

University of York Department of Health Sciences
M.Sc. in Evidence Based Practice, M.Sc. in Health Services Research

Exercise: Combining data from many studies

This paper is taken from the journal *Obstetrics & Gynecology* (Vol. 91, No. 1, January 1998, pages 149-155). The original paper covers all complementary therapies. I have edited it to concentrate on only one: acupressure (acupuncture without needles) on the wrist.

Read the paper and answer the questions.

ALTERNATIVE THERAPIES FOR NAUSEA AND VOMITING OF PREGNANCY

Patricia Aikins Murphy, CNM, DRPH

From the Department of Obstetrics and Gynecology, and The Center for Complementary and Alternative Medicine Research in Women's Health, Columbia University College of Physicians and Surgeons, New, York, New, York.

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Objective. To review available evidence about the effectiveness of alternative therapies for nausea and vomiting of pregnancy.

Data Sources: MEDLINE and 13 additional US and international data bases were searched in 1996-1997 for papers that described use of alternative medicine in the treatment of pregnancy and pregnancy complications, specifically those addressing nausea, vomiting, and hyperemesis. Bibliographies of retrieved papers were reviewed to identify additional sources.

Methods of Study Selection: All relevant English language clinical research papers were reviewed. Randomized clinical trials addressing specifically the use of nonpharmaceutical and nondietary interventions were chosen for detailed review.

Tabulation, Integration, and Results: Ten randomized trials studying the effects of acupressure, ginger, and pyridoxine on nausea and vomiting of pregnancy were reviewed. Evidence of beneficial effects was found for these three interventions, although the data on acupressure are equivocal. Insufficient evidence was found for the benefits of hypnosis. Other interventions have not been studied.

Conclusion: There is a dearth of research to support or to refute the efficacy of a number of common remedies for nausea and vomiting of pregnancy. The best-studied alternative remedy is acupressure, which may afford relief to many women; ginger and vitamin B. also may be beneficial.

Nausea and vomiting of early pregnancy is a common complaint, affecting 50% or more of women in Western societies. The condition is generally self-limited, with symptoms most common and troublesome in early pregnancy and abating by the end of the first trimester. Concerns about the potential teratogenic effects of drugs taken during the critical embryogenic period, especially in the wake of the thalidomide tragedy of the 1960s, limit the use of pharmacologic treatments for this condition. As a result, many women try alternative therapies to treat nausea and vomiting. An informal review of a number of pregnancy self-help books, magazines, and lay alternative therapy publications indicates that therapies range from vitamins to herbals to homeopathic drugs to acupressure or acupuncture.

This review summarizes research on a variety of complementary and alternative remedies for the treatment of nausea and vomiting of pregnancy. [Only acupressure is given here.] Published studies are too few or have used an assortment of exposures and outcome measures, making a statistical meta-analysis difficult, if not inappropriate.

Methodology

A literature search was conducted in 1996, as part of a broad strategy to identify relevant publications relating to the use of complementary or alternative medicine in women's health. References for this review were culled from the overall search results. Databases searched included, in addition to MEDLINE, Acubase (acupuncture), Agricola (National Agricultural Library, USA), Biosis (USA), CATS/AMED (Current Awareness Topics/Alternative and Allied Medicine Database, UK), Cancerline, Cinahl, CISCOM (Centralised Information Service for Complementary Medicine, UK), Embase (coverage of pharmacologic and biomedical research, the Netherlands), and the General Science, Psych Abstracts, Psych Info, and Social Science Citations Indexes.

To identify any additional references not found in the automated search, citations and bibliographies of all retrieved papers were reviewed as well. The search was not limited to English language papers; however, only English language papers or abstracts were read.

Papers were included in this review if they discussed 1) nausea and/or vomiting of early pregnancy as the treatment condition and 2) an intervention or therapy other than Western biomedical pharmacology or standard advice about diet or lifestyle changes. All research studies were reviewed; studies were classified as clinical trials (comparing clinical outcomes of women given the alternative intervention with a control group), observational studies, or case reports or series. Decisions were made *a priori* to exclude papers that represented pooled data from other studies, if the original studies were published in English and retrieved in the literature search.

General Considerations in Evaluating Studies

Issues to consider when evaluating studies of alternative therapies include 1) the highly individualized nature of treatment in many alternative frameworks, 2) the difficulty of creating appropriate placebos for some interventions, and 3) the reliability and validity of exposure and outcome measures. In addition, because nausea and vomiting of pregnancy is a self-limited condition, some women will get better during the period of therapy with or without the intervention. Thus, the effects of time and gestational age must be considered when studying interventions. Many women try multiple remedies, and it often is difficult to distinguish their effects; studies should demonstrate some effort to control for other therapies. In randomized trials, distribution of other interventions might be assumed to be equal across groups, but in other studies, their effects should be controlled. Finally, consideration should be given to the potential for adverse effects on fetal development, given that most of these interventions are used during a critical period of embryogenesis. Additional remedy-specific methodologic considerations will be discussed in the individual sections below.

Acupressure and Related Modalities

There have been several clinical trials³⁻⁹ of acupressure and related modalities in the treatment of nausea and vomiting of pregnancy. All involved stimulation of or pressure on an acupuncture point known as pericardium 6 (P6) or the Neiguan point, on the volar surface of the forearm approximately three fingerbreadths above the wrist. A review¹⁰ of studies of this intervention has demonstrated its beneficial effect in the treatment of postoperative emesis, chemotherapy-associated emesis, and motion sickness.

