A RANDOMIZED ASSESSOR-BLINDED WAIT-LIST CONTROLLED TRIAL TO ASSESS THE EFFECTIVENESS AND COST-EFFECTIVENESS OF ACUPUNCTURE IN THE MANAGEMENT OF CHEMOTHERAPY-INDUCED PERIPHERAL NEUROPATHY

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Background

- Overall incidence of chemotherapy-related peripheral neuropathy (CIPN) is 10-35% of patients during treatment and it may be as high as 100%, depending on the chemotherapy drug, dose-intensity, cumulative dose and other as yet unidentified risk factors (Molassiotis et al 2019; Mols et al 2014; Miaskowski et al 2016).

- Significant implications of CIPN on the quality of life of patients, including dysfunction in daily activities, social well-being, work reintegration and physical impairments such as pain (Mols et al 2014).

- Considerable impact on health care resource utilization: those experiencing CIPN having more outpatient visits and medication use, estimated to be at US$17,000 more in patients with CIPN than non-CIPN cancer patients (Pike et al 2012).
CIPN management

- Largely unsuccessful
- ASCO guidelines provide no recommendation for preventing CIPN, a moderate recommendation for duloxetine in the treatment of CIPN and a few treatment options based on inconclusive evidence for CIPN (Hershman et al 2014).
- Acupuncture may be considered for treating CIPN: small scale, pilot studies (N<30) or case series provide some initial evidence of effect, particularly in decreasing neuropathic pain.
- A systematic review identified three such trials which all used a different approach (acupuncture, auricular acupuncture, acupuncture with moxibustion) (Fanconi et al 2013)
The aim of the study is to test the effectiveness (in terms of neuropathic pain, other neurological sensations and overall quality of life) of an 8-week course of acupuncture in the management of CIPN in cancer patients who are receiving/have received neurotoxic chemotherapy.

Assess its cost-effectiveness
Methods

- Design: randomized assessor-blinded wait-list controlled trial
- Sample size: N=87, fully-powered trial
- Settings: 2 large cancer centers in Hong Kong
- Randomization: computer-generated, balancing for treatment types
- ClinicalTrials.gov Identifier: NCT02553863
**Inclusion criteria**

- Patients with diagnosis of breast, gynecological, colorectal or head & neck cancer, and multiple myeloma
- Patients with cancer stage I-IV;
- Karnofsky Performance score 80-100.
- Currently receiving or having received neurotoxic chemotherapy (taxanes, cisplatin, oxaliplatin, bortezomib, etc).
- Reporting tingling in hands/feet and other clinical indications of CIPN after initiation of cancer treatments,
- Confirmed to be indicative of CIPN by a medical consultant often through brief neurological examination
- Not using any medication for the prevention or treatment of CIPN for the past 3 months.
- Willing to participate and be randomised to one of the study groups.
- No previously established peripheral neuropathy.
Intervention

- Patients received, in addition to standard care, a standardized 30-minute acupuncture session needling specific body points;
- The points were standardized according to the clinical manifestations of the subjects: For upper limbs we used LI4, LI11, PC7, TE5, and/or Baxie points (Ex-UE9)--for lower limbs we used SP6, ST36, LV3, ST41, and/or Bafeng (Ex-LE10);
- An equal ‘dose’ of points was used for all patients (4 points bilaterally);
- Stimulation of the acupoints to achieve de qi sensation;
- Acupuncture sessions were carried out twice weekly for 8 weeks (=a total of 16 sessions);
- Each session was based on a strict protocol followed by all therapists.
Outcome measures [*blinded assessors*]: (Baseline, week 8, follow-up wk 14 & 20)

- Primary outcome at 8-weeks: Pain: ‘worst pain during past week’ measured using the Brief Pain Inventory

Secondary outcomes:

