Is Acupuncture Effective in Reducing Nausea and Vomiting in Patients Undergoing Chemotherapy?

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Is Acupuncture Effective in Reducing Nausea and Vomiting in Patients Undergoing Chemotherapy?

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ABSTRACT

OBJECTIVE- The objective of this systematic review is to determine whether or not acupuncture effective in reducing nausea and vomiting in patients undergoing chemotherapy.


DATA SOURCES- Randomized controlled trials measuring the reduction of nausea and vomiting in chemotherapy patients using acupuncture.

OUTCOMES MEASURED- The outcomes measured were episodes of vomiting or increased nausea that required additional antiemetic as noted on a four point scale. Emesis free days, episodes of emesis and severity and duration of nausea were measured using the Rhodes index of nausea, vomiting and retching scores filled out by patients. A 0-10 point scale was used to measure reduction in severity of nausea.

RESULTS- There was statistically significant changes in nausea and vomiting in only one study. According to Streitberger et al, acupuncture does not reduce vomiting or nausea in patients when used prior to and the day after chemotherapy. You et all found that acupuncture is effective in reducing emesis episodes, but does not increase emesis free days. Mehling et al determined there is no reduction in nausea or vomiting when acupuncture is used in chemotherapy patients.

CONCLUSIONS- The results show that acupuncture is not effective in reducing chemotherapy induced nausea and vomiting. Further research is needed to determine if type of chemotherapy, specific cancer or use of antiemetics skew the results.

KEY WORDS – Nausea, chemotherapy, acupuncture
INTRODUCTION

Cancer is extremely common, affecting all age groups, races, and genders with an incidence of 461.6 cases per 100,000 individuals per year. Chemotherapy is a common cancer treatment, but side effects make it difficult to tolerate, longer for patients recover, and may require a change to treatment protocol. Of cancer patients, 40-70% experience nausea and vomiting due to chemotherapy treatment. The goal of chemotherapy is to reduce or eradicate the cancer, therefore improving quality and length of life, and yet patients may become pessimistic and attempt suicide after only two weeks of nausea and vomiting. Some relief is found with antiemetics, but more effective options need to be evaluated and incorporated into practice. Currently, more than 40% of patients with cancer report using alternative medicine, this paper will concentrate on acupuncture. Acupuncture is based on the ancient Chinese principles of yin and yang, to which balance is achieved by stimulation of various points on the body with needles. It is believed that acupuncture affects the nervous system and releases endorphins.

Physician Assistants are involved in all specialties of medicine. In oncology, the front lines of the cancer battle, the use of acupuncture to treat chemotherapy induced nausea and vomiting can be a vital addition to treatment protocol. In primary care, where the diagnosis of cancer begins, the ability to provide comfort and options for patients worried about the well known side effects of chemotherapy is invaluable. There are 24.6 million healthcare visits per year for cancer patients. The use of antiemetics for chemotherapy induced nausea and vomiting average $267 per day or $90,369-111,239 per year, while the cost of an acupuncture treatment ranges from $75-100 per visit.
There are three types of emesis, acute, delayed and anticipatory. It is unknown which patients will suffer from each type. Chemotherapy medications trigger zones in the medulla, cerebral cortex, and intestinal track utilizing dopamine, serotonin, histamine, opioid, and acetylcholine receptors that lead to vomiting. Antiemetics being used to treat the symptoms are 5-HT3 receptor antagonists and corticosteroids, such as ondansetron. While antiemetics reduce nausea, they are expensive and not 100% effective.

Acupuncture has been used for 4000 years in China to treat disease. Many individual studies and practices have found acupuncture to be helpful in treating nausea and vomiting. Several large organizations have added acupuncture to their recommendations, the American College of Chest Physicians recommended acupuncture as complementary when nausea is poorly controlled post chemotherapy. Also, the NIH states acupuncture is currently showing benefits for the treatment of nausea and vomiting in the chemotherapy patient. If acupuncture can reduce nausea and vomiting in patients undergoing chemotherapy, their quality of life will be improved and their recovery time reduced.

