

Clinical evaluation of the effect of SILVERCEL® Non-Adherent in wound infections

KEY WORDS

- ▶ Wound infection
- ▶ Silver dressings
- ▶ Infection criteria
- ▶ Two-week challenge

The diagnosis and management of wound infection continue to be highly challenging aspects of wound care. In recent years, the role of topical antimicrobial dressings to treat wound infection has gained recognition. However, questions have been raised about the efficacy and apparent expense of silver dressings. This four-week prospective, non-comparative evaluation examined the impact of the silver-containing dressing SILVERCEL® Non-Adherent (Systagenix) on signs and symptoms of infection in wounds of various aetiologies. The evaluation found that when used appropriately SILVERCEL Non-Adherent treated infection effectively and was associated with improvements in malodour, purulent exudate, exudate level, periwound erythema, bleeding at dressing change and pain.

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Wound infection is a major cause of delayed healing and may produce symptoms, such as malodour and pain, which distress patients and are a challenge for clinicians to manage (World Union of Wound Healing Societies [WUWHS], 2008). The cost of healing wounds that have become infected has been found to be up to several times higher than the cost of healing wounds that are not infected (Driver and deLeon, 2008).

When used to treat wound infection, antimicrobial dressings are intended to reduce wound bioburden. However, studies of the use of antimicrobial dressings have often used endpoints that assess healing rather than effect on infection (Wounds UK, 2011), sometimes with unfortunate consequences. For example, the VULCAN study assessed rates of complete healing over 12 weeks in patients with venous leg ulcers who received a silver dressing or a non-antimicrobial control dressing (Michaels et al, 2009a; Michaels et al, 2009b). The study concluded that there was no statistically significant difference in the proportion of wounds healed between the study and control groups and that there was a higher cost associated with silver dressings.

In some areas of the UK, the study was, and continues to be, used to justify withdrawal of silver dressings even though many concerns have been raised over the potentially misleading nature of the

study (Leaper and Drake, 2011; White et al, 2010; Gottrup and Apelqvist, 2010). A major concern has been that the study did not evaluate patients for the presence or risk of wound infection. Consequently, it is not possible to use the VULCAN study to draw conclusions on the efficacy or on the cost-effectiveness of silver dressings in the treatment of wound infection.

Recently published guidelines (WUWHS, 2008; Wounds UK, 2011; Wounds UK, 2013) advocate appropriate use of topical antimicrobials. These recommend that for infected wounds not showing improvement after 10–14 days of topical antimicrobial therapy the patient and management approach should be re-evaluated. A recent consensus document on the use of silver dressings suggested that this initial two-week period could be seen as a two-week 'challenge' during which the efficacy of the silver dressing could be assessed (Wounds International, 2012).

This small-scale prospective clinical evaluation was designed to examine the impact of the silver-containing dressing SILVERCEL® Non-Adherent (Systagenix) on a number of clinical indicators of wound infection when used appropriately in patients with infected wounds of various aetiologies. It was not intended to investigate rates of healing.

SILVERCEL Non-Adherent is a sterile absorbent silver-containing antimicrobial wound dressing

that contains alginate and carboxymethyl cellulose (Clark and Bradbury, 2010, Ivins et al, 2010). SILVERCEL, the absorbent silver-containing core of SILVERCEL Non-Adherent, has been shown in a number of laboratory and clinical studies to have good antimicrobial activity and high absorbent capacity and to be well tolerated (Clark et al, 2009; Teot et al, 2005; Kammerlander et al, 2008; DiLonardo et al, 2006).

METHODS

This was a prospective, non-comparative clinical evaluation of SILVERCEL Non-Adherent in the management of infected wounds. The primary objective was to assess the impact of SILVERCEL Non-Adherent on the signs and symptoms of wound infection in the context of a two-week 'challenge'. The secondary objective was to continue the evaluation for up to four weeks for patients who continued to receive the dressing.

