

Official Title of the study:

Optimization of Post-Operative Therapy for Nausea or
Vomiting

NCT number:

03075163

Protocol Approved by Institutional Review Board on
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Optimization of Post-Operative Therapy for Nausea or Vomiting

1. Protocol Title:

Optimization of Post-Operative Therapy for Nausea or Vomiting

Author of Protocol:

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2. IRB Review History

None previous.

3. Objectives

This is a single site, prospective, single blinded, randomized controlled study designed to evaluate the impact of acupressure when used as an initial treatment before rescue medications in the treatment of post-operative nausea and/or vomiting at UCD.

Specific aims:

- a. Primary: Observe the effect of initial treatment with acupressure for post-operative nausea and vomiting on the amount of ondansetron used for rescue therapy.
- b. Secondary: Observe the effect of initial treatment with acupressure for post-operative nausea and vomiting on
 - i. time to discharge after first postoperative antiemetic therapy is initiated.
 - ii. patients' perception of nausea on a 1-10 scale.
 - iii. patients' satisfaction of their treatment for nausea on a 1-10 scale.

Hypothesis: Bilateral manual acupressure at P6 is effective for post-operative nausea and vomiting and is not inferior to ondansetron as a rescue medication based upon the number needed to treat.

4. Background

Despite our advancements in medical technology, Post Operative Nausea and Vomiting (PONV) continues to negatively affect patients' health care experience. The incidence of PONV varies considerably between surgical settings and is estimated to range from 22%- 38% for nausea and 12%-26% for vomiting.¹ Patients continue to rank nausea and vomiting as the most undesirable surgical outcome and on average would be willing to pay \$100 for a 100% effective antiemetic if they experienced PONV.² This strain on our healthcare system causes an increase in resource utilization. One study showed an increase of time to discharge from the Post Anesthetic Care Unit (PACU) of one hour with an increased requirement of nursing and physician attention.³ PONV can also cause rare but serious medical complications such as aspiration, and wound dehiscence. It is estimated that for an "average" same day surgery center, the annual cost for PONV is \$253,270- 1,519,617.⁴

The use of multimodal pharmacological antiemetic prophylaxis and rescue medication continues to be the backbone of PONV therapy. Patients are typically given antiemetic therapy in both the preoperative and intraoperative periods based on clinical judgment of PONV risk factors. In the post operative period patients who develop PONV are then further treated. Over a 1 week observation of patients recovering in the UC Davis pavilion surgical center, an average 21.4% received some sort of pharmacological antiemetic therapy in PACU and of this population 17.4%

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receive further antiemetic treatment. This multimodal approach is similar to current practice as depicted in figure 1.⁵ At UCD acupressure is offered by some physicians prior to rescue medication. However, acupressure does not play a large role in current UCD treatment strategy. Ondansetron is the current medication used the most in the PACU, regardless of intraoperative use. It carries the risk of prolonged QT, as well as headache, constipation, weakness, tiredness, chills, drowsiness.⁶ In contrast, a small research study showed that implementation of acupressure for treatment of PONV improved patients satisfaction with their treatment for PONV.⁷ This is supported by a recent Cochrane metaanalysis that showed acupuncture stimulation at the P6 acupoint was just as effective as antiemetic drugs in the treatment of PONV.⁸ More specifically studies on acupressure at P6 has shown to be effective and virtually side effect free for pediatric tonsillectomy or adenoidectomy⁹, vertigo related nausea¹⁰, Cesarean Section Under Spinal Anesthesia¹¹, chemotherapy.¹¹⁻¹² P6 stimulation has been shown to stimulate the vagus nerve firing, inducing prolonged slow wave gastric peristalsis. This reduction in antiperistalsis has been correlated with nausea and vomiting.¹³⁻¹⁴

