Evaluation of acupuncture in the management of chemotherapy-induced peripheral neuropathy

Graeme K Donald,1 Irene Tobin,1 Jacqui Stringer1

Abstract
Aim To clinically evaluate the effectiveness of acupuncture when used in the management of chemotherapy-induced peripheral neuropathy (PN).

Background During cancer treatment, certain chemotherapies can cause varying degrees of PN. Patients’ quality of life can be seriously impaired through loss of sensation, pain or mobility problems. Conventional medications routinely used to manage neuropathic symptoms have poor side-effect profiles and there is little or no evidence justifying their use to treat chemotherapy-related neurotoxicities. There are studies suggesting that acupuncture may be an effective therapy in treating PN across a number of different aetiologies.

Design A retrospective service evaluation.

Method Patients (n=18) were referred for acupuncture by the medical staff and/or nurse specialists or they self-referred for treatment. A course of six weekly acupuncture sessions was offered to them, and their details were recorded on an evaluation form prior to session one. Points were selected by acupuncturists, based on patient presentation, and needles remained in situ for 30–45 min. Treatments took place in outpatient clinics, chemotherapy day case ward or a drop-in clinic based in a physiotherapy gym. The evaluation form was completed at the end of session 6 by a therapist who had not been involved in patient care.

Results 82% (n=14) of patients reported an improvement in symptoms following their course of acupuncture; one patient with advanced disease died during the 6 weeks. Some patients derived additional benefits from the treatment including a reduction in analgesic use and improved sleeping patterns. The most common acupoints used were SP6 (n=18), ST36 (n=18) and LV3 (n=14).

Conclusion Although these results are encouraging, they are uncontrolled. They suggest that acupuncture could be an option for these patients and controlled trials using validated patient-reported outcome measures are justified.

INTRODUCTION
Peripheral neuropathy (PN) is a problematic side effect for patients undergoing a variety of chemotherapy regimens. It can be defined as the dysfunction of the sensory, motor and/or autonomic neurons of the peripheral nervous system.1 Patients can experience a variety of symptoms including pain, paraesthesia and loss of proprioception. These effects can have a detrimental impact on the patients’ quality of life by affecting gait and mobility and by limiting their ability to perform simple acts of dexterity, such as buttoning a shirt or tying a shoe lace. PN poses a major problem for patient care as pharmacological treatments are often inadequate2 due to dosing complexities, delayed analgesic onset and common side effects such as somnolence. Crucially, the incidence of PN can be dose limiting for efficacious chemotherapies such as oxaliplatin, thalidomide and bortezomib. Patients whose tumours are responding may well fail to report their symptoms for fear of dose reduction or break in treatment. The challenges associated with pharmacological treatments present an opportunity to investigate alternative methods of management that may complement allopathic care. The evidence is less than robust for the treatment for PN with standard medication. Various studies have been conducted on the conventional treatment of PN using tricyclic antidepressants (TCAs),3 4 gabapentin,5 pregabalin6–8 and opiates.9 The evidence generated from these trials suggests low or no efficacy of TCAs and gabapentin in PN caused by chemotherapy or diabetes. Pregabalin appears to be effective, but it is expensive and retains a poor side-effect profile. In diabetic neuropathy, however, preliminary studies show some promise in using acupuncture as an adjunct to standard medication10–12 and this may translate to chemotherapy-induced PN.

The exact mechanism of acupuncture remains unclear. Recent research has associated acupuncture with a number of biochemical mediators including γ-aminobutyric acid, glutamate, adenosine and β-endorphin, all of which are active within the nervous system.13 14 Nerve growth factor (NGF) is currently the subject of experiments to develop medications for PN but Manni et al15 have reported on their experimental data linking acupuncture with increased NGF production. Furthermore, imaging studies show changes in limbic system and other structures.16 17 Zhao18 also showed that manual acupuncture activates all types of nerve fibres, myelinated and unmyelinated. Although there is no grand unifying theory combining all these data, it points to possible explanations for how and why acupuncture may work for patients experiencing CIPN.

Patients at an acute cancer hospital in the northwest of England with PN refractory to standard care are offered a course of acupuncture; a service that has been available since January 2009. This is an evaluation of the clinical effectiveness of the acupuncture service provided, from January 2009 to August 2010, when used in the treatment of chemotherapy-related PN, as reported by the patients treated.

Aim The aim of this study is to explore the potential effectiveness of acupuncture in the treatment of chemotherapy induced PN.

