

Acupuncture treatment for chemotherapy-induced peripheral neuropathy – a case series

Raimond Wong, Stephen Sagar

Abstract

Chemotherapy induced peripheral neuropathy (CIPN) occurs in 10 to 20% of cancer patients treated with neurotoxic chemotherapy. A mixture of sensory, sensorimotor and autonomic nervous system dysfunction can occur, resulting in deterioration in function and worsened quality of life. A major feature is discomfort and pain. Early termination of treatment and dose reduction of chemotherapy may be necessary. The clinical course is variable and depends on the chemotherapy agents and their cumulative dose. Although symptoms can resolve completely, in most patients CIPN is either only partially reversible or completely irreversible. Current management for CIPN is symptomatic using membrane stabilising medications and antidepressants. The use of nerve growth factors is still experimental.

Dysaesthesia and pain involving the feet and hands are described in both traditional Chinese medicine (TCM) and Western biomedicine. In TCM, the pathogenesis is related to the inability to direct *Qi* and Blood to the extremities, and is associated with *Qi*, Blood, *Yang* and Kidney deficiencies. Acupuncture is moderately effective in treating diabetic neuropathy. However, to date, there is no report of the usefulness of acupuncture for CIPN.

We report the result of a pilot prospective case series of five patients treated with an acupuncture protocol that aims to correct *Qi*, Blood and *Yang* deficiencies and directs *Qi* and Blood to the extremities, with the goal of improving the symptoms of CIPN. The responses were encouraging, and cannot be easily explained by the known neurophysiological mechanisms of acupuncture.

Keywords

Acupuncture, peripheral neuropathy, chemotherapy.

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Introduction

Treatment of cancer often involves chemotherapy as part of the treatment regimen. Neurotoxicity is one of the dose-limiting side effects that can result in a reduction, or even termination, of chemotherapy. The incidence of chemotherapy-induced toxicity is estimated to be as high as 60%.¹ Peripheral neuropathy has been reported to occur in 10% to 20% of cancer patients.² The condition is particularly more common in patients treated with neurotoxic chemotherapy agents including platinum compounds, vinca alkaloids, taxanes and suramin.³⁻⁵ Symptoms of neurotoxicity can appear immediately, during, or after the course of chemotherapy. Their severity depends on the type and the cumulative dose of chemotherapy used. Pre-existing conditions, such as

diabetic or alcoholic neuropathy and primary neurological disorders may also affect the pattern and severity of symptoms. Sensory or sensorimotor peripheral neuropathy is the predominant presenting symptom while autonomic nervous system dysfunction can sometimes be seen. Affected patients commonly complain of pain in the extremities and can have signs of paraesthesia, hyperaesthesia, impaired vibration and joint position sense, ataxia, myalgia and muscle weakness. In most patients, the recovery is incomplete resulting in persistent symptoms and adverse effects on their quality of life.

Current treatments of chemotherapy-induced peripheral neuropathy aim to relieve the symptoms of paraesthesia and pain. Tricyclic antidepressants and membrane stabilising drugs, such as carbamazepine

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and gabapentin, are moderately effective, but are accompanied by severe side effects that include sedation, postural hypotension, dry mouth and cardiac complications. Moreover, symptoms reappear after these medications are discontinued.⁶⁻⁹ New pharmaceutical approaches that include neurotrophic growth factors, insulin-like growth factor, glutamate and alpha-lipoic acid, are still experimental.

Acupuncture has recently been investigated for the treatment of peripheral neuropathy presenting in individuals infected with human immuno-deficiency virus (HIV). There was a reduction in scores for pain (aching and burning), pins and needles, and numbness in the extremities after five weeks of acupuncture.¹⁰ In contrast, another study suggested that acupuncture treatment was no more effective than placebo.¹¹ In patients with diabetic neuropathy, acupuncture treatment has also been shown to induce significant improvement in their symptoms.¹² To date, the effectiveness of acupuncture in treating CIPN has not been reported in the literature. This report describes the results for five consecutive patients with taxane- or platinum-induced CIPN treated with a standardised acupuncture protocol.

Case histories

Characteristics of all patients in the study

Five consecutive patients with greater than WHO grade II CIPN symptoms were referred for acupuncture treatment. (WHO grading system - grade 0: no symptoms; grade I: paraesthesiae and/or decreased tendon reflexes; grade II: severe paraesthesiae and/or mild weakness; grade III: intolerable paraesthesiae and/or marked motor loss and grade IV: paralysis.) Ages ranged from 60 to 71 years of age. All patients had advanced gynaecological cancers requiring chemotherapy with

carboplatin and paclitaxel, and were treated with an average cumulative total dosage of 3500mg and 1860mg for each drug respectively. The duration of CIPN symptoms before acupuncture treatment ranged from 6-38 months (median 18 months). Three patients had Grade II and two patients had Grade III symptoms. Pain, numbness and tingling of fingers and toes were the chief symptoms in all patients. Imbalance in gait was seen in three patients. Average pain score was 7.8 out of 10 (range: 6 to 9). All patients were managed with narcotic analgesics with two patients also on tricyclic antidepressants. One patient had a history of diabetes and multiple sclerosis. Patients' demographics and disease characteristics are summarised in Table 1.

