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Effectiveness of a Novel Antimicrobial Dressing in Treating Chronic Venous Leg Ulcers

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KEYWORDS

Anti-microbial dressing, Biofilm, Venous leg ulcer, Wound healing.

ABSTRACT

Aim and objective: The purpose of this study was to investigate the effectiveness ofSilver containing wound dressing in Leg ulcer patients with chronic venous disease. **Methods:** 60 patients with venous leg ulcers were treated with silver colloid dressings for four weeks, followed by conventional dressings for four weeks with or without having signs ofinfection were treated. Clinical evolution of the wound in terms of size, depth and ulcer painwere monitored for eight weeks. In this study, two participants defaulted and lost to follow up. **Results:** The wound condition has significantly improved after 8 weeks with completely healed ulcers in 4 patients, 48 (76%) patients had improvement and 2 patients had deteriorated wound requiring debridement. An average of 54% reduction in size and 60% reduction in depth of ulcers seen. No adverse events were encountered related to wound dressings. Participants reported less pain on pain scores as the study progressed. **Conclusion:** According to this study, silver wound dressings have an acceptable efficacy for treating chronic venous leg ulcers where biofilm formation might inhibit healing.

1. Introduction

It has long been known that venous leg ulcers pose a problem to patients with considerable costs, recalcitrance, pain, and reduced quality of life [1]. In most cases, such wounds cannot be treated successfully, and ulcers can persist for up to a year [2]. There has been a link between chronic wound micro flora colonization (biofilm) and delayed wound bacterial healing in chronic wounds [3, 4]. As a result of Biofilms, which are found in most chronic wounds can cause impaired wound healing and do not respond to topical and systemic antimicrobial treatments [5, 6]. Biofilms are complex biochemical systems made up of polysaccharides, proteins, and extracellular DNA, heterogeneous community of microorganisms, providing protection and increasing tolerance to antimicrobials, including innate Antibiotics and antiseptics as well as the immune system [6, 7]. Biofilms commonly form in wounds with poor granulation tissue, excessive moisture, surface slime and recurrent infections [8, 9]. Biofilms impede the healing of non-healing and non-responsive wounds to antimicrobial therapies that are susceptible to recurrent infections [8, 9]. To the best of our knowledge, there is no commercially available wound dressing that disrupts biofilms and kills the microorganisms that are associated with them. Ionic silver,in addition to its antimicrobial properties, protects wound from

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inflammation, infection, and odour. The dressing contains silver impregnated in an amorphous hydrogel acting as a surfactant. Biofilm is disrupted, allowing ionic silver to penetrate and act on microorganisms. As a result of the surfactant, the surface tension of the biofilm is reduced and it helps loosen the structure of the biofilm. An evaluation of safety and efficacy was conducted on patients with an infectedchronic venous leg ulcersin this study.

2. Methodology

Dressing witha silver colloid was evaluated for its effectivity in treatingchronic venous leg ulcers in this non-comparative study. All patients enrolled in the study were informed of the study procedures and obtained an informed consent prior to participating.

2.1 Subjects involved

The study included participants with Over the age of 18, an ankle-to-brachial pressure index must be obtained greater than 0.8, surface area ranging from 10 to 40 $cm^2$and having signs of infection likeerythema, edema, malodour, and heavy exudation from wound.At baseline, the ulcers were categorized into clinically infected wounds (requiring topical antibiotic treatment) or non-infected wound that does not require antibiotics or topical antimicrobial treatments, but exhibits some signs and symptoms of infection. A topical anti-biotic or anti-microbial was not administered to the study participants either three weeks prior and throughout the study. All participants wore compression dressings throughout the study period. Exclusion criteria included skin sensitivity to dressing components, or antibiotics administered systemically prior to start of study, malignant leg ulcer, Three months ago, I had a deep vein thrombosis and had a venous surgery, on immunosuppression or prior history of radiotherapy.

2.2 Treatment

As part of the study, an informed written consent was signed by the participants meeting the inclusion criteria and has received silver impregnated dressing forfour weeks, followed by four weeks of conventional dressings. A moisture-retentive secondary dressing was applied over the primary dressing to maintain optimum amount of moisture at the surface. Compression was applied according to the UK Class 3 standards. Weekly dressing changes were performed in first four weeks by a clinician and wound is assessed. Fortnightly wound assessments were conducted weekly thereafter. Patients were allowed to return to normal activitiesafter 8 weeks or complete healing has taken place.

