Section: General Surgery

Original Research Article

A PROSPECTIVE STUDY TO COMPARE THE EFFECTIVENESS OF COLLAGEN GRANULE-BASED DRESSING VERSUS CONVENTIONAL DRESSING IN THE MANAGEMENT OF DIABETIC FOOT ULCERS

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ABSTRACT

Background: Diabetic foot ulcers represent a significant healthcare challenge with substantial morbidity and mortality. This study aimed to evaluate the efficacy of collagen granule-based dressing compared to conventional dressing in the management of diabetic foot ulcers.

Materials and Methods: A prospective study was conducted with 100 patients with diabetic foot ulcers, randomly allocated into two groups of 50 patients each. Group A received collagen granule-based dressing, while Group B received conventional saline-moistened gauze dressing. Wounds were assessed at baseline and weekly for 12 weeks for wound area reduction, granulation tissue formation, wound healing time, infection rates, and adverse events.

Results: The upper middle class participants achieved the highest mean HeLD score of 82.53 ± 13.88 whereas middle class participants scored 70.58 ± 14.41 and lower middle class participants scored 55.64 ± 10.95 with significant differences (p=0.000). Participants in the lower middle socioeconomic status demonstrated the worst OHRQoL scored 16.78 ± 4.97 on the OHIP-14 scale and still upper class respondents displayed the best OHRQoL with 7.00 ± 0.00 yet these scores were significantly different between socioeconomic groups (p=0.013). The scores from the HeLD assessment had a weak inverse relationship (r=-0.193) with OHIP-14 measures (p=0.003) which demonstrates that better oral health literacy leads to improved oral health-related quality of life.

Conclusion: Collagen granule-based dressing demonstrated superior efficacy compared to conventional dressing in the management of diabetic foot ulcers, with faster healing times, greater wound area reduction, and lower infection rates. These findings suggest that collagen granule-based dressing should be considered as an effective treatment option for managing diabetic foot ulcers.

Keywords: Diabetic foot ulcer, Collagen granule-based dressing, Conventional dressing, Wound healing, Randomized controlled trial.

INTRODUCTION

Diabetic foot ulcers (DFUs) are a common and serious complication of diabetes mellitus, affecting approximately 15-25% of diabetic patients during their lifetime (Armstrong et al., 2017).[1] DFUs contribute significantly to morbidity, reduced quality of life, and healthcare expenditure (Driver et al., 2020).[2] Furthermore, DFUs precede 85% of all diabetes-related amputations, highlighting the critical importance of effective management strategies (Lavery et al., 2018).[3]

The pathophysiology of diabetic foot ulcers is multifactorial, involving neuropathy, peripheral vascular disease, mechanical stress, and impaired wound healing (Berlanga-Acosta et al., 2017).[4] The hyperglycemic environment in diabetes leads to delayed cellular migration, reduced growth factor

production, impaired angiogenesis, and decreased collagen synthesis, all of which contribute to compromised wound healing (Brownlee, 2005).[5] Additionally, the risk of infection is heightened due to impaired immune function, further complicating the management of these wounds (Shin & Tatro, 2019).[6]

Current standard care for DFUs includes debridement, infection control, offloading of pressure, and wound dressings (Hingorani et al., 2016).[7] Conventional dressings, typically composed of saline-moistened gauze, have been the traditional approach but have limitations including adherence to wound beds, frequent dressing changes, and suboptimal healing outcomes (Wu et al., 2019).[8] This has led to the development of advanced wound care products aimed at enhancing the healing process.

Collagen, as an essential structural protein, plays a vital role in wound healing by providing a scaffold for cellular migration and proliferation, promoting angiogenesis, and facilitating tissue remodelling (Brett, 2008).[9] Collagen-based dressings have emerged as promising alternatives to conventional dressings, with potential benefits including maintenance of a moist wound environment, protection against bacterial contamination, absorption of exudates, and provision of an extracellular matrix for tissue regeneration (Holmes et al., 2013).[10]

Specifically, collagen granule-based dressings deliver collagen in a particulate form that can conform to the wound bed, potentially enhancing contact with the wound surface and optimizing the biological effects of collagen. These dressings are designed to be biodegradable, biocompatible, and capable of stimulating the natural healing cascade by providing a temporary matrix for cellular attachment and growth factor binding (Fleck & Simman, 2010).[11]

While several studies have investigated various wound care products for DFUs, there remains a gap in the literature regarding the comparative efficacy of collagen granule-based dressings versus conventional dressings in a rigorous randomized controlled trial setting. This study aims to address this knowledge gap by evaluating the clinical outcomes of these two treatment approaches in patients with diabetic foot ulcers.

