

Assessment of Two Different Techniques in the Treatment of Diabetic Foot Ulcer

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Abstract

Aim: The aim of the present study was to evaluate the effect of the collagen dressing and conventional dressing on foot ulcer.

Methods: The present study was carried out in the Department of surgery, JLNMC, BHAGALPUR, Bihar, India for the period of six months. Total one hundred patients with chronic foot ulcer were studied.

Results: We found high number of male (75%) had chronic leg ulcer as compared to female (25%). However, the gender distribution was comparable same in both collagen and conventional dressing groups ($p > 0.05$). There is a clear association between age and chronic leg ulceration. Data suggest that the prevalence of leg ulceration progressively increases with increasing age. In our study, overall, the chronic leg ulcer was found more in older age. Mean age [conventional dressing group (50.55 ± 10.90 years) and collagen dressing group (45.15 ± 6.50 years)].

Conclusion: Diabetic foot ulcers treated with collagen dressing are efficacious in terms of reduction in wound area resulting in early wound healing.

Keywords: Diabetic foot ulcer, Collagen Dressings, Wound Healing, Skin grafts, Non healing wounds

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Introduction

Diabetic Foot Ulcer (DFU) is a chronic condition that resulted from uncontrolled diabetes that leads to peripheral artery disease or neuropathy. A single or combination of both abnormalities will trigger the development of DFU. DFU usually leads to progressive bone, joint, and soft tissue deterioration with commonly seen in the ankle and foot [1], causing severe complications that inflict more than 50% of amputations in diabetic patients. This is mainly caused by

impaired wound healing due to the thickening of the basement membrane, foreign body infection, low proliferation rate, irregular keratinocyte differentiation, and slow angiogenesis that perpetuates the foot deformity. [2,3]

Collagen-containing wound dressings have been used in the treatment of diabetes-related foot ulcers (DFU). Collagen components, such as fibroblast and keratinocytes, are a major part of skin development. Collagen may be harvested

from a variety of sources including living and non-living bovine, porcine, and equine skin. Once harvested (via a proprietary process), a native collagen bioscaffold matrix is created that stabilizes the vascular and cellular components, which become incorporated into the wound bed. [4] Preliminary findings suggest that collagen-containing wound dressings may have several advantageous features. Cullen et al reported the findings from the testing of an oxygenized regenerated cellulose (ORC)/collagen dressing. [5]

The management of diabetic foot ulcers includes relieving the wound using suitable therapeutic footwear. Other recommendations include the use of daily saline or similar dressings that allow a moist wound environment, debridement, antibiotic therapy if osteomyelitis or cellulite 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. In addition to holding the infection, an ideal wound care product should also protect the normal tissues and should not interfere with the normal wound healing. Proteins are the natural polymers, which make up approximately 15% of the human body. Amino acids are the building blocks of all proteins. Collagen is the major protein of the extracellular matrix and is the most abundant protein found in mammals comprising 70%–80% of the skin (dry weight) and 25% of the entire protein. Collagen acts as a structural gallow in the tissues. [6-8]

Regardless of etiology, foot ulcers cause considerable and prolonged distress for patients. Acute pain or continuous aching discomfort is usual, exacerbated with changes of dressings. Often, ulcers become secondarily and heavily infected, with the production of a foul-smelling slough and copious exudate that promote general unhappiness and increasing social

isolation, ultimately reducing quality of life. Other issues for patients include restricted mobility, embarrassing dressings and inability to continue working. [9]

The aim of the present study was to evaluate the effect of the collagen dressing and conventional dressing on foot ulcer.