OBJECTIVE

The objective of this systematic review is to determine whether or not acupuncture is effective in reducing nausea and vomiting in patients undergoing chemotherapy.
METHODS

These studies included men and women over 18 years old undergoing chemotherapy and measured the effect of acupuncture on nausea and vomiting. Included in this analysis were a randomized controlled trial which compared acupuncture with massage to usual hospital care, a single blind randomized controlled trial which compared acupuncture, acupuncture with vitamin B6 injections, and vitamin B6 injections only, as well as a single blind randomized controlled trial which compared acupuncture to sham acupuncture. The outcome of the trials showed reduction in nausea with acupuncture, according to patient reports.

Articles for this systematic review were located by the author using PubMed, OVID, and Cochrane databases with the keywords nausea, chemotherapy and acupuncture. All articles were published in English, in peer reviewed journals. They were selected based on the importance of outcomes to patients. Inclusion criteria included randomized controlled trials involving cancer patients undergoing chemotherapy. Patients under 18 years old were excluded. To successfully measure patient outcomes, the following statistical methods were utilized: RRR, ARR, NNT, t-test, p-value, CI, CER, EER, RBI, Wald test, Nilcoxon rank sum test, Kruskal-Wallis rank test, and mixed effect regression analysis.
1. Table 1: Characteristics of Included Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Type</th>
<th>#Pts</th>
<th>Age (yrs)</th>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
<th>W/D</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streitberger, 2003 (1)</td>
<td>Single Blind RCT</td>
<td>80</td>
<td>Mean of 54</td>
<td>Age ≥18 years. Patients receiving HDCT and PBSCT. No acupuncture treatment during the last 6 months.</td>
<td>In last 24 hours, patients s/o nausea or vomiting or receiving antiemetic drugs Patients treated with benzodiazepines, exception qhs. Already received an antiemetic therapy before the start of chemotherapy with exception of steroids. Eczematous skin changes acupuncture location. Plaster allergy. Other simultaneous acupuncture Start of therapy with opioids or Coagulopathy</td>
<td>0</td>
<td>Acupuncture at P6 30 minutes prior to, and the following day, of high dose chemotherapy</td>
</tr>
<tr>
<td>Mehling, 2007 (2)</td>
<td>RCT</td>
<td>150</td>
<td>Mean of 57 ≥ 18</td>
<td>Scheduled for cancer related surgery, required ≥ 48 hr hospitalization limited to: Breast, Abdominal, Pelvic, Urological or Head and neck surgery</td>
<td>Not fluent in English Diagnosed with DVT On anticoagulants</td>
<td>12</td>
<td>Acupuncture at pericardium-6 and stomach - 36 at various times during the day</td>
</tr>
<tr>
<td>You, 2009 (3)</td>
<td>Single Blind RCT</td>
<td>142</td>
<td>45-65</td>
<td>Pathologically diagnosed with ovarian cancer stages II to III Experienced mild to moderate nausea and/or vomiting Received the same chemotherapy regimen and antiemetic drugs</td>
<td>Other medical disorders that might manifest with nausea or vomiting Mental illness or unable to communicate. Unable to apply instrument or to return on time for the f/u for 3 weeks Arm lymphedema in Active infection</td>
<td>5</td>
<td>Acupuncture treatment every other day at P6 for 20 minutes</td>
</tr>
</tbody>
</table>
OUTCOMES MEASURED

Each study measured individual outcomes using a variety of methods. Streitberger et al measured episodes of vomiting or increased nausea that required additional antiemetics. In this study, patients rated their nausea on a four point scale, which was analyzed in a descriptive comparison and using Fisher’s exact test for categorical variables. You et al measured emesis free days, episodes of emesis and severity and duration of nausea using the Rhodes index of nausea, vomiting and retching scores filled out by patients. Mehling et al measured reduction in severity of nausea which patients reported using a 0-10 point scale and self reported episodes of vomiting.

