ulcers in this trial will not always have the same characteristics as those in other clinical trials.^{3,9,19,20,25}

Wounds at risk of infection are characterised by a high heterogeneity in their clinical characteristics and aetiologies. Therefore, even with a very large sample size, the influence of confounding factors cannot be ruled out, despite randomisation.²⁰

Only three dressing-related local events were documented. All are often observed in leg ulcer management.^{26,27}

The test dressing improved the perilesional skin: nearly 40% of the ulcers showed a healthy surrounding skin at the end of the treatment period compared with an 'altered' state in 87% of patients at baseline.

The acceptability of the dressing (ease of application and removal) to health-care professionals was good. Patients appreciated the painless dressing removal, which supports previous studies undertaken with neutral UrgoCell.²⁸

The investigating physicians considered that the wounds improved (or healed) in nearly 78% of patients after four weeks of treatment, despite their poor prognosis²⁹ and considering the mean initial surface area (12.6cm^2) and ulcer duration (15.2 months).

These results suggest UrgoCell Silver had a favourable influence on the wound prognosis, and was well tolerated and well accepted in the treatment of venous leg ulcers with clinical signs of critical colonisation. However, a randomised clinical evaluation is required to confirm these encouraging clinical results. ■