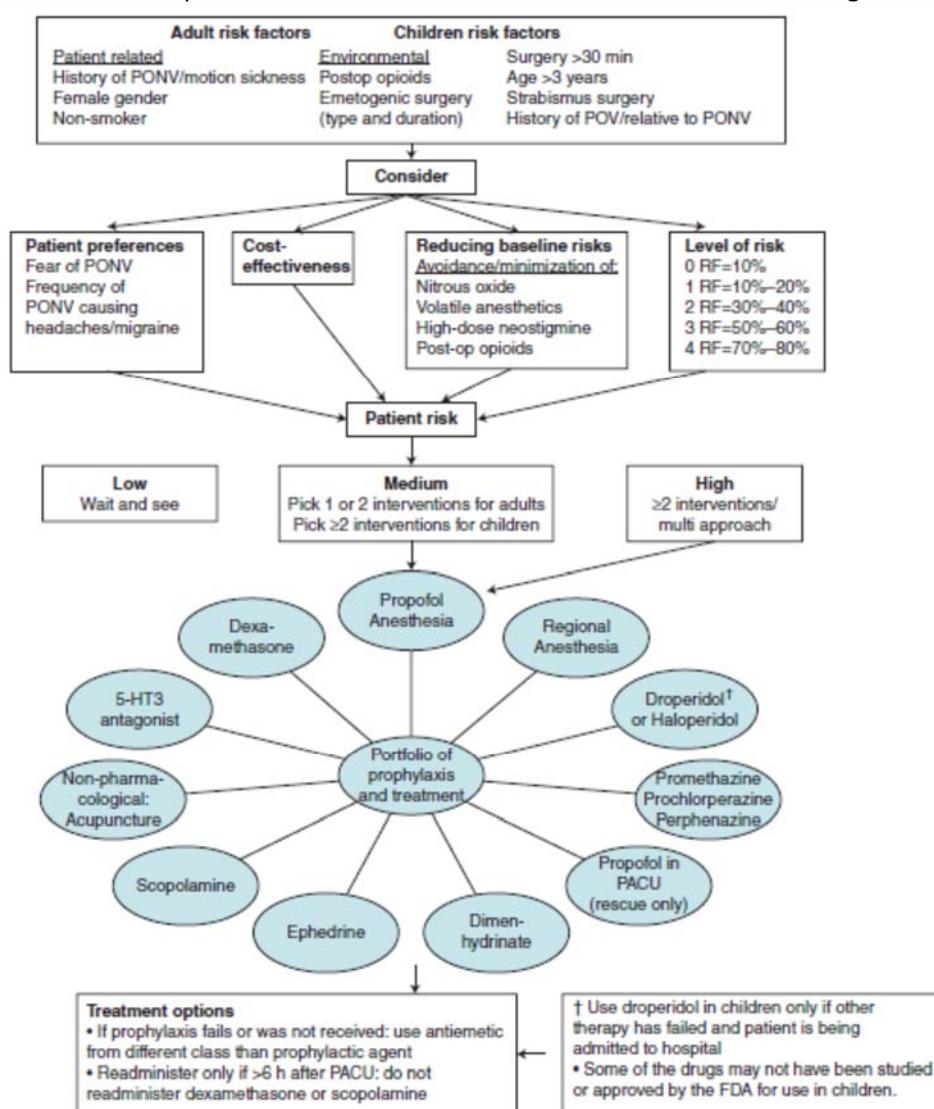


Figure 1: Society for Ambulatory Anesthesia guidelines for the management of postoperative nausea and vomiting.⁵

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It is hypothesized that increasing the use of acupressure can significantly decrease the need for rescue medication in the PACU. This has the potential to increase patient satisfaction, decrease cost and decrease risk of pharmacological side effects. We propose a randomized control trial of acupressure for PONV to test the impact of a no-risk precedent to standard therapy. Patients will be consented for the trial in preoperative period. From the consented patients, only those who develop post-operative nausea requiring antiemetic therapy decided by the patient's nurse or PACU anesthesiology team will continue in the study. Patients will then be randomized into one of 2 groups. The first group will receive pharmacologic antiemetic therapy with no acupressure per our standard regimen. The second group will receive up to 3 minutes of acupressure. At the end of this period, if the patient is still nauseated, they will continue with the same pharmacologic antiemetic therapy as the first group. The test subjects will be blinded to the fact that acupressure is being tested for treatment of PONV before further pharmacologic intervention. This blinding is important to avoid bias of the test subjects. Subjects may be upset if they wanted to be in either the acupressure group or the ondansetron group and were not placed in the desired group. This has the potential to confound the patient's self-reported nausea or vomiting scoring. The patient consent includes that acupressure may be one of the therapies used for treatment.

5. Inclusion and Exclusion Criteria

Patients scheduled for elective surgical procedures requiring general anesthesia in the UC Davis Medical Center main ORs will be screened for potential enrollment.

