

## Acupuncture in adults with Chemotherapy-Induced Peripheral Neuropathy: a systematic review

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**Objective:** to analyze and synthesize knowledge about the effect of acupuncture on chemotherapy-induced peripheral neuropathy symptoms in adults with cancer. **Method:** the method used was a Systematic Review. Potential articles were identified by searching in the PubMed of National Library of Medicine, Cumulative Index to Nursing and Allied Health Literature, Embase, Cochrane Central and Scopus. Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses strategy, 607 articles were identified. After removing the duplicates, all titles and abstracts were reviewed, and seven articles were selected for full review. After the full review, five studies were selected for inclusion. **Results:** of the five articles included, four were cohort studies and one was a quasi-experimental study. All articles showed that acupuncture was associated with an improvement in the peripheral neuropathy, but the type of protocol, use of medications, time of treatment, and different outcome measures made it difficult to compare the studies. **Conclusion:** the use of acupuncture appears to be associated with an improvement in the symptoms of chemotherapy-induced peripheral neuropathy and has no side effects. In order to improve the evidence about benefits associated with acupuncture, more experimental studies using both subjective and objective measures are needed.

**Descriptors:** Neoplasms; Antineoplastic Agents; Acupuncture; Acupuncture Therapy; Acupuncture Points; Peripheral Nervous System Diseases.

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## Introduction

Chemotherapy is one of the most important treatments for cancer, but it has many adverse effects that adversely impact the patient's quality of life. One adverse effect of chemotherapy is chemotherapy-induced peripheral neuropathy (CIPN)<sup>(1)</sup>.

CIPN is a serious problem because it leads to difficulties in adherence to chemotherapy treatment, which may have an impact on both the patient's daily life and the long-term outcome of the treatment. The drugs that can cause CIPN include Cisplatin, Oxaliplatin, Paclitaxel, Thalidomide, and Bortezomib<sup>(1)</sup>. Patients who receive Cisplatin, for example, may experience loss of all sensory modalities, ataxia and gait imbalance, early reduction/loss of deep reflexes, paresthesia (burning sensation, tingling), numbness (loss of sensation), among others. These symptoms may continue for months after the end of treatment<sup>(1)</sup>. The intensity and degree of severity of the symptoms depends on the drug, dose, treatment time, and other co-morbid conditions, such as Diabetes, prior exposure to neurotoxic agents, and alcohol exposure<sup>(2)</sup>.

CIPN is diagnosed by a health care provider, usually based on the patient's self-report, but a growing number of objective measures are becoming available. Objective measures include nerve conduction studies (NCS), neurological examinations, and cytokine assessments. A few studies on pharmacological treatments for CIPN, such as vitamin E, glutathione, and lipoic acid, have been conducted, but their quality is poor and the results are not consistent, owing largely to reliance on self-reported outcomes<sup>(1)</sup>. The primary approach to the management of CIPN is dose delays and dose reductions; thus, it is very important to diagnose CIPN as early as possible, so that the chemotherapy dose can be adjusted<sup>(2)</sup>.

There has been a growing interest in acupuncture, a common complementary therapy, as a new intervention for CIPN. Acupuncture is an ancient practice that originated within the Traditional Chinese Medicine (TCM) in which needles are inserted into the patient's skin at various points in the body<sup>(3)</sup>. Acupuncture results in a sensation known as *De-Qi*, which is considered fundamental to its effect, but the actual receptors and nerve fibers involved are unknown<sup>(4)</sup>. The meaning of *Qi*, which is subjective and dependent on the context and coordinates in which it is experienced, is considered to be the patient's "energy" or "the arrival of vital energy"<sup>(5)</sup>. The mechanisms of action of acupuncture are still not fully understood, but

the most commonly held hypotheses are that acupuncture leads to increased blood flow in the capillaries at the needle insertion sites, releases local opioid peptides, reduces inflammation, and stimulates specific areas of the brain<sup>(6)</sup>.

Researchers have studied the impact of acupuncture on many disorders such as musculoskeletal diseases<sup>(7)</sup>, chronic lower back pain<sup>(8)</sup>, nausea in pregnancy<sup>(9)</sup> and headache<sup>(10)</sup>. Researchers have also shown that acupuncture is effective for the treatment of many cancer symptoms caused by chemotherapy or radiotherapy, such as nausea<sup>(11)</sup>, vomiting<sup>(11)</sup>, cancer pain<sup>(12)</sup>, hot flashes<sup>(13)</sup>, and fatigue<sup>(14)</sup>. Furthermore, recent studies<sup>(15-16)</sup> with other modalities such as laser acupuncture and auricular therapy have demonstrated their efficacy in the management of systemic arterial hypertension and chronic spinal pain. The anatomic points chosen by the person who applies the acupuncture may vary. Some individuals follow specific acupuncture protocols while others develop specific protocols for each patient.

