Addressing local wound infection with a silver-containing, soft-silicone foam dressing: A case series

Kerry Richards, Paul Chadwick

A silver-containing, soft-silicone foam dressing was assessed for its ability to reduce the signs and symptoms of local infection in a series of diabetic foot ulcers. Target ulcers were treated with good traditional wound care and dressed with the test dressing for a period of up to 4 weeks, during which they were evaluated for signs and symptoms of localised infection and pain. Reductions in pain, erythema, oedema, heat and exudate levels were found. Clinical signs of local infection were absent from the majority of target ulcers by study end. Larger clinical trials are required to confirm these findings.

Article points

1. Infection of diabetic foot ulcers needs to be treated with topical and/or systemic antimicrobial therapies urgently.
2. People with diabetic foot ulcers, particularly those with ischaemia, can suffer from wound pain and this should be taken into consideration when dressing choices are made.
3. In the present case series clinical signs of local infection were eradicated by the end of the 4 weeks' treatment with a silver-containing soft-silicone foam dressing.
4. The test dressing was associated with minimal pain at dressing changes.

Keywords

- Antimicrobial silver
- Dressing-related wound pain
- Infection
- Soft-silicone foam dressing

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The incidence of diabetes is escalating worldwide (Wild et al, 2004) and is associated with a number of complications including diabetic foot ulcers (DFUs; Boulton et al, 2005). Good medical management of DFUs should focus on the holistic care of the person with diabetes and specifically on pressure relief of the ulcerated area, wound-bed preparation (especially debridement) and the careful management of exudate levels, infection and pain (Frykberg, 2002).

Infected DFUs have been associated with increased risk of lower-limb amputation (Nather et al, 2008). DFU infection has also been associated with increased wound pain and increased sensitivity to pain, both of which have been implicated in delayed healing and reduced quality of life (White, 2009).

Modern dressings (e.g. soft silicones, hydrogels, hydrofibres, alginates), many combined with atraumatic adhesives, are less likely to cause pain during dressing changes than traditional dressings (White and Morris, 2009). Silver-containing dressings have been shown to be effective against a range of wound pathogens, including *Staphylococcus aureus* and beta-hemolytic streptococci, the most common pathogens associated with mild to moderate DFU infections (Ip et al, 2006; Bader, 2008).

Silver ions have been combined with some modern dressing types to simultaneously combat infection and minimise dressing-related pain (White, 2009). These dressings have been used with and without systemic antibiotics to treat infections in chronic wounds (Lipsky and Hoey, 2009; Ousey and McIntosh, 2009) – and specifically DFUs (Lansdown et al, 2003; Coutts and Sibbald, 2005; Rayman et al, 2005; Lipsky et al, 2006; Tong, 2009) – with success.

Here, the authors report the results of a case series designed to evaluate the effects of a silver-containing, soft silicone foam dressing on DFUs showing signs and symptoms of local infection.

Aims

The primary objective of this preliminary study was to evaluate the signs and symptoms of localised infection in DFUs during the course of treatment that comprised traditional wound care and the use of a silver-containing, soft silicone foam dressing (Mepilex® Ag; Mölnlycke Health Care, Gothenburg; *Box 1*). Secondary objectives were to evaluate and record: (i) the level of pain associated with dressing changes; (ii) change in wound area; (iii) investigator opinion of the test dressing's performance; and (iv) adverse events.

Method

The investigation was designed as a single-centre, open, non-randomised case series. In- and outpatients attending a specialist podiatry clinic with active DFUs exhibiting signs of local infection that, in the opinion of the investigators and in line with the manufacturer's instructions, were suitable for treatment with the test dressing were enrolled (inclusion and exclusion criteria listed in *Table 1*).

Each participant was treated according to local clinical practice and evaluated over a treatment period of 4 weeks (including weekly visits during which assessments for the purposes of this study were undertaken and results recorded) or until the ulcer healed, whichever occurred first. All participants received traditional wound care as part of their treatment (debridement and offloading appropriate for their foot and wound type). Systemic antibiotics were used concomitantly if judged necessary by the investigators. Dressing changes were undertaken according to local clinical practice (usually three times per week).

It was agreed by the local clinical governance committee that research ethics committee approval was not required for this study because it was an in-market evaluation of a CE-marked dressing in accordance with its instructions for use.