Inclusion criteria:

- age greater than 18 years
- scheduled for an elective surgical procedure requiring general anesthesia

Exclusion criteria:

- unable to access pericardial 6 acupressure point bilaterally post procedure
- Adults unable to give primary consent
- allergy to ondansetron
- age less than 18 years
- pregnancy
- prisoners

6. Number of Subjects

Assuming a variation and dropout rate of 10%, approximately 300 patients will be consented to achieve the 28 patients in the acupressure group and the 28 patients in the control group needed for the study. The need for 28 patients in each group was calculated for a 95% confidence, power 80%, and an equivalence limit of 30% with an assumed effectiveness of 82.6% of patients that will not need further treatment. These calculations were done using a binary-equivalence calculator (<https://www.sealedenvelope.com/power/binary-equivalence>). The assumed effectiveness of antiemetic therapy of 82.6% of patients was calculated from the incidence of antiemetic therapy needs in the UCD pavilion PACU during a one week period.

7. Recruitment Methods

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Patient recruitment and informed consent will be obtained in the UCDMC perioperative suite. Recruitment will be by direct discussion between the prospective candidates and the study investigators prior to their scheduled surgical procedure. The investigators will provide the consent form in person and give the prospective subject sufficient time to review the consent form and discuss the study with friends and family. The screening of patients will require the investigators to access personal health information to identify prospective subjects without HIPAA authorization. The research could not be practicably carried out without this waiver of consent. The risk of harm from contacting the participants is greater than the risk of the study procedures. The research is of minimal risk and does not involve any procedures for which written consent is normally required outside the research setting. The participants' rights and welfare will not be adversely affected by waiving consent. This protected health information will not be inappropriately reused or disclosed to any other person or entity. To further safeguard all protected health information, the final data will not be labeled with any personal identifying information, or with a code that this research team can link to personal identifying information. The data will not be stored with any identifiers.

8. Study Timelines

Each individual will only participate in the post anesthetic care unit starting from when the patient's nurse or anesthesiology team deems that the patient needs treatment for PONV. It ends when the patient is discharged from anesthesiology care in the post anesthetic care unit.

9. Study Endpoints

Primary study endpoint is the assessment of acupressure effect on PONV.

10. Procedures Involved

Patients will be asked to score nausea on a 1 to 10 scale before treatment. In the acupressure group, manual pressure will be applied by specifically trained personnel on the wrists bilaterally at the P6 point for up to 3 minutes. The P6 point is located three fingerbreadths from the wrist crease on the volar surface of the arm between the palmaris longus and flexor carpi radialis. (See Figure 2) In the event of failure in the acupressure group, further treatments will be identical to the control group. Since ondansetron is the standard Post Anesthetic Care Unit treatment, it will be first line rescue therapy except in the case that the patient has received 8mg in the past 6 hours. If needed, further antiemetic pharmacologic treatments may include, but are not limited to, phenergan, metoclopramide, haloperidol, diphenhydramine or propofol at the clinical discretion of the patient's anesthesiology care team. Patients will be asked to score nausea and satisfaction with treatment on 1 to 10 scales after treatment

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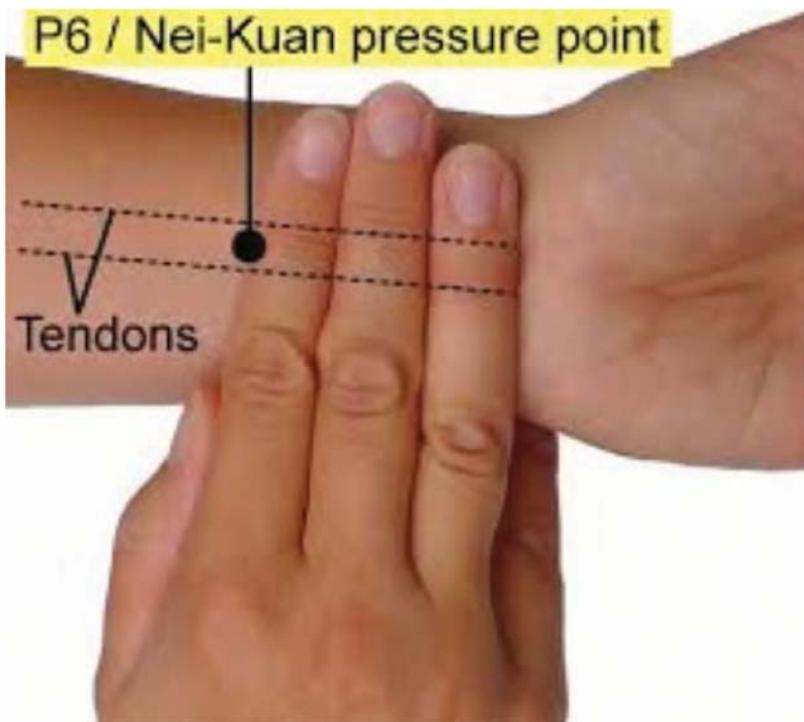


Figure 2: P6 point from¹²

11. Data and Specimen Banking

Not applicable.

