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The Influence of Dressings on Venous Ulcer Healing — A Randomised Trial

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Objective: *To assess the effect of different dressings on venous ulcer healing.*
Design: *A randomised clinical trial.*
Materials: *Patients were randomised to treatment with one of three dressings: a zinc oxide impregnated bandage, a zinc oxide impregnated stockingette, or an alginate dressing. All patients were treated as outpatients and had compression bandaging with two minimal stretch bandages (Elastocrepe) and a stockingette (Tubigrip) to keep the bandages in place.*
Methods: *One hundred and thirteen patients (133 ulcerated limbs) with chronic ulceration of the leg due to venous disease alone, and attending Fremantle Hospital Leg Ulcer Clinic, Western Australia were entered into the study. Healing was measured as complete healing of the ulcerated limb or failure of the limb to heal within 9 months.*
Results: *There was no significant difference between the three groups in ulcer size, duration, and other parameters compared. Healing was affected significantly by ulcer size and which leg was ulcerated. There was significantly faster healing with the paste bandage.*
Conclusion: *The use of a paste bandage significantly improved the healing of chronic venous ulcers when used in combination with compression bandaging, and compared to an alginate dressing and a zinc oxide impregnated stockingette.*

Key Words: Randomised controlled trial; Venous ulcer; Wound dressing.

Introduction

Chronic venous ulceration is a difficult clinical problem that consumes a large amount of resources. These resources include medical and nursing time as well as cleansing solutions, other topical applications, dressing products, bandages and elastic stockings. The treatment of these patients is spread across many areas of health care[1] and the costs have been estimated at between 1.1% and 1.3% of the total health care budget in several European communities.[2]

The treatments used for leg ulcers today differ little from those that have been used for centuries. In spite of the large amounts of money expended on treating these ulcers, there has been little research that actively reflects the effectiveness of the treatments. Many published studies are unable to provide firm conclusions on methods for improving venous ulcer healing. The reasons that most frequently accounts for this are treating ulcerated limbs with more than one aetiology,[3,4] using different bandaging regimens in the different dressing groups that are compared,[5,6] using inadequate measures of healing such as reduction in size at a given time interval,[7–10] using inadequate sample sizes[11] or having no control group.[12] The only effective measure of treating outpatients with dressings is total healing of the ulcerated limb.[13,14] These deficiencies have been part of the reason for the lack of new effective methods for improving the healing of chronic venous ulcers.

In our Leg Ulcer Clinic the standard method of dressing leg ulcers has been to employ a paste bandage (Viscopaste, Smith & Nephew) and minimal stretch bandages (Elastocrepe, Smith & Nephew). The paste bandage has the disadvantage of being an expensive dressing and being time consuming to apply. In this study we compared three different dressings under the same bandages, to see if we could improve the time to healing of the ulcerated limbs using dressings that were easier to apply. In addition we assessed the specific factors that influenced the time to healing.

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Methods

This was a prospective randomised trial. The dressings employed were a zinc oxide impregnated paste bandage (Viscopaste, Smith & Nephew) a zinc oxide impregnated stockingette (Acoband, Auspharm), and a calcium alginate fibre dressing (Kaltostat, Faulding Pharmaceuticals). The zinc oxide stockingette was chosen because it contained zinc but did not have the same non-stretch bandage characteristics present in the paste bandage and would allow a comparison with that dressing. Kaltostat was chosen because of its ease of application and also it has been considered to be an "interactive" dressing that might directly influence wound healing.[15]

For this study only patients with proven venous ulceration were considered. A full history of ulceration was taken and a careful examination was performed. The patient characteristics recorded were: age, sex, duration of the current ulcer, number of ulcer episodes on the affected limb, the time since the first ulcer on the affected limb, the longest time with an unhealed ulcer, the side of the ulcerated limb and the total area of ulceration on the affected limb. Investigations performed to determine the aetiology of ulceration were: a full blood picture and ESR, urea and electrolytes, liver function tests, blood sugar, rheumatoid factors, resting ankle brachial Doppler arterial pressure index (normal >0.90), and venous refilling on photoplethysmography (PPG) (<25 s is abnormal in our laboratory[16]). The venous abnormality was defined as superficial if the refilling time on PPG returned to normal with an above-knee or below-knee tourniquet. If the refilling time did not return to normal with a tourniquet, the venous abnormality was considered to be due to either deep venous disease or communicating vein incompetence.[17]

