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ORIGINAL ARTICLE

Efficacy of a new multifunctional surfactant-based biomaterial dressing with 1% silver sulphadiazine in chronic wounds

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Abstract

Chronic wounds represent a large and growing segment of health care and add considerably to human suffering and economic burden as populations age. More effective materials, especially those promoting ease of use and economy, are needed to treat this increasing number of patients. A case series conducted at a European outpatient tertiary wound centre used a novel surfactant-based biomaterial dressing containing 1% silver sulphadiazine on 226 chronic wound patients with various aetiologies. Eighty-eight patients had been undergoing standard of care treatment at the facility, while the remainder ($n = 138$) began treatment with the surfactant-based biomaterial dressing on enrollment. A total of 73% of the first group healed or showed improvement, with 60% healing by a median of 17 weeks after beginning treatment, and 86% of the group of new enrollees healed or showed improvement, with 73% healing within a median of 12 weeks of beginning treatment with the new product. Patient and clinician reports showed improved compliance, reduced pain and a favourable side-effect profile. Limited economic analysis showed markedly reduced treatment costs compared with standard of care. Further research is recommended.

Introduction

Non-healing wounds are a challenge to health care professionals, as well as the patients who suffer from these wounds with their pain and significant loss of quality of life. These wounds will be a challenge for current and future social and government budgets as the changing demographics show the shift to a much older population. Much research has been performed on chronic wounds, and this has led to a better understanding of how to manage them.

Two concepts that have developed from this recent research are critical colonisation and bacterial biofilm. Critical colonisation describes the level of bacteria in a chronic wound that is not sufficiently high to produce the clinical symptoms of infection, but high enough to delay the healing process (1). A biofilm is a group of bacteria held together by an extracellular polymeric substance associated with a surface and resistant to environmental stresses that could overwhelm a lone bacterium (2). Both of these impediments to wound healing can be resolved with effective topical antimicrobial therapy.

At our ambulatory wound care clinic, we have been introduced to a new multifunctional, biocompatible, surfactant-based, biomaterial dressing with 1% silver sulphadiazine (SSD). SSD is a proven topical antimicrobial agent and, in this new water-soluble gel formulation, can be used in chronic wounds without leaving a residue. In addition, the surfactant properties of the gel assist in penetration and disruption of the bacterial biofilm.

Ideally, wound healing products should also be relatively easy and quick to use, and have a low economic burden.

Key Messages

- a novel biocompatible surfactant-based dressing carrying 1% silver sulphadiazine was used in a case series of treatment of a spectrum of chronic wounds.
- a total of 226 patients with chronic wounds received treatment with the novel product and were followed at an outpatient tertiary care centre.
- the silver sulphadiazine-containing surfactant-based dressing product showed favourable healing rates; patients and clinicians reported reduced pain, lower treatment costs and reported no adverse effects.

Industry has reacted by introducing a multitude of advanced wound dressings that respond to the various issues identified in wound healing research. These new products present additional challenges to the health care professional: finding the best products to help the patient, while at the same time respecting the work load of the wound care staff and the economic impact for administration. The purpose of this report is to describe the benefits achieved from treating 226 patients with chronic wounds from April 2011 to October 2012 with this new surfactant-based gel dressing with 1% SSD.

Material and methods

The multifunctional, surfactant-based biomaterial dressing was in gel form (PluroGel®) containing 1% SSD (PluroGel® PSSD; PluroGen Therapeutics, Inc., Norristown, PA). The surfactant used in PluroGel® has been recognised by the US Food and Drug Administration as safe for use in medical applications.

This was a cohort-design study. The study cohort consisted of any patient presenting to the clinic between April 2011 and October 2012 with a non-healing, chronic wound. Inclusion into the study cohort required that the wound had been treated with acceptable standards of wound care for at least 8 weeks without showing progress towards healing. The comparison group for this study was the same patients who had shown minimal progress in healing for at least the previous 8 weeks before entry into the study.

All patients with non-healing wounds of at least 8 weeks duration and a wound size of $>1\,cm^2$ were included. Wound aetiology was established via several procedures: arterial status was investigated by manual palpation of distal pulses, together with Doppler auscultation. Additional procedures, performed as clinically indicated, included ankle brachial index (ABI), venous mapping with duplex ultrasound, neurologic status including tuning fork test, monofilament Semmes-Weinstein testing and Tip-Therm testing. Magnetic resonance imaging and angiography (MRI/MRA) and/or computed tomography scanning (CT) were performed if clinically indicated for diagnosis or staging of wounds. All procedures were performed in-house. When the wound aetiology was established, an appropriate tool was used to classify the stage or severity.