RESULTS

In the study performed by Streitberger et al, comparing acupuncture with non invasive acupuncture, the primary outcomes were presented as dichotomous data and as an intention to treat analysis with patients who discontinued treatment considered a failure.

The reported incidence of failure, defined as emetic episodes or additional medication on days 1 or 2, was 61% in the acupuncture group and 64% in the control group. This difference is not statistically significant with a p value of 0.82. To improve these symptoms in one patient, 34 must undergo acupuncture.. The absolute risk reduction (ARR) was calculated to be -0.03 and the relative risk reduction (RRR) calculated to be -39%. The confidence interval (CI) was reported to be -18% and 24% of a 3% difference, meaning there is 95% certainty that the true value for the population exists between those values. (Table 2)
Tolerability and safety were both high, as there were no side effects or complications reported that were specific to acupuncture. While no patients withdrew from the study, it was discontinued prematurely at 80 patients, instead of the planned 200, due to the negative results of those patients. The conditional power under the optimistic assumptions of the alternative hypotheses was determined to be 40% at that time, showing a small probability of obtaining different results with additional participants.

Table 2: Efficacy of Nausea/Emesis Prevention with Acupuncture

<table>
<thead>
<tr>
<th>Study</th>
<th>Failure Rate: control</th>
<th>Failure Rate: Acupuncture</th>
<th>p-value</th>
<th>95% CI</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streitberger</td>
<td>0.64</td>
<td>0.61</td>
<td>0.82</td>
<td>-18% and 24%</td>
<td>-34</td>
</tr>
</tbody>
</table>

Failure= emetic episodes or additional medication on days 1 or 2  
NNT = number needed to treat  
CI = confidence interval

In the study performed by You et al, comparing acupuncture with vitamin B6, acupuncture alone, and B6 injections alone, the primary outcomes were continuous data, and unable to be converted into dichotomous form. The data was presented as an intention to treat analysis, using a generalized estimating equation/logistic model with variance estimation.

The reported incidence of emesis episodes, reported as the mean of the groups, was 10.64 for the acupuncture group, 13.15 for vitamin B6, and 5.87 for the combination. This difference is statistically significant with a p value of <0.01. The reported incidence of emesis free days, reported as mean, was 30 for the acupuncture group, 21 for vitamin B6, and 59 for the combination. This was not statistically significant, with a p value of 0.49. (Table 3)
No complications or safety issues were listed in the study, one patient discontinued due to pain upon acupuncture. In total, five patients were dropped from the study, two others lost in follow up, one did not receive chemotherapy, and one missed a treatment session.

Table 3: Mean Emesis Outcomes with the Addition of Acupuncture and Vitamin B6

<table>
<thead>
<tr>
<th></th>
<th>Acupuncture and Vitamin B6</th>
<th>Vitamin B6</th>
<th>Acupuncture</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emesis Episodes per Person</td>
<td>5.87</td>
<td>13.15</td>
<td>10.64</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Emesis Free Days</td>
<td>59</td>
<td>21</td>
<td>30</td>
<td>0.49</td>
</tr>
</tbody>
</table>

In the study performed by Mehling et al, comparing acupuncture and massage with normal hospital care, the primary outcomes were presented as dichotomous and continuous data, and were not all able to be converted in dichotomous data. The data was analyzed using an intention to treat analysis.

The reported change in vomiting, reported as a mean, was -0.6 for acupuncture and -0.1 for the control, with a p value of 0.20, this was not a statistically significantly difference. The change in nausea, reported as a mean, was -0.3 in acupuncture and -0.1 in the control. This was also not a statistically significant difference with a p value of 0.26. (Table 4)

No complications, safety issues, or tolerance issues were listed in the study. Twelve patients were dropped from the study, due to rescheduled surgery or decline participation after surgery.