The objective of this review was to analyze and synthesize the knowledge about the effect of acupuncture on chemotherapy-induced peripheral neuropathy symptoms in adults with cancer. The research question for this review was: Does acupuncture reduce chemotherapy-induced peripheral neuropathy symptoms in adults with cancer?

## Method

The method used was a Systematic Review of the literature (SR). A SR is a strategy that aims to identify, evaluate and synthesize relevant studies on a given topic, gathering evidence that responds to a specific clinical problem. Systematic reviews are used to establish evidence-based clinical practice<sup>(17)</sup>. The present review was conducted using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) strategy<sup>(18)</sup>, with the following inclusion and exclusion criteria:

Inclusion criteria: peer-reviewed English studies of adults (18 years old or more) diagnosed with cancer, who were able to give consent without proxy, with symptoms of CIPN diagnosed by a health care provider and treated with acupuncture (without electrical, laser or auricular stimulation).

Exclusion criteria: case series, case reports, studies with interventions that included electrical or laser stimulation and auricular acupuncture, studies with animals, studies with adults diagnosed with dementia, reviews, conference abstracts, studies with acupuncture and substances other than

prescribed medications, studies about neuropathic pain only, and articles without access to the full text.

The PICO<sup>(19)</sup> statement for this review was: P: adults with chemotherapy-induced peripheral neuropathy; I: acupuncture; C: adults with chemotherapy-induced peripheral neuropathy who did not receive acupuncture treatment; and O: improvement of chemotherapy-induced peripheral neuropathy symptoms. The databases used were: PubMed of National Library of Medicine, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Embase, Cochrane Central and Scopus. The search in all databases included articles published since the beginning of each index until February 2018. The terms used in the search were:

PubMed: ("Peripheral Nervous System Diseases"[Mesh] OR ("peripheral neuropathy"[Text Word] OR "neuropathic pain"[Text Word])) AND (("Neoplasms"[Mesh] OR "Antineoplastic Agents"[Mesh]) OR (chemotherapy[Text Word] OR induced[Text Word] OR cipn[Text Word] OR cancer[Text Word])) AND (((("Acupuncture"[Mesh] OR "Acupuncture Therapy"[Mesh]) OR "Acupuncture Points"[Mesh]) OR "Acupuncture Analgesia"[Mesh]) OR acupuncture[Text Word]).

Embase: chemotherapy-induced peripheral neuropathy/ OR exp \*peripheral neuropathy/ OR (peripheral neuropathy\* or neuropathic pain).ti,ab,kw. AND exp antineoplastic agent/ ae [Adverse Drug Reaction] OR exp neoplasm/ OR (chemotherapy or induced or cipn or cancer). ti,ab,kw. AND acupuncture.ti,ab,kw. or exp acupuncture analgesia/ or exp acupuncture/ or exp acupuncture needle/.

Cochrane Central: [mh "ACUPUNCTURE ANALGESIA"] or [mh ACUPUNCTURE] or [mh "ACUPUNCTURE THERAPY"] or (acupuncture): ti,ab,kw [mh "Peripheral Nervous System Diseases"] or ("peripheral neuropathy\*" or "neuropathic pain"): ti,ab,kw [mh "Antineoplastic Agents"] or [mh Neoplasms] or (chemotherapy or cipn or cancer or induced or complication\*):ti,ab,k.

Scopus: TITLE (acupuncture) AND TITLE-ABS-KEY ("peripheral neuropathy\*" or "neuropathic pain") AND TITLE-ABS-KEY (chemotherapy or cipn or cancer or induced or complication\*).

CINAHL: (MH "Peripheral Nervous System Diseases+") or "peripheral neuropathy\*" or "neuropathic pain" AND (MH "Acupuncture+") or Acupuncture AND (MH "Antineoplastic Agents+/AE") or (MH "Neoplasms") or chemotherapy or induced or cipn or cancer.

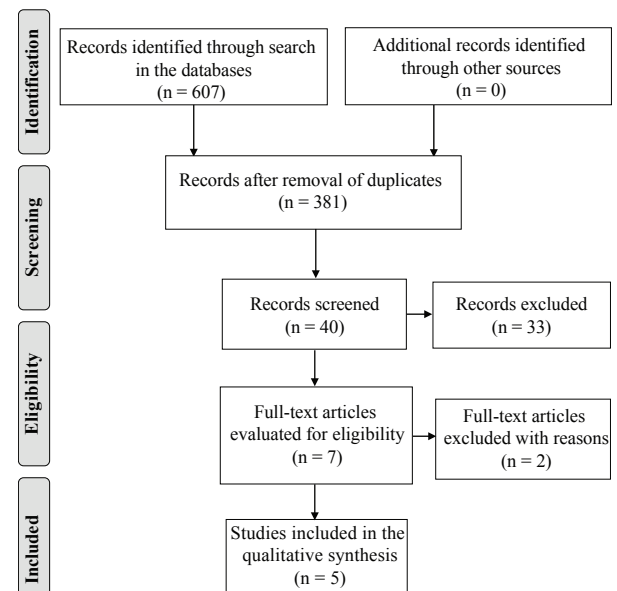
The search resulted in a total of 607 articles (Table 1).

