

Evaluation of a Collagen-Alginate Wound Dressing in the Management of Diabetic Foot Ulcers

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Abstract

Efficacy and safety of a collagen-alginate topical wound dressing (FIBRACOL Collagen-Alginate Wound Dressing) in the treatment of diabetic foot ulcers was compared with that of regular gauze moistened with normal saline. Seventy-five patients with foot ulcers were assigned randomly in a 2:1 ratio to the collagen-alginate test dressing or the gauze dressing. At the end of the study, the mean percent reduction of the wound area was $80.6\% \pm 6\%$ in the collagen-alginate dressing group and $61.1\% \pm 26\%$ in the gauze dressing group ($p = .4692$). Thirty-nine (78%) patients treated with the collagen-alginate dressing achieved $\geq 75\%$ wound area reduction, compared with 15 (60%) of gauze-treated patients. Complete healing was achieved in 24 (48%) of the collagen-alginate dressing group and 9 (36%) of the gauze dressing group.

Wound size, when averaged over the 8-week period and with the duration of the ulcer taken into account, was reduced significantly in the collagen-alginate dressing group, as compared with the gauze dressing group ($df = 1$, $p = .0049$). It is concluded that the collagen-alginate test dressing is as or more effective and safe as the currently used treatment.

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FOOT PROBLEMS RELATED TO DIABETES affect 15% to 20% of all diabetic patients and are the most common indication for hospitalization for these patients, with an annual health care cost of over \$1 billion.^{1,2} The two most common causes of foot problems are neuropathy and peripheral vascular disease, which tend to coexist in the majority of such patients.³

Standard treatment of foot ulcerations, as recommended by the American Diabetes Association, typically includes extensive debridement of necrotic tissue, frequent dressing changes, periods of nonweight-bearing of the affected extremity, and appropriate use of antibiotics when infection is present.⁴ In patients with nonhealing ulcerations due to ischemia, an arterial revascularization procedure also may be required.

In contrast, there is no current consensus regarding the optimal topical treatment for diabetic foot ulcerations. During the past 10 years, numerous topical treatment modalities have been developed to provide coverage and protection of the ulceration, prevent infection, and promote granulation of the wound. The current commercially avail-

able techniques and treatments include total contact casting, hyperbaric oxygen, topical antibiotics, antiseptic solutions, degradable dressings, enzymatic debriding agents, compound impregnated dressing materials, and growth factors.⁵⁻⁹

In a randomized open clinical trial, effectiveness, safety, and patient acceptability of a new wound dressing were evaluated. The dressing (FIBRACOL Collagen-Alginate Wound Dressing, Johnson & Johnson Medical, Arlington, TX) is a combination of collagen and calcium alginate. Collagen, the main component of skin and connective tissue, is believed to encourage wound healing by providing a framework for newly formed tissue; calcium alginate is believed to provide a moist wound interface.

Patients and methods

Seventy-five diabetic patients who were treated for foot ulcerations participated in this trial. The following inclusion criteria were used: at least 21 years of age; adequate nutritional intake, as indicated by a serum albumin of > 2.5 grams/dl; adequate blood flow to the lower ex-

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square or the Fisher's exact test was employed for categorical data. For continuous measurements, the conventional two-sample *t*-test was utilized; however, in cases in which the validity of this test was in question, a nonparametric test was used as an alternative procedure. The life-table (survival) approach and log-rank test statistics were used to analyze the rate of ulcer healing and time to healing. A multivariate analysis of repeated measures to assess the treatment effect on planimetry ulcer areas across nine time points (including the initial measure) was performed.

Results

Sixty-one of the original 75 (81%) enrolled patients completed the study; the percentage of patients in the collagen-alginate test dressing group (44 [88%]) who completed the study was higher than in the gauze dressing control group (17 [68%]), ($p < .05$). Fourteen patients (6 patients in the test dressing group and 8 patients in the gauze dressing group) did not complete the study. Five patients chose to withdraw from the study; 3 patients missed more than 2 consecutive weekly visits, and 6 patients experienced adverse events. No significant demographic differences were found between the two treatment groups (Table 1), and there were no significant differences between them with respect to baseline ulceration characteristics, such as ulcer duration (145 ± 73.4 days vs. 224 ± 104.4 days [mean \pm SE]), size (2.60 ± 0.5 cm² [range 0.6-20.4] vs. 2.99 ± 0.6 cm² [range 0.55-11.6]) or stage of ulceration in the collagen-alginate dressing group and the gauze dressing group, respectively (Table 2).

At the end of the study, the mean percentage reduction of the wound area was $80.6\% \pm 6\%$ in the collagen-alginate dressing group and $61.1\% \pm 26\%$ in the gauze dressing group ($p = .4692$)

