

## Case Report

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# Acupuncture and Low Dose Gabapentin Effectively Treat Paclitaxel Induced Peripheral Neuropathy and Prevent Chemotherapy Dose Reduction

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*The University of Maryland School of Medicine Marlene and Stewart Greenebaum Cancer Center, Baltimore, MD, USA***Abstract**

Peripheral neuropathy is a frequent and well-recognized debilitating complication of taxanes, often necessitating dose-reduction of these effective agents. Here, we present a case in which acupuncture treatments were successfully used in combination with low dose gabapentin to alleviate PIPN symptoms and prevent chemotherapy dose reduction.

**Keywords:** Acupuncture; Peripheral neuropathy; Neoadjuvant chemotherapy

**Introduction**

Peripheral neuropathy is a frequent and well-recognized debilitating complication of taxanes, often necessitating dose-reduction of these effective agents [1,2]. Within the taxane family, paclitaxel is more commonly associated with the development of peripheral neuropathy than docetaxel [1,2]. Management of paclitaxel induced peripheral neuropathy (PIPNe) remains a significant clinical challenge. At present, no pharmacologic therapies have been proven to be universally effective [3]. Medications commonly employed to treat PIPNe include a diverse class of drugs, such as GABA analogs (i.e. gabapentin and pregabalin), tricyclic anti-depressants, selective serotonin reuptake inhibitors (SSRIs) and opioid analgesics. However, these drugs are often reported as either ineffective or fraught with further complications. As such, non-pharmacologic therapies, such as acupuncture, have generated significant interest in the management of PIPNe. Acupuncture has been successfully employed for symptom palliation in patients experiencing peripheral neuropathy secondary to diabetes, HIV and cancer [4-6], and thus presents an attractive treatment option for PIPNe. Here, we present a case in which acupuncture treatments were successfully used in combination with low dose gabapentin to alleviate PIPNe symptoms and prevent chemotherapy dose reduction.

**Case Report**

A 54-year-old postmenopausal African-American female, with no significant past medical history, was diagnosed with stage IIIA (T2N2M0) triple negative breast cancer one month after palpating a left breast mass. She opted to enroll in a clinical trial in which she was randomized to receive neoadjuvant weekly paclitaxel (80 mg/m<sup>2</sup>) for twelve weeks followed by dose-dense doxorubicin and cyclophosphamide for four cycles.

Following her first two doses of weekly paclitaxel, she developed grade 2 peripheral neuropathy according to the National Cancer Institute-Common Toxicity Criteria (NCI-CTC). Neuropathy symptoms presented in her hands and feet, which she described as a sensation of tingling and numbness that interfered with her daily function. She also reported a painful sensation in her feet, which she rated as 7 out of 10 on a standard pain scale. She was initially prescribed gabapentin 100 mg three times a day for relief of her neuropathic pain symptoms, but was also offered the option of receiving acupuncture if her symptoms persisted. At her next follow-up visit, one week later, by which time she had been taking gabapentin at the prescribed dose for approximately 10 days, she reported a worsening of her neuropathy and elected treatment with acupuncture. For the next two weeks, she

was treated with acupuncture per standard protocol once per week as well as taking gabapentin 100 mg three times a day. The standard acupuncture protocol consisted of treatment at the following acupoints: bilateral ear points (shen men, point zero, and two additional auricular acupuncture points where electro-dermal signal was detected); bilateral body acupuncture points LI4, SJ5, LI11, ST40; and Ba Feng located in upper and lower extremities [7]. She experienced an immediate improvement in her neuropathy symptoms right after the acupuncture treatment with pain reduced from 4 to 1 on a ten point scale, and, at each of her subsequent follow-up visits, was found to have an NCI-CTC grade 1 neuropathy with minimal paresthesia and pain. Meanwhile, she continued taking 100 mg of gabapentin three times daily for a total of five weeks, which she discontinued due to dizziness. She continued to receive paclitaxel at full dose and did not require dose reduction or dosing schedule modifications due to neuropathic symptoms. Additionally, she noted that acupuncture also appeared to alleviate her symptom of mild to moderate nausea, also believed to be related to paclitaxel.

After completing twelve weeks of paclitaxel, she proceeded to received four cycles of doxorubicin and cyclophosphamide and had an uncomplicated clinical course without incident. The patient tolerated chemotherapy well, and both gabapentin and acupuncture were discontinued. Her neuropathy symptoms remained minimal during this stage of her treatment. A restaging MRI of the breast following completion of chemotherapy showed significant interval reduction in size of the left breast mass and axillary tail. The patient then underwent left partial mastectomy and left axillary lymph node dissection, which revealed no evidence of invasive ductal carcinoma. To date, she remains in a pathologic complete remission.

