Acupuncture-point stimulation for chemotherapy-induced nausea or vomiting (Review)

Ezzo JM, Richardson MA, Vickers A, Allen C, Dibble SL, Issell BF, Lao L, Pearl M, Ramirez G, Roscoe JA, Shen J, Shivnan JC, Streitberger K, Treish I, Zhang G

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ABSTRACT

Background
There have been recent advances in chemotherapy-induced nausea and vomiting using 5-HT_3 inhibitors and dexamethasone. However, many still experience these symptoms, and expert panels encourage additional methods to reduce these symptoms.

Objectives
The objective was to assess the effectiveness of acupuncture-point stimulation on acute and delayed chemotherapy-induced nausea and vomiting in cancer patients.

Search strategy
We searched MEDLINE, EMBASE, PsycLIT, MANTIS, Science Citation Index, CCTR (Cochrane Controlled Trials Registry), Cochrane Complementary Medicine Field Trials Register, Cochrane Pain, Palliative Care and Supportive Care Specialized Register, Cochrane Cancer Specialized Register, and conference abstracts.

Selection criteria
Randomized trials of acupuncture-point stimulation by any method (needles, electrical stimulation, magnets, or acupressure) and assessing chemotherapy-induced nausea or vomiting, or both.

Data collection and analysis
Data were provided by investigators of the original trials and pooled using a fixed effect model. Relative risks were calculated on dichotomous data. Standardized mean differences were calculated for nausea severity. Weighted mean differences were calculated for number of emetic episodes.

Main results
Eleven trials (N = 1247) were pooled. Overall, acupuncture-point stimulation of all methods combined reduced the incidence of acute vomiting (RR = 0.82; 95% confidence interval 0.69 to 0.99; P = 0.04), but not acute or delayed nausea severity compared to control. By modality, stimulation with needles reduced proportion of acute vomiting (RR = 0.74; 95% confidence interval 0.58 to 0.94; P = 0.01), but not acute nausea severity. Electroacupuncture reduced the proportion of acute vomiting (RR = 0.76; 95% confidence interval 0.60 to 0.97; P = 0.02), but manual acupuncture did not; delayed symptoms for acupuncture were not reported. Acupressure reduced mean acute nausea severity (SMD = -0.19; 95% confidence interval -0.37 to -0.01; P = 0.04) but not acute vomiting or delayed symptoms. Noninvasive electrostimulation showed no benefit for any outcome. All trials used concomitant pharmacologic antiemetics, and all, except electroacupuncture trials, used state-of-the-art antiemetics.

Authors' conclusions
This review complements data on post-operative nausea and vomiting suggesting a biologic effect of acupuncture-point stimulation. Electroacupuncture has demonstrated benefit for chemotherapy-induced acute vomiting, but studies combining electroacupuncture

with state-of-the-art antiemetics and in patients with refractory symptoms are needed to determine clinical relevance. Self-administered acupressure appears to have a protective effect for acute nausea and can readily be taught to patients though studies did not involve placebo control. Noninvasive electrostimulation appears unlikely to have a clinically relevant impact when patients are given state-of-the-art pharmacologic antiemetic therapy.

PLAIN LANGUAGE SUMMARY

Electroacupuncture is effective for first day vomiting after chemotherapy, but trials considering modern antivomiting drugs are needed.

This review looked at whether stimulating acupuncture points could reduce nausea and vomiting caused by chemotherapy. Acupuncture points can be stimulated by acupuncture applied with electricity (electroacupuncture), acupuncture without electricity (manual acupuncture), acupressure (pressing on the points usually with fingertip), or electrical stimulation on the skin surface such as wristwatch-like devices. Electroacupuncture reduced first-day vomiting, but manual acupuncture did not. Acupressure reduced first-day nausea, but was not effective on later days. Acupressure showed no benefit for vomiting. Electrical stimulation on the skin showed no benefit. All trials also gave antivomiting drugs, but the drugs used in the electroacupuncture trials were not the most modern drugs, so it is not known if electroacupuncture adds anything to modern drugs. Trials of electroacupuncture with modern drugs are needed.