Table 1 – Number of studies found in the databases. Edmonton, AB, Canada, 2018

Databases	Nº of studies (n=xx)
PubMed*	146
Embase	260
Cochrane Central	38
Scopus	77
CINAHL†	86
Total: 607	

\*PubMed - PubMed of National Library of Medicine; †CINAHL - Cumulative Index to Nursing and Allied Health Literature

After the removal of duplicates, all titles and abstracts were reviewed and 7 articles were selected for reading of the full text. Two further articles were removed after the full review because they did not meet inclusion criteria (Figure 1).



\*PRISMA - Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Figure 1 - Flowchart, according to PRISMA\*, to select the studies found<sup>(18)</sup>

The characteristics of the studies to be analyzed were: title, authors, year of publication, design, evidence level, population and sample size, measure for CIPN, treatment and results, and comments from the authors about specific characteristics of the study. The studies were evaluated according to the level of evidence required for the question of the systematic review. As the question investigated in this review was the effects of a treatment, the following levels of evidence were considered: Level I: systematic reviews; Level II: individual randomized controlled trials; and Level III: quasi-experimental studies, and cohort studies<sup>(20)</sup>.

The critical evaluation of the studies was done by two independent reviewers, according to the Checklists for Cohort Studies and Quasi-Experimental Studies from the Joanna Briggs Institute Critical Appraisal Tools<sup>(21)</sup>. These instruments were chosen because they allow the methodological evaluation of the studies and of the scientific evidence found in the proposed systematic review.

## Results

The Figures 2 and 3 summarize the characteristics of the quasi-experimental study and of the cohort studies included in the review, according to the assessment of methodological quality from Joanna Briggs Institute Critical Appraisal Tools<sup>(21)</sup>.

Questions	Study Schroeder, Meyer-Hamme and Eplée 2012 <sup>(22)</sup>
1. Is it clear in the study what is the 'cause' and what is the 'effect' (i.e. there is no confusion about which variable comes first)?	Yes
2. Were the participants included in similar comparisons?	Yes
3. Were the participants included in the comparison receiving similar treatment/care other than the exposure or intervention of interest?	Yes
4. Was there a control group?	Yes
5. Were there multiple measurements of the outcome both pre- and post-intervention/exposure?	Yes
6. Was follow-up complete and if not, were the differences between groups adequately described and analyzed in terms of follow-up?	Yes
7. Were the outcomes of participants included in any comparisons measured in the same way?	Yes
8. Were outcomes measured in a reliable way?	Yes
9. Were appropriate statistical analyses used?	Yes

Figure 2 – Evaluation of the methodological quality of the quasi-experimental study included in the review according Joanna Briggs Institute Critical Appraisal Tools<sup>(21)</sup>

Questions	Study Donald, Tobin and Stringer 2011 <sup>(23)</sup>	Bao, et al. 2014 <sup>(24)</sup>	Toftagen, et al. 2015 <sup>(25)</sup>	Russo 2017 <sup>(26)</sup>
1. Were the two groups similar and recruited from the same population?	Not applicable	Not applicable	Not applicable	Not applicable
2. Were the exposures measured similarly to assign people to both exposed and unexposed groups?	Not applicable	Not applicable	Not applicable	Not applicable
3. Was the exposure measured in a valid and reliable way?	No	Yes	Unclear	Yes
4. Were confounding factors identified?	No	Yes	Yes	Yes
5. Were strategies to deal with confounding factors stated?	No	Yes	Unclear	No
6. Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?	Yes	Yes	Yes	Yes
7. Were the outcomes measured in a valid and reliable way?	No	Yes	Yes	Yes
8. Was the follow-up time reported and long enough for outcomes to occur?	Yes	Yes	Yes	Yes
9. Was follow-up complete, and if not, were the reasons for follow-up loss described and explored?	Yes	Yes	Not applicable	Yes
10. Were strategies to address incomplete follow-up used?	Unclear	Not applicable	Not applicable	Not applicable
11. Were appropriate statistical analyses used?	Yes	Yes	Yes	Yes

Figure 3 – Evaluation of the methodological quality of the cohort studies included in the review according Joanna Briggs Institute Critical Appraisal Tools<sup>(21)</sup>

The quasi-experimental study included in this review met all of the criteria outlined by the Joanna Briggs Institute for studies of this design, and thus it is of good quality. One cohort study<sup>(23)</sup> did not meet the Joanna Briggs Institute Checklist for cohort studies,

indicating significant methodological weaknesses. The weaknesses included use of questionnaires that have not been tested for validity and reliability, and failure to identify and control confounding factors in the analysis. In another cohort study<sup>(26)</sup>, the authors

identified possible confounding factors but did not use strategies to control them. The other cohort studies were well done.

