



OUTCOME OF COLLAGEN DRESSINGS IN THE TREATMENT OF DIABETIC FOOT ULCERS: AN OBSERVATIONAL STUDY

Dr. Nikhil Mahajan	M.S General Surgery Adesh Institute of Medical Sciences Bathinda.
Dr. Rahul Jindal	Post Graduate student Adesh Institute of Medical Sciences Bathinda.
Dr. Deepak Gupta*	MS General surgery Adesh Institute of Medical Sciences Bathinda. *Corresponding Author
Dr. Dushyant kumar Garg	M.S General surgery Adesh Institute of Medical Sciences Bathinda

ABSTRACT Diabetic foot ulcers are common and during their lifetime are estimated to affect 15 percent of all diabetic individuals. The treatment of diabetic foot ulcers comprises of protocols aiming for relieving the wound with the help of suitable therapeutic footwear. Other treatment options include the use of daily saline or similar dressings that permits a moist wound environment, debridement, antibiotic therapy if osteomyelitis or cellulitis is present, optimal control of blood glucose level, and assessment and correction of peripheral arterial insufficiency. Hence; the present study was conducted in AIMSR Bathinda for assessing the outcome of collagen dressings on 50 patients with diabetic foot ulcers from June 2018 onwards and it was observed that collagen dressings were efficacious in terms of reduction in wound area resulting in early wound healing in diabetic foot ulcers. This study suggested that future works should focus on biofilms and extracellular regulation in the treatment of diabetic foot ulcers.

KEYWORDS :

INTRODUCTION

Diabetic foot ulcers are common and during their lifetime are estimated to affect 15 percent of all diabetic individuals. It is now recognized that approximately twenty percent of patients with such foot ulcers need amputation. Diabetic foot ulcers are responsible for almost 85% of the total amputation cases. Abundant risk factors for the occurrence of foot ulcers have been proposed, the most crucial being peripheral sensory neuropathy followed by peripheral vascular disease. In diabetic individuals, the proportion of neuropathic, neuroischemic, and purely ischemic lesions is 54, 34, and 10%, respectively.¹⁻³ In India, it is assessed that annually approximately 40,000 legs are being amputated, out of which, approximately 75% are neuropathic with secondary infection, which is potentially preventable. Various parameters, such as, barefoot walking, illiteracy, low socioeconomic status, late presentation by patients, ignorance about diabetic foot care among primary care physicians, and belief in the other substitute systems of medicine add on to this high prevalence.⁴⁻⁷ The most crucial risk factors for foot ulceration are diabetic neuropathy, peripheral arterial disease and repeated trauma of the foot.⁸

The treatment of diabetic foot ulcers comprises of protocols aiming for relieving the wound with the help of suitable therapeutic footwear. Other treatment options include the use of daily saline or similar dressings that permits a moist wound environment, debridement, antibiotic therapy if osteomyelitis or cellulitis is present, optimal control of blood glucose level, and assessment and correction of peripheral arterial insufficiency. Various topical medications and gels have been promoted for ulcer healing and maintenance. Apart from treating the infection, an ideal wound care product should also protect the normal tissues and should not interfere with the normal wound healing. At present, diabetic foot ulcers are being managed by local dressing with agents such as povidone-iodine, eusol, and hydrogen peroxide but they have their own restrictions. Application of collagen sheets may be an efficient alternative to the currently used conventional methods of dressings for diabetic wounds.^{9, 10} Collagen is the major protein of the extracellular matrix. It is also the richest and most abundant protein that is found in mammals. Hence, under the light of above mentioned data, we planned the present study to assess the outcome of collagen dressing in the treatment of diabetic foot ulcers

MATERIALS & METHODS

The present study was conducted in Adesh Institute of Medical Sciences & Research, Bathinda. Ethical approval was obtained from institutional ethical committee and written consent was obtained from all the patients after explaining in detail the entire research

protocol. All the patients who presented with diabetic foot ulcers in AIMSR from June 2018 were enrolled.