If indicated, patients were referred for percutaneous transluminal angioplasty (PTA) or other appropriate vascular procedures; neurology, dermatology and orthopaedic consultations were also obtained as necessary. An orthotist was also available to optimise offloading of plantar ulcers and for specialised footgear as needed.

Before starting treatment, patient and wound histories were recorded by nursing staff performing patient interviews and, when available, by performing record review. Informed consent was obtained.

All study wounds were treated with the surfactant-based biomaterial dressing containing 1% SSD in a regional referral, tertiary level specialised wound care centre of an insurance company.

Before application of the new surfactant-based biomaterial dressing, the wound was cleaned, necrotic tissue was debrided (if necessary), mostly by mechanical means, and the skin around the wound was protected (if necessary). The new surfactant-based biomaterial dressing was either spread with the help of a spatula on a gauze dressing or directly put into the wound using a spatula. This dressing has the characteristic that it stays thick at body temperature and therefore can be applied easily. After application of the new surfactant-based biomaterial dressing, the wound was closed with a secondary dressing (most with simple, inexpensive gauze or non-woven), followed by a moisture barrier film. Dressing change was initially performed daily, and later performed with a frequency ranging from every other day to once weekly as wounds improved, according to clinical discretion.

In some cases, additional foam products were added (49 cases). In cases where specific wound infection was a concern, systemic and/or local antibiotics (53 cases) were administered concomitantly. Compression (125 cases) and/or pressure reduction (87 cases) as well as cortisone therapy (10 cases) or PTA (10 cases) were prescribed when necessary. Wound treatment and healing progress as well as patient comments were documented by patient file and photographs.

The primary outcome parameter for this study was a healed wound. A healed wound was defined as a wound that had developed complete coverage by epithelium without evidence of exudation. All wounds were monitored for their decrease in wound size as treatment progressed. At the termination of the study, any wound that had shown a decrease in wound size of at least 75% was reported as having shown significant progress.

Secondary outcome parameters such as reduction in pain, odour, exudates and inflammation were recorded at each clinic visit using standardised scales.

Results

During the period from April 2011 to October 2012, 103 male and 123 female patients, average age 73·5 years, with a non-healing wound and multiple comorbidities were studied. The comorbidities influencing wound healing were treated concomitantly and included vascular disorders (196 patients with arterial and 101 patients with venous disorders), diabetes mellitus (123 patients), polyneuropathy (57 patients) and coronary artery disease (41 patients).

At the initiation of this study, 88 of the 226 patients were being treated in this wound care centre with different local and systemic wound therapies prior to this study, but without success (group A, consisting of 49 males and 39 females). The other 138 patients were referred by general practice doctors or home care nurses or were self-presenting and started the new surfactant-based biomaterial dressing treatment directly (group B, consisting of 54 males and 84 females).

The patients ($N = 226$) presented with the following wounds: 72 arterial ulcers (32%), 73 venous ulcers (32%), 23 mixed ulcers (10%), 41 diabetic/neuropathic wounds (18%) and 17 other wounds – post-traumatic/postoperative as well as burns (8%).

Results are reported and analyses performed for those patients not lost to follow-up. For patients in group A, 14 patients were lost to follow-up and we therefore were able to follow 74 patients. In group A, 44 patients (59·5%) were healed within a median of 17 weeks, 10 patients (13·5%) were still in treatment at close of data collection showing significant

progress to healing and therapy was changed in 20 patients (27·0%). For patients in group B, 28 patients were lost to follow-up and we were therefore able to follow 110 patients. In group B, 80 patients (72·7%) were healed within a median of 12 weeks, 15 patients (13·6%) were still in treatment at close of data collection showing significant progress to healing and therapy was changed in 15 patients (13·6%). Overall for the total study population, 42 patients were lost to follow-up and we therefore were able to follow 184 patients. For the total study population, 124 patients (67·4%) were healed, 25 patients (13·6%) were still in treatment at close of data collection showing significant progress to healing and therapy was changed in 35 patients (19·0%). The results for healing in groups A and B are summarised in Table 1.