Baseline participant demographic data and the wound history were recorded at the first consultation. At the first consultation and subsequent dressing changes, the following variables were assessed by qualitative visual assessment by the investigators, unless stated otherwise:

- Signs and symptoms of localised infection (i.e. erythema, heat, oedema, exudate levels [Lipsky et al, 2006]); scored as: none, mild, moderate or severe.
- Pain severity reported by participants before, during and after dressing change using a validated visual analogue scale ranging from zero (no pain) to 100 (worst pain ever; Harms-Ringdahl et al, 1986).
- Ulcer size (length at the longest point, width at the widest point; measured in millimetres).
- Proportion of viable tissue in wound.
- Adverse events.

Photographs were taken during dressing removal and after cleansing and/or debridement. At the final dressing change, the investigators gave a rating (very good, good, poor, very poor) for each case for each of the following parameters: (i) overall experience with dressing; (ii) dressing conformability; (iii) dressing flexibility; (iv) fluid handling of dressing; (v) ease of application of dressing; (vi) ease of removal of dressing; (vii) dressing adherence (lack of) to wound bed.

Data generated from this study are presented in a descriptive manner. All efficacy endpoints are summarised by visit number (1–4 visits). No hypothesis testing was planned for this descriptive investigation.

Box 1. Characteristics of the dressings used in the present case series.

The test dressing (Mepilex® Ag; Mölnlycke Health Care, Gothenburg) in this case series consists of a soft-silicone wound contact layer (Safetac®; Mölnlycke Health Care), an absorbent foam pad (containing a silver compound [silver sulphate] and activated carbon) and a vapour-permeable waterproof film.

The wound contact layer adheres to intact dry skin, and remains *in situ* on the surface of a moist wound or damaged surrounding skin without adhering to these fragile tissues. Thus, the dressing does not cause damage to the wound or epidermal stripping in the peri-wound region – even when exudate starts to dry out – and pain on removal in minimised (Cutting, 2008).

A seal forms between the intact skin and the dressing, inhibiting the movement of exudate from the wound to surrounding skin, thereby helping to prevent maceration of the peri-wound region (White, 2005).

In the presence of wound exudate, silver ions are released from the dressing that inactivate a range of wound-related pathogens. *In vitro* studies demonstrate that the dressing provides rapid, sustained (up to 7 days), broad-spectrum antimicrobial action, effective against aerobic and anaerobic, gram-positive and gram-negative bacteria (including meticillin-resistant *Staphylococcus aureus*, vancomycin-resistant enterococci), fungi and viruses (Chadwick et al, 2009).

This dressing has been used with positive results to manage both acute (Bevilacqua and Rogers, 2008; Meuleneire, 2008) and chronic (Barrett, 2009; Barrows, 2009; Tong, 2009) wounds with signs and symptoms of local infection.

Table 1. Inclusion and exclusion criteria.

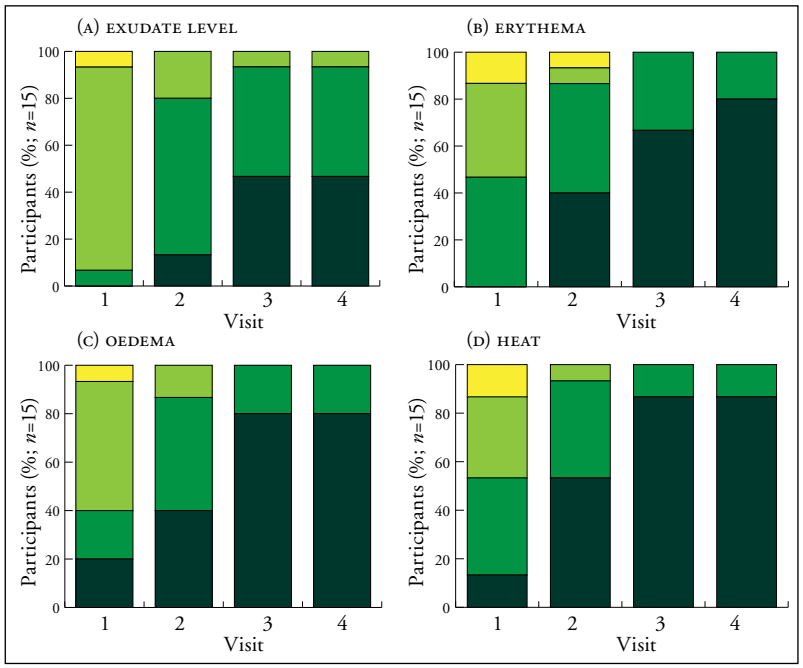
Inclusion criteria

- Aged ≥18 years.
- Type 1 or 2 diabetes.
- An active diabetic foot ulcer (below the ankle) exhibiting at least two signs of local infection (i.e. erythema, heat, oedema, pain, increased exudate) and, in the opinion of the investigator, was considered suitable for treatment with the test dressing.
- Signed informed consent.