Patient selection

Patients aged over 18 years who were considered to have a wound that was infected or that had increased bacterial burden were recruited from a variety of healthcare settings in the British Isles by seven clinicians with specialist interest in wound care. Where a patient had more than one infected wound, the clinician chose which wound to include in the evaluation according to their own preference.

Patients were not eligible if they were unable to give informed consent for inclusion in the evaluation, had a known sensitivity or allergy to any of the components of SILVERCEL Non-Adherent (eg carboxymethylcellulose, alginates, ethylene methyl acrylate or silver), were severely immunocompromised or were non-concordant.

Baseline assessment

At baseline, clinicians used a data collection form to record the aetiology, size and duration of the wound. In addition, they were asked to select from a list of nine criteria which signs and symptoms related to infection were present (*Box 1*). This list was compiled using key triggers for identifying wound infection specified in the World Union of Wound Healing Society consensus document on wound infection (WUWHS, 2008).

Clinicians were also asked to provide indepth information on certain signs and symptoms of infection by indicating their presence and level (*Box 2*). Improvement of these signs and symptoms in a patient with an infected wound may indicate that the infection is resolving.

Following baseline assessment, all patients were treated with the most appropriate size and formulation of SILVERCEL Non-Adherent. The dressings were applied according to the manufacturer's instructions and changed according to local protocols.

Follow-up assessments

Patients were re-assessed for signs and symptoms of infection at approximately weekly intervals for as long as SILVERCEL Non-Adherent was in use, up to a maximum of four weeks. The results were recorded on the data collection form.

At each follow-up assessment, clinicians were asked to record whether or not they thought the wound had improved, and whether or not they considered it to be infected. The clinicians also listed which of the criteria in *Box 1* were present, and provided more detail on the signs and symptoms listed in *Box 2*.

Analysis

Where assessments for individual items were missing from the data collection sheets the patient was omitted from the analysis of that particular item and percentages were calculated on the basis of the number of patients for whom data were available.

RESULTS

A total of 30 clinical evaluations were collected from seven clinicians in six centres. Four of these (13.3%) cases were not included in the analysis because of deviations from the evaluation protocol.

First follow-up assessments were conducted four to nine days after the introduction of SILVERCEL Non-Adherent and second assessments were conducted at nine to 14 days. All 26 patients had data for the second assessment (9–14 days); however, two of these patients did not have data for the first follow-up assessment (4–9 days). Twenty (76.9%) patients continued SILVERCEL Non-Adherent to the third assessment, and 14 (53.8%) to the fourth assessment (*Figure 1*).

Box 1. List of criteria from which clinicians selected after diagnosing a patient with a wound that was infected or that had increased bacterial burden.

- ▶▶ Delayed healing
- ▶▶ Friable/bleeding tissue
- ▶▶ Malodour
- ▶▶ Change in nature of pain
- ▶▶ Discolouration
- ▶▶ Breakdown/increase in size of wound
- ▶▶ Spreading erythema
- ▶▶ Local heat
- ▶▶ Pus/abscess

Box 2. Signs and symptoms for which more detailed data were collected.

- ▶▶ Malodour – none, minimal, moderate or high
- ▶▶ Exudate description – serous, haemoserous or purulent
- ▶▶ Exudate level – none, minimal, moderate or high
- ▶▶ Periwound erythema – none, minimal, all edges of wound or surrounding skin
- ▶▶ Bleeding at dressing change – none, minimal, moderate or severe
- ▶▶ Pain before and during dressing changes – based on a zero–ten scale

Dressing change frequency ranged from weekly to daily, with most patients having twice or thrice weekly changes.

Demographics and wound characteristics

The 26 patients included in the analysis had a mean age of 70.2 years (range 30 to 94 years; *Table 1*). Fifteen patients (57.7%) were treated in hospital (mostly in outpatient clinics), with the remainder treated in nursing homes ($n=8$; 30.8%) or in their own home ($n=3$; 11.5%).