12. Data Management and Confidentiality

Patients' MRN numbers will be on the consent forms along with a patient specific study number (etc. UCD PONV 001). Patient data will be recorded on a data collection sheet using the study number only for identification and then transferred to a laptop for off-line analysis. All computers or laptops holding identifiable data will be password protected and/or encrypted. Data analysis will be done with Prism (Ver. 5.0). All identifiable data, both from the computer and all written forms, will be stored in a locked cabinet in the PI's office in the Department of Anesthesiology and Pain Medicine after the end of the study. All data will be destroyed 1 year following publication of the results of this study.

13. Provisions to Monitor the Data to Ensure the Safety of Subjects

The risks associated directly with acupressure are minimal, but there is a risk for continued discomfort of approximately 3 minutes that would be associated with a delay in treatment. This is covered in the informed consent form.

14. Withdrawal of Subjects

Informed consent discussions will explicitly include emphasis that neither patient enrollment nor patient withdrawal from the study will result in any alterations to the standard clinical care in other aspects than their antiemetic treatment postoperative. Subjects may elect to withdraw at any time.

15. Potential Benefits to Subjects

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This study has the potential to decrease this severity of PONV, decrease the need for drug treatment in the PACU, decrease risk of pharmacological side effects, shorten the duration of PACU stay and increase patient satisfaction. It is a no-risk precedent to standard therapy.

16. Vulnerable Populations

This protocol will not involve the recruitment from any vulnerable patient populations.

17. Multi-Site Research

This is a single-site research study.

18. Community-Based Participatory Research

This project is not designed for community-based participatory research.

19. Sharing of Results with Subjects

There are no plans to share the specific results of this study with the study subjects.

20. Setting

Patient recruitment and informed consent will be obtained in the pavilion preoperative area. All data will be recorded during the post-operative period once the patient is identified as needing antiemetic therapy and is enrolled in the study.

21. Resources Available

Sufficient time and personnel are available for completion of this study. Informed consent and data collection will be performed by collaboration among all members of this research team. All members of the team have participated in the development of the protocol and are familiar with all facets of the study and are able to obtain informed consent. The role of the specialist (UC Davis Chronic pain Acupuncturist Ian Koebner, MSc., MAOM, L.Ac.) for this study will be to educate and train the PI's in acupressure prior to their performing acupressure on the patients enrolled in this study. He will not be required to perform acupressure on every patient in the study.

22. Prior Approvals

Not applicable.

23. Provisions to Protect the Privacy Interests of Subjects

A de-identified patient specific study number will be used to specify research subjects for data collection. Patients' personal antiemetic treatment regimen will only be discussed with the primary care givers when appropriate for patient care. All medications used will be entered into the EMR per standard practice.

Patient recruitment and informed consent will be obtained in the UCDMC perioperative suite only when there is sufficient time for a complete discussion between the investigator and the patient. Recruitment will be by direct discussion between the prospective candidates and the study investigators prior to their scheduled surgical procedure. The investigators will provide the consent form in person and give the prospective subject sufficient time to review the consent form and discuss the study with friends and family.

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24. Compensation for Research-Related Injury

There is no significant side effect profile for acupressure at P6. Research-related injury is not anticipated for this study given the benign natural of manual acupressure limited to 3 minutes.

25. Economic Burden to Subjects

There is no charge or additional cost for participation in this study. Neither the patient nor their insurance carrier will be charged for taking part in the research.

26. Consent Process

Informed consent will be obtained by direct discussion between the prospective candidates and the study investigators in the UCDMC perioperative suite. Recruitment will be prior to their scheduled surgical procedure. The investigators will provide the consent form in person and give the prospective subject sufficient time to review the consent form and discuss the study with friends and family. Informed consent from non-English speaking subjects will be obtained on an individual case basis using an appropriate translator for their native language.

27. Process to Document Consent in Writing

A copy of the form used to document written consent is attached to this application.

28. Drugs or Devices

Standard Antiemetic drugs will be used as needed and include but not limited to ondansetron, phenergan, metoclopramide, haloperidol, diphenhydramine and propofol. No devices will be used.

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