Patients were assessed according to TCM diagnostic methods. A TCM questionnaire was used for symptom enquiry along with tongue and pulse examinations. Kidney and *Qi* deficiencies were the predominant symptom pattern in all five patients.

Treatment methods

Both authors were trained and certified in medical acupuncture and have over seven years of experience; the acupuncture treatments were performed at our cancer centre. We used 34G (0.25mm diameter and 40mm long) sterilised disposable acupuncture needles, without electrical stimulation. The points utilised were CV6, ST36, and LI11. Needles were inserted and withdrawn during patients' inspiration, with pressure on acupuncture points after needle withdrawal ('tonification' technique in TCM acupuncture approach). They were inserted to a depth of 5mm. We did not seek the *de qi* sensation. We performed clockwise twirling of the needle for about 30 seconds for each needle insertion. We needled *Ba Feng* points on both feet and *Ba Xie* points of both hands to 2-

Table 1 Baseline data on five patients with chemotherapy-induced peripheral neuropathy

Patient	Age	WHO grade	Duration (months)	Pain score	TCM patterns	Co-morbidity
1	64	II	6	8	Kidney, Spleen, Qi, Blood	
2	71	III	14	8.5	Kidney, Qi deficiencies	
3	69	III	38	7.8	Kidney, Qi, Blood, Heart deficiencies	diabetes; multiple sclerosis
4	60	II	18	6	Kidney, Qi, Lung deficiencies	
5	67	II	12	9	Kidney, Qi deficiencies	severe varicose veins

3mm depth with needle insertion and withdrawal performed during patients' expiration and with acupuncture points not covered after needle withdrawal ('sedation' technique). We did not perform any twirling of needles. For severe numbness and dysfunction of fingers or toes, *jing* points or tips of affected fingers or toes were also needled with a sedation technique. We left all needles in place for 30 to 45 minutes after insertion. We delivered acupuncture treatment once per week for six weeks (one course) followed by four weeks rest and then followed by another six weeks of treatment (second course).

Treatment Results

For social reasons, one patient discontinued acupuncture after seven treatments. All other patients finished the two courses of treatment. At the end of the acupuncture therapy, all five patients reported improvement of pain, numbness and tingling. Average pain score was reduced to 3 out of 10 (range 1 to 5). Improved symptoms were seen after the first treatment in one patient who had experienced six months of CIPN. Patients with severe numbness in their fingers and toes, who were treated by needling the *jing* points, showed remarkable improvement in the sensation and movement of the treated fingers and toes after the first treatment. All patients had a reduction in analgesic dosage. Gait was significantly improved in all three patients who complained of imbalance. There were no adverse side effects. At six months follow up, symptom control persisted in four patients. The one patient with a history of diabetes and multiple sclerosis reported improvement of symptoms for only one month (Table 2).

Detailed history of one of the five patients

A 71 year old woman presented with malignant ascites due to poorly differentiated adenocarcinoma.

An abdominal CT scan showed multiple intra-abdominal implants. Serum CA 125 was markedly elevated, indicating metastatic ovarian cancer. Her past medical history included left breast cancer, treated with mastectomy and adjuvant radiation 23 years previously. There was no history of diabetes or any neurological disorder. She received six cycles of chemotherapy that consisted of a combination of paclitaxel and carboplatin. The cumulative doses of paclitaxel and carboplatin were 1712mg and 3270mg, respectively. After the fourth cycle of chemotherapy, she developed numbness and lost the positional sense of her fingers. She had difficulties in holding objects and in writing. She also complained of a burning pain and a tingling sensation in her feet that were particularly worse at night. She demonstrated an ataxic gait. Her cancer persisted after six cycles of chemotherapy. One year after presentation, she was restarted on carboplatin followed by oral etoposide. Her neuropathic symptoms became worse and she was referred for acupuncture treatment.

At initial assessment she complained of neuropathic symptoms for 14 months. She was fatigued but still active. There was reduced light touch sensation in the hands and feet. All limb reflexes were diminished but symmetrical. Hand muscles were wasted, especially in the thenar eminence. Motor power was four out of five in the hands only. Varicose veins were present on both lower limbs, and the skin of her lower limbs was slightly purple in colour. Peripheral pulses were normal. Her gait was ataxic. She was not able to button up her shirt. Her pain score was 8.5 out of 10.