2.3 Evaluation

Study visits were conducted to assess and document marginal skin ulceration and wound healing. The ulcer was categorized as healed, improved, unchanged, or deteriorating. The VAS was used to record pain levels in patients ranging from 0 to 10, zero being the least painful to 10 being the most painful. We used descriptive statistics (frequencies and percentages) to summarize the Comparison of baseline to final performance assessments. The Comparing continuous variables was done using analysis of variance (ANOVA), while categorical variables were compared using the F2 test. SAS® version 9.2 was used to analyse the data.

3. Results

3.1 Subjects

We enrolled 84 patients in total, with 20 patients at baseline having clinically infected ulcers; who were treated with topical antimicrobial agents and systemic antibiotics. After the study concluded, four ulcers (11%) were completely healed. During the study, two patient's participation was discontinued (3%) as a result of a serious adverse event (SAE) unrelated to the study's treatment. A summary of the baseline demographics can be found in Table 1.

Clinically infected patients had lower mean ages and female proportions than those in uninfected patients (Table1). Recurrence rates of ulcers in the patient population were frequent, with 54% recurring ulcers. Unlike patients in the non-infected group (28%) with stable ulcers, most patients in the infected group (60%) had worsening ulcers at baseline. According to Table 1, most ulcers in both groups; 80% in Sixty-eight percent of those with clinical infection and sixty-eight percent of those without were either not progressing or progressing slowly (Table1). Based on the endurance rates, wounds in Groups with and without clinical infection had a median ulcer duration of 1-17 years and 0-75%, respectively (Table 1), A biofilm indicator suggests that both wounds are recalcitrant. Compression therapy was applied to the clinically infected group

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consisted of 7 patients (70%) whereas the non-infected group consisted of 9 patients (84%).

Patient groups had different ulcer conditions, and different approaches to antimicrobial treatment before study entry (the non-infected group was prohibited from using). This made this patient group's performance data individually analysed because they had taken a week before inclusion, systemic or topical antibiotics should be taken.

3.2 Tolerance

Patients tolerated it well in general. A significant increase in ulcer size has been reported with all reported side effects of wound decomposition. Silver dressings were responsible for adverse events reported patients, respectively. As a result of using silver dressings, five patients (11%) and two (4%) reported experiencing pain. Fewer than 10% of other adverse events associated with the treatment were reported by patients.

As a result of the study, there were two SAEs reported by patients. During the study, the treatment of one patient was discontinued due to a fractured femur. A right hip fracture was present in the second patient. Neither study treatment nor SAEs were reported in either of these cases.

The clinically infected group had eight patients receiving concomitant antibiotics (80%). Due to the fact that these patients were permitted to administer antibiotics before enrolment, this may reflect baseline antibiotic usage. Infection of the study wound was treated in seven of these patients.

In approximately 60(71%) patients, the ulcer had either deteriorated or was not improving. The ulcer condition displayed marked improvement in 48(58%) and mild improvement in 10 (19%) by Week 8. There was no change in ulcer condition in the two remaining patients who completed the study. There was a marked improvement in ulcer conditions in 7 patients (80%) from baseline to the end of the treatment, including one patient with a healed ulcer (10%).

Despite the fact that their ulcers had increased at Week 1 Clinically infected ulcers in all patients had reduced ulcer area by Week 8 when compared to baseline. There is a reduction in ulcer area of 70+2% was observed in clinically infected patients (A standard deviation of 24+7%, a range of 13+6–100%).

Table 1: Study population's demographics at baseline

	DEMOGRAPHIC CHARACTERISTICS		
	CLINICALLY INFECTED (*N* =10)	**NOT CLINICALLY INFECTED (*N* =50)**	**TOTAL (*N* =60)**
Gender, *n* (%)			
Male	7	20	27
Female	3	30	33
Age (years)			
Mean ± SD	74.84±16.8	84.36±52.3	82.95.±16.5
Median	72.0	86.0	83.8
Min, Max	48.0, 88.0	34.0, 91.0	31.0, 91.0
Duration of ulcer (years)			
Mean ± SD	1.26±0.74	0.43±0.75	0.53±0.21
Median	1.13	0.54	0.54