Figure 1. Evaluation structure.

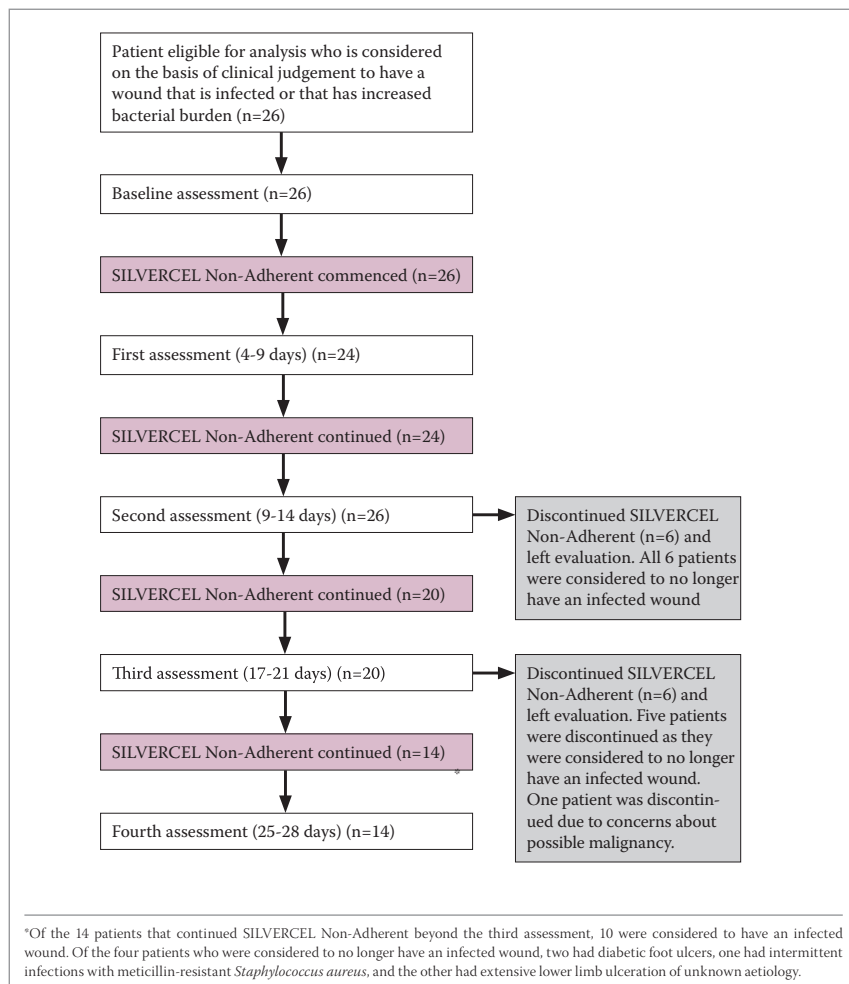


Table 1. Patient demographics.

	N (%)	Mean age (years)	Range (years)
Male	16 (61.5)	70.8	30–94
Female	10 (38.5)	69.2	38–92
All	26	70.2	30–94

Fifty per cent of patients in the evaluation had diabetes, although there were a variety of wound aetiologies (*Table 2*). Wound duration ranged between 4 days and 8 years (*Table 2*).

Criteria of wound infection

Delayed healing and malodour were the most frequently selected criteria of infection at baseline (*Table 3*).

All but two patients (92.3%) had two or more criteria of infection (*Box 1*) at baseline (one had no criteria recorded, and one had one criterion: delayed healing) (mean 3.73; range zero to eight) (*Figure 2*). The mean number of criteria recorded decreased over time, with a more than a 50.0% reduction by second assessment (9–14 days).

However, there was variation between cases in the way that the criterion ‘delayed healing’ was reported. For some patients with long-standing wounds this criterion was not recorded at baseline, for others it was recorded at every assessment and for some it appeared in later assessments only. A further analysis of the mean number of criteria after omitting ‘delayed healing’ from all assessments also found a decrease in mean number of criteria over time (*Figure 2*).

