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Does acupressure help to reduce symptoms in individuals receiving chemotherapy?

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A SELECTIVE EVIDENCE BASED MEDICINE REVIEW

In Partial Fulfillment of the Requirements For

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In

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ABSTRACT

OBJECTIVE: The objective for this selective EBM review is to determine whether or not acupressure can help to reduce symptoms in individuals receiving chemotherapy.

STUDY DESIGN: A systematic review of three peer-reviewed primary studies published between the years of 2007-2014.

DATA SOURCES: Three randomized control trials evaluating if acupressure can reduce nausea and vomiting symptoms in cancer patients undergoing chemotherapy. Sources were chosen from Google Scholar and PubMed based on their relevance to the clinical topic.

OUTCOMES MEASURED: The outcomes that are measured in the articles are chemotherapy-related nausea and vomiting. Two of the articles measured these patient oriented outcomes using Rhodes Index of Nausea, Vomiting, and Retching and the third article measured them using daily patient logs with elements from Rhodes Index of Nausea and Rhodes Index of Nausea, Vomiting, and Retching.

RESULTS: The first study conducted by Molassiotis et al³ and the study by Dibble et al⁵ showed significant improvement of nausea and vomiting in the acupressure group compared to the control group. However, the other study conducted by Molassiotis et al⁴ did not have significant findings between the control and acupressure groups.

CONCLUSION: The data presented in this review suggests that there is mixed evidence regarding whether or not there is a true association between acupressure utilization and reduction of nausea and vomiting. The one study that had significant results did not incorporate a placebo group to evaluate whether or not acupressure caused a true physiologic effect to reduce symptoms in individuals undergoing chemotherapy.³ In the other two studies,^{4,5} there was strong significance between the control groups and placebo groups. Therefore, further research should be conducted to determine if acupressure serves more of a placebo effect rather than causing true physiologic changes leading to reduction of nausea and vomiting in chemotherapy patients.

KEY WORDS: acupressure, chemotherapy, nausea, vomiting

INTRODUCTION

Cancer is unfortunately a disease that affects millions of people of all ages. Each year in the United States alone, more than 1.5 million people are newly diagnosed with some form of cancer.¹ In 2014, the total amount of people living with the 10 most common cancers was 14,483,830.¹ It is the fourth leading cause of death in young adults behind accidents and suicide, resulting in about 9,000 deaths in people 20-39 years of age in the US.¹

According to the American Cancer Society, the estimated total health care cost for cancer in the United States in 2015 was \$80.2 billion. This cost includes all inpatient and outpatient treatment for cancer patients in the US throughout the year.¹ According to the CDC, the number of patients that present to physician offices with cancer as their primary diagnosis is 24.6 million and about 650,000 of those patients receive chemotherapy each year.²

Although there has been extensive research into treatment for the various types of cancer, there is still no definitive cure. The current treatment options for cancer depend on how extensive the cancer is when the person is diagnosed. Chemotherapy, radiation, surgery, or combinations of the three are the most common therapy options for cancer patients.¹ However, these are not always guaranteed to completely cure the disease and often have significant side effects.

Two side effects that most chemotherapy patients experience are nausea and vomiting. In order to overcome these symptoms, people often take traditional antiemetic medication such as ondansetron. In addition to these usual medications, some people also try other therapies that are thought to be effective at relieving nausea and vomiting such as acupressure since the use of antiemetic medications does not always completely relieve the symptoms. Acupressure is a commonly used adjunctive therapy to relieve nausea and vomiting symptoms due to its cheap cost and ease of use. Although many studies have been conducted to analyze the efficacy of

acupressure to relieve these symptoms, there still seems to be varying opinions regarding this matter.

OBJECTIVE

The objective of this selective EBM review is to determine whether or not acupressure helps to reduce nausea and vomiting symptoms in patients undergoing chemotherapy.

METHODS

The three studies used for this systematic review were all randomized controlled trials. These studies all focused on patients with recent cancer diagnoses that were about to start undergoing chemotherapy treatment. They utilized acupressure armbands that applied pressure to the P6 acupoint, which has been thought to help alleviate nausea and vomiting symptoms in chemotherapy patients. In one of the studies, the comparison group was given sham acupressure bands that did not press on the P6 acupoint but instead pressed on a different point of the arm that is not supposedly associated with nausea control. In the two other studies, the comparison groups were only given traditional antiemetic medicine. The outcomes that are measured among the three studies are chemotherapy-related acute and delayed nausea and vomiting.