Inclusion Criteria

·Patients with diabetic foot ulcers.

Exclusion Criteria

·Patients with diabetic foot ulcers who were known cases of carcinomas and connective tissue disorders.
·Patients with diabetic foot ulcer with untreated underlying osteomyelitis.
·Patients with diabetic foot ulcers with unstable fractures or lose fragments of bone.

Complete demographic details of all the patients were obtained. Collagen dressing was given to all the patients and outcome was assessed.

RESULTS

32 percent of the patients (16 patients) belonged to the age group of more than 60 years. 52 percent of the patients (26 patients) and 44 percent of the patients (22 patients) belonged to the age group of 51 to 60 years and 41 to 50 years respectively. 14 percent of the patients (7 patients) belonged to the age group of 30 to 40 years. 6 percent of the patients (3 patients) belonged to the age group of less than 30 years. Out of total of 50 patients with diabetic foot ulcers, 72 percent of the patients (36 patients) were males while the remaining 28 percent of the patients (14 patients) were females. In 42 percent of the patients (21 patients), diabetic foot ulcer was of less than 10 days duration. In 14 percent of the patients (7 patients), and 18 percent of the patients (9 patients), diabetic foot ulcer was of 11 to 20 days and 21 to 30 days duration respectively. In 22 percent of the patients (11 patients) and 6 percent of the patients (3 patients), diabetic foot ulcer was of 31 to 60 days and more than 60 days duration respectively. Mean wound area before dressing as 33.56 mm², while mean wound area second week after dressing was 16.24 mm². Significant results were obtained while comparing the mean wound area before dressing and second week after dressing. Mean number of debridement done was 3.42, while mean hospital stay was found to be 25.16 days.

Table 1: Age-wise Distribution Of Patients

Age group (years)	Number of patients	Percentage of patients
Less than 30	3	6
30 to 40	7	14
41 to 50	11	22
51 to 60	13	26

More than 60	16	32
Total	50	100
Mean age \pm SD	52.57 \pm 12.56	

Table 2: Gender-wise Distribution Of Patients

Gender	Number of patients	Percentage of patients
Males	36	72
Females	14	28
Total	50	100

Table 3: Comparison Of Wound Area At Different Time Interval

Parameter	Before dressing	Second week after dressing	p- value
Mean wound area before dressing (mm ²)	33.56	16.24	0.001 (Significant)
\pm SD	3.26	3.48	

Table 4: Number of debridement, hospital stay and percentage shrinkage of wound

Parameter	Mean	SD
Number of debridement required	3.42	0.64
Hospital stay (days)	25.16	2.61
Percentage shrinkage of wound	50.79	13.39

DISCUSSION

In 42 percent of the patients (21 patients), diabetic foot ulcer was of less than 10 days duration. In 14 percent of the patients (7 patients), and 18 percent of the patients (9 patients), diabetic foot ulcer was of 11 to 20 days and 21 to 30 days duration respectively. In 22 percent of the patients (11 patients) and 4 percent of the patients (2 patients), diabetic foot ulcer was of 31 to 60 days and more than 60 days duration respectively. In a study conducted by Motzkau M et al, diabetic foot ulcer was of 26 days duration. In another study conducted by Donaghue VM et al, diabetic foot ulcer was of 8 weeks duration. Ravari H et al reported the duration of diabetic foot ulcer to be 4 weeks in their study¹⁰⁻¹²

In a previous study conducted by Blume P et al, authors assessed the safety and efficacy of Formulated Collagen Gel (FCG) alone and with Ad5PDGF-B (GAM501) compared with Standard of Care (SOC) in patients with 1.5–10.0 cm² chronic diabetic neuropathic foot ulcers that healed <30% during Run-in. Wound size was assessed by planimetry of acetate tracings and photographs in 124 patients. Comparison of data sets revealed that acetate tracings frequently overestimated areas at some sites. For per-protocol analysis, 113 patients qualified using acetate tracings but only 82 qualified using photographs. Prior animal studies suggested that collagen alone would have little effect on healing and would serve as a negative control. Surprisingly trends for increased incidence of complete closure were observed for both GAM501 (41%) and FCG (45%) vs. Standard of Care (31%). By photographic data, Standard of Care had no significant effect on change in wound radius (mm/week) from during Run-in to Week 1 but both FCG and GAM501 significantly increased healing rates that gradually declined over subsequent weeks. Both GAM501 and FCG appeared to be safe and well tolerated, and alternate dosing schedules hold promise to improve overall complete wound closure in adequately powered trials.¹³