In addition, there were some inconsistencies between the recording of the presence of the numbered criteria and the recording of the signs and symptoms selected for more detailed reporting. For example, a criterion may have been listed as present, but not referred to in the more detailed reporting section, and vice versa.

Table 2. Wound aetiology and duration.

Wound aetiology	N (%)
Diabetic foot ulcer	6 (23.1)
Trauma	4 (15.4)
Surgical dehiscence	4 (15.4)
Pressure ulcer	3 (11.5)
Malignancy	2 (7.7)
Lower limb ulceration of unknown aetiology	2 (7.7)
Miscellaneous*	5 (19.2)
Total	26 (100)
Wound duration	Days
<30	10 (38.5)
≥30–90	4 (15.3)
≥90	12 (46.2)

*One each of: surgical site infection, post-surgical neuropathy, rheumatoid arthritis, breakdown of an old abdominal suture line, and breakdown over a post-traumatic bone fragment

Table 3. Criteria selected at baseline.

Criterion	N (%)
Delayed healing	17 (65.4)
Malodour	17 (65.4)
Friable/bleeding tissue	14 (53.8)
Local heat	12 (46.2)
Breakdown/increase in size of wound	9 (34.6)
Discolouration	9 (34.6)
Spreading erythema	7 (26.9)
Change in nature of pain	6 (23.1)
Pus/abscess	5 (19.2)

*Number of patients with criterion (% of evaluation group; n=26).

Infected

All wounds were considered by the clinicians to be infected (n=24) or to have increased bacterial burden (n=2) at baseline. At the second assessment (9–14 days), 34.6% (n=9) of wounds were classified as being no longer infected (Figure 3). At the third and fourth assessments, respectively, 45.0% (n=9) and 57.1% (n=8) of the evaluation group were no longer considered to have an infected wound.

Improved

At the second assessment (9–14 days), 22 (84.6%) of wounds were categorised as having improved with a more than 50.0% reduction in mean number of criteria recorded. Of patients who continued to receive SILVERCEL Non-Adherent beyond the second assessment (9–14 days), 85.0% (17 out of

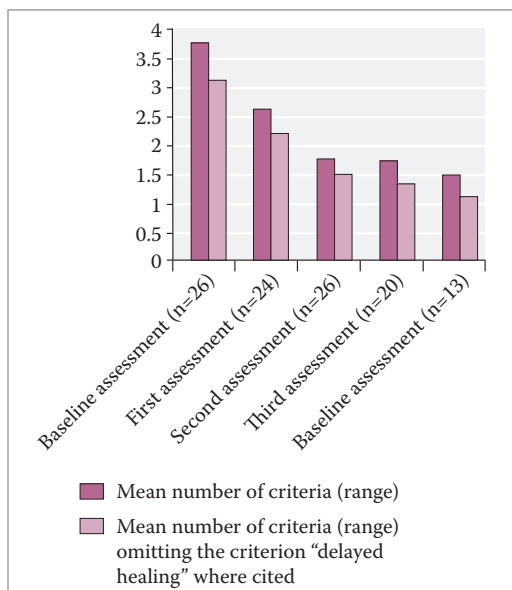
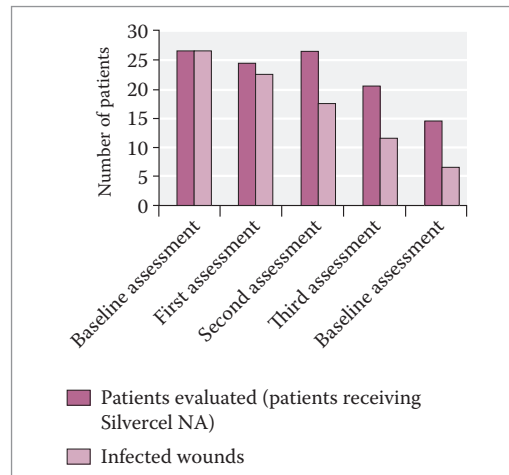


Figure 2. Mean number of criteria of infection.