She gave a TCM history of frequent urination, weak back and knees. Her skin complexion was slightly pale. Her pulse examination revealed weak Kidney pulses but the rest of the pulse was quite

Table 2 Pain scores and WHO grades of patients before and after acupuncture treatment

Patient	Pain score pre-acupuncture	Pain score post-acupuncture	WHO grade pre-acupuncture	WHO grade post-acupuncture
1	8	2	II	I
2	8.5	3	III	II
3	7.8	3	III	I
4	6	3	II	I
5	9	3	II	I

strong. Her tongue was pinkish to red in colour and the tongue coating was scanty. The presumptive TCM diagnosis was *Qi* and Kidney deficiency leading to a reduction of Blood and *Qi* flow to the hands and feet.

She was treated with the standard acupuncture protocol described above in the 'treatment method' section. She was treated once weekly for a total of seven treatments. Therapy was discontinued because of sickness of one of her family members.

At the end of the seven treatments, her pain symptoms improved to a score of three out of 10 (from 8.5), associated with a reduction in analgesic consumption. The sensation in her fingers almost returned to normal. The sensation in her feet also improved and she was able to keep her balance while walking. She was followed for 10 months without further deterioration of symptoms.

Discussion

CIPN is a common complication of chemotherapy treatment. Taxanes, platinum analogues and vinca alkaloids are the main chemotherapy compounds that are associated with CIPN. There is a paucity of data in the literature to ascertain the overall proportion of patients who experience symptoms due to CIPN and their natural history. One study reported that CIPN occurred in 10 to 20% of patients.² With the increased use of these chemotherapy agents in current practice, the incidence of CIPN will increase. Currently there are no effective means for treating or preventing CIPN. Available treatments with medications are mainly for temporary symptomatic relief and carry major adverse side effects.

To date there is no report in the literature regarding the use of acupuncture in CIPN. We report the results of our empirical attempt to treat CIPN with acupuncture in five patients. Our choice in using acupuncture for CIPN is based on some positive study results for acupuncture treatment in patients with diabetic and HIV/AIDS related peripheral neuropathy.^{11,12} Our acupuncture protocol for treating CIPN was developed from the treatment approach for patients described in TCM classics.¹³ In the TCM model, a free flow of *Qi* and Blood is important to maintain optimal health. The symptoms of CIPN are considered to be a state of deficiency of *Qi* and Blood, and the body's failure to direct these components to the four limbs, resulting in sensory

symptoms and impaired limb function. We describe successful treatment with acupuncture based on an approach that supports body *Qi* and Blood, and directs their flow to the extremities.

The acupuncture protocol that we used was developed empirically. The acupuncture point, CV6 (*Qi Hai*) was used, based on its described effect in strengthening original *Qi*, regulating the flow of *Qi* and tonifying the Kidneys. ST36, LI11 (*Zu San Li, Qu Chi*), the *He Sea* points of the Stomach and Large Intestine meridians respectively, were used to further tonify the *Qi* and Blood. Given both meridians are in the *Yang Ming* category, the effects of each point are believed to reinforce each other. ST36 was also indicated for pain in the lower legs. *Ba Xie* and *Ba Feng* points help to direct *Qi* and Blood to the hands and feet, respectively, leading to a reduction in pain and numbness. Three of the described patients suffered from severe numbness with consequent impairment of fine motor skills of the fingers. Needling the *jing* point of the affected fingers caused a marked improvement in numbness after three to four treatments.

Our results suggest that the effect of an empirical protocol on CIPN is promising. However, since we treated only five patients, a definitive conclusion that acupuncture is generally effective for CIPN needs to be proven in larger trials.

The precise physiological mechanism by which acupuncture treatment can improve the symptoms of CIPN are not known. The possibility of a placebo effect cannot be excluded. However, the fact that acupuncture was associated with a considerable sustained remission after prolonged periods of experiencing CIPN is encouraging. Acupuncture may exert its effect through the spinal cord pain gate. An induced increase in endorphin production may result in an improvement in pain symptoms.¹⁴⁻¹⁶ The improvement in sensory function, however, cannot be explained by increased endorphin levels. Acupuncture may stimulate nerve growth factors. Recent animal studies have shown that acupuncture treatments can accelerate nerve regeneration.^{17,18} This may explain the sustained response of our patients after acupuncture treatments. It is still controversial to claim that specific acupuncture point stimulation leads to specific functions. However, a recent fMRI study has suggested a difference in the cerebral cortex areas that showed increased activities after specific

acupuncture point stimulation as compared to non-acupuncture point stimulation.¹⁹ We are currently designing a larger phase I/II trial to further examine the efficacy of acupuncture treatment in CIPN.

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