Methods

The present study was carried out in the Department of surgery, JLNMC, Bhagalpur, Bihar, India for the period of six months. Total one hundred patients with chronic foot ulcer were studied

Inclusion Criteria:

1. Patients with chronic foot ulcer (diabetic/burn patients).
2. Patient willing to give informed consent
3. In case of diabetic patients- diabetes mellitus is defined as per World Health Organization (WHO) criteria of age and duration of therapy

1. Age ≥ 35 years
2. Absence of insulin requirement in the first 5 years after diagnosis.

Exclusion Criteria:

1. Critically ill patients
2. Patient refusal
3. Any evidence of underlying bone osteomyelitis
4. Malignancy

All patients underwent a standard clinical and laboratory evaluation. Briefly, information about age, known DM duration, smoking habits, arterial blood pressure, and anthropometric measurements was collected. Patients with chronic foot ulcer (diabetic/burn patients) who were willing to give informed consent were considered. Critically ill patients and patients who refused were excluded. In case of Type II diabetic patients, WHO criteria of age and duration of therapy (Age ≥ 35 years & absence of insulin

requirement in the first 5 years after diagnosis) were used.

In all patient's wound size was noted before treatment initiation. A collagen or conventional dressings were applied to wound, and all patients were followed as per standard post-application treatment protocol. Patients underwent dressing changes every 3 to 4 days until wound healing or for maximum period of 12 weeks. Changes in wound size were recorded when the dressing was removed; and at 4 and 12 weeks.

Healing time, duration of antibiotic therapy, follow up period were noted. All patients were also followed up for adverse

events. All the data were captured in the pre-printed pro-forma (given below).

Statistical analysis

'Chi-Square test' or 'Fisher exact test' was applied as appropriate for comparison of nominal data. 't test' was applied for comparison of continuous data. Additional exploratory (parametric as well as non-parametric) analysis of the data was performed as deemed essential by using appropriate statistical tests. P-value of 0.05 was considered as statistically significant.

Results

Table 1: Comparison of sex in both the groups

| Parameter | Treatment | | | | P value |
|-----------|-------------------|-----|-----------------------|-----|---------|
| | Collagen dressing | | Conventional dressing | | |
| | N | % | N | % | |
| Sex | | | | | 0.80 |
| Female | 20 | 25 | 10 | 25 | |
| Male | 60 | 75 | 30 | 75 | |
| Total | 80 | 100 | 40 | 100 | |

We found high number of male (75 %) had chronic leg ulcer as compared to female (25 %). However, the gender distribution was comparable same in both collagen and conventional dressing groups ($p > 0.05$).

Table 2: Comparison of age in both the groups

| Parameter | Treatment | | | | P value |
|-----------|-------------------|------|-----------------------|-------|---------|
| | Collagen dressing | | Conventional dressing | | |
| | Mean | SD | Mean | SD | |
| Age | 45.15 | 6.50 | 50.55 | 10.90 | 0.01 |

There is a clear association between age and chronic leg ulceration. Data suggest that the prevalence of leg ulceration progressively increases with increasing age. In our study, overall, the chronic leg ulcer was found more in older age. Mean age [conventional dressing group (50.55 ± 10.90 years) and collagen dressing group (45.15 ± 6.50 years)].

Table 3: Comparison of Size of ulcer in both the groups

| Parameter | Treatment | | | | P value |
|-----------|-------------------|------|-----------------------|------|---------|
| | Collagen dressing | | Conventional dressing | | |
| | Mean | SD | Mean | SD | |
| Size | 6.50 | 3.45 | 8.80 | 2.70 | 0.01 |

The mean wound size was 6.50 ± 3.45 cm in collagen dressing group and 8.80 ± 2.70 cm in conventional dressing group. Significantly high mean age, duration of ulcer and wound size in patients receiving conventional dressing could be because of chance, and partly because of non-randomized nature of the study.

Table 4: Comparison of healing time in both the groups

| Parameter | Treatment | | | | P value |
|--------------------|-------------------|------|-----------------------|------|---------|
| | Collagen dressing | | Conventional dressing | | |
| | Mean | SD | Mean | SD | |
| Healing time (Wks) | 4.50 | 1.20 | 7.75 | 1.60 | 0.01 |

The healing time use was significantly lower in patients receiving collagen dressing (4.63±1.18 weeks) as compared to conventional dressing (7.79±1.61 weeks).