Table 4: Percent Mean Change from Baseline

<table>
<thead>
<tr>
<th></th>
<th>Acupuncture</th>
<th>Control</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea: Same day surgery</td>
<td>4.5</td>
<td>2.1</td>
<td>0.13</td>
</tr>
<tr>
<td>Nausea baseline to post op day 3</td>
<td>-0.3</td>
<td>-0.1</td>
<td>0.26</td>
</tr>
<tr>
<td>Vomiting baseline to post op day 3</td>
<td>-0.6</td>
<td>-0.1</td>
<td>0.20</td>
</tr>
</tbody>
</table>
In the three studies, acupuncture was compared to different controls; usual hospital treatment, placebo acupuncture, and vitamin B6. One of these studies added massage to all acupuncture treatments and another added an additional experimental group combining acupuncture and B6 injections. Each study used the P6 acupuncture site, proximal to the anterior wrist, while one of the studies added additional sites based on patient’s symptoms.

Each study further narrowed their patient populations, one study included only ovarian cancer patients, another only those scheduled for cancer related surgery, and the last included patients undergoing stem cell transplantation.

All of the patients involved were given antiemetics, which is the standard treatment. The data analysis of Mehling et al and Streitberger et al compared the standard medications with the experimental acupuncture treatment. You et al compared all experimental treatments for the most effective.

There was statistically significant changes in nausea and vomiting in only one study. According to Streitberger et al, acupuncture does not reduce vomiting or nausea in patients when used prior to and the day after chemotherapy, see table 2. You et al found that acupuncture is effective in reducing emesis episodes, but does not increase emesis free days, see table 3. Mehling et al determined there is no reduction in nausea or vomiting when acupuncture is used in chemotherapy patients, see table 4.

Compliance was not addressed by any study. You et al removed one patient from the study for missing a treatment session. Only hospitalized patients were enrolled in the other two studies, removing some possible noncompliance. Of those studies, one required patients to keep a diary of symptoms, which was not addressed as a potential compliance issue.
There were no reported safety issues or side effects. Of all the studies, one patient dropped out due to the pain of acupuncture. While potential side effects such as pain, hematoma, and fainting were explained to patients in at least one study, no reports of such incidences in the patients were mentioned.

DISCUSSION

Many previous studies have shown improvement in nausea with acupuncture, but these were done before the 5-HT$_3$ antiemetics were developed.\textsuperscript{5} Other studies have found improvement with the use of acupressure.\textsuperscript{5}

Acupuncture is considered a safe procedure, with rare side effects such pain, bleeding, syncope and minimal contraindications. It is currently used to treat headaches, back pain, nausea, stress, infertility and many more.\textsuperscript{5} The majority of insurance plans do not cover acupuncture services, with each session ranging from $75 to $100; out of pocket expense for the length of chemotherapy is excessive.

There are limitations in the reviewed studies, such as the difficulty in double blinding and use of acupressure. Sample size and a wide variety of cancer types were also limitations in these studies.

CONCLUSION

The studies reviewed demonstrate overall that acupuncture is not effective in treating nausea and vomiting in chemotherapy patients. One study showed a significant decrease in emesis episodes, but did not increase emesis free days.
Each study used different chemotherapeutic agents for patients with different cancers and different antiemetics. One study stated that women experienced nausea more severely and the resulting decrease in symptoms seen in patients may be hormone related. Future research in the role of hormones and nausea is needed to confirm that theory. Another study used a placebo needle that did not puncture the skin; it is possible that the acupressure could influence symptoms. Double blinding is a virtual impossibility when administering acupuncture, unless a method to blind those performing the acupuncture is implemented, pure unbiased results are impossible.

Future trials should focus on one chemotherapeutic agent, as different drugs have different side effects. Also, to collect the most accurate data, future research studies should include an acupuncture variable group without antiemetics, but ethical concerns and difficulty maintaining participation would hinder that study.

There are many studies performed previously that have shown acupuncture to an effective treatment of nausea and vomiting, enough so that The American College of Chest Physicians include the procedure in their guidelines. More study is necessary to determine the true validity of this addition.
REFERENCES


