A Prospective, Randomized, Blinded, Comparative Study of Injectable Dehydrated Human Amniotic/Chorionic Membrane (dHACM) in the Treatment of Recalcitrant Plantar Fasciitis

Charles Zelen, DPM
Attila Poka, MD
James Andrews, MD
A Prospective, Randomized, Blinded, Comparative Study of Injectable Dehydrated Human Amniotic/Chorionic Membrane (dHACM) in the Treatment of Recalcitrant Plantar Fasciitis

Presenter: Charles M Zelen, DPM

My disclosure is in the Final AOFAS Program Book. I have a potential conflict with this presentation due to:

Research funding was provided by MiMedx.

Co-authors: Attila Poka, MD and James Andrews, MD disclose no conflicts relevant to this study.
Introduction

- Plantar fasciitis, a degenerative syndrome, is one of the most common orthopedic complaints relating to the foot, affecting more than one million persons per year.
  - Goff JD, Am Fam Physician 2011

- Conservative management leads to resolution of symptoms in most patients, although several months to even years of treatment is often required.
  - Scioli M, Techniques in Foot & Ankle Surgery 2011

- A treatment which reduces inflammation and heals soft-tissue damage, allowing for rapid return to pain free activities of daily living is desirable.
Human Amniotic Membrane

- Has been used to enhance healing for >100 years.
- In vivo and in vitro studies have shown that the biochemical properties of amniotic membrane help to reduce inflammation and enhance soft tissue healing.
  - Niknejad H, Eur Cell Mater 2008
- Repair is mediated through contained growth factors including EGF, TGF-β, FGF which are known to stimulate epithelial cell migration and proliferation, and PDGF A and B which stimulate many metabolic processes, including general protein and collagen synthesis, collagenase activity, and chemotaxis of fibroblasts and of smooth muscle cells.
  - Parolini O, Human Placenta: Structure and Development 2010
Dehydrated Human Amniotic/Chorionic Membrane (dHACM) Allograft

- The PURION® process is a method of gently cleaning, sterilizing, and drying human amniotic/chorionic membrane prior to injection or application.

- The dHACM allograft material can be micronized to create a powder that can be suspended in saline for injection (AmnioFix®, MiMedx, Marietta, GA).

Study Objective

To examine the efficacy of micronized, dHACM in suspension with 0.9% saline as an injectable treatment for refractory plantar fasciitis (PF).
Methods

- Central IRB approved prospective, randomized, single-blind, clinical trial comparing improvement of PF symptoms in patients receiving standard of care treatment alone versus standard of care with the injection of micronized dHACM allograft.

- Patients with PF recalcitrant to standard treatments were randomized to receive placebo injection, 0.5 cc of dHACM, or 1.25 cc dHACM.

- PF symptoms were evaluated weekly for 6 weeks then at week 8 using AOFAS Hindfoot Scale, Wong-Baker FACES™ Pain Rating Scale. QualityMetric’s SF-36v2® Standard Health Survey was completed at baseline and week 8.

- Primary outcome was difference in AOFAS Hindfoot Score from baseline and week 8.

- Intention-to-treat methods were used to compare data within and across the three study groups. The Mann-Whitney test or Kruskal-Wallis test was used to perform a comparison between two or > two samples of continuous data respectively. The Chi-squared test was used to compare two or more samples of binary data. The level of statistical significance was set at \( p < 0.05 \).
## Results - Patient Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intervention Group</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Controls</td>
<td>0.5cc dHACM</td>
</tr>
<tr>
<td>Sample Size</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>Female (#/%)</td>
<td>12 (80)</td>
<td>7 (47)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>50.5 ± 9.9</td>
<td>56.1 ± 12.8</td>
</tr>
<tr>
<td></td>
<td>53.0 (33, 63)</td>
<td>60.0 (30, 72)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>29.2 ± 6.3</td>
<td>29.7 ± 5.6</td>
</tr>
<tr>
<td></td>
<td>27.3 (22.3, 42.3)</td>
<td>28.7 (22.5, 43.6)</td>
</tr>
<tr>
<td>PF symptoms</td>
<td>20.6 ± 13.8</td>
<td>24.2 ± 13.0</td>
</tr>
<tr>
<td>(weeks)</td>
<td>16.0 (8, 51)</td>
<td>21.0 (8, 48)</td>
</tr>
</tbody>
</table>
Primary Outcome: Mean Difference in AOFAS Hindfoot Score Compared to Baseline Measurement During the Study Period

- Within each group significantly higher scores were observed between baseline and week eight (all $p \leq 0.01$), although significantly greater improvement was noted in the groups receiving dHACM vs. controls (all $p < 0.001$).

- Similar improvement in AOFAS Hindfoot scores were observed for those patients receiving 0.5cc or 1.25cc dHACM at any week.
Other Outcome Measures

Wong-Baker FACES™ Score:
- Patients receiving dHACM reported significantly greater reductions in pain from baseline reports (all \( p < 0.001 \) controls vs. 0.5cc dHACM, and all \( p < 0.004 \) controls vs. 1.25cc dHACM).
- Pain reduction from baseline appears similar for the dHACM groups.

QualityMetric's SF-36v2® Standard Health Survey:
- Patients receiving dHACM had significantly greater improvement in physical and mental scores vs. controls (all \( p \leq 0.002 \)).
- The magnitude of difference between baseline and week 8 appears similar when comparing the dHACM groups.
Conclusions

- This is the 1st randomized trial on the use of dHACM for treatment of Plantar Fasciitis.
- Patients with chronic/refractory PF receiving a single-dose injection of dHACM allograft experienced significant improvement in symptoms and increased function within 1 week of injection and had continued improvement over the 8 week study period.
- Limitations of the present study are those inherent to small sample size. Further studies are needed to better assess the utility of dHACM within current treatment guidelines for the management of PF.

The results of our clinical trial show that dHACM allograft injection is an effective treatment for patients with chronic plantar fasciitis and may reduce costs by decreasing the need for repeat office visits or costly surgical interventions.