Table 2 reports healing rates for each wound type. Analysis of healing rate by wound type showed that the new surfactant-based biomaterial dressing was associated with improved healing rates in all wound types studied. There was a significantly higher healing rate for arterial and venous ulcers in group B compared with group A. In group A, 11 arterial ulcers (45·8%) were healed and 3 were in significant progress to healing at close of data collection; 10 venous ulcers (50·0%) were healed and 3 were in significant progress to healing at close of data collection; 5 mixed ulcers (62·5%) were healed and 2 were in significant progress to healing at close of data collection; 9 diabetic/neuropathic ulcers (69·2%) were healed and 2 were in significant progress to healing at close of data collection; and 9 other wounds (100·0%) were healed. In group B, 27 arterial ulcers (79·4%) were healed; 29 venous ulcers (67·4%) were healed with 8 in significant progress to healing at close of data collection; 3 mixed ulcers (60·0%) were healed with 2 in significant progress to healing at close of data collection; 15 diabetic/neuropathic ulcers (68·2%) were healed with 5 in significant progress to healing; and 6 other wounds (100·0%) were healed. Overall, for the total study population, 38 arterial ulcers (65·5%) were healed with 3 in significant progress to healing; 39 venous ulcers (61·9%) were healed with 11 in significant progress to healing at data collection; 8 mixed ulcers (61·5%) were healed with 4 in significant progress to healing at close of data collection; 24 diabetic/neuropathic ulcers (68·6%) were healed with 7 in significant progress to healing at close of data collection; and 15 other wounds (100·0%) were healed.

Analysis of healing rate by age group showed that the new surfactant-based biomaterial dressing was associated with improved healing rates in all age groups including the difficult to heal older population (>70 years). The results show little difference in healing rate between the studied age groups with the greater difference in healing rate again shown between groups A and B. In group A, 73·0% of all patients followed were healed or showed significant progress to healing at the end of data collection, of whom 59·5% were healed. In group B, 86·4% of all patients were healed or made significant progress to healing at the end of data collection, of whom 72·7% were healed. Overall, 81·0% of all patients followed were healed or showed significant progress to healing at the end of data collection, of whom 67·4% were healed.

Use of the new surfactant-based biomaterial dressing product resulted in a number of additional clinical observations of performance that were beneficial in patient care (Table 3). It is noted that the new surfactant-based biomaterial dressing was consistently accepted by patients and the medical staff.

No adverse affects from long-term topical use of SSD were observed. SSD was used during all phases of wound healing without any problems.

We hypothesised that there may be a cost reduction due to the use of this new surfactant-based biomaterial dressing product. We therefore identified a specific difficult patient and performed an economic analysis (3). This patient (female, 86 years, diabetic foot ulcer left heel; several comorbidities) was treated unsuccessfully with no change in the wound for 20 weeks using three different treatment modalities. This resulted in 78 dressing changes (3·9 dressing changes per week) having overall cost for materials of €742·23 and an average material cost per dressing change of €9·52. Following the three unsuccessful treatment modalities, we began treatment with the new surfactant-based biomaterial dressing product.

The patient was treated with the new surfactant-based biomaterial dressing for 12 weeks, resulting in complete closure of the wound. Over the 12-week treatment period with the new surfactant-based biomaterial dressing, we made 40 dressing changes (mean 3·3 dressing changes per week). Overall cost of materials using the new surfactant-based biomaterial dressing was €184·40 and mean cost per dressing change was €4·61.

In this cost analysis, neither did we calculate the savings from the reduction in the number of dressing changes per week (reduced from 3·9 to 3·3 changes per week), nor did we include the savings in clinical staff costs as a result of the use of the new surfactant-based biomaterial dressing product. With regard to material cost only, the treatment with the surfactant-based biomaterial dressing was over 50% less expensive per dressing change than the initial three different treatment costs. The new surfactant-based biomaterial dressing realised an additional and large cost savings (which for this study we did not attempt to calculate) because its use resulted in complete wound closure. These figures suggest that a further detailed study of the new surfactant-based biomaterial dressing treatment (including staff costs) may show significant economic savings.

To establish baseline results expected when standard products and treatments for chronic wounds are used enabling comparison to the results reported here for the new surfactant-based biomaterial dressing product, we performed a search of the published literature. This search provided the following standard of care data: Wolcott *et al.* reported a 48·5% healing rate in 503 patients (4); Mostow *et al.* reported a 34% healing rate in 58 patients (5); Da Costa *et al.* reported a 19% healing rate in 21 patients (6); Osiris Therapeutics, Inc. reported a 21·3% healing rate in 16 patients (7); Blume *et al.* reported a 31% healing rate in 16 patients (8). In total, these five publications reported 645 chronic wound patients receiving standard of care products and treatments with an average chronic wound healing rate of 43·8%.