For the purposes of this study only ulcers with a minimum diameter of 0.5cm and a maximum diameter of 10cm, in the longest diameter, were included. Patients with evidence of diabetes, rheumatoid arthritis, arterial disease or any other possible contributing factor to the ulceration were excluded. Patients who had evidence of cellulitis at the time of randomisation were also excluded from this study.

Treatment was performed on an outpatient basis in a specialised Leg Ulcer Clinic. The leg and foot were washed in a soap-water bath and any loose debris was debrided from the surface of the ulcer. Viscopaste was applied in a spiral fashion from the base of the toes to just below the knee, Acoband was applied from the base of the toes to just below the knee, and Kaltostat was applied only over the ulcer itself and was moistened with saline at the time of application. Over each of these dressings two Elastocrepe bandages (Smith & Nephew) were applied from the base of the toes to just below the knee and a Tubigrip stockingette (Seton) was placed over the bandages to keep them in place. The dressings were changed once weekly. However, in the very early stages, if there was excessive exudate, the dressings were changed twice and, on some occasions, three times a week. Once the exudate had subsided they reverted to weekly dressings.

Patients were considered withdrawals from the study if the dressings had to be discontinued for reasons other than failure of the ulcer to heal. These causes of withdrawal included allergy to the dressings, excessive pain with the application of the dressing, the development of cellulitis in the leg, or if the patient had some medical or personal reason which prevented them from continuing with the dressings. Data up to the point of withdrawal were included in the final analysis.

Dressings were continued for 9 months or until the limbs had healed. Treatment was considered to have failed if the limb remained unhealed at 9 months, if there was marked deterioration of the ulcer with a rapid increase in size such that outpatient treatment could no longer be justified, or if over any 3 month period there was a failure of the ulcer to reduce in size. These patients were then considered for admission to hospital, bed rest and preparation for skin grafting.

The pressures exerted under the bandages and dressings were measured using a Medical Stocking Tester (Salzman, St Gallen) with the patients both lying and standing. These pressures were assessed for eight patients in each group, with sub-bandage pressures being recorded at three sites: 2.5cm above the medial malleolus (P1), mid calf (P2), and upper calf (P3).

The characteristics of the three groups were assessed by Chi-squared analysis for sex, and Kruskal-Wallis one way analysis of variance for other characteristics. Pressures beneath bandages were analysed using Kruskal-Wallis one way analysis of variance for unpaired data, and Wilcoxon rank sum test for paired data. The time to healing was used as the dependent variable in a Cox regression analysis with the patient characteristics and the type of dressing considered as covariates.

The rate of reduction of ulcer size in cm^2 per week was calculated for each patient for the time that they were in the study. This included patients who healed, those who did not heal and those who were withdrawn. The rate of reduction in ulcer size was compared for each group using a one way analysis of

variance with post hoc Bonferroni test to assess differences between groups.

The sample size was assessed in order to provide an 80% chance of detecting a 15% difference between the groups at the 5% level of significance.

Results

A total of 113 patients with 133 ulcerated limbs were entered into the study. The median age was 73 years with a range of 31–92 years. There were 67 females and 46 males entered into this study. Forty-three ulcerated limbs were randomised to Viscopaste, 46 to Kaltostat and 44 to Acoband.

The characteristics of the patients in the three groups are shown in Table 1. The ulcer size data has been shown as both a mean and a median value, since other reports commonly use the mean value to represent the ulcer sizes of groups, however the median more accurately reflects the size of the ulcers in the study. There was no difference between the three treatment groups for any aspect of the ulcer history. This included duration of the current ulcer, the number of ulcer episodes on the affected limb, the time since the first episode of ulceration or the longest time that the patient had had an unhealed ulcer on the affected limb. There was a difference in the number of patients with superficial venous disease alone in the three treatment groups, with more limbs in the Kaltostat group (54%) having superficial venous disease compared to those treated with Viscopaste (33%) and Acoband (32%).