Exclusion criteria

- Known allergy or hypersensitivity to any of the test dressing components.
- Uncontrolled diabetes (HbA_{1c} ≥12% [≥108 mmol/mol]).
- High level of wound exudate.
- Treatment of the target ulcer with a silver-containing dressing within the preceding 7 days.
- University of Texas Diabetic Wound Classification Stages C, D and Grade 3.
- Those who would have had difficulty following the study protocol.
- Those participating in other clinical investigation, either ongoing or within the preceding 30 days.

Figure 1. Change in signs and symptoms of local infection of target ulcers between visits 1 and 4 (■ severe; ■ moderate; ■ mild; ■ none).



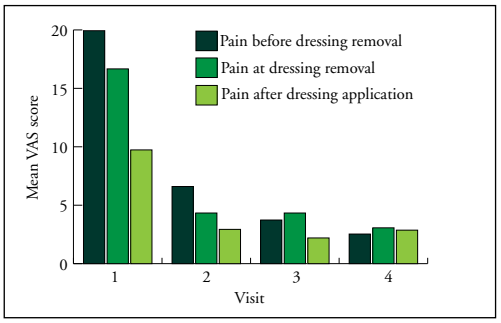


Figure 2. Change in level of pain reported by participants before, during and after dressing removal/application. VAS, visual analogue scale ranging from zero (no pain) to 100 (worst pain ever).

Table 2. Participant and target ulcer data at baseline.

No.	Target ulcer foot	Location of target ulcer	Prior amputation on foot with target ulcer	Palpable foot pulse	Neuropathy	Texas Grade†		Diabetes type	Diabetes duration (years)	HbA_{1c} (mmol/mol)‡
						Grade	Stage			
101	Right	Hallux, plantar	Yes	Yes	Yes	1	B	2	9	68
102	Left	Heel	No	Yes	Yes	1	B	2	1	50
103	Left	Heel, plantar	No	Yes	Yes	2	B	2	30	66
104	Left	Plantar surface	Yes	Yes	Yes	0–1	B	2	29	86
105	Right	Dorsal area	Yes	Yes	Yes	2	B	2	11	60
106	Right	Hallux, plantar	No	Yes	Yes	0–1	B	2	4	57
107	Right	Plantar surface	No	Yes	Yes	1	B	2	3	46
108	Left	Hallux, plantar	No	Yes	Yes	2	B	2	7	50
109	Left	Plantar surface	Yes	Yes	Yes	1	B	2	14	49
110	Right	Plantar surface	No	Yes	Yes	1	B	2	3	55
111	Right	Digitalis II-V, plantar	No	No	Yes	1	D	2	12	72
112	Right	Hallux	No	Yes	Yes	1	B	2	20	46
113	Right	Plantar surface	Yes	Yes	No	1	B	2	13	65
114	Left	Plantar surface	Yes	Yes	Yes	2	B	2	0.16	79
115	Left	Digitalis II-V	No	Yes	Yes	1	B	2	9	57

†University of Texas Diabetic Wound Classification System (Lavery et al, 1996); ‡HbA_{1c} was measured in % but is presented here converted to the International Federation of Clinical Chemistry and Laboratory Medicine's measures.

Results

Fifteen participants (11 men, four women) met the inclusion criteria. All participants had type 2 diabetes. Mean participant age was 63.7 years (median 65 years; minimum 47 years; maximum 78 years; concurrent medical conditions listed in *Appendix I*). Data for each target ulcer at baseline are presented in *Table 2*. The majority (13/15, 86.6%) of target ulcers presented as Grade 1 or 2 in the University of Texas Diabetic Wound Classification System (Lavery et al, 1996).