BACKGROUND

Progress in the prevention and treatment of chemotherapy-induced nausea and vomiting has been achieved with the advent of 5-HT_3 receptor antagonists such as dolasetron, granisetron, and ondansetron (Campora 1994; Hesketh 1999; Oettle 2001; Stewart 1999) and dexamethasone (Ioannidis 2000). However, many patients still experience these symptoms (Gralla 1999), and expert panels (Gralla 1999; Hesketh 1998) emphasize the need for additional ways to reduce symptoms. Chemotherapy-induced nausea and vomiting can impair a patient's quality of life (Osoba 1997), cause emotional distress (Love 1989), and aggravate cancer-related symptoms of cachexia, lethargy and weakness (Griffin 1996; Roscoe 2000).

The need for additional relief has led to interest an in nonpharmacological adjuncts to drugs. Acupuncture, one nonpharmacological adjunctive treatment, has gained increasing popularity since the National Institutes of Health 1997 Consensus Statement stating that "promising results have emerged showing efficacy of acupuncture in adult postoperative and chemotherapy nausea and vomiting" (Anonymous 1998a). At that time, however, only two small randomized controlled trials (RCTs) had been published on acupuncture for chemotherapy-induced nausea and vomiting (Dundee 1987; Dundee 1988), and both predated the widespread use of 5-HT_3 antagonists.

The acupuncture point, Pericardium 6 (P6), or Neiguan, is the most commonly used acupuncture point to control nausea and vomiting (Dundee 1988). P6 is located on the anterior surface of the wrist between the tendons of the flexor carpi radialis and the palmaris longus. It is usually measured as three patient finger breadths from the flexor crease (Pearl 1999). Two systematic reviews (Lee 2004; Vickers 1996) suggest that P6 stimulation reduces nausea and vomiting related to morning sickness and postoperative distress; another review (Jewell 2002) reported unclear benefit for morning sickness.

P6 can be stimulated by various methods. The most well-known technique is manual stimulation by insertion and manual rotation of a very fine needle (manual acupuncture). Electrical current can be passed through the inserted needle (electroacupuncture). Electrical stimulation can also be applied via electrodes on the skin surface or by a ReliefBand, a wristwatch-like device (noninvasive electrostimulation). Pressure can be applied either by pressing on the point with the fingers or by wearing an elastic wristband with an embedded stud (acupressure).

Initial clinical trials show that the protective effects of P6 stimulation by acupuncture on chemotherapy-related illness last about eight hours (Dundee 1988b). The inconvenience of applying acupuncture at regular intervals throughout chemotherapy has raised interest in the more convenient stimulation methods such as noninvasive electro stimulation or acupressure. Comparisons of various P6 stimulation modalities suggest that treatment benefit correlates with intensity of stimulation, with acupuncture having the greatest effect and manual stimulation the least (Dundee 1991a; McMillan 1991). However, given the popularity of self-administered techniques, we planned to evaluate the effectiveness of all modalities. Moreover, as some trials were conducted before the advent of 5-HT_3 antagonists, we planned to evaluate the possible impact of type of concurrent pharmacologic antiemetics on effectiveness.

OBJECTIVES

To conduct a systematic review and meta-analysis on acupuncture-

point stimulation for chemotherapy-induced nausea and vomiting in cancer patients. Secondary objectives were to assess the individual effectiveness of each modality (i.e. manual acupuncture, electroacupuncture, noninvasive electrostimulation, acupressure) and to conduct sensitivity analyses within each modality by examining:
(a) sham-controlled trials separately from non-sham trials;
(b) adequately concealed trials from unclear or inadequately concealed trials;
(c) trials that gave concomitant state-of-the-art antiemetic medications from those that did not;
(d) a final objective was to assess the safety of acupuncture-point stimulation by assessing reports of adverse events in included trials.

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

Trials explicitly stated as randomized.

Types of participants

Cancer patients receiving chemotherapy.