The primary objective of this study was to compare the efficacy of collagen granule-based dressing versus conventional saline-moistened gauze dressing in terms of wound healing time, percentage reduction in wound area, and complete wound closure rates in the management of diabetic foot ulcers. Secondary objectives included assessment of granulation tissue formation, incidence of wound infection, and adverse events associated with both dressing types.

MATERIALS AND METHODS

This prospective, randomized, controlled, parallel-group trial was conducted at the Department of Surgery at Tirunelveli Medical College between May 2023 and February 2024. The study protocol was approved by the Institutional Ethics Committee. All procedures were performed in accordance with the ethical standards of the Declaration of Helsinki.

Eligible participants were patients aged 18-75 years with type 1 or type 2 diabetes mellitus who presented with foot ulcers of Wagner grade 1 or 2, with a wound area between 2 cm^2 and 25 cm^2, and an ankle-brachial index (ABI) ≥ 0.7. Patients were excluded if they had severe peripheral arterial disease (ABI < 0.7), osteomyelitis, active wound infection requiring systemic antibiotics, exposed bone or tendon, malignancy at the ulcer site, known hypersensitivity to collagen, HbA1c > 12%, serum creatinine > 3.0 mg/dL, or if they were receiving immunosuppressive therapy. Patients participating in another clinical trial or who had received any advanced wound therapy in the preceding 30 days were also excluded.

Based on previous studies, we estimated that the mean time to complete healing would be approximately 8 weeks in the collagen group and 10 weeks in the conventional dressing group, with a standard deviation of 3 weeks. To detect this difference with 80% power and a 5% significance level, 44 patients per group were required. Allowing for a 10% dropout rate, we enrolled 50 patients in each group. After obtaining written informed consent, eligible patients were randomly allocated in a 1:1 ratio to either the collagen granule-based dressing group (Group A) or the conventional dressing group (Group B) .

All patients underwent comprehensive assessment including detailed history, physical examination, laboratory investigations (complete blood count, fasting and postprandial blood glucose, HbA1c, serum creatinine, liver function tests), and radiological evaluation to exclude osteomyelitis. Peripheral vascular assessment was conducted using Doppler ultrasonography to determine the ankle-brachial index.

Group A (Collagen Granule-Based Dressing): After wound preparation, collagen granules (derived from bovine Achilles tendon, >95% type I collagen) were applied to cover the entire wound surface to a depth of approximately 2-3 mm. The wound was then covered with a non-adherent secondary dressing and secured with hypoallergenic tape.

Group B (Conventional Dressing): After wound preparation, saline-moistened gauze was applied to the wound bed and covered with dry gauze and secured with hypoallergenic tape.

Dressings in both groups were changed every 48-72 hours depending on exudate levels, or sooner if clinically indicated. All patients received appropriate systemic antibiotics if wound cultures indicated infection, based on sensitivity reports.

Outcome measures included time to complete wound healing, percentage reduction in wound area at 4, 8, and 12 weeks and proportion of wounds with complete closure by 12 weeks.

Secondary outcome measures included rate of granulation tissue formation (assessed weekly using a validated 5-point scale, incidence of wound infection.

Wounds were photographed at baseline and weekly using standardized techniques. Granulation tissue formation, wound edge advancement, and overall wound appearance were assessed by two independent evaluators using standardized scoring systems.

Patients were followed weekly for 12 weeks or until complete wound healing, whichever occurred first. At each visit, wound assessment, dressing change, and documentation of adverse events were performed. Patients who did not achieve complete wound healing by 12 weeks were referred for appropriate further management but were included in the final analysis based on the intention-to-treat principle.

Statistical analysis was performed using SPSS version 26.0. Continuous variables were expressed as means and standard deviations or medians and interquartile ranges, as appropriate. Categorical variables were expressed as frequencies and percentages. The Student's t-test or Mann-Whitney U test was used for comparison of continuous variables between groups, and the chi-square test or Fisher's exact test was used for categorical variables. A p-value < 0.05 was considered statistically significant.

RESULTS

Of 126 patients screened, 100 met the eligibility criteria and were randomized to either the collagen granule-based dressing group (n=50) or the conventional dressing group (n=50). Four patients (two from each group) were lost to follow-up, and their last observation was carried forward for the intention-to-treat analysis.

The demographic and baseline clinical characteristics of both groups are presented in [Table 1]. There were no significant differences between the groups in terms of age, gender, body mass index, diabetes duration, HbA1c levels, or baseline wound characteristics, indicating effective randomization.