When searching for data sources, the search engines used were Google Scholar and PubMed. The keywords “acupressure”, “nausea”, and “chemotherapy” were used in order to find the best studies that analyzed this topic. The articles were carefully selected based on if they included outcome measures that were patient oriented and their relevance to the clinical topic. The inclusion criteria when searching for articles included participants that have been diagnosed with cancer, outcomes that were patient oriented, and articles that were published in 2007 or later. Exclusion criteria included articles published before 2007, those that were not patient oriented, and prior use of acupressure. All the chosen studies were published between 2007 and

2014 in peer-reviewed journals in the English language. The statistics that were used in the studies included p-values and odds ratios.

Table 1 - Demographics & Characteristics of included studies

Study	Type	# Pts	Age (yrs)	Inclusion Criteria	Exclusion Criteria	W/D	Interventions
Molassiotis (2007)	RCT	54	32-76	Breast cancer diagnosis, cancer stage I-III, no prior chemo experience, receiving doxorubicin and cyclophosphamide, and willing to sign a consent to be randomized to one of two groups	Received palliative chemo, life expectancy <3 months, had metastatic disease, bowel obstruction, undergoing concurrent radiotherapy, lymphedema of the arms	18	Acupressure wristband to P6 acupoint
Molassiotis (2014)	RCT	500	>16 (does not specify range, but majority >50)	scheduled to receive first cycle of chemotherapy; scheduled to receive chemo as a single or multiple administration repeated in 2, 3, or 4 week cycles; acupressure wristband naïve; either gender and older than 16 years old; cancer diagnosis receiving chemo without concurrent use of radiotherapy; receiving chemo as outpatients or inpatients; willing to be randomized to a group	scheduled to receive radiotherapy with chemotherapy; unable to provide self-care; liver disease; metabolic or mechanical risk factors for nausea; experiencing nausea and/or vomiting as a result of use of opioids; lymphedematous arms; chronic alcohol use	139	Acupressure wristbands to P6 acupoint
Dibble (2007)	RCT	160	49 +/- 9	Women receiving chemo for treatment of breast cancer; nausea intensity score with chemo of at least 3 on Morrow scale; starting 2 nd or 3 rd cycle of chemotherapy; able to communicate in English	Nausea score of less than 3; has not had cycle of chemotherapy yet; cannot communicate in English	13	Acupressure wristbands to P6 acupoint

OUTCOMES MEASURED

The outcomes that are measured in the articles are chemotherapy-related nausea and vomiting. Two of the articles measured these patient oriented outcomes using Rhodes Index of Nausea, Vomiting, and Retching and the third article measured them using daily patient logs with elements from Rhodes Index of Nausea and Rhodes Index of Nausea, Vomiting, and Retching.

RESULTS

This review of three randomized controlled trials analyzed the efficacy of acupressure in reducing nausea and vomiting symptoms in cancer patients undergoing chemotherapy.

In the study conducted by Molassiotis et al 2007³, fifty-four patients were recruited and randomized into two different treatment groups by drawing from an envelope. The control group, which consisted of participants taking traditional antiemetic medication only, included 19 people.³ The experimental group was instructed to wear wristbands that pressed on the P6 acupoint in addition to traditional antiemetic medication and consisted of 17 participants.³ All participants were newly diagnosed with cancer and new to chemotherapy treatment at the start of the study. Inclusion criteria for the participants consisted of a breast cancer diagnosis stage I-III, no prior chemotherapy, receiving doxorubicin and cyclophosphamide chemotherapy, and willing to be randomized to a group.³ Subjects were excluded if they have had prior chemotherapy, life expectancy was less than three months, had metastatic cancer, were undergoing radiation in addition to the chemotherapy, or had lymphedema of the arms.³ All participants received a serotonin antagonist, such as ondansetron, and dexamethasone for acute nausea and vomiting.³ The experimental group was given elastic wristbands with a 1 cm round plastic stud that presses on the P6 acupoint, which is located on the anterior forearm about three finger width distance up

from the wrist. The participants were adequately trained to identify the acupoint and how to properly wear the band.³ They were instructed to wear the bands bilaterally, to only take them off while taking a shower, and to apply pressure to the stud for 2-3 minutes every 2 hours. All subjects completed the Rhodes Index of Nausea, Vomiting, and Retching for 5 consecutive nights after their chemotherapy treatment of the day.³ The data in this study was presented as continuous using R-ANOVA to compare the effect that acupressure had on the patients that used acupressure during chemotherapy treatment versus those that did not.

