Evidence Table


Study Type: Randomized controlled trial.

Study Aim: To evaluate the clinical role of noncontact, low-frequency ultrasound therapy (MIST therapy) in the treatment of nonhealing leg and foot ulcers associated with chronic critical leg ischemia.

Outcomes

Primary: Incidence of wound healing in 12 weeks in the two study groups.
Secondary: Degree of wound healing associated with TcPO2 levels of 20-40 mmHg and levels <20 mmHg in the supine and dependent positions.

Design

- **Number of subjects:** N=70 (n=35 in treatment group, and n=35 in control group).
- **Description of study population:** MIST therapy group: Mean age 74 years, 80% men, 69% had prior revascularization, 11% never smoked. Control group: Mean age 76 years, 74% men, 80% had prior revascularization, 26% never smoked. Overall in the two groups 76% had CAD, 67% DM, and 80% had hypertension or dyslipidemia.
- **Inclusion criteria:** Documented chronic limb ischemia evaluated by transcutaneous oximetry (TcPO2), wounds present for a minimum of 8 weeks before enrollment.
- **Exclusion criteria:** Evidence of erythema or purulent discharge at enrollment, undergoing chemotherapy, or inability to attend three treatment sessions per week.
- **Intervention:** Patients were randomly assigned to receive either standard wound care alone or standard wound care plus ultrasonic MIST therapy. Standard wound care comprised topical therapy using principles of moist wound healing, daily dressing changes, and weekly debridement. The types of dressings used or technique of debridement was not specified. Systemic therapy included aggressive medical management to optimize cardiovascular health, diabetic management, offloading, and compression therapy when indicated. Ultrasonic MIST therapy (Celleration Inc., Eden Prairie, MN) was delivered as 5-minute sessions 3 times weekly for 12-weeks.
- **Source of outcome data:** Weekly evaluation of the wound including wound measurement and digital photography of the wound bed. Wound volume was based on ruler measurements using length by width by depth calculations. Wound depth was obtained using a sterile cotton-tip applicator and ruler.
- **Length of follow-up:** 12 weeks.

Validity

- **Blinding? No**
- **Appropriate randomization procedures? No discussed.**
- **Appropriate comparison intervention?** MIST therapy plus standard treatment was not compared to a sham or an alternative intervention, but to standard therapy alone.
• Treatment/control groups comparable at baseline? Yes.
• Other than intervention, was care/follow-up similar in each group? Yes.
• Adequate compliance with intervention? Not provided.
• Sufficient statistical power? No discussed.
• Intention to treat analysis? Not discussed but apparently all patients had follow-up data.
• Completeness of follow-up: The authors did not report any dropout.
• Industry funding? Yes.

Conclusions regarding validity of methods:

The trial was randomized and controlled but was not blinded, conducted in a single site, and sponsored by the manufacturer, all of which are sources of bias.

Results

Proportion of patients with >50% wound healing after 12 weeks of treatment

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<thead>
<tr>
<th></th>
<th>MIST therapy plus Standard care group</th>
<th>Standard care only group</th>
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<tbody>
<tr>
<td>n=35</td>
<td></td>
<td>n=35</td>
</tr>
<tr>
<td>&gt;50% healing, No (%)</td>
<td>22 (63%)</td>
<td>10 (29%)</td>
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<tr>
<td>*NNT 3</td>
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<td>&lt;0.001</td>
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Only 1% of the patients in the 2 treatment groups with >50% wound healing, had a baseline TcPO2 <20 mmHg with dependency

Authors’ Conclusions

The authors concluded, “The rate of healing and of cutaneous foot and leg ulceration in patients with chronic ischemia improved significantly when MIST therapy was combined with the standard of wound care.”

Reviewer’s Conclusions

The trial was randomized and controlled, but was not blinded and was supported by the manufacturer which is a potential source of bias. Moreover, the outcomes were mainly based on measurements which are subject to potential error, the authors did not discuss if there were any dropouts, rate of compliance, or adverse events associated with the intervention.

The results of the trial show that patients managed with MIST therapy in addition to standard treatment achieved a significantly higher >50% wound closure rate in 12 weeks than those managed with standard therapy alone. A secondary analysis of the trial showed that patients with critical limb ischemia with baseline TcPO2 <20 with dependency were significantly less likely to achieve >50% healing by week 12, using standard treatment with or without MIST therapy.