The articles included in the review are summarized in Figure 4. All authors found that acupuncture had a positive effect on CIPN symptoms in at least some

participants, with no adverse events. However, there were also some individuals who did not report a reduction in CIPN symptoms after acupuncture. Based on this review, it seems reasonable to support the use of acupuncture by cancer patients interested in reducing CIPN symptoms.

Title and author of the article	Acupuncture for chemotherapy-induced peripheral neuropathy (CIPN*): a pilot study using neurography Schroeder, Meyer-Hamme and Epplée 2012 <sup>(22)</sup>
Design	Quasi-Experimental Study
Evidence level	III
Population + sample size	11 patients with CIPN*: 6 best medical care for CIPN* + acupuncture (3 men and 3 women, mean age of 64) and 5 best medical care for CIPN* but no specific treatment for CIPN* (4 men and 1 woman, mean age of 65). Many types of cancer. Best medical care: carbamazepine or pregabalin. The study was done in Portugal.
Measure for CIPN*	Neurological examination and nerve conduction studies. Nerve conduction studies data were collected before treatment and after 6 months of treatment by examination of the sural and tibial nerves. In the nerve conduction studies, a change of velocity in the sural nerve of 2m/s slower or faster was considered significant and a change in the amplitude of the sensory nerve action potential of more than 2uV was seen as a significant impairment or improvement in the sural nerve.
Treatment	Used of traditional Chinese acupuncture. Treatment: 10-week treatment with the ST34, five extra points EX-LE12 and four additional points at EX-LE8 (Ba Feng). The needles were inserted bilaterally.
Results	Acupuncture group: all had hypoesthesia in stocking distribution. After 6 months, five patients had improvement in the conduction velocity of the sural nerve and one did not have change. Control group: all reported hypoesthesia in stocking contribution. After six months, three patients showed no change in the conduction velocity of the sural nerve, one had improvement and one had increased neuropathic pain. No adverse effects were reported.
Comments	The sample size was small. The same acupuncture protocol was used to treat all patients in the experimental group. Patients had many types of cancer. Patients of the acupuncture group completed chemotherapy 2-21 months before acupuncture, but those of the control group completed chemotherapy 1-14 months before acupuncture.
Title and author of the article	Evaluation of acupuncture in the management of chemotherapy-induced peripheral neuropathy Donald, Tobin and Stringer 2011 <sup>(23)</sup>
Design	Cohort
Evidence level	III
Population + sample size	Eighteen patients (eight men and ten women, with mean age of 51.83 years) in England. Seventeen patients completed the study but one died. Fourteen patients were referred for acupuncture to complement their conventional treatment for CIPN* (drugs not identified).
Measure for CIPN*	Self-report
Treatment	Use of traditional Chinese acupuncture. Acupoints were selected based on patient presentation at each session and the needles remained in place for 30-45 minutes. One patient received acupuncture twice a week for 3 weeks while 16 received weekly treatments for 6 weeks. The points used and the numbers receiving treatment at each point in brackets were: SP6 (18), ST36 (18), LV3 (14), LI4 (13), BL60 (12) and Ba Feng/Ba Xie (10).
Results	Fourteen patients reported that acupuncture improved their CIPN* and three reported no change. Six reported one additional benefit such as improved sleeping and relaxation, and reduced stress, seven reported more than one additional benefit and four had no additional benefits. No adverse effects were reported.
Comments	Patients had different types of cancer and used different chemotherapy drugs. No control group. Eight patients had other comorbidities such as Type 2 diabetes mellitus, which may have affected outcomes. A different protocol was used for each patient.

(the Figure 4 continue in the next page...)