The data from this study led to the conclusion that the acupressure bands decreased the occurrence of nausea and vomiting in the breast cancer patients undergoing chemotherapy. Across the five assessment days, nausea occurred significantly less frequent in the experimental group compared to the control group.³ In addition, there was a significant improvement with vomiting in the experimental group, especially during days four and five.³

The acupressure wristbands were very tolerated by the subjects for the most part. The only complaint was from one subject who reported that she took the bands off because they were tight and left marks on her arms for a few days after removing them.³

Table 2: Effectiveness of Acupressure to Reduce Nausea and Vomiting During One Round of Chemotherapy conducted by Molassiotis et al.³

Study: Molassiotis et al 2007	F value	P value
Nausea occurrence in acupressure group compared to control group	23.4	<0.001
Vomiting occurrence in acupressure group compared to control group	4.26	0.047

In the other study by Molassiotis et al,⁴ participants were randomly allocated to three different groups, the control group, experimental acupressure group, and the sham acupressure group through computer-generated randomization. In the acupressure group (n=186), participants were instructed to wear the acupressure bands bilaterally throughout all seven days of data collection and were shown how to properly wear them over the P6 acupoint.⁴ The sham acupressure group (n=166) was given identical bands, but was instructed to wear them with the pressure stud on the exterior of the band and on the opposite side of the arm from where the P6 acupoint is.⁴ The control group (n=166) was simply given standard antiemetic medication to take throughout the study.⁴ 500 subjects were randomized among the three trial groups, but only 361 cases were completed by the end of the study.⁴ The participants filled out the Rhodes Index of Nausea, Vomiting, and Retching for eight days per chemotherapy cycle for a total of 4 cycles. The possible range for values was 0-12, with higher numbers indicating worse nausea and vomiting symptoms.⁴

The data from this study showed that more people in the acupressure group reported no nausea throughout chemotherapy treatment compared to those in the control group, but there was no statistical significance between the two groups.⁴ There was a very skewed distribution in the continuous data between trial arms so the Mann-Whitney U-tests with Bonferroni adjustments was used to analyze the effectiveness of acupressure between the trial groups. In addition to the lack of statistical significance between the control and real acupressure band groups, the data showed statistical significance between the control and sham acupressure groups. Therefore, the overall data from this study suggests that there is no true association between the use of acupressure therapy and reduced symptoms of nausea and vomiting in patients undergoing chemotherapy treatment.

Table 3: Effectiveness of Acupressure to Reduce Nausea and Vomiting During the First Round of Chemotherapy conducted by Molassiotis et al.⁴

Study: Molassiotis et al. 2014	P Value
Control vs. Real Acupressure Bands	0.23

In the study by Dibble et al⁵, 160 women who were starting their second or third cycle of chemotherapy for treatment of breast cancer were randomly assigned to a control group, placebo group, or acupressure group. The patients in the control group (n=54) did not receive any additional intervention other than the usual antiemetic medications they were being prescribed by their physicians.⁵ The patients in the experimental acupressure group (n=53) in this study were not given bands but were instead instructed on proper location of the P6 acupoint, which is on the anterior forearm, and were told to use the thumb of the opposite hand to press on that point on each forearm.⁵ Nausea supposedly makes these points on the forearm tender to touch so the subjects were instructed to press on the P6 points each morning and any time throughout the day when they feel nauseous until the point no longer feels tender.⁵ The placebo group (n=53) was given the exact same instructions as the experimental acupressure group, but the only difference was that they were told to press on the S13 acupoint around the base of the fifth digit, which served as the placebo point in this study.⁵ Throughout an entire round of chemotherapy, all participants filled out a daily log that consisted of a nausea experience scale from the Rhodes Index of Nausea and a numeric rating scale and also documented the usual prescribed antiemetic medications they were taking. Out of the 160 participants in the beginning of the study, 36 women did not complete the logs, and the reason is not known.⁵