Mean wound area before dressing as 33.56 mm², while mean wound area second week after dressing was 16.24 mm². Significant results were obtained while comparing the mean wound area before dressing and second week after dressing. Our results were in concordance with the results obtained by Shimikore SS et al, who reported similar findings in their study. In their study, mean wound area before dressing was 32.30 mm², while on second week follow-up, the mean wound area was found to be 15.77 mm².¹⁴ Mean number of debridement done was 3.42, while mean hospital stay was found to be 25.16 days. Mean percentage shrinkage of wound in the present study was found to be 50.79%. Our results were in concordance with the results obtained by Gottrup F, et al, who reported that 100 percent epithelialization occurred in 52 percent of the patients and 50 percent shrinkage of the wound occurred in 43 percent of cases. Also, in a study conducted by Fleischli JG et al, 100

percent epithelialization occurred in 47 percent of the cases.¹⁵ Wound cleansing and debridement physically remove microbes and their secreted products from the wound. In addition the removal of devitalized tissue likely reduces an important nutrient source of the microbes and therefore reduces the microbial bioburden. Several studies suggested that bioburden is a barrier to healing, and research that specifically targets wound bacteria populations has been promising.^{13, 14}

Kirsner and colleagues evaluated Apligraf application on 163 DFUs from 155 patients with an average wound area of 6.0 \pm 5.5 cm² and wound duration of 4.4 \pm 2.6 months. Sixty five percent of patients required multiple applications but overall, there was a 70 percent improvement in wound closure in 12 weeks. The study authors concluded that DFUs treated with Apligraf had higher, faster healing rates. They also found an increase in the probability of healing by 97 percent in comparison to dehydrated amniotic membranes.¹⁷ The mode of action (MoA) of collagen-based dressings is also addressed. Due to a number of potential stimuli (local tissue ischemia, bioburden, necrotic tissue, repeated trauma, etc.), wounds can stall in the inflammatory phase contributing to the chronicity of the wound. One key component of chronic wounds is an elevated level of matrix metalloproteinases (MMPs). At elevated levels, MMPs not only degrade nonviable collagen but also viable collagen. In addition, fibroblasts in a chronic wound may not secrete tissue inhibitors of MMPs (TIMPs) at an adequate level to control the activity of MMPs. These events prevent the formation of the scaffold needed for cell migration and ultimately prevent the formation of the extracellular matrix (ECM) and granulation tissue. Collagen based wound dressings are uniquely suited to address the issue of elevated levels of MMPs by acting as a 'sacrificial substrate' in the wound. It has also been demonstrated that collagen breakdown products are chemotactic for a variety of cell types required for the formation of granulation tissue. In addition, collagen based dressings have the ability to absorb wound exudates and maintain a moist wound environment.¹⁸ Limited data are available on the effect of topical collagen granule-based dressing in diabetic foot ulcers. Veves et al. conducted a randomized controlled trial (RCT) in which the collagen dressing was compared with standard treatment in diabetic foot ulcers. The results showed that collagen granules have wound-healing property. In another study by Lázaro-Martínez et al., it was demonstrated that protease-modifying dressings in patients with neuropathic diabetic foot ulcers initiate better tissue regeneration.¹⁹

CONCLUSION

Diabetic foot ulcers treated with collagen dressing are efficacious in terms of reduction in wound area resulting in early wound healing. Collagen-based wound dressings can be an effective tool in the healing of diabetic foot wounds. This study suggests that future works focus on biofilms and extracellular regulation, and include high risk patients.

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