Table 1: Demographic and Baseline Clinical Characteristics of Study Participants

Characteristic	Collagen Group (n=50)	Conventional Group (n=50)	p-value
Demographic Parameters			
Age (years), mean ± SD	58.3 ± 9.7	59.1 ± 10.2	0.68
Gender, n (%)			0.84
- Male	32 (64)	33 (66)	
- Female	18 (36)	17 (34)	
Body mass index (kg/m²), mean ± SD	27.6 ± 3.8	28.1 ± 4.1	0.52
Diabetes-Related Parameters			
Diabetes duration (years), mean ± SD	12.4 ± 6.2	13.1 ± 5.8	0.56
Diabetes type, n (%)			0.74
- Type 1	5 (10)	6 (12)	
- Type 2	45 (90)	44 (88)	
HbA1c (%), mean ± SD	8.3 ± 1.4	8.5 ± 1.5	0.48
Insulin therapy, n (%)	34 (68)	36 (72)	0.67
Neuropathy present, n (%)	42 (84)	41 (82)	0.79
Ankle-brachial index, mean ± SD	0.89 ± 0.11	0.87 ± 0.12	0.38
Wound Characteristics			
Ulcer location, n (%)			0.86
- Plantar forefoot	28 (56)	26 (52)	
- Heel	7 (14)	9 (18)	
- Midfoot	10 (20)	11 (22)	
- Dorsum	5 (10)	4 (8)	
Wagner grade, n (%)			0.69
- Grade 1	21 (42)	19 (38)	
- Grade 2	29 (58)	31 (62)	
Duration of ulcer (weeks), median (IQR)	8.2 (4.5-12.6)	7.8 (4.2-13.1)	0.74
Initial wound area (cm²), mean ± SD	7.8 ± 4.3	8.1 ± 4.6	0.73
Wound depth (mm), mean ± SD	4.2 ± 1.7	4.5 ± 1.9	0.40

Wound Healing Outcomes: The mean time to complete wound healing was significantly shorter in the collagen granule-based dressing group compared to the conventional dressing group (7.2 ± 1.8 weeks vs. 9.4 ± 2.1 weeks, p<0.001). Kaplan-Meier survival analysis confirmed this difference, with the log-rank test showing statistical significance (p<0.001).

Wound Area Reduction: The mean percentage reduction in wound area at different time points is presented in [Table 2]. The collagen group demonstrated significantly greater wound area reduction at all-time points compared to the conventional dressing group.

Table 2: Percentage Reduction in Wound Area at Different Time Points

Time Point	Collagen Group (n=50)	Conventional Group (n=50)	p-value
Week 2	28.7 ± 7.4%	16.5 ± 6.2%	<0.001
Week 4	56.3 ± 12.1%	32.7 ± 10.8%	<0.001
Week 6	67.8 ± 14.3%	42.5 ± 12.7%	<0.001
Week 8	78.9 ± 15.6%	51.4 ± 14.5%	<0.001
Week 10	89.2 ± 12.3%	64.8 ± 17.2%	<0.001
Week 12	94.5 ± 9.7%	76.3 ± 19.4%	<0.001

Complete Wound Closure: By the end of the 12-week study period, complete wound closure was achieved in 43 patients (86%) in the collagen group compared to 32 patients (64%) in the conventional dressing group (p=0.01). The difference in complete wound closure became apparent from week 6 onwards and continued to increase throughout the study period.

Granulation Tissue Formation: The formation of healthy granulation tissue was more rapid and robust in the collagen group compared to the conventional dressing group. By week 4, 38 patients (76%) in the collagen group had achieved >50% granulation tissue coverage (grades 3-4) compared to 21 patients (42%) in the conventional group (p<0.001). The mean granulation tissue score at various time points is presented in [Table 3].

Table 3: Granulation Tissue Formation at Different Time Points

Time Point	Collagen Group (n=50)	Conventional Group (n=50)	p-value
Baseline	0.74 ± 0.56	0.78 ± 0.62	0.73
Week 2	2.26 ± 0.78	1.48 ± 0.65	<0.001
Week 4	3.12 ± 0.72	2.04 ± 0.81	<0.001
Week 6	3.58 ± 0.54	2.64 ± 0.85	<0.001
Week 8	3.84 ± 0.37	3.02 ± 0.77	<0.001

Values represent mean ± standard deviation on a scale of 0-4 (0=none, 1=<25%, 2=25-50%, 3=50-75%, 4=>75% of wound bed)

Wound Infection and Adverse Events: The incidence of wound infection requiring systemic antibiotics was significantly lower in the collagen group (6 patients, 12%) compared to the conventional dressing group (14 patients, 28%) (p=0.04). The most common organisms isolated were Staphylococcus aureus, Pseudomonas aeruginosa, and Escherichia coli in both groups.

No serious adverse events attributable to either dressing were reported during the study period. Minor adverse events included mild pain during dressing changes (collagen group: 4 patients, 8%; conventional group: 12 patients, 24%; p=0.03) and local skin maceration (collagen group: 3 patients, 6%; conventional group: 9 patients, 18%; p=0.04). No allergic reactions to the collagen material were observed.