- Functional Assessment of Cancer Therapy (FACT/GOG-Ntx)
- Neurotoxicity examination [baseline and at the end of acupuncture course].
- The 7-domain Total Neuropathy Score-clinical version (TNSc).
- Neurophysiological testing (n=22)
- Health economics evaluation
Results
Pain severity

Baseline | Wk 8 | Wk 14 | Wk 20
---|---|---|---
Control gr | | | |
Exp gr | | | |

Graph showing pain severity over time with different groups.
Physical well-being

![Graph showing physical well-being over time with two groups: Control gr and Exp gr.](image-url)
Neurotoxicity score (FACT-G Ntx)
FACT/COG-Ntx Trial Outcome Index changes over time
# Changes in TNS score & CTCAE

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>8 weeks</th>
<th>p-value vs baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Neuropathy Score (TNSc)</strong>&lt;br&gt;p for group by time interaction 0.01</td>
<td>Control group Intervention Effect size</td>
<td>7.6 (0.5) 8.1 (0.5)</td>
<td>7.6 (0.6) 6.2 (0.5) 0.42</td>
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<tr>
<td><strong>p-value#</strong></td>
<td>0.43</td>
<td>0.10</td>
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<tr>
<td><strong>NCI-CTCAE-sensory (Moderate/severe)</strong>&lt;br&gt;p for group by time interaction 0.046</td>
<td>Control group Intervention</td>
<td>N=27 (63%) N=29 (66%)</td>
<td>N=26 (62%) N=16 (37%)</td>
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<tr>
<td><strong>p-value#</strong></td>
<td>0.76</td>
<td>0.02</td>
<td></td>
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<tr>
<td><strong>NCI-CTCAE motor (Moderate/severe)</strong>&lt;br&gt;p for group by time interaction 0.07</td>
<td>Control group Intervention</td>
<td>N=30 (70%) N=33 (75%)</td>
<td>N=28 (67%) N=21 (50%)</td>
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<tr>
<td><strong>p-value#</strong></td>
<td>0.59</td>
<td>0.11</td>
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## Cost-effectiveness of acupuncture

<table>
<thead>
<tr>
<th>Treatment group</th>
<th>Cost (HKD$) Mean (SD)</th>
<th>Incremental cost</th>
<th>QALYs Mean (SD)</th>
<th>Incremental QALYs</th>
<th>ICER (HK$/ QALY)</th>
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<tbody>
<tr>
<td><strong>Health care provider perspective</strong></td>
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<tr>
<td>Usual care</td>
<td>$3,286.16 (6009.04)</td>
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<td>0.200 (0.022)</td>
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<tr>
<td>Acupuncture</td>
<td>$8,849.25 (6182.91)</td>
<td>$5,563.09</td>
<td>0.209 (0.021)</td>
<td>0.009</td>
<td>$616,965.62</td>
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<td><strong>Societal perspective</strong></td>
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<tr>
<td>Usual care</td>
<td>$12,384.40 (19230.74)</td>
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<td>0.200 (0.022)</td>
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<tr>
<td>Acupuncture</td>
<td>$19,815.03 (22955.75)</td>
<td>$7,430.63</td>
<td>0.209 (0.029)</td>
<td>0.009</td>
<td>$824,083.44</td>
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<td><strong>Patient perspective</strong></td>
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<tr>
<td>Usual care</td>
<td>$7,919.19 (17636.65)</td>
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<td>0.200 (0.022)</td>
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<td>Acupuncture</td>
<td>$12,794.84 (17793.87)</td>
<td>$4,875.65</td>
<td>0.209 (0.029)</td>
<td>0.009</td>
<td>$540,727.56</td>
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Discussion

- Trial confirmed beneficial effect of acupuncture in the management of CIPN, in this first fully-powered trial
- Key outcomes met with MCID changes
- Some effects were not sustained at week 14 and 20, suggesting the need for ‘boosting’ sessions
- Acupuncture can be a treatment option for CIPN, in a field that options are few
- Consider ‘dose’, duration & acupoints
- Effective but not cost-effective treatment
Questions and comments