Discussion

Although this was not a controlled study, it was a routinely accepted and used cohort study with a significant patient population showing that the rate of wound healing was dramatic

Table 1 Summary of healing rate results for the new surfactant-based biomaterial dressing product by length of time for treatment: (a) group A: authors' patients prior to new surfactant-based biomaterial dressing product; (b) group B: direct start with new surfactant-based biomaterial dressing product; and (c) groups A and B: total

Pre-treatment months	Total patients	Treatment weeks	Lost to follow-up	Patients followed up	Therapy change	Healed	Progressing to healing at data collection	% healed of patients followed up	% healed plus progressing to healing of patients followed up
(a)									
<3	14	0–8	3	11	4	7		63·6	63·6
<3	8	9–12	1	7	2	5		71·4	71·4
<3	11	13–26	3	8		7	1	87·5	100·0
<3	10	>26	1	9	5	2	2	22·2	44·4
Subtotal	43		8	35	11	21	3	60·0	68·6
4–6	1	0–8	0	1		1		100·0	100·0
4–6	0	9–12	0	0					
4–6	2	13–26	1	1		1		100·0	100·0
4–6	3	>26	1	2		1	1	50·0	100·0
Subtotal	6		2	4	0	3	1	75·0	100·0
>6	5	0–8	1	4	1	3		75·0	75·0
>6	6	9–12	0	6	2	4		66·7	66·7
>6	8	13–26	2	6	3	3		50·0	50·0.0
>6	20	>26	1	19	3	10	6	52·6	84·2
Subtotal	39		4	35	9	20	6	57·1	74·3
Total	88		14	74	20	44	10	59·5	73·0
% of patients followed up					27·0	13·5	59·5		
(b)									
0	52	0–8	16	36	5	30	1	83·3	86·1
0	18	9–12	4	14	1	12	1	85·7	92·9
0	30	13–26	5	25	4	20	1	80·0	84·0
0	38	>26	3	35	5	18	12	51·4	85·7
Total	138		28	110	15	80	15	72·7	86·4
% of patients followed up					13·6	72·7	13·6		
(c)									
Total	226	0 > 26	42	184	35	124	25	67·4	81·0
% of patients followed up					19·0	67·4	13·6		

using the new surfactant-based biomaterial dressing. Patients in group A were being treated by the authors in a regional referral tertiary level specialised wound care centre with best practice protocols and advanced wound care products. However, the rate of healing was slow. When these patients were started on the new surfactant-based biomaterial dressing, their wounds showed immediate improvement. A total of 59·5% of these patients achieved complete wound closure within a median of 17 weeks.

In group B patients, the surfactant-based biomaterial dressing was started upon their referral to the clinic. Again, wound improvement was immediate and 72·7% of these wounds healed within a median of 12 weeks.

When the two groups of patients were combined, the wound closure rate was 67·4%. Other wound healing studies (4–8) using standard of care practices and products have reported closure rates of 19–48·5%, with an average of 43·8%.

Historical results for the use of SSD in other carriers cannot fully explain the healing results reported here for the new surfactant-based biomaterial dressing. The surfactant used in this dressing has been used in other medical applications and has demonstrated unique biophysical properties. These properties include wound cleansing (9), cyto-protection (10), rheological enhancement of the wound border (11), reduced inflammation (12) and enhanced wound blood flow (13). Preliminary results also suggest that the surfactant disrupts existing biofilm and prevents its redevelopment (14). Each of these factors can improve the capability of wounds to heal.

SSD has been used effectively in burn care for decades without complications. Its use in wounds has been limited because its formulations in the past have not been water-soluble. With this new surfactant-based biomaterial, the product can be used effectively in the wound without concern of difficult-to-remove residue. Thus, this new surfactant-based biomaterial containing 1% SSD can be used in all phases of wound healing. The enhancement of wound healing without complication provides further documentation of the safety and efficacy of SSD reported by an expert working group (15).