Method Patients were referred by the medical staff and/or nurse specialist or they...
self-presented for treatment. Although patients may have been experiencing more than one problematic symptom, the primary purpose for the provision of acupuncture was to treat the PN; other conditions were secondary. Once the patients’ clinical condition had been assessed as suitable for acupuncture (ie, platelet count >100×10^9/l), they were initially offered a course of six weekly treatments. Patient suitability to receive acupuncture was assessed prior to each session. All acupuncturists were qualified nurses trained in the western medical approach (WMA) and needles remained in situ for 30–45 min. Acupuncturists selected points to be used based on patient presentation at each session. Treatments took place either in an outpatient clinic, chemotherapy day case ward or a drop-in clinic based in a physiotherapy gym.

An evaluation form was completed by the therapist prior to the first session and on completion of the final (sixth) session. A different member of the team completed this final evaluation in order to minimise bias. Details of the patient and their treatment were captured and the treatment response after the 6 weeks was categorised as improved, unchanged, aggravated, increased or other. Additional benefits were also recorded, which included tick-boxes indicating relaxation, reduced stress, better sleep, improved mood, less medication and other.

This was an evaluation of the service being offered to patients as part of routine hospital activity; hence, no attempts were made to control variables. Furthermore, no validated questionnaires were used and no baseline measurements were taken. The results are based purely on patient opinion following completion of the treatment. Electronic records were accessed following treatment to retrieve demographic data and to identify, by cross-referencing with the literature and symptom onset, the likely agent causing the neuropathy. This ongoing evaluation takes place with every patient in the hospital who accesses the acupuncture service, in order to monitor efficacy. This paper, however, focuses on those whose primary concern was PN.

**RESULTS**

A total of 18 patients (eight males, 44%, and ten females, 56%) were referred to the service for the management of their PN (September 2008 to June 2010). The mean age was 51.83 years (SD 12.97); 17 patients fully completed the course of acupuncture and one patient died during the 6 weeks. Of the patients commencing treatment, 94% (n=17) were White-British and 6% (n=1) was White-Irish. The primary cancer diagnoses are shown in table 1. Fourteen patients were referred for acupuncture to complement conventional treatment, two patients requested acupuncture from their clinician and two were referred as conventional treatment was unsuccessful. One patient received acupuncture twice a week for 3 weeks while the remaining 16 received weekly treatments for 6 weeks.

Of the 17 patients completing the course of treatment, 82% (n=14) reported that acupuncture had improved their neuropathy symptoms, 18% (n=3) reported no change and there were no reports of deterioration in PN. Thirty-five per cent (n=6) reported one additional benefit from the acupuncture while 41% of patients (n=7) documented more than one additional benefit. Twenty-four per cent of the patients (n=4) had no additional benefits to report from the treatment.