Discussion

Collagen has a crucial role in wound healing. Local tissue ischemia, bioburden, necrotic debris, recurrent trauma, and other variables cause wounds to stall in the inflammatory phase, increasing their chronicity. Collagen breakdown products are chemotactic agents for many cells that are required for the production of granulation tissue. Collagen-based dressings can also remove wound exudates while maintaining a moist wound environment. Collagen is a biological substance that aids wound healing by forming and arranging newly produced fibers and granulation tissue in the wound bed, creating an ideal wound healing environment. [10] Collagen granules help angiogenesis and strengthen the body's healing processes when sprinkled over a wound. [11,12] This provides mechanical assistance by lowering oedema and fluid loss from the ulcer site, stimulating fibroblast recruitment into the ulcer, and enhancing granulation tissue metabolic activity. Collagen dressings are simple to apply to wounds and have the added benefit of stopping bleeding. [13]

Since the study was not randomized we found unequal distribution of patients in both the groups. Collagen dressing was applied to 75 % patients, whereas conventional dressing to 25 % patients.

There is a clear association between age and chronic leg ulceration. Data suggest that the prevalence of leg ulceration progressively increases with increasing

age. In our study, overall, the chronic leg ulcer was found more in older age. Mean age [conventional dressing group (50.58 ± 10.96 years) and collagen dressing group (46.13±6.70 years)]. The finding is in the line with published literature. Studies by Callam et al [14]; Baker et al [15]; Baker and Stacey [16]; O'Brien et al [17] reported prevalence estimates in age bands and all show an increase in prevalence with each decade of life.

In the present study, we have found an overall benefit of collagen on the rate of wound healing compared with moistened gauze. The healing time use was significantly lower in patients receiving collagen dressing (4.50±1.20 weeks) as compared to conventional dressing (7.80±1.60 weeks). Further, the follow up period was significantly lower in collagen dressing patients (2.13±1.11) days as compared to conventional dressing patients (2.92±1.41). Our results showed that collagen dressing is effective in promoting complete wound healing in the studied patient population. The analysis indicated that collagen dressing was of greater benefit, compared with saline-moistened gauze, in treating foot ulcers with duration of less than 6 months. The results are in the line with published literature.

In a study by Veves in 276 patients with diabetic foot ulcer, after 12 weeks of treatment, 51 (37.0%) Promogran'-a collagen/oxidized regenerated cellulose dressing-treated patients had complete wound closure as compared to 39 (28.3%) patients of control group (moistened gauze), but this difference was not statistically significant (P=0.12). In this study, author found an overall benefit of

collagen on the rate of wound healing compared with moistened gauze. [18]

In this study, the collagen sponge proved to be efficacious in the promotion and stabilization of granulation tissue. The collagen available for this use comes in the form of soft sponges, which are lyophilized and sterilized. It has been proven that the material implanted, lysed by enzymatic digestion by leukocytic proteases, maintains intimate contact with the bottom of the lesion, is embedded into the granulation process, and forms plastic scaffolding over which fibroblast migration takes place followed by endogenous cell invasion. [19]

The wound healing process involves phenomena such as proliferation, migration, and cell differentiation—all of which are influenced by the presence of collagen. In the final stage of repair with a continuity tissue solution, the maturation of collagen takes place and collagen fibers create a bridge between the edges of the damaged tissues, going on to form or favor a scar with elasticity and mechanical strength.

Conclusion

Diabetic foot ulcers treated with collagen dressing are efficacious in terms of reduction in wound area resulting in early wound healing. Collagen dressing increases the rate of wound healing as compared to moistened gauze. Further, it also reduces the follow up period and antibiotic use significantly as compared to conventional dressing. Probably, its spongy network contributes to exudate absorption and blocking of possible extensions of the wound, preventing bacterial growth that would delay the healing process. However, further studies are recommended.