Figure 3. Wound infection status for the evaluation period.



20) and 92.9% (13 out of 14) patients were classified as improved at the third and fourth assessments, respectively. This is further demonstrated through analysis of improvements in certain signs and symptoms of infection.

Malodour

The majority of patients (n=22; 84.6%) had malodour at baseline. By the second assessment (9–14 days), 16 of the 22 patients (72.7%) had shown improvement in level of malodour and eight of the 26 patients (30.8%) had no malodour (Figure 4). Improvements in level of malodour continued after the second assessment. Ten of the 20 patients (50.0%) who continued to receive the study dressing had a reduction in level of malodour at the third assessment and four of the 13 remaining patients (30.8%) had a reduction in malodour at the fourth assessment.

Exudate level

Twenty three (88.5%) patients had moderate or high exudate levels at baseline (Figure 5). More than half of patients (n=14; 53.8%) had a lower exudate level at second assessment (9–14 days) than at baseline. By third assessment, 65% had a lower exudate level than at baseline. At fourth assessment, this proportion was higher at 76.9%.

Exudate descriptor

At baseline, 14 patients (53.8%) had purulent exudate. At first assessment (4–9 days), the

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Figure 4. Malodour.

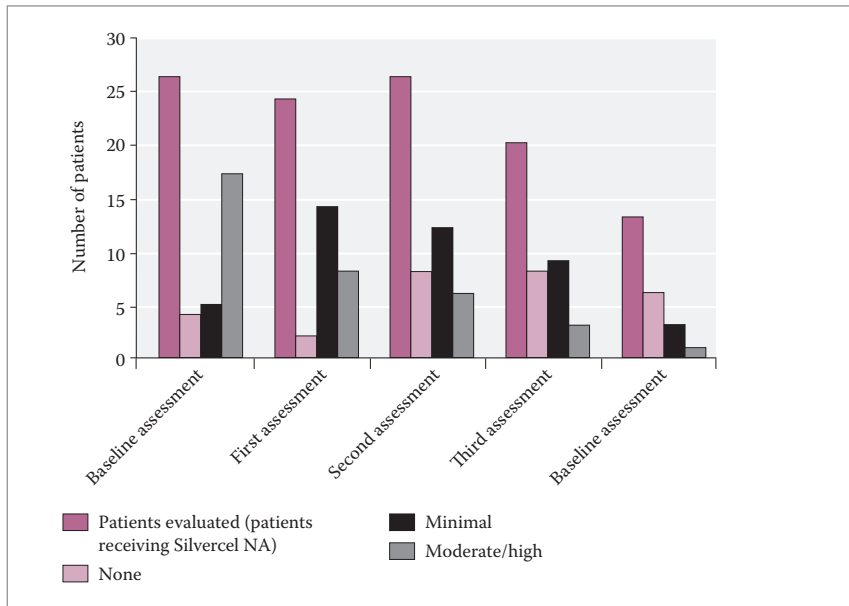
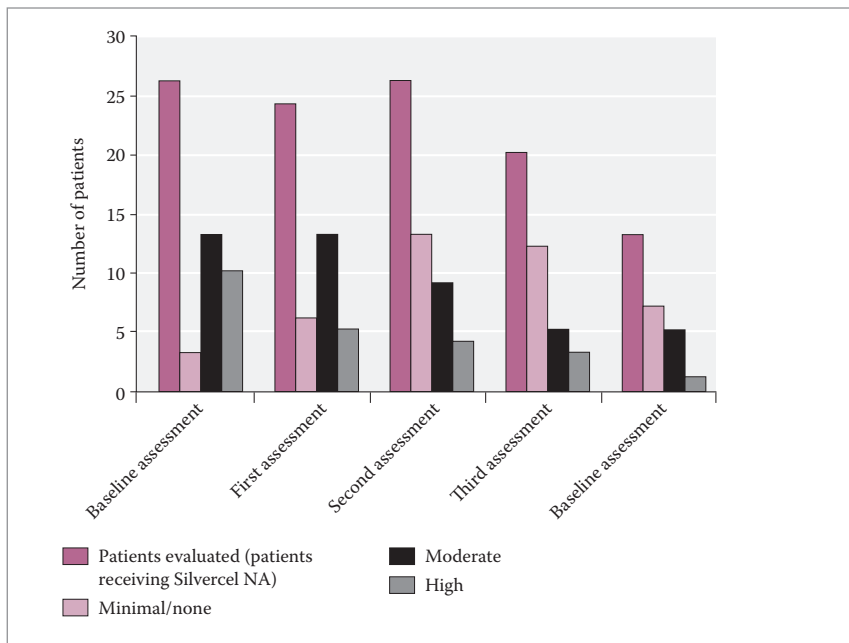