Signs and symptoms of local infection

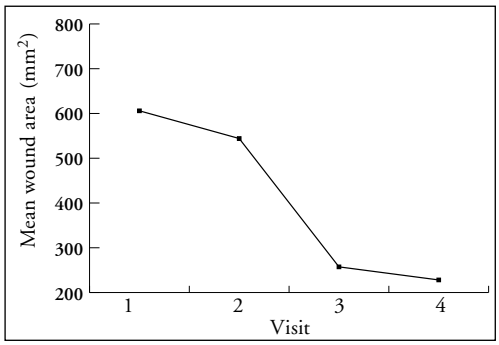
At baseline, erythema (13/15, 86.7%), oedema (11/15, 73.3%), heat (11/15, 73.3%) and exudate level (14/15, 93.3%) were mostly rated as mild or moderate, with a small percentage (2/15, 13.3%; 1/15, 6.7%; 2/15, 13.3; 1/15, 6.7%; 1/15, 6.7%, respectively) rated as severe. During the course of treatment, erythema, oedema and heat reduced and by the final visit these symptoms were rated as mild or none in all target ulcers (*Figures 1b-d*). Exudate levels followed a similar trend, with 93.3% (14/15) of target ulcers producing none or mild exudate by study end (*Figure 1a*). Visit-by-visit levels of local infection are detailed in *Appendix II*.

Two participants received adjunctive antibiotic therapy to manage DFU infection during the study period. One participant (participant 104) exhibited increased clinical signs of infection in the target ulcer after 7 days of treatment with the test dressing; one participant (participant 105) was receiving systemic antibiotic therapy (amoxicillin) prior to enrolment, which was continued into and beyond the study period. Participant 104 was also receiving trimethoprim for the treatment of a urinary tract infection at enrolment, which resolved and the trimethoprim was discontinued between visits 1 and 2.

Pain

At baseline, mean pain severity scores reported by participants prior to, during and after dressing removal/application were 19.9, 16.7 and 9.7, respectively. At subsequent visits, the pain severity scores were lower than that recorded at baseline (*Figure 2*).

Figure 3. Average change in wound size (length × width) by visit.



Wound size reduction

During the study period, a trend toward reduction in wound area was seen (*Figure 3*). Visit-by-visit wound size are detailed in *Appendix II*.

Investigator ratings

The overall experience of using the dressing was rated by investigators as good (20.0%) or very good (80.0%). Conformability was rated as good (6.7%) or very good (93.3%) and the ease of application/removal, lack of adherence to the wound bed, fluid handling and flexibility of the dressing were all rated as very good (*Table 3*).

Adverse events

One adverse event occurred during the study; a target ulcer exhibited increased clinical signs of infection after 7 days of treatment with the test dressing. The participant concerned was treated with systemic antibiotics (doxycycline) and the infection resolved 2 days later. It is generally accepted clinical practice to use topical antimicrobial agents as an adjunct to antibiotics (European Wound Management Association, 2006), hence it was deemed appropriate by the investigators that this participant continue in the study.

Table 3. Investigator evaluation of study dressing.

	Description	*n* (%)
Overall experience	Good	3 (20.0)
	Very good	12 (80.0)
Conformity	Good	1 (6.7)
	Very good	14 (93.3)
Ease of application	Very good	15 (100)
Ease of removal	Very good	15 (100)
Adherence to wound bed	Very good	15 (100)
Flexibility of dressing	Very good	15 (100)
Fluid handling	Poor	1 (6.7)
	Good	7 (46.7)
	Very good	7 (46.7)

Discussion

The findings of the present study suggest that the signs and symptoms of local infection in DFUs can be efficiently resolved by use of a silver-containing, soft-silicone foam dressing regimen in conjunction with good traditional wound care and, where necessary, systemic antibiotics. While case series alone cannot demonstrate the efficacy of an intervention, they do provide insight into how the intervention may be used to overcome clinical challenges. However, a randomised controlled trial is required to definitively assess the efficacy of this intervention.

Coutts and Sibbald (2005), Rayman et al (2005), Jude et al (2007) and Tong (2009) report results similar to those presented here for resolution of local infection associated with the use of silver-containing dressings in the treatment of DFUs. A 2006 Cochrane Database Systematic Review (Bergin and Wraight) on silver-containing dressings and topical agents for the treatment of infected DFUs highlighted that, to date, no randomised or controlled clinical trials have evaluated the effectiveness of these agents. Yet, it should be recognised – especially in the area of wound care – that data obtained from lower down the hierarchy of clinical evidence (e.g. case studies) may be more representative of clinical practice and should be taken into account when reviewing treatment options for suitable patient groups (Gottrup, 2008).

