A New Powder Dressing for Management of Chronic Venous Ulcers

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BACKGROUND A new powder dressing (TPD) is a methacrylate-based powder formulation that transforms in situ into a shape-retentive matrix upon hydration to create optimum moist wound healing conditions. The following randomized, controlled, clinical study aimed to evaluate the role of TPD in the management of chronic venous ulcers (CVU).

METHODS The randomized controlled prospective study enrolled 60 CVU patients. After randomization, patients in the treatment group (n = 30) were treated with TPD, whereas those in the control group (n = 30) received conventional compression dressing therapy.

RESULTS After treatment, patients in the TPD group had significantly higher rates of complete ulcer healing at 12 weeks (43.3% vs 10.0%, p = .004) and 24 weeks (86.7% vs 40.0%, p = .001) when compared with conventional dressing group. Moreover, patients in the TP dressing group had significantly shorter time to complete ulcer healing [mean (95% CI): 16.7 (14.1–19.3) versus 37.0 (30.8–43.2) weeks, p = .001]. In addition, patients in the TPD group had significantly fewer number of dressings, less severe pain after dressing, and lower need for systemic analgesics.

CONCLUSION Use of TPD in management of CVUs was associated with significantly higher healing rates, shorter duration to healing, and lower pain.

Chronic venous ulcers (CVUs) are common lesions affecting more than 1.0% of the general population and over 4% of the elderly with significant negative impact on quality of life. Management expenditures account for ~1% of healthcare budgets in many Western countries.[1–3]

The underlying pathogenesis entails a complex interplay between venous hypertension, impaired microcirculation, altered cellular function, and activation of local inflammatory mediators, ultimately resulting in chronic venous insufficiency and ulcer formation.[4,5]

Management of CVUs is challenging. Compression bandages and wound management are the mainstay of CVUs treatment,[6] Investigated pharmacological adjuncts include pentoxifylline,[7] papain gel,[8] and sevoflurane[9]. In some patients, surgical interventions including superficial vein reflux eradication[10] and mechanochemical and thermal ablation[11] have also been used.

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However, management of CVUs notably lacks clinical evidence derived from randomized clinical trials.[12,13] Moreover, different clinical guidelines lack consensus regarding the recommended interventions.[14,15] This makes pursuit of new modalities for CVUs management a vital clinical and economic priority.

Transforming powder dressing (TPD) is a methacrylate-based formulation that transforms in situ into a shape-retentive matrix upon hydration, creating optimum conditions for moist wound healing. The powder is a polymer mixture of poly-2-hydroxy-ethyl-methacrylate (84.8%), poly-2-hydroxy-propyl-methacrylate (14.9%), and sodium deoxycholate (0.3%). This technology has been successfully used in management of soft tissue wounds of variable etiologies, including diabetic foot wounds after debridements for necrotizing fasciitis,[16] partial-thickness skin graft donor sites in burn patients[17] and other lower leg wounds.[18]

The present randomized controlled study evaluated the role of TPD (Altrazeal, ULURU Inc., Addison, TX) in management of CVU.

Patients and Methods

The randomized controlled prospective study was conducted at Helwan University Hospitals, Cairo, Egypt and other private hospitals. The study protocol was approved by the local ethical committee of Helwan Faculty of Medicine and all patients gave informed consent before enrollment. The study was registered at clinicaltrials.gov (NCT04793074).

Patients were diagnosed on the basis of clinical findings and vascular Doppler ultrasonography. Exclusion criteria included associated infections and ulcers of other etiologies.

