

A Long-term Follow-up Study of Chronic Diabetic Foot Ulcers Healed with Dehydrated Human Amniotic/Chorionic Membrane Allografts

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Abstract

Identification and implementation of an ideal treatment regimen for diabetic foot ulcers (DFU) is a common issue faced by clinicians. Therapies that promote rapid and complete healing reduce the risk for infection and amputation, can substantially improve quality-of-life while decreasing financial burdens.¹ Even in cases where primary healing occurs, DFUs frequently recur. Human amniotic membrane has been used to treat cutaneous wounds for over a century.² Recent improvements in preparation have led to development of a commercially available dehydrated human amnion/chorion membrane (dHACM) allograft. Studies have shown the effectiveness of dHACM for rapid healing of DFUs.^{3,4,5} We sought to evaluate rates of recurrence of chronic DFUs healed with use of dHACM. Twenty-five patients were enrolled in the initial randomized trial.⁴ Of those 25, 13 were randomized to receive dHACM and 12 of 13 (92.3%) healed (mean 2.5 ± 1.9 weeks).⁴ Of 12 patients randomized to receive standard care, one healed, and 11 exited the randomized study without healing and subsequently received dHACM. Of these 11 patients, 10 (91%) healed completely within 12 weeks of starting dHACM treatment (mean 4.2 ± 3.1 weeks).⁵ Twenty-two of 25 DFUs (88%) completely healed after dHACM treatment, and these patients were eligible for inclusion in the follow-up study. Follow-up examinations were conducted 9-12 months after healing. Eighteen of 22 patients returned for follow-up examination. Only one had recurrent DFU while 17 (94.4%) remained fully healed. These findings support the effectiveness of dHACM for treatment of DFU. dHACM is a clinically viable and economically feasible treatment option.

Introduction

Identification and implementation of an ideal treatment regimen for diabetic foot ulcers (DFUs) are increasingly common issues faced by clinicians. DFUs are notoriously slow to heal and even in cases where primary healing is achieved ulcers frequently recur. An optimal treatment for DFUs would be one that supports both rapid and long-term healing. Human amniotic membrane has been used as an allograft to treat cutaneous wounds for over a century.² Recent improvements in preparation have led to the development of a commercially available dehydrated human amnion/chorion membrane (dHACM) allograft.

Amniotic Membrane²

- Encapsulates the fetal compartments: composed of amnion and chorion layers
- Non-vascular tissue consisting of epithelium cells, basement membrane, a thick compact layer, and fibroblast layer
- Fibrous layer contains cell anchoring collagen types: I, III, IV, V, and VII
- Biochemical properties help to reduce inflammation and enhance soft tissue healing
- Fresh amniotic membrane has antibacterial and pain reduction properties, is self-signaling and mediates tissue repair via the contained growth factors

EpiFix® - A Dehydrated Human Amnion/Chorion Membrane Allograft

- A biologically active implant or graft for tissue regeneration application
- Amniotic membrane obtained from screened and tested donors to ensure safety
- Cleaned, dehydrated, and sterilized by the proprietary PURION® Process which produces a tissue with a 5 year, ambient temperature shelf life

Purpose

Our purpose is to evaluate the rates of recurrence of chronic DFUs healed with the use of dHACM.



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Methods

We conducted a follow-up study of patients with chronic DFUs previously enrolled in an IRB approved randomized clinical trial comparing rates of primary healing with dHACM versus a standard protocol of wound care.⁴ The study was conducted in a single center in Southwest Virginia under the direction of a senior clinician with expertise in diabetic foot care. All patients signed an IRB approved informed consent form prior to enrollment in the initial study and provided additional IRB approved consent for the current review of subsequent data and outcomes.

Included

- Patients from the initial randomized trial that were randomized to the dHACM treatment group and healed within 12 weeks (n=12)⁴
- Patients that were randomized to standard treatment with moist wound care that subsequently received dHACM and healed after initial study completion (n=10)⁵

Study Outcome

- Rate of ulcer recurrence in patients 9-12 months after primary healing with the use of dHACM

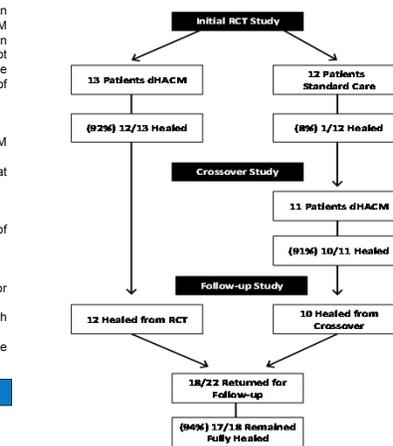
Data Analysis

- 22 patients with chronic DFUs that healed with the use of dHACM were eligible for inclusion
- Follow-up examinations were conducted at ≥9 months after primary healing with dHACM
- Complete healing was defined as a total epithelialization of the open area of the wound

Results

Table 1. Patient Characteristics

Variable	N=18
Male gender (n%)	5 / 27.8
Age (yr)	58.8 ± 12.8
BMI (kg/m ²)	32.7 ± 6.7
Obese (>29.9 kg/m ²) (n%)	10 / 55.5
Smoker (n%)	3 / 16.7
Caucasian race (n%)	15 / 83.3
Wound size (cm ²) at 1 st application of dHACM	3.1 ± 3.8
Wound duration (weeks) at 1 st application of dHACM	1.7 (0.7, 13.5)
Forefoot or digital ulcer (n%)	19.4 ± 13.6
Heel or midfoot ulcer (n%)	14.0 (6.0, 54.0)
Time to healing with dHACM (weeks)	9 / 50
	9 / 50
	3.1 ± 2.8
	2.0 (1.0, 9.0)



Summary Results from RCT, Crossover and Follow-up Study

- 25 patients were enrolled in the initial randomized trial⁴
- Of those 25, 13 were randomized to receive dHACM and 12 of 13 (92.3%) healed (mean of 2.5 ± 1.9 weeks)⁴
- Of the 12 patients randomized to receive standard care, one healed, and 11 exited the randomized study without healing and subsequently received dHACM
- Of these 11 patients, 10 (91%) healed completely with dHACM (mean 4.2 ± 3.1 weeks)⁵
- 22 of 25 patients (88%) ultimately had complete healing of DFUs after treatment with dHACM, and were eligible for inclusion in the follow-up study
- Long-term follow-up occurred in 18 of 22 patients at 9-12 months post-healing
- 17 of 18 patients (94.4%) remained fully healed without DFU recurrence

References

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Results

Examples of Subjects Healed with dHACM



Conclusions

- In the present study of 18 patients with chronic DFUs that healed within 12 weeks after treatment with dHACM, all but one treated ulcer (94.4%) remained healed approximately one year later.
- Findings from this long term follow-up study support the results of the original randomized trial and the second crossover study showing that dHACM is an effective treatment for both rapid and sustained healing of DFUs.
- These results illustrate that the addition of dHACM to routine wound management can enhance wound healing in patients with DFUs.
- Limitations of the current study are inherent to those of a retrospective study design and small sample size. These findings should be confirmed and expanded with subsequent clinical trials.