**Discussion**

This case report suggests that acupuncture in addition to low dose gabapentin may be effective to treat paclitaxel-induced peripheral

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neuropathy (PIPNe) and to prevent chemotherapy dose reduction. In addition to the direct benefits of symptomatic relief and reduction of neuropathic severity, improvement of PIPNe allowed this patient to continue receiving paclitaxel at full-dose, a factor that arguably contributed to her excellent treatment response.

Paclitaxel, and other taxanes, commonly referred to as microtubule stabilizing agents (MTSAs) lead to disruption of mitosis in the G2 phase, and exert a broad spectrum of cytotoxic effects in cancers of the breast, ovary and lung [8].

Despite its efficacy, the development of peripheral neuropathy remains the most common cause for paclitaxel dose modifications [1]. PIPNe is characterized as an axonal, predominantly, sensory neuropathy [1,9]. Symptoms are typically described as numbness and tingling in a “stocking-and-glove” pattern, particularly in the distal lower extremities. Patients may also report intermittent sharp, shooting pains in the legs. Loss of deep tendon reflexes and sensation to pain and temperature are also commonly reported [1]. The incidence of PIPNe varies from 2-33% [10-15] and is based largely on several predisposing risk factors such as dose per cycle, concurrent therapy with other neurotoxic agents, treatment schedule, cumulative dose, duration of infusion and pre-existing neuropathy from other medical conditions such as diabetes [1,2]. Furthermore, a reported 58% of patients develop paclitaxel-associated acute pain syndrome (P-APS). This is a distinct clinical entity, recently characterized by Loprinzi and colleagues, which may also predispose patients to PIPNe later in their treatment course [16].

The precise pathogenesis through which paclitaxel exerts its neurotoxic effects is unknown. However, pre-clinical rat models have demonstrated that taxanes disrupt axonal transport, and affect all sensory nerve fibers, particularly large myelinated nerve fibers involved in vibration and proprioception [8,17,18].

Management of PIPNe remains challenging considering that commonly used pharmacologic therapies have varying rates of success and often carry their own adverse effects. So far, the only successful clinical trial for treatment of chemotherapy induced peripheral neuropathy (CIPNe) treatment clinical trial showed 60 mg daily duloxetine caused a modest 0.7 point pain reduction (on a ten point scale) when compared to placebo, and was also associated with common side effects such as fatigue and nausea [19].

Acupuncture is a well-tolerated; low-risk non-pharmacologic intervention which has been successfully used to treat chemotherapy induced peripheral neuropathy [6,7]. Although the mechanism of acupuncture remains unclear, it has been proposed that acupuncture works through its effect on neurotransmitters and neurohormones. Animal research suggests that acupuncture accomplishes its analgesic effect by stimulating nerves in the muscle, which then relay the signal to the spinal cord, midbrain and hypothalamus-pituitary system. This signaling leads to the release of neurotransmitters and hormones such as endorphins and enkephalins [20-22]. Several other mechanisms have also been suggested to explain the effect of acupuncture analgesia. These include: activation of descending pain inhibiting pathways; deactivation of the limbic system as well as cortical and subcortical regions; cortical cerebral vasodilation causing release of neuropeptide; and inhibition of the release of inflammatory factors [23-27].

In this particular case, the benefit of acupuncture in addition to low dose gabapentin appeared to be two-fold. In addition to providing symptomatic relief, this combination treatment potentially prevented paclitaxel dose reduction, allowing this patient to receive the full

benefit of chemotherapy and achieve a pathologic complete response. The role that acupuncture may have in preventing chemotherapy dose reductions is an important consideration in the care of cancer patients receiving neurotoxic chemotherapy regimens. It is also interesting that the patients’ PIPNe symptoms resolved after 5 weeks of low dose gabapentin in combination with weekly acupuncture treatment. This suggests there may be synergistic effects between the two modalities that warrant further research.

Our case report provides encouraging results regarding the use of acupuncture plus low dose gabapentin in treating PIPNe. However, one potential limitation is that it is difficult to discern which component of this patient’s treatment played the primary role in palliating her symptoms. The patient did comment that she did not experience any improvement in symptoms during the 10 days of gabapentin treatment before acupuncture was started. Her symptoms greatly improved, however, promptly following initiation of acupuncture treatments. While gabapentin typically takes several weeks to demonstrate its therapeutic effect, we would not expect such a dramatic decline in symptoms on the low dose that this patient received [28]. Importantly, the patient experienced no adverse treatment effects from either gabapentin or acupuncture. Further studies should examine potential synergistic effects of acupuncture combined with low dose anti-neuropathy agents, with the goal of providing patients with effective treatment with minimal side effects.

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