References

1. Mishra SC, Chhatbar KC, Kashikar A, Mehndiratta A. Diabetic foot. *Bmj*. 2017 Nov 16;359.

2. Fauzi AA, Chung TY, Latif LA. Risk factors of diabetic foot Charcot arthropathy: a case-control study at a Malaysian tertiary care centre. *Singapore medical journal*. 2016 Apr; 57(4):198.
3. Tsourdi E, Barthel A, Rietzsch H, Reichel A, Bornstein SR. Current aspects in the pathophysiology and treatment of chronic wounds in diabetes mellitus. *BioMed research international*. 2013 Jan 1;2013.
4. Landsman A, Taft D, Riemer K. The role of collagen bioscaffolds, foamed collagen, and living skin equivalents in wound healing. *Clin Podiatr. Med Surg*. 2009;26(4):525–533.
5. Cullen B, Watt PW, Lundqvist C, et al. The role of oxidised regenerated cellulose/collagen in chronic wound repair and its potential mechanism of action. *Int J Biochem Cell Biol*. 2002; 34(12):1544–1556.
6. Honnegowda TM, Kumar P, Padmanabha Udupa EG, Sharan A, Singh R, Prasad HK, Rao P. A comparative study to evaluate the effect of limited access dressing (LAD) on burn wound healing. *International wound journal*. 2016 Oct;13(5):791-8.
7. Price BL, Lovering AM, Bowling FL, Dobson CB. Development of a novel collagen wound model to simulate the activity and distribution of antimicrobials in soft tissue during diabetic foot infection. *Antimicrobial Agents and Chemotherapy*. 2016 Oct 21;60(11):6880-9.
8. Park YJ, Hwang Y, Park KH, Suh JW, Shim DW, Han SH, Lee JW, Choi WJ. Collagen Dressing in the Treatment of Diabetic Foot Ulcer: A Prospective, Randomized, Placebo-Controlled, Single-Center Study. *Foot & Ankle Orthopaedics*. 2016 Aug 19;1(1):2473 011416S00080.
9. Bauling PC. A review of the impact of dressings on quality of life. In *International Congress And Symposium Series-Royal Society Of*

- Medicine. Royal Society of Medicine Services Ltd. 1998; 227: 39-42.
10. Nataraj C, Ritter G, Dumas S, Helfer FD, Brunelle J, Sander TW. Extracellular wound matrices: Novel stabilization and sterilization method for collagen-based biologic wound dressings. *Wounds*. 2007;19(6):148-56.
 11. Park SN, Lee HJ, Lee KH, Suh H. Biological characterization of EDC-crosslinked collagen-hyaluronic acid matrix in dermal tissue restoration. *Biomaterials*. 2003;24(9):1631-41.
 12. Lazovic G, Colic M, Grubor M, Jovanovic M. The application of collagen sheet in open wound healing. *Ann Burns Fire Disasters*. 2005; 18 (3) :151-6.
 13. Motta G, Ratto GB, De Barbieri A. Can heterologous collagen enhance the granulation tissue growth? An experimental study. *Ital J Surg Sci*. 1983;13(2):101-8.
 14. Callam MJ, Harper DR, Dale JJ, Ruckley CV. Chronic ulcer of the leg: clinical history. *Br Med J (Clin Res Ed)*. 1987 May 30;294(6584):1389-91.
 15. Baker SR, Stacey MC, Jopp-McKay AG, Hoskin SE, Thompson PJ. Epidemiology of chronic venous ulcers. *Journal of British Surgery*. 1991 Jul;78(7):864-7.
 16. Baker SR, Stacey MC. Epidemiology of chronic leg ulcers in Australia. *Australian and New Zealand Journal of Surgery*. 1994 Apr;64(4):258-61.
 17. O'Brien JF, Grace PA, Perry IJ, Burke PE. Prevalence and aetiology of leg ulcers in Ireland. *Irish journal of medical science*. 2000 Apr;169(2):110-2.
 18. Donaghue VM, Chrzan JS, Rosenblum BI, Giurini JM, Habershaw GM, Veves A. Evaluation of a collagen-alginate wound dressing in the management of diabetic foot ulcers. *Advances in Wound Care: The Journal for Prevention and Healing*. 1998 May 1;11(3):114-9.
 19. Salih A. A., Saedi S. M., & Ghali K. H. Impact of Fibrosis Related to TGF- β 1 and TNFR-1 Growth Factors in Renal Failure Patients. *Journal of Medical Research and Health Sciences*, 2022; 5(7): 2105–2111.