### Table 1 Patient summaries

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Sex</th>
<th>Age</th>
<th>Likely agent(s) causing PN</th>
<th>Acupuncture effect on symptoms</th>
<th>Relevant comorbidities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemato-oncology</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MM</td>
<td>F</td>
<td>58</td>
<td>Bortezomib</td>
<td>Improved</td>
<td>Extensive bony (spinal) involvement</td>
</tr>
<tr>
<td>ALL</td>
<td>M</td>
<td>43</td>
<td>Vincristine</td>
<td>Improved</td>
<td>Nil</td>
</tr>
<tr>
<td>MM</td>
<td>M</td>
<td>46</td>
<td>Thalidomide</td>
<td>Improved</td>
<td>Extensive bony (spinal) involvement</td>
</tr>
<tr>
<td>MM</td>
<td>M</td>
<td>68</td>
<td>Bortezomib</td>
<td>Improved</td>
<td>Nil</td>
</tr>
<tr>
<td>ALL</td>
<td>F</td>
<td>28</td>
<td>Vincristine</td>
<td>Improved</td>
<td>Nil</td>
</tr>
<tr>
<td>ALL</td>
<td>F</td>
<td>23</td>
<td>Vincristine</td>
<td>Unchanged</td>
<td>Steroid-induced diabetes mellitus</td>
</tr>
<tr>
<td>MM</td>
<td>F</td>
<td>53</td>
<td>Bortezomib</td>
<td>Improved</td>
<td>Nil</td>
</tr>
<tr>
<td>ALL</td>
<td>M</td>
<td>44</td>
<td>Vincristine</td>
<td>Improved</td>
<td>Nil</td>
</tr>
<tr>
<td>MM</td>
<td>M</td>
<td>48</td>
<td>Thalidomide</td>
<td>Improved</td>
<td>Nil</td>
</tr>
<tr>
<td>CML</td>
<td>M</td>
<td>59</td>
<td>Vincristine</td>
<td>Unchanged</td>
<td>Nil</td>
</tr>
<tr>
<td>MM</td>
<td>F</td>
<td>66</td>
<td>Bortezomib</td>
<td>Unchanged</td>
<td>Plasmacytoma compressing S1 nerve root</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colon adenocarcinoma</td>
<td>M</td>
<td>57</td>
<td>Oxaliplatin</td>
<td>Improved</td>
<td>Nil</td>
</tr>
<tr>
<td>Colon adenocarcinoma</td>
<td>F</td>
<td>49</td>
<td>Oxaliplatin</td>
<td>Improved</td>
<td>Hypothyroidism</td>
</tr>
<tr>
<td>Colon adenocarcinoma</td>
<td>M</td>
<td>58</td>
<td>Oxaliplatin</td>
<td>Improved</td>
<td>Type 2 diabetes mellitus</td>
</tr>
<tr>
<td>Caecum adenocarcinoma</td>
<td>F</td>
<td>59</td>
<td>Oxaliplatin</td>
<td>Improved</td>
<td>Nil</td>
</tr>
<tr>
<td>Breast</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left invasive ductal carcina</td>
<td>F</td>
<td>43</td>
<td>Docetaxel</td>
<td>Improved</td>
<td>Guillain–Barrè syndrome</td>
</tr>
<tr>
<td>Left invasive ductal carcina</td>
<td>F</td>
<td>74</td>
<td>Paclitaxel</td>
<td>Improved</td>
<td>Type 2 diabetes mellitus</td>
</tr>
<tr>
<td>Gynaecological</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ovarian adenocarcinoma</td>
<td>F</td>
<td>57</td>
<td>Carboplatin/Paclitaxel</td>
<td>Patient died</td>
<td>Nil</td>
</tr>
</tbody>
</table>

AML, acute myeloid leukaemia; ALL, acute lymphoblastic leukaemia; CML, chronic myeloid leukaemia; MM, multiple myeloma; PN, peripheral neuropathy.
Table 2  Frequent acupoints (n=18)

<table>
<thead>
<tr>
<th>Acupoint</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>SP6</td>
<td>18</td>
</tr>
<tr>
<td>ST36</td>
<td>18</td>
</tr>
<tr>
<td>LV3</td>
<td>14</td>
</tr>
<tr>
<td>LI4</td>
<td>13</td>
</tr>
<tr>
<td>BL60</td>
<td>12</td>
</tr>
<tr>
<td>Ba Feng/Ba Xie</td>
<td>10</td>
</tr>
</tbody>
</table>

Table 3  Additional acupuncture benefits (n=17)

<table>
<thead>
<tr>
<th>Benefit</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleeping</td>
<td>8</td>
<td>47</td>
</tr>
<tr>
<td>Relaxed</td>
<td>8</td>
<td>47</td>
</tr>
<tr>
<td>Reduced stress</td>
<td>4</td>
<td>24</td>
</tr>
<tr>
<td>Less medication</td>
<td>4</td>
<td>24</td>
</tr>
<tr>
<td>Improved mood</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Other</td>
<td>4</td>
<td>24</td>
</tr>
</tbody>
</table>

Table 1 gives a treatment summary of all 18 patients involved in the evaluation and Table 2 displays the acupoints most frequently used by practitioners. Table 3 shows the breakdown of the additional benefits derived by the patients.

DISCUSSION

It is proposed that, with the 82% reported success rate seen in this evaluation, acupuncture may be worth further exploration in the management of chemotherapy-related PN. The effectiveness rate expressed by this cohort of patients is similar to that of Zhang et al 10 and Abuaisha et al 12, who achieved success rates of 87.5% and 77%, respectively, in managing diabetic PN.

The similarity between the results for diabetic neuropathy and those described here suggests that there may be aspects of neuropathy that are common across differing aetiologies and that acupuncture could be effective in addressing this commonality. Furthermore, in the only other study of this nature, Wong and Sagar 18 evaluated acupuncture in the management of PN caused by carboplatin and paclitaxel. This involved a small number of patients (n=5); however, 100% reported reductions in their pain scores. Participants were treated weekly for 6 weeks, had a treatment break for 4 weeks and then repeated the original 6-week cycle. Ostensibly, patients in this study received double the acupuncture dose of our participants. Although very preliminary, these findings compiled with our own and demonstrate potential and the need for further research into this novel method of treatment.

