PRESS RELEASE

EDITOR'S CHOICE

Acupuncture for chemotherapy-induced peripheral neuropathy (CIPN): a pilot study using neurography

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ABSTRACT

Objectives Chemotherapy-induced peripheral neuropathy (CIPN) can produce severe neurological deficits and neuropathic pain and is a potential reason for terminating or suspending chemotherapy treatments. Specific and effective curative treatments are lacking.

Methods A pilot study was conducted to evaluate the therapeutic effect of acupuncture on CIPN as measured by changes in nerve conduction studies (NCS) in six patients treated with acupuncture for 10 weeks in addition to best medical care and five control patients who received the best medical care but no specific treatment for CIPN.

Results In five of the six patients treated with acupuncture, NCS improved after treatment. In the control group, three of five patients did not show any difference in NCS, one patient improved and one showed impaired NCS.

Conclusion The data suggest that acupuncture has a positive effect on CIPN. The encouraging results of this pilot study justify a randomised controlled trial of acupuncture in CIPN on the basis of NCS.

INTRODUCTION

Chemotherapy-induced peripheral neuropathy (CIPN) involves damage to the peripheral nervous system and can produce severe neuropathic pain or gait impairment and may be a reason to terminate or suspend chemotherapy treatments. Specific and effective curative treatments are lacking. The major groups of drugs that induce CIPN include the taxanes, vinca alkaloids and platinum compounds. The incidence of CIPN is high and can reach levels of up to 92%.[1]

Publications in English language journals on acupuncture as a symptomatic treatment for CIPN have been limited to only a few case studies, all of which report an improvement in symptoms.[2 3] A Chinese study described acupuncture as more effective than cobamamide for the treatment of sensory symptoms in paclitaxel-induced CIPN.[4]

We conducted a pilot study in 2006 in 192 patients with peripheral neuropathy diagnosed on the basis of nerve conduction studies (NCS). Patients were evaluated over a period of 1 year, measured by NCS. The aim of this non-randomised non-blinded study was to determine whether there is evidence of effective treatment of peripheral neuropathy (PN) with acupuncture assessed by objective measurements and whether further prospective studies on the basis of the above criteria are warranted. We have previously published data on the treatment of PN of unknown aetiology and diabetic neuropathy with acupuncture, and found an improvement in NCS in 76% of patients after a treatment period of 10 weeks, one treatment per week.[5 6] In this paper we report our results in patients with CIPN.

METHODS

A total of 192 consecutive patients with PN of the lower extremities were diagnosed by NCS and treated in a neurologist's outpatient clinic for a period of 1 year. Patients with PN confirmed by neurological examination and NCS were included in the study. Patients with alcohol abuse, drug usage, a history of diabetes, toxic drugs (except a history of chemotherapy) or inflammatory disease documented as underlying causes for PN were excluded from the study. This was confirmed by standard screening.[5]

Of this group, 11 patients had developed symptoms of PN during the course of chemotherapy and were identified as having CIPN. Chemotherapy had been given for different types of cancer (table 1).

Acupuncture treatment was offered to all the patients with CIPN. Six patients agreed to receive acupuncture treatment and five refused owing to personal inconvenience of the appointments offered. These five patients (four men, one woman) of mean age 65 years who received the best medical care but no specific treatment for PN thus served as a control group. Six patients (three men, three women) of mean age 64 years received the best medical care and additionally were treated with acupuncture for PN of the lower extremities. Patients in both groups did not receive any other treatment for PN except stable doses of carbamazepine or pregabalin during the observation period. The characteristics of the acupuncture and control groups are shown in table 1.

Measurements of nerve conduction velocity (NCV) were performed with a Neuropack-Sigma, MEB-9400, EMG/NCV/EP-System (Nihon-Khoden, Tokyo, Japan). The amplitudes of the motor and sensory responses were measured to the first negative peak. All studies of NCV were done at room temperature (22–24°C). Skin temperature was measured at the sites of sensory nerve measurements and values were analysed, adjusting for the effects of temperature. Follow-up NCS data were collected after a period of 6 months (±2 weeks) by examination of the sural and tibial nerves in the same calf as in the initial assessment. Standard orthodromic needle recording methods were used for sural nerve assessment while standard surface recording methods were used for tibial nerve recordings.[7 8] A change in NCV in the sural nerve of 2 m/s slower or faster than the initial measurement was considered significant. A change in the amplitude of the sensory nerve action potential of more than 2 μV was defined as a significant impairment or improvement in the sural nerve.

