Acupuncture and massage therapy for neuropathic pain following spinal cord injury: an exploratory study

Cecilia Norrbrink,1,2 Thomas Lundeberg3

ABSTRACT

Objective The study sought to explore the possibility of using acupuncture and massage therapy for relieving neuropathic pain following spinal cord injury (SCI).

Design 30 individuals with SCI and neuropathic pain were assigned to treatment of either massage or acupuncture, with 15 individuals in each group. Both groups received treatment twice weekly for 6 weeks. Treatments were evaluated at the end of treatment and 2 months later (follow-up).

Results Data were analysed on an intention-to-treat basis. Within the groups, ratings of present pain, general pain, pain unpleasantness and coping improved significantly at the end of treatment after acupuncture compared to baseline values, and following massage therapy ratings of pain interference on the Multidimensional Pain Inventory improved. At follow-up no significant improvements were seen.

Between-group differences were seen regarding ratings of worst pain intensity at the end of treatment, and regarding pain unpleasantness and coping with pain at follow-up, both in favour of acupuncture.

At the end of treatment, eight of the 15 individuals receiving acupuncture and nine receiving massage reported an improvement on the Patient Global Impression of Change Scale, and at follow-up six patients in the acupuncture group and one patient in the massage group still reported a favourable effect from the treatment.

Few side effects were reported and neither dropout from the study did this due to adverse events.

Conclusion Neuropathic pain following SCI is often only partially responsive to most interventions. Results from this study indicate, however, that both acupuncture and massage therapy may relieve SCI neuropathic pain. For this reason, larger randomised controlled trials are warranted for assessing the long-term effects of these treatments.

INTRODUCTION

We lack knowledge of how to treat neuropathic pain due to spinal cord injury (SCI) satisfactorily. Treatment is therefore a great challenge for care givers.1 Current treatment recommendations are based on the few studies of this patient group and on algorithms for treating peripheral neuropathic pain. With these tools we can sometimes relieve such pain following SCI to some extent, but rarely enough for the individuals to be satisfied. The lack of satisfaction can also be related to the fact that many of the drugs used have severe unwanted side effects.

Regarding other treatments, sensory stimulation with transcutaneous electrical nerve stimulation has been studied mainly in peripheral neuropathic pain conditions and is considered to be an effective complement.3 In some individuals with central neuropathic pain, transcutaneous electrical nerve stimulation may induce pain alleviation1 but often less than in peripheral neuropathies.

In rodent studies, acupuncture has been studied after peripheral nerve injury and is effective for hyperalgesia4 and allodynia5,6 signs considered as consequences of nerve damage and associated with neuropathic pain. Treatment with acupuncture has, however, not been extensively studied in peripheral or central neuropathic pain conditions in humans. Only two randomised controlled studies have been carried out4,8 and both report no or very little difference between acupuncture and the control treatment. However, in one of these studies verum acupuncture was compared to sham acupuncture, defined as needle insertions in deep muscles but not in acupuncture points followed by needling stimulation. This type of control is controversial since it is most likely not an inert treatment.9 Two uncontrolled studies showed positive effects compared to baseline values when treating diabetic neuropathy10 and HIV-related neuropathic pain.11

In SCI, a within-subject-design study using acupuncture showed promising results for treating overall pain but less good for the cohort with central neuropathic pain.12 Still, in 42% of those individuals, pain intensities were alleviated by at least two units on a 0–10 numerical rating scale (NRS)—which is not a negligible effect in this patient group.

Massage therapy has not been studied for treating neuropathic pain following SCI but it decreased anxiety13 in individuals with SCI.