Title and author of the article	A Pilot Study of acupuncture in treating bortezomib-induced peripheral neuropathy in patients with multiple myeloma Baο, et al. 2014 <sup>(24)</sup>
Design	Cohort
Evidence level	III
Population + sample size	Twenty-seven patients with multiple myeloma (mean age of 63) treated in United States of America with bortezomib and with persistent CIPN* (grade 2 or more) - criteria NCI-CTC 4.0 <sup>f</sup> .
Measure for CIPN*	FACT/GOG-Ntx <sup>z</sup> , Neuropathic Pain Scale, nerve conduction studies, and assessment of proinflammatory cytokines (such as interleukin-6, 8, 10, macrophage inflammatory protein -1 $\alpha$ ). Data were collected at baseline, twice during acupuncture (weeks 4 and 10), and then 4 weeks after acupuncture (week 14).
Treatment	Use of traditional Chinese acupuncture. Ten acupuncture sessions (twice a week for 2 weeks, once a week for 4 weeks, and biweekly for 4 weeks). Points: bilateral ear points (shen men, point zero and 2 additional points where electrodermal signal was detected), bilateral body points LI4, TE5, LI11, ST40 and Ba Feng in upper and lower extremities. The needles remained in the skin for 20 minutes. Patients continued using the prescribed medications for CIPN* but the drugs used were not identified.
Results	Nerve conduction studies: (n =15) five showed at least 10% increase in motor nerve amplitude, eight showed no significant changes and two showed at least 10% decrease. No significant correlations between symptoms and nerve conduction results. Cytokine studies: no correlation with other measures or grade. Significant reduction in FACT/GOG-NTx <sup>z</sup> score (p < .0001) and Neuropathic Pain Scale score (p < .0001). Eighteen of 26 (69%) patients had at least 30% reduction in Neuropathic Pain Scale score. No adverse effects reported.
Comments	Only 14 weeks of treatment. All patients received the same protocol. Median time after discontinuation of bortezomib was 19 months.
Title and author of the article	Evaluation of group acupuncture for cancer-related symptoms: a retrospective analysis Toftthagen, et al. 2015 <sup>(25)</sup>
Design	Cohort
Evidence level	III
Population + sample size	Forty-two patients participated in the study. Mean age was 66.1 and the majority of patients were women. Breast cancer was the main diagnosis. Thirty-five had Chemotherapy-Induced Peripheral Neuropathy. The study was done in the United States of America.
Measure for CIPN*	The patients were questioned about their symptoms using a 0-10 symptom severity scale.
Treatment	Use of traditional Chinese acupuncture. The points used were determined by the areas of body where neuropathy was reported. Points used: HT-8, PC-8, LI-4, Baxie, ST-36, SP-9, GB-34, KD-3, BL-60, ST41-BL57, SP-3 and BL-66. Needles remained in the skin for at least 25 minutes.
Results	The participants reported a reduction in CIPN* and other symptoms after four acupuncture sessions. No adverse effects reported.
Comments	It was unclear how many treatments were applied or what the frequency of the treatments was. The outcome was only measured through self-report. Different acupoints for each patient were used.
Title and author of the article	The feasibility of an acupuncture protocol in the treatment of chemotherapy induced peripheral neuropathy - a pilot study Russo 2017 <sup>(26)</sup>
Design	Cohort
Evidence level	III
Population + sample size	Eleven patients (three men and eight women) with CIPN* grade II or greater, based on the World Health Organization criteria. The mean age was 65.9 years. The study was done in the United States of America.
Measure for CIPN*	Neuropathic Pain Scale, QLQ-C30 <sup>s</sup> and QLQ-CIPN20 QOL scales <sup>l</sup> . Each patient completed the questionnaires before the first session, at the fourth acupuncture session, and at the final acupuncture session.

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Title and author of the article	The feasibility of an acupuncture protocol in the treatment of chemotherapy induced peripheral neuropathy - a pilot study Russo 2017 <sup>(26)</sup>
Treatment	Traditional Chinese acupuncture was not used (no further information was given). Protocol: the Hua Tuo Jia Li, UB 32, Ba Xie, Ba Feng, LI 10, LI 11 to LI5, GB 34. Needles remained in the skin for 20 minutes. Acupuncture sessions occurred once a week for 10 weeks. The same protocol was applied to all subjects. The patients were taking various supplements and medications, but there was no pattern in the medications taken.
Results	Significant improvement in neuropathic pain, CIPN* symptoms, and sensory condition. The sample was small and many statistical analyses were conducted on the same sample, with no Bonferroni correction. No adverse effects reported.
Comments	Included both patients with acute and chronic CIPN*. The cancer diagnoses of participants were not stated. Data were collected only at the end of the study, and no results of each individual treatment were available. Authors were unsure whether the tools used accurately measured symptom experience.

\*CIPN - Chemotherapy-Induced Peripheral Neuropathy; †NCI-CTC 4.0 - National Cancer Institute-Common Toxicity Criteria 4.0; ‡FACT/GOG-NTx - Functional Assessment of Cancer Therapy/Gynecologic Oncology Group - Neurotoxicity questionnaire; §QLQ-C30 - Quality of Life Questionnaire; ||QLQ-CIPN20 QOL scales - Quality of Life Questionnaire-Chemotherapy-Induced Peripheral Neuropathy 20 Quality of Life scales

Figure 4 - Summary of studies on acupuncture intervention

## Discussion

One quasi-experimental study and four cohort studies were included in this review. The authors of all studies showed that acupuncture was associated with an improvement in CIPN symptoms in at least some participants and no one experienced adverse events. The cohort and quasi-experimental studies were classified as having evidence level III, which is defined as less reliable studies. The methodological quality of the articles, however, was very good, which indicates that they were good studies of the effects of the intervention in CIPN patients.

The antineoplastic agents used in the studies in this review (Oxaliplatin, Cisplatin, Vincristine and Bortezomib) affect the nervous system differently, and all can reach the ganglion cells of the dorsal roots to the distal axons<sup>(27)</sup>. The use of different chemotherapeutic agents across the studies included in this review may explain some of the variability in the findings<sup>(28)</sup>. The authors of one study<sup>(28)</sup> also noted that the development and intensity of symptoms were related to the dose of the chemotherapeutic drug, what is something that could have been better explored by the authors of the included studies.