The patients were asked at the time of the second NCS to tick one box to indicate whether their condition had improved, worsened or remained unchanged.

Acupuncture treatment was based on a neurophysiologcial approach to traditional Chinese medicine (TCM) theory.[9] Point selection followed the training curriculum at the TCM-Master Education at the Instituto de Ciências Biomédicas Abel Salazar, University of Porto, Portugal. The specific acupuncture protocols employed in this study are described below, point location and depth of insertion were as described in standard textbooks[10] and disposable sterile steel needles of 0.30×30 mm were used and left in place for 20 min to a depth of 10–30 mm. Each patient received a standard 10-week treatment of the ST34 (*Liangqiu*) as well as the five extra points EX–LE12 (*Qiduan*) and the four extra points EX–LE8 (*Bafeng*). The needles were inserted bilaterally. Twenty needles were inserted per session. Needle stimulation techniques were not used. We did not employ manipulation in order to elicit a *de qi* sensation. Acupuncture was performed in all cases by the same senior physician who had received >1000 h of acupuncture training before participating in the trial and had used acupuncture for 20 years. The six patients in the acupuncture group were examined by NCS 2–21 months (mean 10.3) after chemotherapy. NCS was performed before treatment and again 6 months later (ie, 3 months (±2 weeks) after the end of treatment).

The five patients in the control group were examined by NCS 1–14 months (mean 10.8) after chemotherapy and routinely again at 6 months.

Table 1 Cancer types and chemotherapy of patients with chemotherapy-induced peripheral neuropathy

Patient groups	Chemotherapy
Acupunture group	
Breast	Docetaxel/doxorubicin/cyclophosphamide
Colon	Oxaliplatin
Colon (sigmoid)	Cisplatin
Bronchial	Cisplatin
Lymphoma	Rituximab/fludarabin/cyclophosphamide
Lymphoma	Rituximab/fludarabin/cyclophosphamide
Control group	
Breast	Docetaxel/doxorubicin/cyclophosphamide
Colon (sigmoid)	Oxaliplatin
Colon	5-fluorouracil/oxaliplatin
Pleura mesothelioma	Alimta/cisplatin
Lymphoma	Rituximab/fludarabin/cyclophosphamide

RESULTS

All six patients in the acupuncture group had hypoesthesia in a stocking distribution; three had additional neuropathic pain. There was no clinical motor involvement and no motor involvement in NCS. NCS showed mixed damage of the axon and the myelin sheath of the sensory sural nerve in all six acupuncture-treated patients. All five patients in the control group had hypoesthesia in a stocking contribution; three had additional neuropathic pain. There was no clinical motor involvement and no motor involvement in NCS. NCS revealed mixed damage to the axon and myelin sheath of the sensitive sural nerve in two patients in the control group while three had pure axonopathy. The results of the NCS of the sural nerve as well as the subjective outcomes are shown in table 2. A comparison of the mean values for the two groups is shown in table 3.

DISCUSSION

This pilot study shows improvement in NCS after acupuncture treatment in CIPN. The use of NCS as an

Table 2 Nerve conduction studies of the sural nerve and subjective outcome in acupuncture-treated and control groups

Acupuncture (10 treatments over 3 months)						Control (no specific treatment)					
Patient no	NCV (m/s)		Amplitude (μV)		Patients' evaluation	Patient no	NCV (m/s)		Amplitude (μV)		Patients' evaluation
	Initial	After 6 months	Initial	After 6 months	After 6 months		Initial	After 6 months	Initial	After 6 months	After 6 months
1	0	30.6	0	0.8	Improvement	1	42	42	3.9	3.9	No change
2	0	0	0	0	No change	2	42	42	3.6	3.8	No change
3	36	45	0.2	1.7	Improvement	3	36	42	3.2	3.1	No change
4	0	42	0	1.2	Improvement	4	42	42	2.3	5	Improvement
5	0	42	0	2.2	Improvement	5	37	0	2	0	Impairment
6	34	45	1.5	2	Improvement						

NCV, nerve conduction velocity.