Pain in people with diabetes is complex: loss of protective sensation is often a key factor in the development of DFUs, however recent research has highlighted that pain can be associated with both neuropathic and neuroischaemic ulceration (Bengtsson et al, 2008). It has also been suggested that nerves play a central role in tissue homeostasis and may orchestrate complex reparative processes (Schaper et al, 2008). Interestingly, a genetic link has been identified that may predict which people will suffer DFU-related pain (Cheng et al, 2009).

In a randomised controlled trial to determine

Page points

1. The findings of the present study suggest that the signs and symptoms of local infection in diabetic foot ulcers can be efficiently resolved by use of a silver-containing, soft-silicone foam dressing regimen in conjunction with good traditional wound care and, where necessary, systemic antibiotics.
2. Several authors report results similar to those presented here, however no randomised or controlled clinical trials have evaluated the effectiveness of silver-containing dressings.
3. Data obtained from lower down the hierarchy of clinical evidence (e.g. case studies) may be more representative of clinical practice and should be taken into account when reviewing treatment options for suitable patient groups.

"These results suggest that the dressing – when used as one component of a regimen that includes holistic patient care, good traditional wound care and systemic infection control when necessary – is a useful therapeutic modality."

the comparative effectiveness and cost-effectiveness of three dressing products for DFUs, between 13% and 22% of participants reported pain in the region of the wound at all visits, with least pain reported by those receiving non-adherent dressings (P=0.012; Jeffcoate et al, 2009). In the present study, all participants reported experiencing dressing change-related pain at baseline. The pain severity scores relating to subsequent visits were all lower than that recorded at baseline. Importantly, the greatest reduction in pain scores occurred between baseline and the first visit, suggesting a dressing effect rather than simply a reduction in the pain associated with resolution of infection or healing of the wound – a finding in line with that of Jeffcoate et al (2009).

Clinicians should consider dressing-related pain when managing DFUs and when possible select dressings that lessen this pain. Adhesive dressings may damage fragile diabetic skin (Holewski et al, 1989; Tantisiriwat and Janchai, 2008; Lawton and Langoen, 2009). The belief that people with diabetic peripheral neuropathy do not suffer wound and/or dressing-related pain should be set aside and treatments that reduce these burdens embraced.

During the study period, a trend toward reduction of wound area was seen. The rate of healing was consistent with that reported by other authors working in DFU populations (Coutts and Sibbald, 2005; Rayman et al, 2005; Jude et al, 2007; Tong, 2009), although direct comparison with these studies would not be appropriate due to differences in study protocols and populations.

Conclusion

Infection is a significant problem in DFU management; it delays healing and increases wound-related pain and risk of amputation, and is a burden on the healthcare economy. The use of a silver-containing, soft-silicone foam dressing in the cases reported here resulted, in the majority, in the rapid resolution of the signs and symptoms of local infection, and reduced the levels of pain associated with dressing change. These results suggest that the dressing – when used as one component of a regimen that includes holistic patient care, good traditional wound care and systemic infection control when necessary – is a useful therapeutic modality. ■

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APPENDIX I. Medical history and previous surgical interventions for each participant.

No.	Condition	C/P	Ongoing medication	Previous surgeries
101	Chronic renal impairment	C	No	Right foot osteomyelitis; surgical debridement
	Hypothyroidism	C	Yes	
	Essential hypertension	C	Yes	
	Retinopathy	C	No	
102	Hypertension	C	Yes	None
	Hypercholesterolaemia	C	Yes	
103	Nephropathy	C	No	Renal transplant
	Hypertension	P	No	
	Hyperlipidaemia	C	Yes	
	Retinopathy	C	Yes	
104	Depression	C	Yes	Left/1st symes amputation
	Neuropathic pain	C	Yes	
	Hypercholesterolaemia	C	Yes	
	Urinary tract infection	C	Yes	
105	Chronic renal disease	C	No	Forefoot amputation
106	Congenital talipes equinus	C	No	Incision and drainage of foot
	Diabetic retinopathy	C	No	
107	Rheumatoid arthritis	C	Yes	Osteomyelitis (2nd toe)
	Hypertension	C	No	
	Pulmonary vasculitis	P	No	
108	Lung cancer	C	Yes	None
	Cardiovascular protection	C	Yes	
	Dyslipaemia	C	Yes	
109	Renal impairment	C	No	None
	Angina	C	No	
	Cardiovascular accident	P	Yes	
110	Psoriasis	C	No	None
	Raised blood pressure	C	Yes	
	Raised cholesterol	C	Yes	
111	Hypertension	C	No	None
	Asthma	C	Yes	
112	Hypertension	P	No	None
	Renal disease	C	Yes	
113	Hypertension	C	Yes	Toe amputation
	Neuropathic pain	C	Yes	
	Retinopathy	C	Yes	
114	Hypertension	C	Yes	Left hallux amputation
115	Hypertension	C	Yes	None
	Hypercholesterolaemia	C	Yes	