In a previous survey14 individuals with SCI reported massage to be one of the most effective non-pharmacological treatments for SCI chronic pain but spoke less of acupuncture. Similar results have been reported in other studies.15,16
Based on these results an exploratory study was designed to assess the possibility of using medical acupuncture and massage therapy for relieving neuropathic pain due to SCI. Both treatment modalities activate endogenous pain inhibitory systems, however they are believed to act through different mechanisms.\(^\text{17–18}\)

**METHODS AND INDIVIDUALS**

**Individuals**

Individuals with SCI and pain were recruited from a spinal unit in Stockholm, Sweden through advertisements and through mailed enquiries. Inclusion criteria were an SCI more than 2 years previously and pain diagnosed as neuropathic at or below level\(^\text{19}\) due to the SCI of more than 6 months duration. All individuals were asked not to change current pain medication or any other treatments during the treatment period but were allowed to stay on concurrent medication.

**Study design**

The study was carried out using a sequential controlled design. The first 15 individuals giving informed consent for the study and fulfilling the inclusion criteria were assigned to western medical acupuncture and the following 15 to massage. The assignation procedure was unknown to the individuals who were all willing to receive both acupuncture and massage. The treatment period consisted of 6 weeks with treatment twice weekly. The treatments were evaluated at the end of treatment and at follow-up 2 months later using a mailed questionnaire.

**Acupuncture**

Acupuncture points were chosen individually and needles were inserted in areas with preserved sensation. Points were chosen from a western medical perspective, that is, placed in areas with pain and in strong general acupuncture points. In addition, earpoint Shenmen and GV20 were selected as possible complements. Needle insertion was carried out using the recommended depth allowing for muscle stimulation.\(^\text{20}\) Stimulation was initially manual and from the third or fourth session four points were stimulated with high frequency (80 Hz) electroacupuncture (CEFAR Acus 4; Cefar AB, Lund, Sweden). Points stimulated in the upper extremity were either LI11–LI4, LI15–LI11 or LI15–LI4, and in the lower extremity ST32–GB34, ST32–ST36 or BL54–BL54. In total 13–15 points were used in each session. The intensity was high, giving non-painful paresthesia. During manual acupuncture de qi was elicited three times at each session of 30 min.

The acupuncture procedure is described according to the Standards for Reporting Interventions in Clinical Trials of Acupuncture.\(^\text{21}\)

**Massage**

Classical massage therapy was carried out in areas with pain and preserved sensation with individuals lying on a massage table. The massage consisted of non-painful light pressure effleurage and petrissage. It was important that the massage did not cause discomfort for the individuals and therefore stimulation in areas with allodynia or unpleasant feelings from touch were avoided.

**Outcome measures**

**Primary outcome measures**

The individuals rated their general and their worst pain intensities, and pain unpleasantness, during the last week using a visual analogue scale (VAS). They also rated present pain intensity at baseline, at the end of treatment (6 weeks) and at follow-up (2 months). In addition they rated the global pain-relieving effect on the Patient Global Impression of Change Scale (PGIC)\(^\text{22}\) at both end of treatment and follow-up.

A decrease of two units or more in pain intensity ratings on a 0–10 NRS\(^\text{23}\) has been considered clinically significant, and 1.8 units or more in individuals with SCI (defined as ‘my pain decreased to a meaningful extent’).\(^\text{24}\) Translated to a VAS with a range of 0–100, a decrease of 18 units or more was considered to identify a responder.

**Secondary outcome measure**

As secondary outcome measures the Hospital Anxiety and Depression Scale was used to rate anxiety and depression,\(^\text{25}\) the Multidimensional Pain Inventory—Swedish language version (MPI-S)\(^\text{26}\) part I, to assess the psychosocial consequences of pain, and a sleep questionnaire\(^\text{27}\) to assess quality of sleep. Further, Fugl-Meyer’s Life Satisfaction instrument (LiSat – 9)\(^\text{28,29}\) was used. In the analysis only the global rating of life satisfaction was considered. In addition, individuals rated how well they were able to cope with their pain on an 11-point NRS anchored ‘not at all’ (0) and ‘very good’ (10).

Spasticity was assessed using the modified Penn Spasm Frequency Scale,\(^\text{30}\) for frequency and severity. Spasm frequency is reported from 0=no spasms to 4=spontaneous spasms occurring >10/h, and severity of spasms from 1=mild to 5=severe.

The study was approved by the Regional Ethics Approval Board in Stockholm, Sweden.