A number of additional factors may have also contributed to the difficulty to compare the findings. First, while some authors<sup>(22,24,26)</sup> used the same acupuncture protocol for all patients, others<sup>(23,25)</sup> did not do so, but rather adapted the protocol to each patient's unique problems. Second, in most studies some patients also used medications such as pregabalin and carbamazepine to treat CIPN symptoms during the time they received acupuncture. Medication use was not controlled in the analysis, making it difficult to know whether acupuncture was responsible for the changes in CIPN symptoms or not. Third, the time of the protocols varied considerably

from only a few weeks to 14 weeks. Finally, although some acupoints such as Ba Feng, Ba Xie, LI11 and LI4 were used in several studies<sup>(23-26)</sup>, there were no studies using exactly the same acupoints.

The authors of one study<sup>(24)</sup> discussed the possible mechanisms of action of acupuncture, but its findings did not support any of these mechanisms. In general terms, analgesia in the context of acupuncture occurs through the activation of a pain control system, which is a complex system involving the stimulation of neurons from different regions of the brain. These neurons send a signal of inhibition of pain to the spinal cord. In this system, there are neurotransmitters such as serotonin, enkephalin and endorphin that are also released to aid in the analgesic effect of acupuncture<sup>(29)</sup>. This may explain why nerve conduction studies had no significant correlation with pain improvement, as these studies merely analyzed the speed and amplitude of action potentials, but did not analyze the substances involved in the process. According to the International Association for the Study of Pain (IASP), neuropathic pain is "the pain caused by injury or disease of the somatosensory system". It is present in 40% of cancer patients, and CIPN patients have a three-fold greater chance of developing neuropathic pain, a condition that is characteristic of CIPN<sup>(30)</sup>. This finding supports the importance of identifying some other objective measure of CIPN symptoms.

The evaluation of CIPN is difficult. In clinical settings, health care providers typically depend on the patient's subjective report of CIPN symptoms using short questionnaires or other tools<sup>(31)</sup>. Thus, it is not surprising that most of the authors of the studies included in this review also used subjective measures for their dependent variable.

Two groups of authors in this review<sup>(22,24)</sup> used both objective measures, such as nerve conduction

studies (NCS), and subjective measures to evaluate the effects of acupuncture. Nerve conduction studies measure the amplitude and velocity of conduction of composite motor and sensory action potentials<sup>(32)</sup>. The use of NCS is problematic because it requires referral to specialized laboratories and causes discomfort to patients<sup>(31)</sup>.

In this review, none of the authors were able to demonstrate a correlation between objective and subjective measures of CIPN symptoms. This could be due to low sensitivity of the subjective and objective measures used. Further research on the identification of tools for accurately measuring the symptoms associated with CIPN is urgently needed. Such work should ideally be conducted with scholars fluent in the languages used by those who have studied the effects of acupuncture within the Traditional Chinese Medicine tradition, so that new approaches can be built upon gains made by these individuals.

This study had two main limitations. First, the number of available studies was small, due to limited research in this area. Second, it was difficult to compare results among studies due to differences in outcomes and in measurement tools used. Some research teams used only subjective measures while others used both subjective and objective measures.

Based on this systematic review, we developed several recommendations for future research. First, the use of an experimental study design is strongly encouraged as it incorporates a control group to which the outcomes in the experimental group can be compared. A related point is the recruitment of a homogenous sample, such as those who are in treatment or those who have finished treatment, large enough to detect possible differences between the experimental and control group.

Second, it seems from the studies included in this review that there is a dose-response effect between acupuncture and outcome. For this reason it would be interesting to see if patients who receive more sessions over a longer period of time are likely to have better outcomes on both objective and subjective measures.

Finally, better measures for evaluating the impact of acupuncture on CIPN symptoms and quality of life are urgently needed. One group of authors<sup>(33)</sup> evaluated eight articles that showed an inverse relationship between CIPN and quality of life, which is not surprising as CIPN is characterized by numbness and burning sensation in lower and upper extremities, which leads to difficulties to drive, write and walk. Researchers planning to conduct studies of acupuncture in the future are, therefore, encouraged to use quality of life instruments to analyze the effect of acupuncture in this important factor in adults with CIPN.

Subjective measures involving patient report are the gold standard in symptom management. Although objective measures are of interest, the most important symptom measure is the perception of the patient. We recommend the use of robust symptom measures such as the Memorial Symptom Assessment Scale (MSAS), with the assessment of severity and frequency of the symptoms, and distress. In addition, quality of life should always be included as a dependent variable, as CIPN appears to significantly reduce the ability to perform activities of daily life.

## Conclusion

This systematic review was based on five studies about the use of acupuncture as intervention for improving the symptoms of chemotherapy-induced peripheral neuropathy. Acupuncture appears to be an effective intervention for treating some adult CIPN patients and is not associated with adverse events. More experimental studies with larger and more homogeneous samples over longer periods of time are urgently needed. In addition, it is important to develop new measurement approaches for the assessment of CIPN symptoms and include quality of life as an outcome measure.