Subgroup Analysis: Subgroup analysis based on initial wound size revealed that the benefit of collagen granule-based dressing was consistent across different wound size categories [Table 4]. Similarly, the advantage of collagen dressing was maintained in subgroups stratified by diabetes duration, glycaemic control, and wound location.

Table 4: Complete Wound Closure Rates by Initial Wound Size

Initial Wound Size	Collagen Group	Conventional Group	p-value
Small (2-5 cm²)	18/19 (94.7%)	15/18 (83.3%)	0.27
Medium (5-10 cm²)	17/19 (89.5%)	12/20 (60.0%)	0.03
Large (10-25 cm²)	8/12 (66.7%)	5/12 (41.7%)	0.21
Overall	43/50 (86.0%)	32/50 (64.0%)	0.01

DISCUSSION

This prospective study demonstrated that collagen granule-based dressing is superior to conventional saline-moistened gauze dressing in the management of diabetic foot ulcers across multiple clinically relevant outcomes. The significant improvements in healing time, wound area reduction, complete closure rates, and reduced infection incidence suggest that collagen granule-based dressing represents an effective treatment option for patients with diabetic foot ulcers.

The accelerated wound healing observed in the collagen group is consistent with the known biological properties of collagen in wound repair. Collagen serves as a natural scaffold that supports cellular migration, proliferation, and organization, which are essential processes in wound healing (Chattopadhyay & Raines, 2014).[12] Additionally, collagen fragments (peptides) can act as chemotactic agents for fibroblasts and promote angiogenesis, further enhancing the healing process (Frantz et al., 2010).[13] The granular formulation of collagen used in this study likely facilitated intimate contact with the irregular wound surface, optimizing the delivery of collagen to the wound bed.

The significantly greater reduction in wound area observed in the collagen group from the early weeks of treatment indicates that collagen dressing promotes the early phases of wound healing. This

early advantage was maintained throughout the study period, culminating in higher complete closure rates by 12 weeks. The more rapid formation of granulation tissue in the collagen group further supports the biological activity of collagen in stimulating the proliferative phase of wound healing. The lower incidence of wound infection in the collagen group is noteworthy and may be attributed to several factors. Collagen has been reported to have some antimicrobial properties and may create a physical barrier against bacterial contamination (Chattopadhyay & Raines, 2014).[14] Furthermore, the more rapid progression through the inflammatory phase of wound healing in the collagen group may have reduced the window of vulnerability to infection. The lower rate of dressing-related adverse events in the collagen group, particularly pain during dressing changes and maceration, suggests that collagen dressing may also contribute to improved patient comfort and compliance.

Our findings are consistent with previous studies that have examined the efficacy of various collagen-based products in wound healing. Veves et al. (2002) reported that a collagen-oxidized regenerated cellulose dressing was effective in the management of diabetic foot ulcers, with improved healing rates compared to standard care. Similarly, Motzkau et al. (2011) demonstrated that collagen-based wound dressings enhanced healing in neuroischemic diabetic foot ulcers. However, our study specifically evaluated collagen in granular form, which offers the advantage of conforming to irregular wound surfaces and potentially enhancing the biological activity of collagen through increased surface area.[15]

The subgroup analysis revealed that the benefit of collagen granule-based dressing was most pronounced in medium-sized wounds (5-10 cm^2), where the complete closure rate was significantly higher compared to conventional dressing. In small wounds (<5 cm^2), both treatments achieved high closure rates, though there was still a trend favouring collagen. In large wounds (>10 cm^2), the difference did not reach statistical significance despite a numerically higher closure rate in the collagen group, possibly due to the small sample size in this subgroup.

Future research should focus on longer-term follow-up to assess recurrence rates, comparison with other advanced wound care products, and more comprehensive economic analyses. Additionally, studies investigating the cellular and molecular mechanisms underlying the enhanced healing with collagen granule-based dressing would provide valuable insights into its mode of action.

CONCLUSION

Our study demonstrates that collagen granule-based dressing is superior to conventional saline-moistened gauze dressing in the management of diabetic foot ulcers, with significant improvements in healing time, wound area reduction, and complete closure rates. Additionally, collagen dressing was associated with faster granulation tissue formation, lower infection rates, and fewer dressing-related adverse events. These findings suggest that collagen granule-based dressing should be considered as an effective treatment option in the management of diabetic foot ulcers, particularly for medium-sized wounds. Implementation of collagen granule-based dressing in clinical practice has the potential to improve outcomes for patients with diabetic foot ulcers, reduce complications, and potentially decrease the overall burden on healthcare resources.

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