Human Amniotic Membrane in the Treatment of Non-Healing Diabetic Foot Ulcers: A Prospective Randomized Controlled Trial

Abstract

A retrospective crossover study of patients with Type 1 or Type 2 diabetes, having a diabetic foot ulcer of at least 6 weeks duration that failed to heal with standard care (SOC) treatment. Twenty-five consecutive patients were enrolled from one site. Two outside wound care physicians reviewed and validated the clinical photos and data. All patients failed at least one month of conservative care prior to randomization. At 8 weeks 93% (10/11) of patients treated with dHACM were healed versus 8% (1/12) with SOC (p<0.001). At week 12 only one patient from the dHACM cohort had failed to heal all remaining SOC patient’s wounds remained open. Upon conclusion of the prospective trial, the SOC group of 11 patients failing to heal were offered bi-weekly treatment with dHACM. At that time their wounds had been present for a mean of 21 weeks and a wound size of 4.7cm². A central IRB approved retrospective analysis of this group was performed and complete healing was achieved in 91% (10/11) by 12 weeks. These prospective and retrospective results are compelling and show that treating diabetic foot ulcers with serial debridement, wet-to-moist dressings, application of enzymatic agent, and the application of dHACM is more effective than SOC and suggests that early effective treatment may decrease clinical operational costs and may prevent longer term medical complications.

Introduction

Diabetes affects at least 6% of the population, or approximately 16 million people in the United States. Lower extremity ulcers are a serious complication for people with diabetes, developing in some 25% of individuals with the disease. These ulcers are often difficult and expensive to treat, and lead to severe morbidity. Conservative treatments are based on clinical evaluation and judgment and may include sharp debridement, wet-to-dry dressings, application of enzymatic agent, and the application of standard dressings. Advanced therapies and biologic dressings are often initiated after conservative treatments have failed.

Amniotic Membrane

• Encapsulates the fetal compartments: composed of amnion and chorion layers
• Non-vascular tissue consisting of epithelial cells, basement membrane, a thin compact layer and fibril network layer
• Fibrous layer contains cells anchoring collagen types: I, IV, and VII
• Biochemical properties help to reduce inflammation and enhance soft tissue healing
• Has antibacterial and pain reduction properties, are self-signaling and mediate tissue repair via the contained growth factors

Epidermis® - A Dehydrated Human Amniotic-Chorionic Membrane Allograft

• Allogenic and acellular active implant or graft for tissue regeneration and replacement
• Amniotic membrane obtained from screened and tested donors to ensure safety
• Cleared, detoxified, and sterilized by the proprietary PURR® process which produces a safe tissue with a 5 year, room temperature, shelf life

Study Design and Purpose

A retrospective crossover study of patients with Type 1 or Type 2 diabetes, having a diabetic foot ulcer (DFU) of at least 6 weeks duration that failed to heal with standard care (SOC) was conducted. All patients had previously been enrolled in a prospective randomized trial comparing the efficacy of dHACM with SOC treatment in RCT (SOC). With the addition of dHACM (Epidermis®, MiMedx, Kennesaw, GA) and that completed study without healing of their DFU.

Methods

This retrospective study was conducted under an IRB approved protocol in Southwest Virginia. Patients read and signed an approved informed consent prior to any study intervention.

Included

Patients with DFU previously randomized to SOC (n=11) who failed to heal upon completion of the prospective trial (dHACM vs. SOC). Twenty-five consecutive patients were enrolled from one site. Two outside wound care physicians reviewed and validated the clinical photos and data. All patients failed at least one month of conservative care prior to randomization. At 8 weeks 93% (10/11) of patients treated with dHACM were healed versus 8% (1/12) with SOC (p<0.001). At week 12 only one patient from the dHACM cohort had failed to heal all remaining SOC patient’s wounds remained open. Upon conclusion of the prospective trial, the SOC group of 11 patients failing to heal were offered bi-weekly treatment with dHACM. At that time their wounds had been present for a mean of 21 weeks and a wound size of 4.7cm². A central IRB approved retrospective analysis of this group was performed and complete healing was achieved in 91% (10/11) by 12 weeks. These prospective and retrospective results are compelling and show that treating diabetic foot ulcers with serial debridement, wet-to-moist dressings, application of enzymatic agent, and the application of dHACM is more effective than SOC and suggests that early effective treatment may decrease clinical operational costs and may prevent longer term medical complications.

Table 1. Patient characteristics.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ($)</td>
<td>61.5 ± 16.5</td>
</tr>
<tr>
<td>Smoking (%)</td>
<td>35.4 ± 24.5</td>
</tr>
<tr>
<td>smoker (%)</td>
<td>92.7%</td>
</tr>
<tr>
<td>Caucasian (%)</td>
<td>100.0%</td>
</tr>
<tr>
<td>Wound size (cm²)</td>
<td>4.7 ± 5.0</td>
</tr>
<tr>
<td>Wound duration (weeks)</td>
<td>21.1 ± 12.4</td>
</tr>
</tbody>
</table>

Results

Table 2. Mean percent reduction in wound size vs. baseline during each treatment period.

<table>
<thead>
<tr>
<th>Treatment week</th>
<th>SOC Period (RCT)</th>
<th>After dHACM (Epidermis)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 1 (%)</td>
<td>21.4 ± 35.8</td>
<td>62.5 ± 29.3</td>
<td>0.013</td>
</tr>
<tr>
<td>Week 2 (%)</td>
<td>15.5 ± 52.5</td>
<td>76.2 ± 25.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Week 3 (%)</td>
<td>13.3 ± 45.3</td>
<td>87.5 ± 15.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Week 4 (%)</td>
<td>26.6 ± 45.3</td>
<td>87.5 ± 15.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Week 6 (%)</td>
<td>6.7 ± 65.8</td>
<td>92.6 ± 12.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Week 8 (%)</td>
<td>-16.6 ± 65.8</td>
<td>93.9 ± 11.1</td>
<td></td>
</tr>
</tbody>
</table>

Figure 1. Rates of wound healing with SOC vs. dHACM (Epidermis®).

Figure 2. Percent of patients completely healed with dHACM after failing SOC.

Figure 3. Time to healing with SOC and dHACM.

Results

• In the initial study period while receiving SOC only, measurements of wound size were inconsistent week to week and by week 8 the overall mean wound size had increased over baseline. During the dHACM treatment period consistent reduction in wound size was noted week to week (Figure 1).
• Wounds were reduced by >50% in 81.8% patients (9/11) by week 2 (1 dHACM application).
• By week 4 (2 dHACM applications) all patients had >50% reduction in wound size.
• Complete healing was achieved by 10/11 (91%) of patients once they received dHACM treatment (Figure 2).

Conclusion

• These findings should be confirmed and expanded with subsequent clinical trials.
• The initial study period while receiving SOC only, measurements of wound size were inconsistent week to week and by week 8 the overall mean wound size had increased over baseline. During the dHACM treatment period consistent reduction in wound size was noted week to week (Figure 1).
• Wounds were reduced by >50% in 81.8% patients (9/11) by week 2 (1 dHACM application).
• Complete healing was achieved by 10/11 (91%) of patients once they received dHACM treatment (Figure 2).

Case 1. Patient healed in 2 weeks (1 Epidermis® application)

Case 2. Healed in 9 weeks (5 Epidermis® applications)

Data presented as mean ± SD or percent as indicated. BMI = body mass index.

References