Table 3 Mean (SD) differences in nerve conduction studies of the sural nerve in acupuncture-treated and control groups

Acupuncture (10 treatments over 3 months)					Control (no specific treatment)				
Initial	After 6 months	Paired t test	p Value	Mean difference	Initial	After 6 months	Paired t test	p Value	Mean difference
Mean NCV (m/s)									
11.67 (18.09)	34.1 (17.54)	t=3.0278 df=5	0.03	+22.43 (18.15)	39.8 (3.03)	33.6 (18.78)	t=0.7962 df=4	NS	−6.20 (17.41)
Mean amplitude (μV)									
0.28 (0.60)	1.32 (0.83)	t=3.2604 df=5	0.02	+1.03 (0.77)	3.0 (0.88)	3.16 (1.89)	t=0.214 df=4	NS	+0.06 (1.49)
Product of NCV and amplitude									
9.70 (20.44)	55.55 (37.66)	t=3.4289 df=5	0.02	+45.85 (32.75)	120.29 (37.32)	132.72 (79.5)	t=0.4163 df=4	NS	+12.43 (66.78)

NCV, nerve conduction velocity.

objective parameter is promising for future acupuncture studies, although the number of cases is limited. Interestingly, an improvement in NCS after acupuncture was shown in CIPN as well as in previous studies on PN of undefined aetiology and diabetic neuropathy.[5 6] The results are consistent with previously published case studies on acupuncture treatment of CIPN.[4]

Although PN has numerous causes including genetic, toxic, metabolic, infectious, inflammatory, ischaemic and paraneoplastic disorders, the nerve can be destroyed in a limited number of ways because the damage can only occur at the level of the axon or the myelin sheaths.[11 12] Differentiating whether neuropathy is axonal, demyelinating or both is achieved by NCS.[11–14] It is generally accepted that compromised nerve conduction in PN mainly depends on structural changes of the myelin sheaths, while the amplitude is correlated with the number of functional axons.[7 8] Consequently, one may speculate that repeated therapeutic interventions with acupuncture over a period of 10 weeks improves the symptomatic state of PN and also induces a normalisation of histological morphology. It has been shown by Litscher *et al*[15] that acupuncture may increase the blood flow in the limbs. Increased blood flow to the vasa nervorum and dependent capillary beds supplying the neurons[16] may contribute to nerve repair with measurable improvement of axons or myelin sheaths. Peripheral mechanisms possibly involved may include other types of fibres, such as the small unmyelinised or thinly myelinised fibres commonly believed to be undetected by NCS.

In addition, the symptomatic effect of acupuncture may reflect morphological changes in the anatomy of peripheral nerves and also complex derangements of central and peripheral regulation.[17 18] One hypothesis relates to the enhancement of conduction by the dorsal column[19–21] or higher centres.[22 23]

CONCLUSION

The data suggest that acupuncture has a positive effect on CIPN as measured by objective parameters (NCS). The results are comparable to previous studies in diabetic neuropathy and PN of undefined aetiology. These findings are of special significance since PN is otherwise almost untreatable but seems to respond to treatment by acupuncture. This pilot study shows encouraging results for the application of acupuncture in CIPN, justifying a randomised controlled trial.

Contributors SS designed data collection tools, monitored data collection for the whole trial, wrote the statistical analysis plan, cleaned and analysed the data and drafted and revised the paper. MH-G analysed the data and drafted and revised the paper. ES monitored data collection and revised the draft paper.