The data obtained from this study suggests that acupressure is effective in helping to reduce nausea and vomiting throughout chemotherapy treatment. The continuous data obtained from days 2-11 of the chemotherapy cycle measured the effect of acupressure on delayed emesis and nausea between trial arms using multilevel Poisson regression.⁵ The results regarding the incidence of emesis showed a greater decline in how often participants in the P6 acupressure group vomited compared to participants in the usual care group. The data regarding delayed nausea showed that women in the acupressure group reported a greater decline in nausea throughout the chemotherapy cycle compared to the women in the usual antiemetic care group on both the Rhodes Index of Nausea (RIN) scores and nausea numeric rating scale.

Table 4: Efficacy of Acupressure to Reduce Delayed Emesis and Nausea conducted by Dibble et al.⁵

Study: Dibble et al.	OR/IRR	P value
Emesis Incidence- Control group vs. Acupressure group	OR= 1.4	p<.001
Decline in Nausea- Control group vs. Acupressure group	RIN: IRR= 1.05	RIN: p<.006
	NRS: IRR= 1.05	NRS: p=.006

DISCUSSION

Acupressure is a very simple, safe, and cost-effective therapy. It is also very safe to use since it is an external, non-invasive device. The only complaint in one of the studies was from a woman who thought the bands were too tight and had to take them off.³ Other than that complaint, there were no other documented side effects throughout the studies.

Although all three studies were randomized and controlled, there were factors that could have served as significant limitations on the accuracy of the data. One limitation was the inability

to monitor if the participants were utilizing the acupressure and sham wristbands appropriately. The subjects were instructed on how to properly apply the acupressure either manually or with the bands, but there is always a chance that they were not continually wearing the bands in the correct spot or manually applying pressure to the exact point. In addition to possible incorrect use of the acupressure, the subjects may have also been noncompliant with how often they used it. The experimental and placebo groups were instructed to wear the bands and apply pressure to the acupoint locations throughout the day so there was not a completely reliable way to tell how compliant the participants truly were. Although the subjects could have reported on their compliance in the surveys, they may have been reluctant to admit to any noncompliance to the research study.

Another limitation in the study by Dibble et al⁵ could have been the fact that the usual antiemetic treatment that all participants were taking no matter which trial arm they were assigned to was not regulated by the researchers. In the daily logs, they noted which prescribed antiemetic medication they were taking, but it differed among all the patients so this served as an uncontrolled variable in the data.⁵

Another thing to consider is that placebo groups were included in the studies by Molassiotis et al 2015⁴ and Dibble et al.⁵ Even though those trial arms were not focused on in this review, it is worth noting that in both studies the control groups vs placebo groups did have statistical significance. This should be taken into consideration when evaluating the true efficacy of acupressure in reducing nausea and vomiting symptoms since there seems to be evidence of a placebo effect.

CONCLUSION

The findings presented in this review reveal that there is mixed evidence regarding the association between correct acupressure use and reduction of nausea and vomiting symptoms in chemotherapy patients. In two of the studies,^{3,5} the results showed that there was a relationship due to the significance between the control and real acupressure groups, but in the third study there was no statistical significance between the group that used acupressure in addition to antiemetic medication and the group that only took medication.⁴ In two studies, placebo groups were incorporated, and the patients that were using sham acupressure bands reported significant reduction in the negative chemotherapy symptoms.^{4,5} In the study by Malossiotis et al,⁴ the placebo group versus control group showed statistical significance while the control group versus real acupressure group did not. This data strongly suggested that there was no true relationship between correct acupressure use and reduction of nausea and vomiting symptoms. However, the other two studies suggest that the effectiveness of acupressure in reducing the symptoms may be a combination between true efficacy and a placebo effect.^{3,5}

Although there is mixed evidence regarding whether or not acupressure has a true impact on reducing nausea and vomiting from chemotherapy, the articles suggest that acupressure has a strong placebo effect on patients. Even if a therapy does not have a true physiological effect on a person, it is just as beneficial if that person perceives the symptom differently due to it. Since acupressure is such a safe and cost-effective therapy, it should be used in addition to traditional antiemetic medications to help reduce nausea and vomiting in chemotherapy patients. For future research on this topic, there should be more emphasis on how much of the treatment efficacy is due to true physiologic effects versus how significant the placebo effect is.

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