One notes that it probably is impossible to perform a true double-blind trial compared with no intervention. Because of the nature of acupressure or acupuncture, subjects will be aware that the intervention is being applied, and any reduction in symptoms could be due to the placebo effect. Sham acupressure (applying pressure at a point other than the one thought to be important) has been used in some trials. However, the correct point can be identified easily in any number of self-help books. In addition, even sham acupressure may elicit a therapeutic response.¹¹ Finally, these studies³⁻⁹ represent a variety of intervention and placebo approaches, differing treatment lengths, varying outcomes measures, and an assortment of outcome categories. Therefore, statistical meta-analysis was deemed inappropriate.

Table 2. Randomized Clinical Trials of Acupressure-

Study	Number of subjects	Intervention	Results
Dundee <i>et al</i> , 1988 ³	350	Manual acupressure over the P6 or a dummy point, compared with control group with no intervention. Intervention of 4 days' duration.	"Severe" or "troublesome" morning sickness noted in 24% using P6 acupressure, 37% using dummy point acupressure, and 56% using no intervention ($p < .005$).
Hyde, 1989 ⁴	16	Acupressure wristbands vs. no intervention. 5 days intervention, followed by crossover to other group for 5 days.	Relief of morning sickness in 75% using wristbands ($P < .025$); reduction of anxiety, depression, and behavioral dysfunction, as measured by standard psychometric tools ($P < .05$).
DeAloysio <i>et al</i> , 1992 ⁵	60	Unilateral (right or left wrist) or bilateral acupressure wristbands* vs. placebo wristbands (no pressure exerted on P6 point). Each version of intervention given for 3 days in a crossover design.	Reduction or elimination of symptoms in 65-69% while using acupressure vs. 29-31% while using placebo ($P < .05$).
Bayreuther <i>et al</i> , 1994 ⁶	16	Acupressure wristbands* vs. placebo wristbands (applied over a dummy point). Seven-day intervention followed by crossover to the alternative intervention for 7 days.	Nausea score (using a visual acuity scale) was lower in the group using acupressure compared with the placebo ($P = .019$). No effect on vomiting.
Belluomini <i>et al</i> , 1994 ⁷	60	Manual acupressure on the P6 point vs. pressure on a dummy point for 3 days.	Nausea decreased significantly in treatment group ($P = .0021$). No difference in severity or frequency of vomiting.
O'Brien <i>et al</i> , 1996 ⁸	161	Acupressure wristbands* vs. wristbands over a dummy point vs. a control group with no intervention. Seven-day intervention.	No differences across groups in nausea or vomiting.
Evans <i>et al</i> , 1993 ⁹	23	Continuous electric current stimulation at the P6 point vs. no stimulation. Forty-eight-hour intervention followed by crossover to alternative intervention.	Improvement in symptoms of nausea and vomiting in 87% of experimental group vs. 43% of controls ($p < .05$).

P6 = pericardium 6.

* Sea Bands (Sea Band International, Greensboro, NC).

Other studies were identified,¹²⁻¹⁴ but they did not meet the criteria for randomized controlled clinical trials. Those reporting benefits were essentially single-group observational studies¹²⁻¹⁴ with no controls and examined both acupressure and acupuncture. A randomized trial of acupuncture for the treatment of nausea and vomiting in early pregnancy is under way in Australia (personal communication, Caroline Smith, 1997).

Discussion

The best-studied remedy appears to be acupressure over the Neiguan point. A systematic review of this literature,³⁰ which excluded studies of poor methodologic quality and those whose data could not be combined, found the effects of acupressure to be comparable to those of anti-emetic medications but cautioned that the evidence is equivocal. Indeed, clinical trials on the use of acupressure or related modalities have not produced consistent findings, although before the publication of the study by O'Brien and colleagues,⁸ results of published trials^{3-7,9} were largely positive. It is clear that acupressure of the Neiguan point benefits many women. One could infer that in studies that did not provide an intervention to the control group or arm of the trial, positive findings might be due only to the placebo effect, because of the difficulty of creating a true double-blind trial. However, there may be value in mobilizing such a mind-body interaction if the intervention is simple and inexpensive, if it results in reduction of symptoms, and if it is not associated with any risk. Properly applied pressure would seem to produce little risk of adverse effect. There are acupressure and acupuncture points that are contraindicated in pregnancy because of their potential to produce uterine contractions, but these are not near the Neiguan point. Such an intervention also would be inexpensive to implement and readily available without a medical visit. No evaluable trials of the related modality, acupuncture, were found. The latter intervention would be more costly, in terms of time and travel for treatment visits and provider fees.

In summary, women seeking alternative, nonpharmacologic therapies for nausea and vomiting of early pregnancy have few evidence-based guidelines to assist them. They may be advised to try acupressure over the Neiguan point; this can be achieved through the use of commercially available wristbands or by applying manual pressure to the appropriate spot on the volar surface of the wrist. [The paper reported studies which suggested that ginger and vitamin B₆ may also be efficacious.] Women should be cautioned that apart from these few studies, there is little evidence to support or refute the benefits or risks of other remedies.

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References omitted.

QUESTIONS ABOUT THIS REPORT:

- (a) What kind of study is this?
- (b) Why does the author think that statistical meta-analysis would be inappropriate? Do you agree?
- (c) What problems are caused by the results being reported in terms of significance tests?
- (d) What are the author's conclusions concerning acupressure and are they justified by the data?