Competing interests None

Patient consent Obtained

Ethics approval Ethical approval was obtained from the Ethik Kommission der Hamburger Ärztekammer

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REFERENCES

1. Oxaliplatin Prescribing Information. http://www.drugs.com/pro/oxaliplatin.html (accessed 3 August 2011).
2. Donald GK, Tobin I, Stringer J. Evaluation of acupuncture in the management of chemotherapy-induced peripheral neuropathy. *Acupunct Med* 2011;29:230–3.
3. Wong R, Sagar S. Acupuncture treatment for chemotherapy-induced peripheral neuropathy–a case series. *Acupunct Med* 2006;24:87–91.
4. Xu WR, Hua BJ, Hou W, *et al.* [Clinical randomized controlled study on acupuncture for treatment of peripheral neuropathy induced by chemotherapeutic drugs]. *Zhongguo Zhen Jiu* 2010;30:457–60.
5. Schröder S, Liepert J, Remppis A, *et al.* Acupuncture treatment improves nerve conduction in peripheral neuropathy. *Eur J Neurol* 2007;14:276–81.
6. Schröder S, Rempiss A, Greten T, *et al*. Quantification of acupuncture effects on peripheral neuropathy of unknown and diabetic cause by NCS. *J Acupunct Tuina Sci* 2008;6:312–14.
7. Stoehr M. *Atlas der klinischen Elektromyographie und Neurographie*. Stuttgart: Kohlhammer, 1998.
8. Eduardo E, Burke D. The optimal recording electrode configuration for compound sensory action potentials. *J Neurol Neurosurg Psychiatry* 1988;23:1.
9. Greten HJ. *Kursbuch Traditionelle Chinesische Medizin*. Second edition. Stuttgart-New York: Thieme Publishing House, 2005
10. Deadman P, Baker K, Al-Khafaji M. *A Manual of Acupuncture* (2nd edition). East Sussex: Journal of Chinese Medicine Publications, 2007.
11. Asbury AK, Gilliatt RW. The clinical approach to neuropathy. In: Asbury AK, Gilliatt RW, eds. *Peripheral Nerve Disorders: A Practical Approach*. London: Butterworths, 1984:1–20.
12. Bosch EP, Mitsumoto H. Disorders of peripheral nerves. In: Bradley WG, Daroff RB, Fenichel GM, Marsden CD, eds. *Neurology in Clinical Practice*. Boston: Butterworth-Heinemann, 1991:1720–6.
13. Donofrio PD, Albers JW. AAEM minimonograph #34: polyneuropathy: classification by nerve conduction studies and electromyography. *Muscle Nerve* 1990;13:889–903.
14. McLeod JG, Tuck RR, Pollard JD, *et al.* Chronic polyneuropathy of undetermined cause. *J Neurol Neurosurg Psychiatry* 1984;47:530–5.
15. Litscher G, Wang L, Huber E, *et al.* Changed skin blood perfusion in the fingertip following acupuncture needle introduction as evaluated by laser Doppler perfusion imaging. *Lasers Med Sci* 2002;17:19–25.
16. Diabetes Control and Complication Trial Group (DCCT). The effect of intense treatment on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med* 1993;329:977–86.
17. Ma S, Cornford ME, Vahabnezhad I, *et al.* Responses of nitric oxide synthase expression in the gracile nucleus to sciatic nerve injury in young and aged rats. *Brain Res* 2000;855:124–31.

18. Ma SX. Nitric oxide synthase in the gracile nucleus isincreased by stimulus-evoked excitatory somato-sympatheticreflexes. *FASEB J* 1998;2:A691.
19. Al-Chaer ED, Lawand NB, Westlund KN, *et al.* Pelvic visceral input into the nucleus gracilis is largely mediated by the postsynaptic dorsal column pathway. *J Neurophysiol* 1996;76:2675–90.
20. Al-Chaer ED, Lawand NB, Westlund KN, *et al*. Visceral nociceptive input into the ventral posterolateral nucleus of the thalamus: a new function for the dorsalcolumn pathway. *J Neurophysiol* 1996;76:2661–74.
21. Al-Chaer ED, Westlund KN, Willis WD. Nucleus gracilis: an integrator for visceral and somatic information. *J Neurophysiol* 1997;78:521–7.
22. Samso E, Farber NE, Kampine JP, *et al.* The effects of halothane on pressor and depressor responses elicited via the somatosympathetic reflex: a potential antinociceptive action. *Anesth Analg* 1994;79:971–9.
23. Sato A, Schmidt RF. Somatosympathetic reflexes: afferent fibers, central pathways, discharge characteristics. *Physiol Rev* 1973;53:916–47.