## References

1. Cavaletti G. Chemotherapy-induced peripheral neurotoxicity (CIPN): what we need and what we know. *J Peripher Nerv Syst.* 2014; 19(2):66–76. doi: <http://dx.doi.org/10.1111/jns5.12073>
2. Tzatha E, Deangelis LM. Co-Morbidity Consult: Chemotherapy-Induced Peripheral Neuropathy. *Oncology.* [Internet]. 2016 Mar [cited May 12, 2018]; 30(3):240-4. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5653267/>
3. Bao T, Zhi WI, Vertosick EA, Li QS, Derito J, Vickers A, et al. Acupuncture for breast cancer-related lymphedema: a randomized controlled trial. *Breast Cancer Res Treat.* 2018; 170(1):77-87. doi: <http://dx.doi.org/10.1007/s10549-018-4743-9>.
4. Kawakita K, Okada K. Acupuncture therapy: mechanism of action, efficacy, and safety: a potential intervention for psychogenic disorders? *Biopsychosoc Med.* 2014; 8:4. doi: <http://dx.doi.org/10.1186/1751-0759-8-4>
5. Yang XY, Shi GX, Li QQ, Zhang ZH, Xu Q, Liu CZ. Characterization of Deqi Sensation and Acupuncture Effect. *Evid Based Complement Alternat Med.* 2013;2013:319734. doi: <http://dx.doi.org/10.1155/2013/319734>
6. Cheng KJ. Neurobiological Mechanisms of Acupuncture for Some Common Illnesses: A Clinician's Perspective. *J Acupunct Meridian Stud.*