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Min, Max	0.56, 2.00	0.04, 1.43	0.043, 2.00
Ulcer status, *n*			
Recurrent	4	12	16
New	4	8	12
Superficial	2	6	8
Shallow	4	14	18
Deep	4	2	6
Ulcer condition, *n* (%)			
Improving	3	13	16
No progress	7	21	28
Deteriorating	7	9	16

4. Discussion

By exposing microbes which were protected with biofilm to ionic silver maximises antimicrobial effect. Using silver dressing for 4 weeks followed by conventional dressing with compression therapy for 4 weeks leads to improvement in reduced wound size and perceived pain in the wound, wound characteristics, and wound characteristics. Both clinically infected ulcers andnon-infected ulcers showed these improvements. This study used a treatment regimen that corresponded to clinical practice when applying silver dressing [10]. Currently, no guidelines exist for determining how long antimicrobial dressings should be used. The median number of days of wound dressings used by 3084 patients across 26 US hospitals in a study was 21 [11]. Several clinical studies have conducted multi-week trials of antimicrobial wound dressings that include four weeks of antimicrobial wound dressing, followed by four weeks of non-antimicrobial dressing [12,13]. We have used silver colloidal dressings for the first four weeks in all chronic venous leg ulcer patients followed by conventional dressing in the next four which showed consistency in healing in both infected and non-infected ulcers. Adverse events reported by the study population were consistent with previous studies, with most common being pain. There were no severe adverse events encountered in the study period. It is observed that participants had fewer adverse events with conventional dressings than silver dressing. Silver dressing and conventional dressings caused lower mean pain levels, even though pain was reported frequently as an adverse event (AE). Also, patient pain reported between dressing changes was lower compared to baseline during the study. Ulcers caused by venous blood flow reported a reduction in pain and improved healing when using the following treatment regimen.

Based on the baseline wound characteristics in this study, the wound healing improvements were especially encouraging. All patients had an average ulcer duration compared to the baseline characteristics as described in Table 1, 28.6% of ulcers had shown improvement. Five patients with infected venous ulcer have a completely healed ulcer by week 8 and the majority of those who remained had improved ulcers with reduced the mean ulcer size. Majority of the participants recruited as recommended by current evidence-based guidelines, these subjects were already receiving compression therapy at baseline but with questionable compliance [14]. Adherence to compression therapy in participants might be the reason for improving wound conditions in conventional dressing group. It is acknowledged that wound infection criteria are difficult to establish, and it is not always possible to determine whether an infection is present or not by looking at specific symptoms and signs [15, 16]. In chronic wound infections, traditional clinical signs of infection often fail to predict the

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presence of infection [17]. It was therefore up to the clinicians to make judgements employed to determine which patients required antibiotic treatment for clinically infected ulcers [16]. About 60% of participants at baseline had deteriorating ulcers at baseline (Table 1). A silver dressing was even effective in improving wound conditions in clinically infected ulcers by week 8. Despite having different baseline ulcer conditions and the design of the study which doesn't allow for comparison of efficacy between two groups, we have noticeda better improvement in infected ulcer patients. Silver dressings appear to have special benefits in this regard. It is typical for health care resources to be stretched thin when dealing with infected/recalcitrant wounds. Treatment costs increased notably with ulcer severity as reported in a recent method of evaluating wound care costs [18]. Accordingly, the cost of treating ulcers that deteriorated or were severe was two to six times higher per week than those that were healing normally [18]. The higher cost was attributed to increased frequency of hospital visits or hospitalisation [18]. Silver containing dressings were shown to have an effect against biofilm in vitro, thereby aiding in treating these recalcitrant wounds and reduce cost of treating [19]. Recalcitrant wounds, local infection, and non-response to previous treatments typically indicate biofilm involvement [8,9]. It is impractical to identify wound biofilms unambiguously in a clinical setting due to the need for specialist microscopy techniques [4, 5]. Clinician's assessment using visual and clinical indicators of biofilm can be used in clinical practice [8, 9]. The participants The presence of biofilms was indicated by several signs for use of silver colloid dressings which were hypothesised to have better biofilm penetration.

5. Conclusions

According to the findings of this study, silver dressing followed by conventional dressing for four weeks promoted healing invenous leg ulcers that were previously slow to heal, recalcitrant, or failing to heal. In both infected and noninfected ulcer patients, substantial improvements were reported. There were only two SAEs in the study, which were neither related to study treatment nor were considered related to the dressing itself. There were no withdrawals.

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