TABLE 1. Comparison Between the Studied Groups Regarding Baseline Characteristics

	TP Dressing $N = 30$	Standard Dressing $N = 30$	p
Age (yr), mean ± SD	53.5 ± 9.0	50.1 ± 8.6	.14
Male/female, *n*	20/10	22/8	.57
BMI (kg/m^2), mean ± SD	30.7 ± 2.8	29.6 ± 3.2	.16
Comorbidities, *n* (%)			
Diabetes	20 (66.7)	19 (63.3)	.79
CHD	8 (26.7)	6 (20.0)	.54
Hypertension	17 (56.7)	14 (46.7)	.44
COPD	3 (10.0)	2 (6.7)	.64
CVD	4 (13.3)	2 (6.7)	.39
Ulcer site, *n* (%)			
Left foot	10 (33.3)	5 (16.7)	.56
Left hand	3 (10.0)	3 (10.0)	
Left leg	10 (33.3)	10 (33.3)	
Right foot	2 (6.7)	3 (10.0)	
Right leg	5 (16.7)	9 (30.0)	
Ulcer size (cm^2), mean ± SD	20.7 ± 6.9	19.3 ± 6.2	.41
Ulcer duration (mo), mean ± SD	30.0 ± 14.0	32.4 ± 12.8	.48
Baseline pain (VAS), mean ± SD	4.5 ± 1.5	4.6 ± 1.4	.73

BMI, body mass index; CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; CVD, cerebrovascular disease; TPD, transforming powder dressing; VAS, Visual analog scale.

Simple equal randomization of subjects across the 2 groups was conducted using computer generated numbers and sealed envelopes. Randomization and allocation of subjects to the 2 study groups were performed by an independent blinded researcher.

Recruited patients underwent thorough clinical examinations, standard laboratory investigations, and vascular ultrasound assessments. Demographic data (age, sex and body mass index), associated comorbidities, ulcer duration and size, and history of previous interventions were recorded for all subjects.

After randomization, subjects in the treatment group ($n = 30$) were treated with TPD every 5/6 days, whereas those in the control group ($n = 30$) received daily conventional compression dressings. In both groups, the ulcers were thoroughly cleaned before application of the respective dressings. In the treatment group, a thin layer of TPD powder was applied to the ulcer surface and hydrated with saline. Any excess powder was removed from the ulcer. A secondary protective gauze dressing was applied (Figure 1). In the control group, a compression dressing was used. No compression dressing was applied in the TPD group. Ulcer pain was assessed at baseline using the visual analog scale (VAS) with 0 meaning no pain and 10 indicating maximal experienced pain. Patients were followed until complete healing or until the end of the study with a minimum follow-

TABLE 2. Comparison Between the Studied Groups Regarding Treatment Outcome

	TP Dressing $N = 30$	Standard Dressing $N = 30$	p
Complete ulcer healing at 12 weeks, *n* (%)	13 (43.3)	3 (10.0)	.004
Complete ulcer healing at 24 weeks, *n* (%)	26 (86.7)	12 (40.0)	<.001
Time to complete healing (wk), mean (95% CI)	16.7 (14.1–19.3)	37.0 (30.8–43.2)	<.001
Dressings mean ± SD	23.9 ± 9.7	196.0 ± 85.5	<.001
Postdressing pain (VAS), mean ± SD	1.4 ± 1.1	2.9 ± 1.3	<.001
Need for analgesics, *n* (%)	2 (6.7)	11 (36.7)	.005
Recurrence, *n* (%)	—	—	—

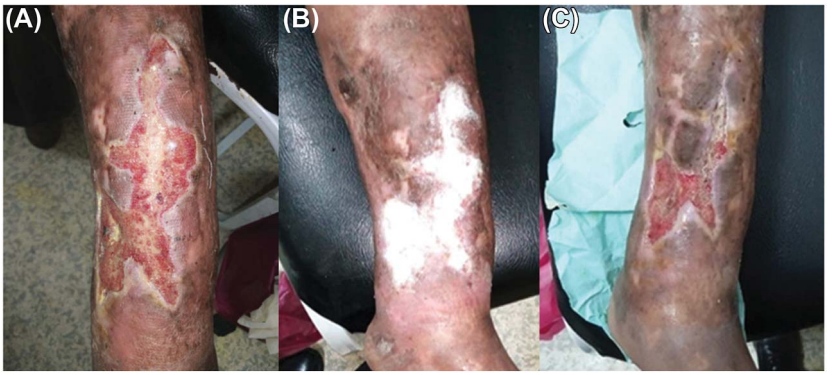

Figure 1. (A) Extent of ulcer before TPD application (B), TPD application, and (C) extent of ulcer 2 months after application of TPD. TPD, transforming powder dressing.

up duration of 24 weeks. None of the studied patients was lost to follow-up.