C, current; P, previous

APPENDIX II. Signs of local infection and wound size by visit for each participant.

No.	Visit	Signs of local infection					Wound size (mm)	
		Redness	Heat	Oedema	Pain	Exudate	Width	Length
101	1	Mod	Mild	None	None	Mod	21	16
	2	Mild	None	None	None	Mild	12	6
	3	None	None	None	None	Mild	5	6
	4	None	None	None	None	None	2	2
102	1	Mild	Mod	Mod	None	Mod	40	28
	2	Mild	Mild	Mod	None	Mod	40	26
	3	None	None	None	None	Mild	40	25
	4	None	None	Mild	None	Mild	24	39
103	1	Mild	Mild	None	None	Severe	26	10
	2	None	None	None	None	Mild	25	2
	3	None	None	None	None	Mod	25	7
	4	None	None	None	None	Mild	25	7
104*	1	Mod	Mod	Mod	Mod	Mod	20	10
	2	Severe	Mod	Mod	Mild	Mild	18	10
	3	None	None	None	Mild	None	15	8
	4	None	None	None	None	None	18	11
105**	1	Mod	Severe	Severe	Mild	Mod	40	30
	2	Mild	None	None	Mild	Mod	38	28
	3	None	None	None	Mild	Mild	39	31
	4	None	None	None	Mild	Mild	41	32
106	1	Mild	Mild	Mild	None	Mod	9	6
	2	None	None	None	None	None	5	5
	3	None	None	None	None	None	15	15
	4	None	None	None	None	None	8	5
107	1	Mild	None	Mod	None	Mod	5	5
	2	Mild	Mild	Mild	None	Mild	2	3
	3	Mild	Mild	Mild	None	None	1	1
	4	Mild	Mild	None	None	None	1	1
108	1	Mild	Mild	Mod	None	Mod	14	10
	2	Mild	None	None	None	Mild	15	15
	3	Mild	None	Mild	None	None	7	12
	4	None	None	None	None	Mild	6	11
109	1	Mod	Mod	Mod	Mod	Mod	30	30
	2	None	Mild	Mild	None	None	10	10
	3	None	None	None	None	Mild	5	5
	4	None	None	None	None	None	5	8
110	1	Mod	Mild	Mild	Mod	Mod	8	9
	2	Mild	Mild	None	Mod	Mod	8	9
	3	Mild	None	None	Mild	Mild	8	7
	4	Mild	Mild	Mild	Mild	Mild	1	1
111	1	Severe	Severe	Mod	Severe	Mod	20	20
	2	None	Mild	Mild	Mild	Mild	20	35
	3	None	Mild	Mild	Mild	None	14	18
	4	None	None	None	Mild	Mild	15	7
112	1	Severe	Mod	Mod	None	Mild	12	25
	2	None	None	Mild	None	Mild	13	22
	3	None	None	None	None	Mild	13	6
	4	None	None	None	None	None	13	6
113	1	Mild	Mild	Mod	None	Mod	18	25
	2	None	None	Mild	None	Mild	20	22
	3	None	None	None	None	None	15	19
	4	None	None	None	None	Mild	11	14
114	1	Mild	None	Mild	Mild	Mod	32	112
	2	Mild	None	Mild	None	Mild	35	111
	3	Mild	None	None	None	Mild	30	100
	4	None	None	Mild	None	Mod	30	100
115	1	Mod	Mod	None	None	Mod	8	6
	2	Mod	Mild	Mild	None	Mild	4	4
	3	Mild	None	None	None	None	4	5
	4	Mild	None	None	None	None	4	3

Mod, moderate. *Increased clinical signs of infection after 7 days of treatment with the test dressing, doxycycline initiated, infection resolved 2 days later. **Receiving amoxicillin prior to enrolment, treatment continued into and beyond the study period.