**Statistics**

Data were analysed on an intention-to-treat basis with missing data in dropouts replaced using the last-observation–carried-forward method.

Patient and treatment characteristics are presented using descriptive statistics: number of observations, mean and SD. Outcome variables are further presented by group using median and IQR before and after treatment.

Determination of the between-treatment difference measured with the PGIC was tested with the Mann–Whitney U test and the difference in number of respondents using the two-tailed Fisher exact test.

Svensson’s rank-invariant method\(^\text{31}\) was used to estimate systematic changes in outcome variables (pain intensity, pain unpleasantness, coping, sleep quality, mood, life...
satisfaction, psychosocial consequences and spasticity) directly after treatment compared to baseline, and also 2 months after treatment compared to baseline.

Systematic group changes are explained by relative change in position (RP), that is, the proportion of individuals with a higher level minus the proportion of those with a lower level in the outcome variable. RP values range from −1 (all individuals decreased) to +1 (all individuals increased). Values close to 0 indicate a negligible systematic group change in the outcome measure. When RP≠0, the values after treatment are systematically higher (+) or lower (−) for the group than the initial values. RP was estimated together with the corresponding 95% CI. SE was calculated using the jack knife method. Differences between acupuncture and massage was estimated as the difference between RPs together with the corresponding 95% CI. Negative differences between interventions (acupuncture vs massage) indicate that a larger proportion of individuals in the massage group decreased (or increased less) from baseline to the end of treatment, compared to those in the acupuncture group in the outcome variable.

All the tests were two-sided, and a significance level of 0.05 was chosen. All descriptive statistics were produced in STATISTICA V.7.0 (StatSoft, Tulsa, Oklahoma, USA) and RP values were calculated in SYSRAN V.1.0 (JK Biostatistics, Stockholm, Sweden) for Matlab V.6.0 (The MathWorks, Natick, Massachusetts, USA).

RESULTS
Altogether 30 individuals were included in the study; 15 received acupuncture and 15 massage. The acupuncture group consisted of 12 males and 3 females with a mean age of 47.1 years (SD 11.1) and the massage group of 13 males and 3 females, mean age 49.8 (SD 9.2). Mean time since injury was 11.9 years (SD 12.3) in the acupuncture group and 12.9 years (SD 9.0) in the massage group. In the acupuncture group, 11 had a traumatic injury compared to 10 in the massage group.

Five of those receiving acupuncture and six of those receiving massage had tetraplegia. Ten of those in the acupuncture group and eight of those in the massage group were on concomitant pain medication including adjuvant analgesics.

TREATMENT
The acupuncture group received a mean of 10.5 treatments (SD 2.9) and the massage group 11.1 treatments (SD 2.1). One acupuncture patient’s treatment was concluded after only eight sessions due to complete pain relief. Lacking compliance, one individual received only three sessions of electroacupuncture and thereafter manual stimulation. Two individuals dropped out of the study, one in each treatment group, for reasons not related to the treatment itself. The acupuncture-group member moved abroad after one treatment and the massage-group member was hospitalised for pneumonia after eight treatments. One massage-group member did not return the follow-up questionnaire.

Adverse events
Compliance was high for both types of treatment. Almost half of those in the acupuncture group (n=7) reported being tired after the treatment initially and one reported a pain increase lasting 4–5 h after the treatment. Of those receiving massage, two reported soreness, one increased pain and one feeling extremely cold 4–5 h after the treatment resulting in poor sleep the first night after treatment.

Positive events
The acupuncture group reported the following positive side effects at the end of the treatment period: improved sleep (n=2), improved bladder (n=1) and bowel (n=1) function, decreased spasticity, less allodynia, more energy, less pain medication, feeling calm and relaxed (n=1 each). The massage group reported: improved function/less stiffness (n=6), improved sleep (n=5), improved relaxation...
(n=2), less spasticity (n=3), improved circulation (warm legs; n=2), less allodynia (n=2), fewer painful attacks (n=2), less medication (n=1).