The primary study outcome was complete ulcer healing at 12 and 24 weeks and time to complete ulcer healing. Healing was considered complete when cutaneous integrity was re-established. Other outcome parameters included number of required dressings, postdressing pain assessed by VAS, need for analgesics, and ulcer recurrence.

Data obtained from the study were presented as numbers and percentages for categorical data and mean ± SD for numerical data. Categorical data were compared using Fisher exact test or chi–square test as appropriate and the numerical data were compared using t-tests. Kaplan–Meier survival analysis with log-rank comparison was used to compare the time to healing between the 2 groups. Results were declared statistically significant if *p*-values were less than 0.05. All statistical calculations were processed using SPSS 26.0 (IBM, Chicago, IL).

Results

The present study included 60 patients with CVUs. They were equally randomized to receive TPD or conventional dressings. Comparison between the studied groups regarding the baseline characteristics revealed no significant differences (Table 1).

After treatment, patients in the TPD group had significantly higher rates of complete ulcer healing at 12 weeks (43.3% vs 10.0%, $p = .004$) and 24 weeks (86.7% vs 40.0%, $p < .001$) when compared with conventional dressing group (Table 1). Moreover, patients in the TP dressing group had significantly shorter time to complete ulcer healing [mean (95% CI): 16.7 (14.1–19.3) versus 37.0 (30.8–43.2) weeks, $p < .001$] (Table 2, Figure 2). In addition, patients in the TP dressing group had significantly fewer number of dressings (23.9 ± 9.7 vs 196.0 ± 85.5, $p < .001$), less severe pain after dressing (1.4 ± 1.1 vs 2.9 ± 1.3, $p < .001$), and lower need for systemic analgesics (6.7% vs 36.7%, $p = .005$) (Table 2). No ulcer recurrence was noted in the studied groups.

Comparison between the studied groups categorized according to different clinical variables showed significantly shorter time to complete healing in almost all categories (Table 3).

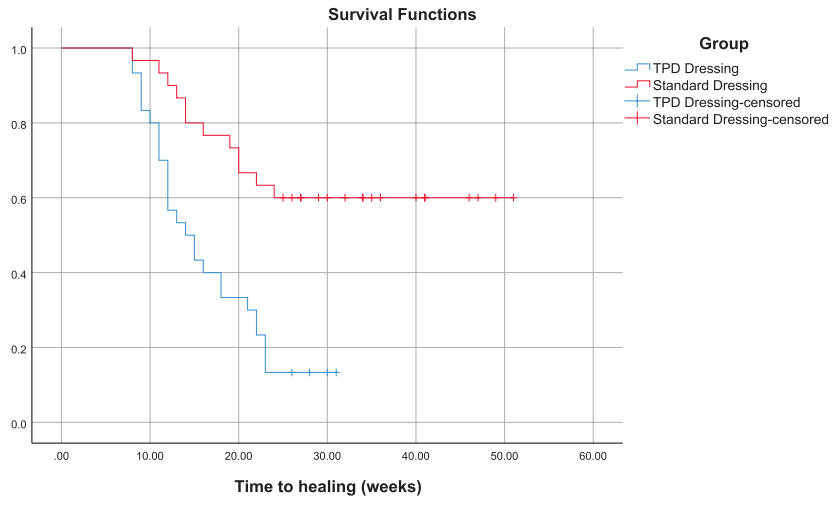

Figure 2. Time to healing in the studied patients.