Types of intervention

Stimulation of acupuncture points by any method (i.e. electroacupuncture, manual acupuncture, acupressure, surface electrodes, or magnets) with or without antiemetic medications.

Types of outcome measures

Acute or delayed chemotherapy-induced nausea or vomiting, or both.

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: Cochrane Pain, Palliative and Supportive Care Group methods used in reviews.

We searched MEDLINE, EMBASE, PsycLIT, MANTIS, Science Citation Index, CCTR (Cochrane Controlled Trials Registry), Cochrane Complementary Medicine Field Trials Register, Cochrane Pain, Palliative Care and Supportive Care Specialized Register, Cochrane Cancer Specialized Register, and conference abstracts. Search strategies for databases other than MEDLINE appear in Table 01.

MEDLINE(R) Search Strategy (1966 - June 2005)
1. ACUPUNCTURE/ (288)
2. exp Acupuncture Therapy/ (8851)
3. Transcutaneous Electric Nerve Stimulation/ (2119)
4. (acupuncture$ or acupoint$ or meridian$).mp. [mp=ti, ot, ab, nm, hw] (11414)
5. alternative medicine$.mp. [mp=ti, ot, ab, nm, hw] (2489)
6. (electroacupuncture or electro-acupuncture).mp. [mp=ti, ot, ab, nm, hw] (1625)
7. moxibustion.mp. [mp=ti, ot, ab, nm, hw] (434)
8. Medicine, Chinese Traditional/ (5157)
9. (acupressure or "traditional chinese medicine" or "relief band$" or bioband$).mp. [mp=ti, ot, ab, nm, hw] (2332)
10. ("transcutaneous electric$ nerve stimulation" or "transdermal electric$ nerve stimulation").mp. [mp=ti, ot, ab, nm, hw] (2368)
11. tens.ti. (285)
12. tens.ab. (2897)
13. or/1-12 (24104)
14. NAUSEA/ (8918)
15. VOMITING/ (13244)
16. (nausea or vomiting).mp. [mp=ti, ot, ab, nm, hw] (44305)
17. (emesis or antiemetic$ or anti-emetic$).mp. [mp=ti, ot, ab, nm, hw] (8357)
18. ANTIEMETICS/ (4438)
19. or/14-18 (47188)
20. exp Antineoplastic Agents/ (570443)
21. (antineoplastic$ or cytotoxic$).mp. [mp=ti, ot, ab, nm, hw] (300063)
22. chemo$.mp. (257640)
23. exp NEOPLASMS/ (1589749)
24. (neoplasm$ or cancer$ or tumour$ or tumor$ or carcinoma$ or "marrow transplant$").mp. [mp=ti, ot, ab, nm, hw] (1639857)
25. CISPLATIN/ (25752)
26. cisplatin.mp. (32511)
27. or/20-26 (2278324)
28. 13 and 19 and 27 (84)
29. randomized controlled trial.pt. (201327)
30. controlled clinical trial.pt. (68374)
31. randomized controlled trials.sh. (37275)
32. random allocation.sh. (53114)
33. double blind method.sh. (81591)
34. single blind method.sh. (8947)
35. or/29-34 (342253)
36. (ANIMALS not HUMAN).sh. (3743484)
37. 35 not 36 (315367)
38. clinical trial.pt. (405946)
39. exp clinical trials/ (165173)
40. (clin$ adj25 trial$).ti,ab. (113500)
41. ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).ti,ab. (82419)
42. placebos.sh. (23692)
43. placebo$.ti,ab. (90640)
44. random$.ti,ab. (321363)
45. research design.sh. (40605)
46. or/38-45 (741293)
47. 46 not 36 (654500)
48. 47 not 37 (348970)
49. 37 or 47 (664337)
50. 28 and 47 (39)

51. from 50 keep 1-39 (39)

METHODS OF THE REVIEW

Selection of studies
Two review authors (AV, JE) reviewed all potentially relevant manuscripts to determine which trials met inclusion criteria.