Figure 5. Exudate level.



number of patients with purulent exudate had dropped to six (57.1% reduction from baseline) (Figure 6). By second assessment (9–14 days), only five of these patients had purulent exudate (64.3% reduction from baseline). At third and fourth assessments, respectively, of patients with exudate descriptors recorded, only one of the 19 and none of 12 patients had purulent exudate.

Periwound erythema

Periwound erythema was seen to decrease over the course of the evaluation. The number of patients with no or minimal periwound erythema increased from 11 (42.3%) at baseline to 17 (65.4%) at second assessment (9–14 days) (Figure 7). At the third and fourth assessments, respectively, 16 of the 20 (80.0%) and 11 of the 13 patients (84.6%) for whom assessment of periwound erythema was available had no or minimal periwound erythema.

Bleeding at dressing change

None of the patients were classified as having severe bleeding during dressing change at any point in the evaluation, and at the first follow-up assessment (4–9 days) no patient had moderate bleeding. At the third and fourth assessments, 14 of 19 (73.7%) and 8 of 13 (61.5%) patients who had continued SILVERCEL Non-Adherent had no bleeding at dressing change.

Pain

Patients rated pain on a scale of zero to ten before and during dressing changes. Patients with known neuropathy ($n=9$ at baseline; eight due to diabetes and one due to trauma) were pain-free at all assessments and were excluded from the analysis of pain scores.

In patients with recorded pain scores who did not have neuropathy, mean pain scores were higher during dressing changes than before, but both mean scores showed a marked reduction over the first and second follow-up assessments (Figure 8). The reduction was sustained in those patients who continued treatment to the third and fourth assessments.

DISCUSSION

This clinical evaluation examined the impact of SILVERCEL Non-Adherent in a diverse range of often complex infected wounds. Many of the patients had diabetes and other risk factors for delayed healing and infection. Patients with diabetic foot infection often have poor vascular supply with impaired ability to fight infection. Treating these wounds effectively at an early stage may prevent any localised infection spreading to the deeper tissues and limb loss.

The evaluation showed that SILVERCEL Non-Adherent had a positive effect by the second assessment (9–14 days) on all clinical criteria examined. Particularly notable were the overall reductions in the proportion of patients with malodour, purulent exudate or bleeding at dressing change, and in pain scores.

The positive effects on all criteria were apparent by the first follow-up assessment (4–9 days) with more than a 50% reduction in mean number of criteria of infection present by the second assessment (9–14 days).

The improvements in symptoms such as malodour and pain at dressing change seen with use of SILVERCEL Non-Adherent have the potential to improve patients' quality of life. Malodour is one of the most distressing symptoms of having a wound (Lindahl et al, 2012; Grocott, et al, 2013) and for about 40% of patients pain at dressing change is the worst part of living with a wound (Price et al, 2008). Comments from the attending clinicians suggested that the non-adherent property of SILVERCEL Non-Adherent made it easy to remove and was beneficial in reducing pain levels and anxiety at dressing change for some patients. Clinicians also commented on the relief felt by some patients when malodour was reduced or resolved.

