Does Therapeutic Massage Ameliorate Chemotherapy-Induced Peripheral Neuropathy?

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INTRODUCTION and CONCEPT

Chemotherapy-induced peripheral neuropathy (CIPN):
- Common, potentially severe, dose-limiting side effect of many 1st and 2nd line chemotherapy regimens.
- Affects ~1/3 of cancer patients who receive chemotherapy,
- often requiring dose reduction or interruption of treatment.
- Affects feet and often hands as well.
- Long-lasting or permanent in some patients.
- Profound impact on quality of life (QoL).
- Long-lasting or permanent in some patients.
- Etiology unclear, but causative agents include:
  - Taxanes: e.g. Docetaxel, Paclitaxel, Taxol
  - Platin: e.g. Cisplatin, Carboplatin, Oxaliplatin.

Current Treatment for CIPN:
- No established and acceptable standard of care.
- Standard practice (for other chronic nerve pain):
  - Steroids, numbing agents, antidepressants, anticonvulsants, opioids/narcotics
- In long-term these drugs can themselves be toxic.
- During anti-cancer chemotherapy:
  - Reduce chemotherapy dose and/or discontinue it.
- Interest in alternative, non-pharmacologic approaches.

HYPOTHESES

Primary:
Therapeutic massage reduces sensory signs and symptoms of CIPN, and improves quality of life.

Secondary:
Effects are mediated by, or reflected in, improved peripheral blood flow.

METHODS

Non-randomized controlled design (Grade 2 CIPN):
- Treatment Group (n=15):
  - 12 treatments in 5 weeks: 15 minutes per lower extremity
  - Follow for 19 additional weeks
  - Monitoring Group (observation only) (n=8):
  - Eligible but cannot accommodate treatment schedule
  - Monitor for 6 weeks.

Assessments
- Neuropathic symptoms (NPS-CIN, CINPAT, EORTC QLQ-CIPN-20): severity, quality, anatomic symptom extension
- Neuropathic signs: monofilament, vibration sensitivity (TNSr)
- Cancer-specific quality of life (EORTC QLQ-30), including impacts on activities of daily living
- Superficial circulation of feet: emitted heat (FLIR camera), localized temperature.

PREVIOUS WORK


PRELIMINARY RESULTS: TREATMENT GROUP

STUDY POPULATION (N=10)
Grade 2 CIPN:
- Moderate; Limiting instrumental ADL
- secondary to taxane or platin.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>8 (80%)</td>
</tr>
<tr>
<td>Male</td>
<td>2 (20%)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>61.2 ± 11.9 (48 – 82)</td>
</tr>
<tr>
<td>CIPN (years)</td>
<td>2.0 ± 3.0 (0.3–7.4)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1 (10%)</td>
</tr>
<tr>
<td>Smoker</td>
<td>2 (20%)</td>
</tr>
<tr>
<td>Prior anti-CIPN Rx</td>
<td>3 (30%)</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>Platin: 2, Taxane: 7, Both: 1</td>
</tr>
<tr>
<td>Primary site</td>
<td>Breast: 6, Colon: 2, Lung: 4</td>
</tr>
</tbody>
</table>

SYMPTOM SEVERITY (CIPNAT SUBSET)

<table>
<thead>
<tr>
<th>Score (0 – 10)</th>
<th>Before Mean (Median)</th>
<th>After Mean (Median)</th>
<th>Change</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite</td>
<td>4.6 (4.0)</td>
<td>1.4 (0.8)</td>
<td>-3.2 (-3.0)</td>
<td>0.006*</td>
</tr>
<tr>
<td>Numbness</td>
<td>6.5 (5.8)</td>
<td>2.8 (2.7)</td>
<td>-3.6 (-4.0)</td>
<td>0.011*</td>
</tr>
<tr>
<td>Cold Sens.</td>
<td>5.8 (7.5)</td>
<td>1.6 (1.0)</td>
<td>-4.1 (-5.0)</td>
<td>0.011*</td>
</tr>
<tr>
<td>Tingling</td>
<td>5.4 (5.8)</td>
<td>1.6 (1.0)</td>
<td>-3.8 (-4.2)</td>
<td>0.006*</td>
</tr>
<tr>
<td>Aches</td>
<td>3.7 (4.0)</td>
<td>0.6 (0.0)</td>
<td>-3.1 (-3.5)</td>
<td>0.011*</td>
</tr>
<tr>
<td>Nerve pain</td>
<td>3.6 (3.8)</td>
<td>0.7 (0.0)</td>
<td>-3.0 (-3.2)</td>
<td>0.011*</td>
</tr>
<tr>
<td>Weakness</td>
<td>3.3 (2.5)</td>
<td>0.6 (0.0)</td>
<td>-2.8 (-2.2)</td>
<td>0.011*</td>
</tr>
</tbody>
</table>

1 Wilcoxon matched-pairs signed-rank test.
N=10 participants. Higher score = more severe.

Composite Symptom Severity

QUALITY OF LIFE (EORTC QLQ)

NEUROPATHIC PAIN SCORE (NPS)
Significant reductions (improvement) in 5-point Pain Quality scores using NPS-CIN.

FLIR THERMOGRAPHY: EXAMPLE
Pre Tx 10 minutes after Tx 15 minutes after Tx

Composite 4.6 (4.0) 1.4 (0.8) -3.2 (-3.0) 0.006*
Numbness 6.5 (5.8) 2.8 (2.7) -3.6 (-4.0) 0.011*
Cold Sens. 5.8 (7.5) 1.6 (1.0) -4.2 (-5.0) 0.011*
Tingling 5.4 (5.8) 1.6 (1.0) -3.8 (-4.2) 0.006*
Aches 3.7 (4.0) 0.6 (0.0) -3.1 (-3.5) 0.011*
Nerve pain 3.6 (3.8) 0.7 (0.0) -3.0 (-3.2) 0.011*
Weakness 3.3 (2.5) 0.6 (0.0) -2.8 (-2.2) 0.011*

Composite Symptom Severity

Tingling

PREVIOUS WORK


FUNDING SOURCES

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CONCLUSIONS

Major Findings to Date:
- Improvements in symptoms “As good as expected with drugs”!
- Are additional treatments advisable for patients with worse or more established symptoms?
- Durability: “maintenance treatments”?
- Mechanism: temperature appears to increase after treatment is completed. Analyses are pending.

Issues for Future Consideration:
- Planning randomized clinical trial (RCT):
  - No acceptable standard of care for “control”
  - Impossible to be “blinded”.
- Which patients are most likely to benefit?
- Does efficacy vary by chemo agent, total dose?
- Does variability in delivery of treatment elements affect efficacy?

FUTURE RESEARCH PLANS

Address Efficacy and Physiologic Mechanisms:
- RCT in patients with established CIPN.
- RCT for prevention or reduction of CIPN in patients receiving chemotherapy
- Case-control study:
  - Blood circulation in feet of CIPN patients vs non-CIPN cancer controls
- Cohort study:
  - Among patients receiving chemo, do changes in superficial circulation predict risk for, or onset of, symptomatic CIPN?

SPECIFIC AIMS

Aim 1
Aim 2
Aim 3