CHEMOTHERAPY-SPECIFIC EFFECTS

Most oxaliplatin neuropathies are reversible and the majority of patients recover within 6–12 months.19 It is important to note that 100% of patients reported that this symptom was controlled at 6 weeks, rather than requiring the 6–12-month recovery period identified by Saif and Reardon.23 If validated, this level of success could potentially spare patients months of distress coping with their PN.

Vincristine is another chemotherapy agent well known for its neurotoxic properties and PN has been quoted as occurring in up to 57% of patients.20 As 60% of the patients with vincristine PN treated here (3/5) reported a decrease in symptoms, our results suggest that acupuncture may be a useful addition to the care options offered to this group of patients.

Although open to debate, many workers in the field have linked the therapeutic dose of bortezomib given for multiple myeloma with PN.21 Table 1 shows a 75% recovery rate (3/4) through acupuncture in this patient group, however, the extent to which these neuropathies were caused by bortezomib is unclear. Multiple myeloma can cause neuropathy as part of the disease process and many patients receiving bortezomib have already been treated with thalidomide, another agent known to cause PN. Table 1 also shows a 100% success rate in the two patients treated for PN caused by thalidomide. While it is more difficult to rationalise the cause of PN in multiple myeloma, as the patient may have already developed a pre-clinical neuropathy, our results demonstrate an 83% (5/6) success rate with all patients with myeloma, irrespective of the cause.

POINT SELECTION FOR RESEARCH

Acupuncture treatments were planned by practitioners according to individual clinical need. As all the practitioners are trained in the WMA to acupuncture and are also qualified nurses, patient care was planned to include their diagnosis and presentation accordingly, thus providing an approach integrating acupuncture into their medical care. The most common points used were SP6 and ST36, which were used in all cases; LV3 was used in 14 of 18 cases. Should the practitioners have been TCM trained, point selection may have varied. Abuaisha et al 12 used a myriad of points including BL18, BL20, BL23, BL58, ST36, SP6, SP9 and ST36, so there is a great deal of overlap between our points. However, Zhang et al 10 used a myriad of points including BL18, BL20, BL23, BL58, ST36, SP6, SP3, CV6, CV4, ST40 and GB34. This brings us to a problem within acupuncture research. Kaptchuk,22 for example, criticised Shlay et al 23 for poor point selection in their large-scale study showing acupuncture to be no better than placebo in HIV-related PN. Entire studies may be planned, funded and carried out but if ineffective points are chosen within a study protocol then the results may be invalid and much time and money will have been wasted. Furthermore, as there are two different theoretical backgrounds for the practice of acupuncture, there may be arguments across ideological lines.

LIMITATIONS

This article describes the results of a retrospective evaluation of an acupuncture service conducted within a clinical setting as part of routine care and so there was no control of variables. Baseline data were not collected and validated questionnaires were not used. Therefore, the findings described are the results of patient opinion at one point in time and the placebo response may be at work here. For this reason,
further research is required to elicit whether the improvements observed are the result of a genuine acupuncture response, placebo response or a combination of both. Those patients who had been referred into the service had displayed symptoms of PN, however, only one had been sent for formal nerve conduction studies. Reports of reduction in pain medication were offered by patients, however, a formal examination of drug charts has not been undertaken.

RECOMMENDATIONS
Uncontrolled data from case work now exist in this method of managing chemotherapy-related PN. It is recommended that more controlled trials be conducted to strengthen the evidence base. Any such trials should take PN risk factors into account, such as diabetes mellitus, HIV or alcohol dependence, as these comorbidities may influence the development of PN. Validated patient-reported outcome measures should be utilised to assess neuropathy pre- and post-intervention. If possible, trials should involve the use of core acupuncture points, as identified by our results. In the creation of a standard treatment, factors into account, such as diabetes mellitus, HIV or alcohol dependence, as these comorbidities may influence the development of PN. Validated patient-reported outcome measures should be utilised to assess neuropathy pre- and post-intervention. It may be acceptable to allow practitioners to add to this core list, based on clinical presentations. In essence, this would lead to a standardised protocol whereby all participants would receive the same core treatment but that individual treatments may be slightly adapted to meet patients’ needs.

CONCLUSION
This service evaluation has provided some evidence suggesting acupuncture has a degree of effectiveness in managing the symptoms of chemotherapy-related PN. Although the specific mechanism for any efficacy shown by acupuncture is unknown, there is a growing base of evidence indicating physiological responses that may explain the neurological effects of acupuncture. While there are still questions around the efficacy of allopathic medication in alleviating chemotherapy-induced PN, acupuncture is a legitimate area for future research that shows promise.

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