An important part of the evaluation was the diagnosis of wound infection, which is reliant on clinical decision-making skills. A recently published debate has highlighted difficulties in defining wound infection and the problems that under- or over-diagnosis can cause (White et al, 2013). Development of a scoring system for diagnosis and for monitoring progress during treatment may be beneficial in ensuring accurate diagnosis and appropriate initiation (and discontinuation) of antimicrobial dressings. However, it is unclear from this evaluation whether tracking numbers of criteria over time is a useful way of monitoring the continued presence of infection because inconsistencies in reporting were seen. These may be the result of confusion over definitions and terminology. In addition, some of the criteria used, eg delayed healing, may be useful for initial diagnosis but may not be suitable for monitoring purposes. Indeed, delayed healing may be related to underlying cause or issues such as nutrition and may warrant re-assessment before drawing conclusions about infection. Further investigation is required to determine which signs and symptoms of wound infection are useful for monitoring progress.

The findings of this evaluation also highlight the value of adopting standardised protocols for the management of wound infection, such as the two-week 'challenge', to ensure appropriate use of

Figure 6. Exudate descriptor.

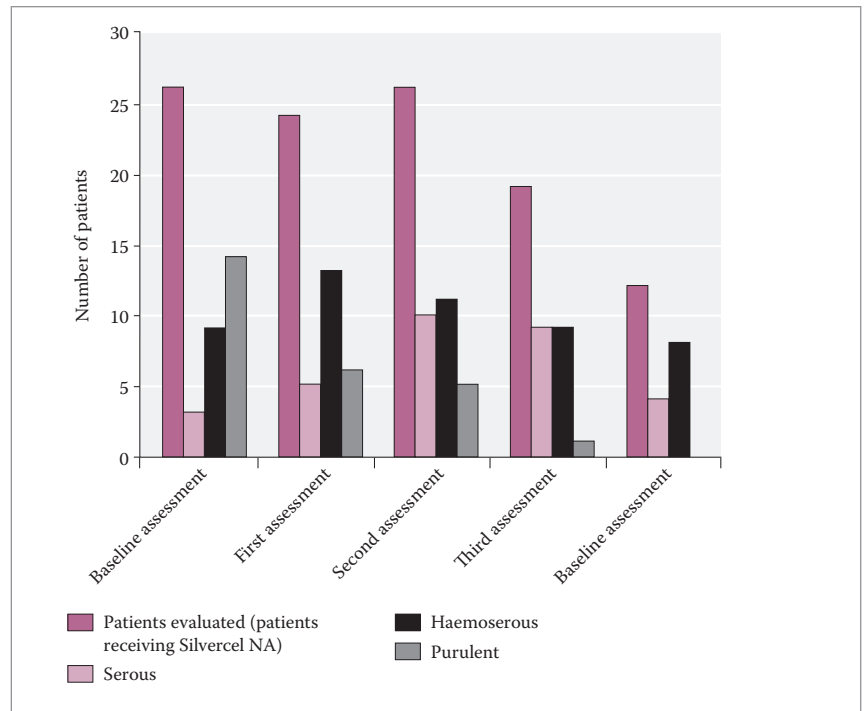
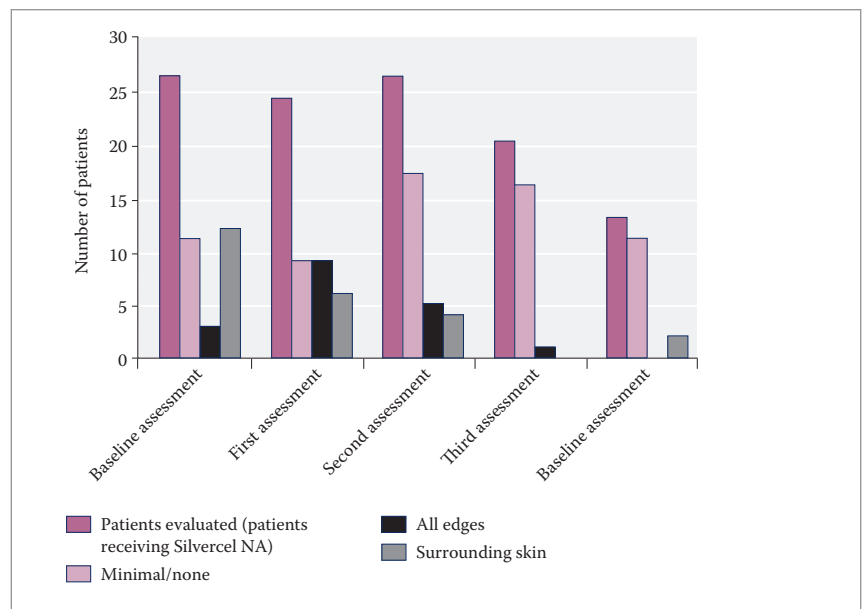