Table 2
COMPARISONS OF THE ULCER CHARACTERISTICS
BETWEEN THE TWO GROUPS AT BASELINE

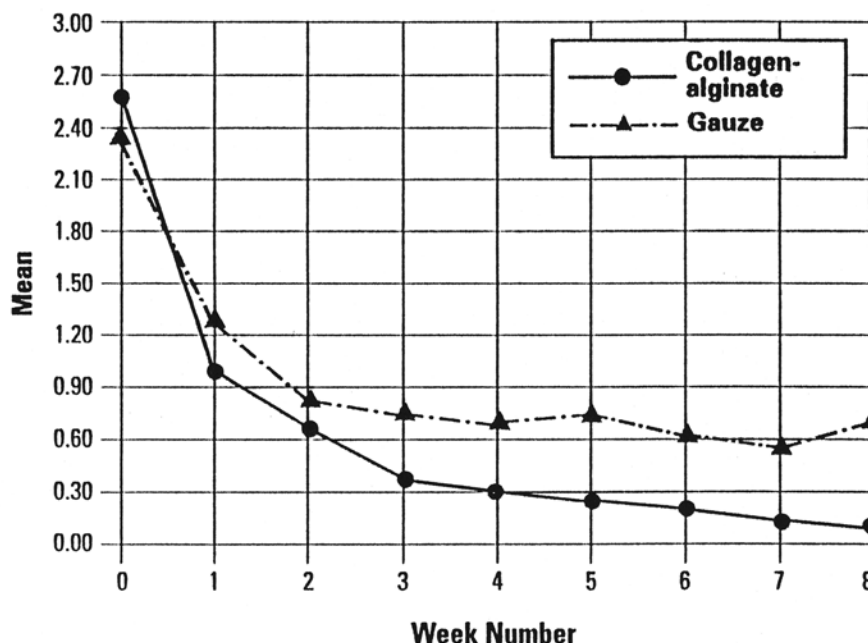
	TEST DRESSING GROUP	GAUZE DRESSING GROUP	STATISTICS
No. of patients who completed the study	50	25	
Ulcer duration (days)	146 \pm 73	225 \pm 104	[T] = .6204, $p = .5369$
Range (days)	1-365	1-1,825	
Ulcer size (cm ²)	2.6 \pm 0.50	2.99 \pm 0.62	[T] = .49, $p = .6237$
Wagner Ulcer Stage			$p = .310$
I	8 (16%)	1 (4%)	
II	36 (72%)	20 (80%)	
III	6 (12%)	4 (16%)	

(Figure 1). Complete healing was achieved in 24 of 50 patients (48%) in the collagen-alginate dressing group and 9 of 25 patients (36%) in the gauze dressing group (log-rank test, $p = .3933$). The mean time to complete healing was 6.2 ± 0.4 weeks for the collagen-alginate dressing group vs. 5.8 ± 0.4 weeks for the gauze dressing group (Figure 2). The results also showed that $\geq 75\%$ healing (75% or greater wound area reduction) was achieved in 39 patients (78%) in the collagen-alginate group and 15 patients (60%) in the gauze dressing group (log-rank test, $p = .1737$); the mean time to 75% healing was 3.46 ± 0.4 vs. 3.72 ± 0.5 weeks, respectively. The median time to 75% healing was 2 weeks for patients in the collagen-alginate group,

compared with 4 weeks for patients in the gauze dressing group ($p = .2551$).

Irrespective of treatment, ulcers of less than 6 months' duration healed at a significantly faster rate than those of more than 6 months' duration ($p = .0001$). The majority of patients in both groups (41 of 50 [82%] in the collagen-alginate dressing group, 21 of 25 [84%] in the gauze dressing group), had a wound of less than 6 months' duration. Multivariate analysis, which included all participants on repeated measurements of ulcer areas over the 8-week study period, indicated that the overall treatment effect on ulcer areas was significant in favor of the collagen-alginate dressing, as compared with the gauze dressing, when factoring in the duration of the ulcer ($p = .0401$). Averaged

Figure 3
MEAN OF PLANIMETRY ULCER AREAS
WOUND DURATION \leq 6 MONTHS



foot ulcers. Results showed that the test dressing was as effective as the gauze dressing in reducing wound area in the studied patient population. Multivariate analysis indicated that the collagen-alginate dressing was of greater benefit, as compared with the gauze dressing, in treating diabetic foot ulcers when wound duration was taken into account. Patients treated with the collagen-alginate dressing had a similar number of adverse events when compared with patients treated with the gauze dressing. Furthermore, patients enrolled in the study reported greater satisfaction with the collagen-alginate dressing than with their previous topical treatment because it was easier to use and it reduced the amount of time required for wound care.

Wound healing is a complex process that involves three separate biologic mechanisms: epithelialization (cellular migration and proliferation), wound contraction, and collagen deposition (fibroblasts are recruited to the site and a new

connective tissue matrix is produced).¹⁴ Diabetic foot ulcers have an abnormal histologic profile, with cessation of epidermal growth or migration over the wound surface and the presence of small abnormal blood vessels in the surrounding skin.¹⁵ The combined use of collagen to provide a framework for enabling the formation of new tissue and calcium alginate to keep the wound moist would be expected particularly to benefit patients with such ulcers.

A limiting factor of a dressing material such as the collagen-alginate test dressing is its relatively high cost when compared with dry gauze and normal saline solution. Significant cost savings can be achieved by cutting the large dressing sheet into pieces approximately equal to the size of the ulcer, thus potentially reducing costs to less than a dollar a day. Furthermore, cost disadvantages probably are balanced by the study's results showing that the collagen-alginate dressing was more likely than

the gauze dressing to be changed only once a day. In addition, patient satisfaction with the collagen-alginate dressing was high because the dressing keeps wounds moist and makes dressing removal and redressing easier. As a significant number of diabetic patients live independently and perform their own wound dressing, higher patient compliance is expected, which would offset the small increase in cost.

A variety of treatment methods currently are advocated for the management of diabetic foot ulcers. Platelet-derived growth factors are believed to promote cellular migration and proliferation to the wound site and are recommended for the management of nonhealing chronic ulceration.⁸ Despite encouraging findings, the results of clinical trials are not consistent,^{8,9} and more detailed information may be required before such a high-cost treatment is accepted as standard practice. The same applies to other experimental treatments such as hyperbaric oxygen,⁷ and it should be mentioned that even the use of local antiseptic solutions is not without controversy, as there are suggestions that these solutions may be toxic to the regenerating endothelium and actually may impede the healing process.^{16,17}

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