At the follow-up individuals could report late-onset improvements. One patient reported improved sleep after acupuncture. In the massage group one reported using less muscle relaxants, and another increased wellbeing and mobility.

**Primary outcome measures—pain and PGIC**

**Between-group differences**

At the end of treatment (6 weeks), there was a significant difference between the two groups in ratings of worst pain intensity (figure 1). There was also a significant change at follow-up (2 months) regarding ratings of pain unpleasantness; both in favour of acupuncture. No other differences between the two groups were detected.

At the end of treatment, 8/15 individuals on acupuncture and 9/15 on massage reported an improvement on the PGIC (minimally improved–very much improved, figure 2). At follow-up 6/15 on acupuncture and 1/15 on massage still reported a positive outcome. The difference between the two groups was not statistically significant.

Numbers of responders calculated as all those reporting a decrease in pain ratings of ≥18 mm measured with VAS are shown in figure 3. The differences seen were not statistically significant.

Ratings of general pain intensity and pain unpleasantness at end of treatment and follow-up are shown in figure 4 plotted against the baseline values.
puncture reported improvement in coping with pain, and those on massage reported less pain interference. At follow-up no improvements were seen, but massage-group members reported worsened coping.

To see whether any of the assessed variables were important for ratings of coping with pain, a Spearman regression analysis was carried out. Pain intensity ($r=−0.57$), pain unpleasantness ($r=−0.61$), mood ($r=−0.58$), sleep ($r=−0.55$), MPI-pain severity ($r=−0.67$), MPI-pain interference ($r=−0.59$), MPI-perceived life control, ($r=0.61$) and MPI-affective distress ($r=−0.65$) all correlated moderately ($r=0.50$ to $0.69$) with ratings of coping. Ratings of global life satisfaction had low ($r=0.26$–$0.49$) correlation with coping ($r=0.46$), and MPI-social support little if any ($r<0.25$; $r=−0.06$).

Within-group differences

Ratings of general and present pain, and of pain unpleasantness, all decreased significantly at end of treatment with acupuncture but not after massage. In terms of median decrease in pain intensity ratings measured with VAS, this was similar in the two groups (table 1).

At follow-up no within-group differences were seen between pain variables.

Secondary outcome measures

At the end of treatment there were no between-group differences regarding the secondary outcome measures for pain or spasticity; but at follow-up, ratings of coping with pain as shown with a 0–10 NRS were in favour of acupuncture (figure 1). Within the groups, individuals on acupuncture reported improvement in coping with pain, and those on massage reported less pain interference. At follow-up no improvements were seen, but massage-group members reported worsened coping.

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### DISCUSSION

In this exploratory study the average pain alleviation following a treatment course of acupuncture or massage was small but significant. It was larger for the affective component of pain than for the sensory component (intensity). At follow-up no significant effects on pain intensity or unpleasantness were maintained, but six of 15 acupuncture-group members versus one of 15 on massage still reported an improvement on the PGIC. Between-group differences, in favour of acupuncture, were seen only regarding ratings of worst pain intensity. Both methods presented few unwanted side effects and compliance was high. None dropped out due to adverse events.

The most pronounced effects were those of acupuncture on ratings of pain unpleasantness where a median decrease of 23/100 VAS units was seen immediately after the treatment course. Acupuncture treatment reportedly modulates activity in limbic structures,33 which could partly explain these findings.

Effects of treatment on pain unpleasantness are not always assessed in clinical trials but they are recommended as an outcome measure.22

Ratings of pain intensity also decreased significantly after treatment with acupuncture. The median decrease in ratings of present pain intensity was 19/100 VAS units following acupuncture (general pain—15 units) and eight units following massage (general pain—14 units). In a large study of SCI neuropathic pain concluding that pregabalin has a positive effect on this type of pain,34 the mean reduction in pain scores on a 0–10 NRS was 1.92 before controlling for placebo. In a comparative study on gabapentin and amitryptiline35 in SCI and neuropathic pain, a mean decrease of VAS 2.14 was seen after treatment with amitryptiline and of VAS 0.75 after gabapentin.