Table 1. Characteristics of the patients, history of ulceration and ulcer size in each group.

	Viscopaste	Acoband	Kaltostat	
Number of limbs	43	44	46	
Sex M:F	17:24	16:25	22:24	p=0.36
Age (years)				
Median	73	76	70.5	p=0.36
(Range)	(33–89)	(31–89)	(36–92)	
Ulcer size (cm^2)				
Mean	10.11	9.14	11.02	p=0.20
Median	3.60	2.94	4.57	
(Range)	(0.15–57.46)	(0.24–75.37)	(0.36–61.32)	
Duration of current ulcer (months)				
Median	6.00	6.00	4.00	p=0.87
(Range)	(0.25–192)	(0.25–5.04)	(0.25–2.64)	
Number of ulcer episodes				
Median	2.0	2.0	3.0	p=0.38
(Range)	(1–23)	(1–20)	(1–40)	
Longest time with unhealed ulcer (months)				
Median	8	7	6	p=0.75
(Range)	(0.25–192)	0.5–504	0.25–264	
PPG (Superficial c.f. deep or communicating vein)	14:29	14:30	25:21	p<0.05

Table 2. Pressures beneath different dressing treatments with patients supine and erect, immediately after applying dressing and bandages (Median values mm Hg).

		After application	
		Supine	Erect
Viscopaste	P1	23	39
	P2	35	42
	P3	31	43
Acoband	P1	42	44
	P2	48	57
	P3	44	45
Kaltostat	P1	28	40
	P2	36	48
	P3	27	43

P1=2.5cm above medial malleolus; P2=mid calf; P3=upper calf.

The pressures achieved under the different dressing methods are shown in Table 2. The pressures measured after application of the dressings were significantly lower in the supine compared to the erect position ($p < 0.01$ for each measurement site, Wilcoxon rank sum test). There was no difference between the three dressings in the erect position ($p > 0.05$ for each position, ANOVA). However, in the supine position there was a significant difference, and the highest pressures were recorded under Acoband and Elastocrepe ($p < 0.01$ for each position, ANOVA). Due to the fragile nature of the probes, it was not possible to leave these in place for 1 week to enable assessment of pressures during the whole period for which the dressings and bandages were applied.

A total of 21 limbs were withdrawn from the study for reasons unrelated to healing of the ulcer (Table 3). The number of patients with allergic reactions to each dressings were approximately the same. Three patients developed an intense, painful response to Kaltostat which ceased with removal of the Kaltostat. There was also one painful response with Viscopaste

Table 3. Results of all ulcerated limbs entered into the study.

	Viscopaste	Acoband	Kaltostat
Withdrawals			
Allergy	2	1	1
Pain	1	1	3
Cellulitis		1	3
Medical/Personal	2	3	3
Completed trial			
Unhealed at 9 months	3	3	1
Ulcer Deteriorated	1	9	9
Ulcer Healed	34	26	26
Total	43	44	46

and one with Acoband. Patients with cellulitis were withdrawn from the study and were admitted to hospital for treatment with intravenous antibiotics. The medical/personal reasons for withdrawal from the study included: admission to hospital with other medical problems (4), moving away from the city in which the study was performed (1), wrong dressing applied (2) and non-compliance with dressing (1). The patients who completed the trial therefore consisted of those who reached an end point of either healing, deterioration of ulceration requiring cessation of treatment or failure to heal with 9 months treatment.

Viscopaste was clearly the most acceptable single treatment with 37/43 (86%) patients able to continue until healing or for 9 months compared to 29/44 (66%) for Acoband and 27/46 (59%) for Kaltostat. (Chi-squared = 8.43, $p < 0.05$).

The influence on the time to healing of the patient variables and the different dressings are shown in Table 4. This clearly demonstrates that the type of dressing used, the initial size of the ulcer, and the side of the ulcerated limb all had a significant influence on the time to complete healing. Other parameters such as duration of the ulcer, the number of ulcer episodes, and the state of the deep veins did not have a significant impact on healing.