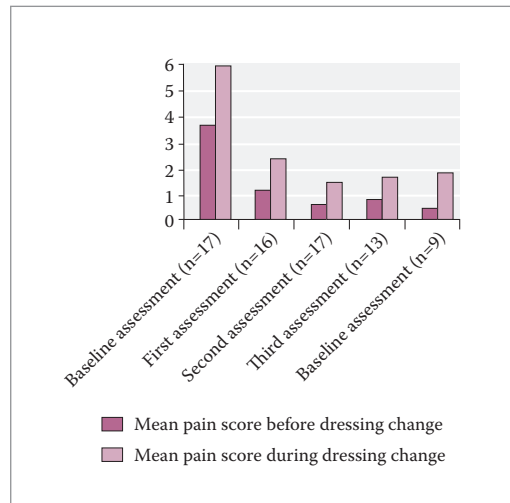
Figure 7. Periwound erythema.



antimicrobial dressings in infected wounds. Almost one-quarter of patients discontinued SILVERCEL Non-Adherent at the second assessment (9–14 days) because the wound was no longer infected, with 84.6% of wounds categorised as having improved. This reinforces the value of re-evaluating antimicrobial therapy at two weeks.

“It [was] demonstrated that SILVERCEL Non-Adherent produced more than a 50.0% reduction in the mean number of clinical criteria at 1–2 weeks, and infection was considered to be cleared within 2 weeks for about one-third of patients.”

Figure 8. Mean pain score before and during dressing changes (excluding patients with neuropathy) on a zero to ten scale.



Clinicians are increasingly being asked to justify the use of an intervention in terms of cost and patient benefits (Wounds International, 2013). Unfortunately, the negative findings of the VULCAN study (Michaels et al, 2009a; b) have been used to label silver dressings as expensive and ineffective. However, this evaluation of SILVERCEL Non-Adherent has shown that appropriate use can be effective in the context of a two-week challenge, and so would be expected to contribute to reducing the cost of managing infected wounds.

CONCLUSIONS

This evaluation provides a valuable insight into the clinical practicality of the two-week ‘challenge’ for the use of antimicrobial dressings in infected complex wounds referred for specialist wound care. It demonstrated that SILVERCEL Non-Adherent produced more than a 50.0% reduction in the mean number of clinical criteria at 1–2 weeks, and infection was considered to be cleared within two weeks for about one-third of patients. Where the use of SILVERCEL Non-Adherent was continued beyond two weeks it was shown to be beneficial with more wounds no longer infected and further reductions in the signs and symptoms of wound infection. The evaluation has also highlighted the need for further research in a number of areas. There is a need to develop and validate protocols for identifying and monitoring infected wounds. **WUK**

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