- 2014; 7(3):105-14. doi: <http://dx.doi.org/10.1016/j.jams.2013.07.008>
7. Yuan QL, Wang P, Liu L, Sun F, Cai YS, Wu WT, et al. Acupuncture for musculoskeletal pain: A meta-analysis and meta-regression of sham-controlled randomized clinical trials. *Sci Rep*. 2016; 6: 30675. doi: 10.1038/srep30675
8. Li J, Zhang JH, Yi T, Tang WJ, Wang SW, Dong JC. Acupuncture treatment of chronic low back pain reverses an abnormal brain default mode network in correlation with clinical pain relief. *Acupunct Med* 2014; 32:102-8. doi:10.1136/acupmed-2013-010423
9. Smith C, Crowther C, Beilby J. Acupuncture to treat nausea and vomiting in early pregnancy: a randomized controlled trial. *Birth*. 2002 Mar;29(1):1-9. doi: <https://doi.org/10.1046/j.1523-536X.2002.00149.x>
10. Mayrink W, Garcia J, Santos AD, Nunes J, Mendonça T. Effectiveness of acupuncture as auxiliary treatment on chronic headache. *J Acupunct Meridian Stud*. 2018 Jul 27. pii: S2005-2901(17)30061-4. doi: 10.1016/j.jams.2018.07.003
11. Li QW, Yu MW, Yang GW, Wang XM, Wang H, Zhang CX, et al. Effect of acupuncture in prevention and treatment of chemotherapy-induced nausea and vomiting in patients with advanced cancer: study protocol for a randomized controlled trial. *Trials* (2017) 18:185. doi: 10.1186/s13063-017-1927-2
12. Lam TY, Lu LM, Ling WM, Lin LZ. A pilot randomized controlled trial of acupuncture at the Si Guan Xue for cancer pain. *BMC Complement Altern Med*. 2017;17:335. doi: 10.1186/s12906-017-1838-5
13. Lesi G, Razzini G, Musti MA, Stivanello E, Petrucci C, Benedetti B, et al. Acupuncture As an Integrative Approach for the Treatment of Hot Flashes in Women With Breast Cancer: A Prospective Multicenter Randomized Controlled Trial (AcCliMaT). *J Clin Oncol*. 2016 May 20;34(15):1795-802. doi: 10.1200/JCO.2015.63.2893.
14. Smith C, Carmady B, Thornton C, Perz J, Ussher JM. The effect of acupuncture on post-cancer fatigue and well-being for women recovering from breast cancer: a pilot randomised controlled trial. *Acupunct Med* 2013;31:9-15. doi:10.1136/acupmed-2012-010228
15. Pereira RDM, Alvim NAT, Pereira CA, Gomes Junior SCS. Laser acupuncture protocol for essential systemic arterial hypertension: randomized clinical trial. *Rev. Latino-Am. Enfermagem*. 2018; 26:e 2936. doi: <http://dx.doi.org/10.1590/1518-8345.1887.2936>
16. Moura CC, Iunes DH, Ruginsk SG, Souza VHS, Assis BB, Chaves ECL. Action of ear acupuncture in people with chronic pain in the spinal column: a randomized clinical trial. *Rev. Latino-Am. Enfermagem*. 2018; 26: e3050. doi: <http://dx.doi.org/10.1590/1518-8345.2678.3050>
17. Doolen J. Meta-Analysis, Systematic, and Integrative Reviews: An Overview. *Clin Simul Nurs*. 2017;(1):28-30. doi: <http://dx.doi.org/10.1016/j.ecns.2016.10.003>.
18. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Loaniddis JPA, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ*. 2009;339:b2700. doi: <https://doi.org/10.1136/bmj.b2700>
19. Joanna Briggs Institute (JBI). Reviewers' manual 2014. Adelaide: University of Adelaide, Joanna Briggs Institute. [Internet] 2014. [cited Oct 3, 2018]. Available from: <http://joannabriggs.org/assets/docs/sumari/reviewersmanual-2014.pdf>.
20. Polit DF, Beck CT. Fundamentos de pesquisa em enfermagem: avaliação de evidências para a prática de Enfermagem. 9º Ed. Porto Alegre. Artmed; 2018.
21. Joanna Briggs Institute (JBI). Critical Appraisal Tools. Adelaide: University of Adelaide, Joanna Briggs Institute. [Internet] 2017. [cited Oct 5, 2018]. Available from: <http://joannabriggs.org/research/critical-appraisal-tools.html>
22. Schroeder S, Meyer-Hamme G, Epplée S. Acupuncture for chemotherapy-induced peripheral neuropathy (CIPN): a pilot study using neurography. *Acupunct Med*. 2012 Mar; 30(1):4-7. doi: 10.1136/acupmed-2011-010034
23. Donald GK, Tobin I, Stringer J. Evaluation of acupuncture in the management of chemotherapy-induced peripheral neuropathy. *Acupunct Med*. 2011 Sept; 29(3):230-3. doi: 10.1136 / acupmed.2011.010025
24. Bao T, Goloubeva O, Pelsler C, Porter N, Primrose J, Hester L, et al. A pilot study of acupuncture in treating bortezomib-induced peripheral neuropathy in patients with multiple myeloma. *Integr Cancer Ther*. 2014 Sep; 13(5):396-404. doi: 10.1177/1534735414534729
25. Toftagen C, Boses S, Healy G, Jooma N. Evaluation of Group Acupuncture for Cancer-Related Symptoms: A Retrospective Analysis. *J Palliat Med*. 2015 Oct; 18(10):878-80. doi: 10.1089/jpm.2015.0143
26. Russo AJ. The Feasibility of an Acupuncture Protocol in the Treatment of Chemotherapy Induced Peripheral Neuropathy – A Pilot Study. *Orient Med*. [Internet]. 2017 [cited May 12, 2018]:3-36. Available from: <https://www.slideshare.net/DrFredRusso/cipndrrusso>
27. Caponero R, Montarroyos ES, Tahamtani SMM. Post-chemotherapy neuropathy. *Rev Dor. São Paulo*. 2016; 17(Suppl 1):S56-8. doi: <http://dx.doi.org/10.5935/1806-0013.20160049>
28. Grisold W, Cavaletti G, Windebank AJ. Peripheral neuropathies from chemotherapeutics and targeted agents: diagnosis, treatment, and prevention. *Neuro Oncol*. 2012 Sep; 14(4):45-54. doi: 10.1093/neuonc/nos203

29. Cabyoglu MT, Ergene N, Tan U. The Mechanism of Acupuncture and Clinical Applications. *Int J Neurosci*. [Internet]. 2006 Feb [cited May 12, 2018];116(2):115-25. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/16393878>
30. Simão DAS, Murad M, Martins C, Fernandes VC, Captein KM, Teixeira AL. Chemotherapy-induced peripheral neuropathy: review for clinical practice. *Rev Dor*. [Internet] São Paulo, 2015 [cited Oct 8, 2018] Jul-Sep;16(3):215-20. Available from: <http://www.scielo.br/pdf/rdor/v16n3/1806-0013-rdor-16-03-0215.pdf>
31. Matsuoka A, Mitsuma A, Maeda O, Kajiyama, H, Kiyoi H, Kodera Y, et al. Quantitative assessment of chemotherapy-induced peripheral neurotoxicity using a point-of-care nerve conduction device. *Cancer Sci*. 2016 Oct; 107(10):1453-7. doi: 10.1111/cas.13010
32. Park SB, Goldstein D, Krishnan AV, Lin SYC, Friedlander ML, Cassidy J, et al. Chemotherapy-Induced Peripheral Neurotoxicity: A Critical Analysis. *CA Cancer J Clin*. 2013 Nov/Dec;63(6):419-37. doi: 10.3322/caac.21204
33. Mols, F, Beijers, T, Vreugdenhil G, Van de Poll-Franse L. Chemotherapy-induced peripheral neuropathy and its association with quality of life: a systematic review. *Support Care Cancer*. 2014 Aug;22(8):2261-9. doi: 10.1007/s00520-014-2255-7

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