The relative risks of healing for the limbs treated with Viscopaste compared with all limbs in the study, the limbs with smaller ulcers compared to larger ulcers (half ulcer area) and ulceration in the right leg compared to the left leg are shown in Table 5. These relative risks indicate that these limbs are 1.67, 1.96 and 1.34 times more likely to heal. A life table showing the times to healing for the three different dressings is shown in Fig. 1 and clearly indicates the more rapid time to total limb healing seen in those patients treated with Viscopaste.

The mean rate of reduction in ulcer size for each group was 0.83cm^2/week (C.I. 0.52–1.14) for Viscopaste, 0.53cm^2/week (C.I. 0.17–0.89) for Acoband, and 0.02cm^2/week (C.I. –0.45–0.50) for Kaltostat. There was a significant difference in the rate of reduction in ulcer size for the groups ($p < 0.05$). The post hoc Bonferroni test indicated a significant difference between the Viscopaste and Kaltostat treated groups ($p < 0.05$), with no significant differences between other groups.

Table 4. Results of Cox regression analysis of influence of different variables on time to total limb healing.

	Coefficient	S.E.	p-Value
Sex	–0.1752	0.1174	0.14
Age	–0.001	0.0086	0.92
Ulcer size	–0.0336	0.0102	0.001
Ulcer duration	0.0013	0.0068	0.85
Number of ulcer episodes	0.0239	0.0231	0.30
Longest time with unhealed ulcer	–0.0032	0.0053	0.54
Time since first ulcer	–0.0013	0.001	0.07
PPG (Deep venous abn)	–0.2664	0.2377	0.26
Limb	0.2582	0.1109	0.02
Dressing			
Viscopaste	0.5156	0.1605	0.001
Acoband	–0.2678	0.1637	0.10
Kaltostat	–0.2478	0.1761	0.16

Table 5. Odds ratio and confidence intervals for dressing, ulcer size and limb.

		95% Confidence Intervals	
	Relative risk	Lower	Upper
Viscopaste	1.67	1.24	2.24
Size (half ulcer area)	1.96	1.55	2.47
Limb (Right leg)	1.34	1.08	1.66

Discussion

This study clearly demonstrated that there was improved healing when a zinc oxide impregnated paste bandage was used under compression bandaging compared to the use of zinc oxide impregnated stockingette or a local alginate fibre dressing. This study evaluated healing as total healing of the limb, which is the only effective measure for evaluating treatments proposed as clinical treatment for venous ulcers.

The rate of reduction in ulcer size did not clearly identify differences between the treatment groups that were more apparent when complete healing was assessed by Cox regression analysis. Analysis of complete healing identified Viscopaste treatment as a significant factor influencing the time to healing. However, analysis of the rate of reduction in ulcer size identified that the Viscopaste treated group healed faster than the Kaltostat group, but not the Acoband group. Clearly the measurement of time to healing allows multivariate analysis which may permit a more accurate determination of the effects of different treatments when considered in combination with other factors that influence ulcer healing. Assessment of rate of reduction in ulcer size does give some indication of differences between treatments, however, this evaluation is not as sensitive as multivariate analysis.

Clearly the topical zinc oxide did not directly influence ulcer healing when compared to an alginate dressing. Zinc oxide was present in both the zinc oxide

impregnated stockingette and the paste bandage, and the healing of the patients treated with the stockingette was slower than for a paste bandage, but no different to that of a locally applied dressing.

The major difference would seem to be in the extra bandaging that the paste bandage employs. The paste bandage consists of a zinc oxide impregnated non-stretch cotton bandage which differs from the Acoband, which is zinc oxide impregnated stockingette. The sub-bandage pressures measured in the supine position were higher with Acoband which has some elasticity. However, there was no difference in the pressures measured in the erect position. The limitations of the measuring device prevented assessment of pressures at the times when they are most likely to be different — throughout the week of application and during exercise. The implication of this study would be that on exercise the non-stretch bandage of Viscopaste imparts some added improvement in venous return in addition to that achieved by the compression bandaging.