TABLE 3. Relation Between Clinical Data and Time to Healing in the Studied Groups

	Time to Healing (wk)		
	TP Dressing	Standard Dressing	*p*
Age			
≥Mean	17.6 ± 7.4	28.5 ± 9.6	<.001
<Mean	14.7 ± 5.9	27.8 ± 13.8	<.001
p Value	0.27	0.88	
Sex			
Male	15.2 ± 6.2	28.2 ± 11.3	<.001
Female	18.8 ± 8.0	27.9 ± 15.3	<.001
p Value	0.18	0.95	
BMI (kg/m^2)			
≥Mean	17.8 ± 7.9	29.5 ± 13.4	<.001
<Mean	14.3 ± 4.7	27.1 ± 11.6	<.001
p Value	0.14	0.6	
Diabetes			
+ve	17.1 ± 6.7	31.5 ± 12.2	<.001
−ve	15.0 ± 7.6	22.2 ± 10.3	<.001
p Value	0.44	0.041	
CHD			
+ve	18.3 ± 8.0	31.3 ± 12.6	<.001
−ve	15.7 ± 6.5	27.3 ± 12.3	<.001
p Value	0.39	0.48	
Hypertension			
+ve	14.5 ± 5.5	26.9 ± 12.7	<.001
−ve	18.9 ± 7.9	29.1 ± 12.1	<.001
p Value	0.08	0.63	
COPD			
+ve	14.3 ± 7.8	33.0 ± 4.2	<.001
−ve	16.6 ± 6.9	27.8 ± 12.6	<.001
p Value	0.59	0.57	
CVD			
+ve	18.0 ± 9.2	16.0 ± 5.7	.8
−ve	16.2 ± 6.7	29.0 ± 12.1	<.001
p Value	0.63	0.15	
Ulcer duration (mo)			
≥Mean	16.7 ± 6.7	33.7 ± 10.6	<.001
<Mean	16.2 ± 7.2	22.5 ± 11.4	<.001
p Value	0.84	0.01	
Ulcer size (cm^2)			
≥Mean	19.7 ± 7.7	31.7 ± 13.3	<.001
<Mean	13.1 ± 4.0	24.9 ± 10.6	<.001
p Value	0.007	0.13	

Discussion

The present study demonstrated significantly higher healing rates and shorter times to healing in CVU patients treated with TPD in comparison to conventional dressing. To the best of our knowledge, this is the first randomized study to assess value of TPD in management of CVUs.

Our findings are in line with conclusions of previous reports using TPD as a sole or adjuvant wound healing agent. Smith and Konnikov[19] reported the outcome of treating difficult postsurgical wound in a 94-year-old patient subjected to Mohs surgery for skin cancer of the central scalp vertex. Surgery resulted in a sizable 4.6- × 4.6-

cm defect. Applying TPD resulted in complete healing of the wound with excellent cosmetic appearance after 2 months of treatment.

Similar results were identified by another report documenting the outcome of TPD application in another 2 skin cancer patients with significant postsurgical wounds.[18] In another report, TPD was used as an adjuvant for treatment of a wound resulting from treatment of hardware infection after osteosynthesis of the lower leg. TPD used after application of negative pressure wound therapy resulted in wound filling with granulation tissue.[20]

The wound healing capabilities of TPD are essentially credited to 2 main factors: first, generous wound oxygenation assisted by the highly porous dressing created by the polymer particles, and second: the disinfected wound environment. The polymer micropores constitute a mechanical barrier against invasion by exogenous micro-organisms.[16]

Interestingly, our study noted a significant reduction in ulcer pain experienced by patients after application of TPD as compared to the control group. The pain-relieving effect of TPD was also reported by Assadian and colleagues,[17] randomized study that used transforming powder for healing of split-thickness skin graft donor sites. This marvelous effect is probably attributed to reduced inflammation, inhibition of substance *p* release, and plentiful wound moisture.[16,21]

As noted by our study, patients subjected to TPD had significantly lower frequency of dressings and subsequently lower frequency of follow-up visits. Even if the relatively high cost of TPD is considered, it can be regarded as a cost-effective option keeping in mind the costs of the lengthy healing process with conventional dressing.

In conclusion, the present randomized study noted use of TPD in management of CVUs was associated with significantly higher healing rates, shorter duration to healing, and less severe pain.

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