The results of this study lead us to conclude that regardless of whether the practitioner starts immediately with the new surfactant-based biomaterial dressing product, or uses it after standard common therapies fail, the new surfactant-based biomaterial dressing with SSD is a promising approach to overcome the challenges which wound care managers face every day. This new product can help with the challenges of balancing patient comfort and quality of life, the staff's overload on the one hand and on the other, the wish to perform

Table 2 Summary of healing rate results for the new surfactant-based biomaterial dressing product by wound type: (a) group A: authors' patients prior to new surfactant-based biomaterial dressing product; (b) group B: direct start with new surfactant-based biomaterial dressing product; and (c) groups A and B: total

Wound type	Total patients	Lost to follow-up	Patients followed up	Therapy change	Progressing to healing at data collection	Healed	% healed of patients followed up	% healed plus progressing to healing of patients followed up
(a)								
Arterial	30	6	24	10	3	11	45·8	58·3
Venous	22	2	20	7	3	10	50·0	65·0
Mixed	11	3	8	1	2	5	62·5	87·5
Diabetic/neuropathic	15	2	13	2	2	9	69·2	84·6
Other	10	1	9			9	100·0	100·0
Total	88	14	74	20	10	44	59·5	73·0
(b)								
Arterial	42	8	34	7		27	79·4	79·4
Venous	51	8	43	6	8	29	67·4	86·0
Mixed	12	7	5		2	3	60·0	100·0
Diabetic/neuropathic	26	4	22	2	5	15	68·2	90·9
Other	7	1	6			6	100·0	100·0
Total	138	28	110	15	15	80	72·7	86·4
(c)								
Arterial	72	14	58	17	3	38	65·5	70·7
Venous	73	10	63	13	11	39	61·9	79·4
Mixed	23	10	13	1	4	8	61·5	92·3
Diabetic/neuropathic	41	6	35	4	7	24	68·6	88·6
Other	17	2	15	0	0	15	100·0	100·0
Total	226	42	184	35	25	124	67·4	81·0

Table 3 Other performance characteristics of the new surfactant-based biomaterial dressing product

Debridement was less necessary compared with other wound management strategies
The wound was always clean and therefore, it was easy to visually assess the wound bed
The new surfactant-based biomaterial dressing was helpful and therefore used in all stages of the wound healing process
The new surfactant-based biomaterial dressing could be used in combination with other therapies and wound care products
Improved patient compliance to the clinical instructions on the care of the wound
Patients had reduced pain during dressing change and during activities at home and out-door pursuits
Patients had less odour in the wound
Due to less pain and less odour, a noticeable increase of patient quality of life was observed
Easy and fast dressing changes were very well accepted by the staff
Easy and fast dressing changes allowed the patient or the patient's family to do the dressing change at home
There were no negative side effects observed for use of the SSD antimicrobial, even when SSD was used for several months

a progressive and effective wound care therapy, at the same time being constantly under economic pressure.

To fully explain the healing results reported here for the new surfactant-base biomaterial dressing, which the authors could not fully attribute to the SSD, presented in this article were the published reports of the multiple profound biophysical characteristics of the new surfactant-based biomaterial dressing (wound cleansing, rheologic, antithrombotic, anti-inflammatory and cyto-protective attributes, as well as powerful effects against biofilm). These effects may be attributed to the molecular structure of the new dressing product's surfactant-based biomaterial, as it interacts with hydrophobic and hydrophilic wound substances. The patient results reported here are consistent with the published reports on the biophysical characteristics of the new surfactant-based biomaterials.

Furthermore, SSD antimicrobial activity neither provides a complete explanation for the marked decrease in pain, debris and exudate, nor does it have any known effect against biofilm. Based on the published reports about how the new surfactant-based biomaterial functions, we believe that the new surfactant-based biomaterial dressing has its own specific effect on the conditioning of the wound bed and that it is possible that a majority of the positive benefits and outcomes are a result of the surfactant-based biomaterial dressing. Further studies of the new surfactant-based biomaterial dressing including its use with other antimicrobials or with no antimicrobial are suggested.

Helpful performance characteristics in the use of the new surfactant-based biomaterial dressing product were observed and reported (Table 3). Many of these reported performance characteristics, including ease of use, application at home,

minimal or no pain during dressing change and improved patient compliance to follow clinical instructions, all contributed to improved healing results.

While the overall healing rate when using the new surfactant-based biomaterial dressing was improved over the reported healing rates for standard of care products and treatments, there was a significant, higher healing rate for arterial and venous ulcers in group B compared with group A. One explanation for this may be that the wounds in group A were older and therefore more difficult to treat, and they continued to be difficult to treat when changing to the new surfactant-based biomaterial dressing. However, another explanation for the improved results of group B may be evidence that it is useful to start the treatment of the new surfactant-based biomaterial dressing as soon as possible, establishing the cleanliness of the wound and an optimal wound environment to heal the wound faster, not allowing the wound to further worsen. Additional studies are suggested to support this conclusion.

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