The times to healing using the zinc oxide bandage and compression bandaging were equivalent to those reported for the four layer system,[16] with 64% of ulcers in this group healed at 12 weeks. The ulcers were also of a similar size when the mean values are compared. This is not a good descriptive statistic for ulcer size even though it has been used in many previous studies. Median area is a much better indicator of ulcer size in these patients.

Further, from this study it is apparent that no single dressing is suitable in all patients. There are specific reasons why different dressings may not be used in individual patients. These are related mainly to allergy, pain caused by application of the dressing, and a failure of the ulcer to begin to heal. In this study, the single dressing that was most acceptable once applied to the patients was the paste bandage.

Many factors were considered in the analysis of this study, and we found that only ulcer size, ulceration on the right leg and the use of a paste bandage, had a significant impact on the time to healing of venous ulcers. Factors such as duration of ulceration, other features of the ulcer history, sex and age of the patient had no effect on the healing. This is in contrast to a previously reported study which suggested that ulcer duration, age of the patient and the extent of venous disease on PPG are significant factors in predicting the time to ulcer healing.[18] This difference may have occurred because the number of ulcerated limbs assessed in this study was smaller than that in the previously reported study (133 in this study compared to 200[18]), because of differences in the dressings and bandages used (Elastocrepe bandages and dressings in this study compared to Elastic stockings or double Tubigrip with local dressings[18]), or because of the duration of the study period (9 months in this study compared to 4 months[18]). The influence of factors such as age, ulcer duration and the extent of the venous disease may therefore only be significant predictors of ulcer healing when less effective methods of compression or less accurate data on the time to ulcer healing

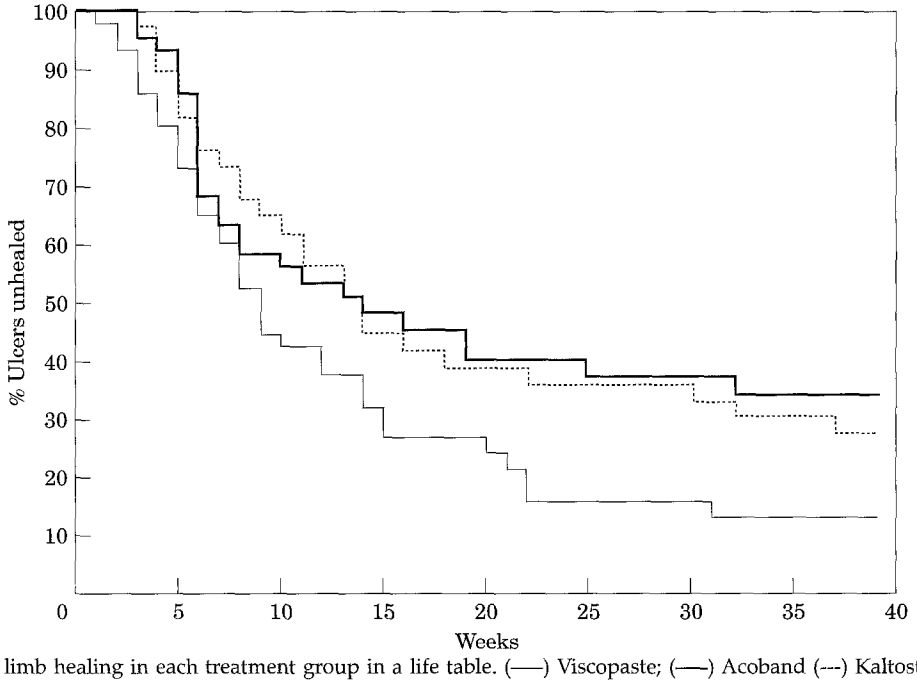

Fig. 1. Time to total limb healing in each treatment group in a life table. (——) Viscopaste; (——) Acoband (---) Kaltostat.

are used in the study design. These factors may not be significant when optimal compression and measures of healing are used.

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