Hanley et al34 reported that in SCI a reduction of 1.8 units or more on a 0–10 NRS was a clinically significant alleviation of pain, which we translated to 18 units on a 0–100 point VAS, and those reporting these values are defined here as responders. Even though no significant differences were seen between the two groups, immediately after the treatment course more individuals on acupuncture reported this amount of pain alleviation. Forty per cent (six of 15) versus 13% (two of 15) were responders regarding ratings of present and general pain intensity, figures similar to those found by Nayak et al35 in SCI and central neuropathic pain. Those authors found that 42% (five of 12 individuals) reported a decrease of at least two units on an NRS following 15 treatment sessions with acupuncture. Even though both studies used very small samples, these results are considered promising.

None of the present respondents reported worsening of pain using the PGIC, but one patient on acupuncture reported being minimally worse at the 2-month follow-up. Whether this was associated with the treatment course is not clear. In the study by Nayak and colleagues,12 four of the total sample (22 individuals reported this amount of pain alleviation. Forty per cent (six of 15) versus 13% (two of 15) were responders regarding ratings of present and general pain intensity, figures similar to those found by Nayak et al35 in SCI and central neuropathic pain. Those authors found that 42% (five of 12 individuals) reported a decrease of at least two units on an NRS following 15 treatment sessions with acupuncture. Even though both studies used very small samples, these results are considered promising.

None of the present respondents reported worsening of pain using the PGIC, but one patient on acupuncture reported being minimally worse at the 2-month follow-up. Whether this was associated with the treatment course is not clear. In the study by Nayak and colleagues,12 four of the total sample (22 individuals reported an increase in pain intensity at end of treatment and that this persisted at follow-up. The reported average increase was 1.08 on a 0–10 NRS.

Nowadays it is recommended22 36 that the PGIC be added when evaluating the results of a clinical trial, since this instrument covers more aspects than only pain reduction. Our evaluation showed that the effects of both treatments rated on the PGIC were similar, with nine of 15 individuals (60%) on massage and eight of 15 (53%) on acupuncture.
reporting a favorable effect. At follow-up, six of 15 (40%) on acupunture still reported an improvement but only one of 15 (7%) on massage. In a study on pregabalin for SCI neuropathic pain,34 57% of those on active drug reported an improvement, using the PGIC immediately after the treatment period. This result is similar to those of both acupuncture and massage seen in the present study.

Both methods of sensory stimulation assessed in this study seemed to be able to decrease pain short-term in individuals with SCI and neuropathic pain. However, a difference between the two stimulation methods was seen: many individuals reported a small reduction following massage, but few reported a major alleviation following acupuncture. Three on acupuncture experienced a dramatic effect and long-term improvement. These long-term pain-alleviating effects have been attributed to activation of pain-inhibiting systems in cortical and subcortical pathways. While individuals with SCI and neuropathic pain may have symptoms in common, the origins and the mechanisms of their pain may vary. Different mechanisms can lead to different responses to therapy, and for this reason larger studies are warranted where possible effects can be studied in subgroups.

Both treatment modalities were safe and compliance was high. No individuals dropped out due to adverse events and no severe adverse events were reported. This is rare in pharmacological trials in the same patient group where the dropout rates are reportedly high with commonly used drugs: 16% on gabapentin, 18% on amitryptiline,35 30% on pregabalin,34 48% on tramadol37 and 50% on gabapentin.38

The treatments assessed had effects mainly on the primary outcome variable—pain. However, individuals also reported that their coping ability had improved after treatment with acupuncture. This might be associated with the decrease seen in pain ratings. Ratings of pain interference also decreased after massage. No other effects on mood, sleep quality, life satisfaction or spastic-pain interference also decreased after massage. No other effects on mood, sleep quality, life satisfaction or spastic-pain interference also decreased after massage.

CONCLUSION
Neuropathic pain following SCI is a condition unresponsive to many interventions. Results from this study indicate that both acupuncture and massage therapy may relieve SCI neuropathic pain and for this reason larger randomised controlled trials are warranted for assessing the long-term effects of these treatments.

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