Data extraction
Two review authors (JE, MR) extracted information on study populations and procedures; two review authors (AV, JE) extracted data on methodological quality (Table 02), and two review authors (MR, BI) extracted chemotherapy and antiemetic-related information (Table 03). Original patient data was obtained from the authors of the studies and reanalyzed when possible (AV). The summary data from each trial were then meta-analyzed using a fixed effect model.

Assessment of antiemetic regimen
Antiemetic regimens were evaluated according to ASCO (American Society of Clinical Oncology) recommendations (Gralla 1999). For acute symptoms in patients receiving chemotherapy with a high risk of emesis, ASCO recommendations include 5-HT_3 plus corticosteroid before chemotherapy. For delayed symptoms in patients receiving cisplatin, the guidelines suggest a corticosteroid plus either metoclopramide or a 5-HT_3 antagonist. For patients receiving noncisplatin, high-risk-of-emesis chemotherapy, the guidelines include a prophylactic corticosteroid alone or with either metoclopramide or a 5-HT_3 antagonist (Gralla 1999).

Two review authors (BI, JE) scored the antiemetic regimen of each study. If consistent with ASCO guidelines, the study scored 'consistent'. If only partly consistent (i.e. 5-HT_3 without corticosteroid for highly emetogenic chemotherapy), the study scored 'partially consistent'. If the study did not satisfy any condition of current recommendations, the study scored 'not consistent' (Table 03).

Assessment of nausea and vomiting outcomes
Outcomes were based on the ASCO expert panel (Anonymous 1996; Gralla 1999) and the Multinational Association of Supportive Care in Cancer (MASCC) Consensus Conference (Hesketh 1998) guidelines. Acute vomiting or nausea was defined as an event occurring within the first 24 hours post-chemotherapy. Delayed vomiting or nausea was defined as an event occurring after the first 24 hours and up to five to eight days post-chemotherapy, as defined by the authors of each study. Delayed symptoms were not calculated for any study that a) gave acupuncture-point stimulation only on day one or b) provided exclusively multiday chemotherapy, which made it impossible to distinguish delayed and acute symptoms after day one. In crossover studies, we extracted data on the first cycle only, when possible, to avoid carryover effects.

Acute outcomes included:
1) incidence of acute vomiting, and
2) mean nausea severity.

Delayed outcomes included:
1) mean number of delayed vomiting episodes, and
2) mean delayed nausea severity.

Assessment of the acupuncture-point stimulation procedure
The optimal acupuncture-point stimulation procedure is not known; therefore, we relied on acupuncturists' clinical experience to assess whether the acupuncture-point stimulation procedure was reasonable and adequate. Two acupuncturists (GZ, LL) were given acupuncture-point stimulation descriptions for each trial and blinded to study results. They rated each procedure (i.e. adequate, not adequate, or not enough information).

Assessment of methodological quality of included studies
The assessment of trial quality consisted of five quality items:
(1) was randomization adequate?
(2) was a sham control used?
(3) was the outcomes assessor blinded?
(4) were dropouts and withdrawals accounted for?
(5) was allocation concealed?

When data were missing from the manuscripts, the authors were contacted and asked to provide the methodological details. Studies were rated on each item as 'yes' if the item was present as either reported in the paper or by personal communication with the author; 'no' if the item was reported in the paper or by the author as not present; or 'not reported' if the item was not reported in the paper and the author could not be located.

Item 1. 'Randomization adequate?' scored 'yes' if the randomization sequence was generated by a table of random numbers, a computer, or drawing numbers from a hat, 'no' if alternate assignment had been used, and 'not reported' if details were not provided in the paper, and the author could not be contacted.

Item 2. 'Sham control used?' score 'yes' if there was a control group established to mimic the acupoint-stimulation treatment. This could include a placebo stimulation of the real point, such as with a noninvasive needle or a sham surface electrode device, or it could include the stimulation of wrong point(s) by needles, acupressure, or surface electrodes. This item scored 'no' if the control group received only antiemetic medications but not a treatment mimicking the acupuncture-point stimulation.

Item 3. 'Blinded outcomes assessor?' scored 'yes' if the paper or author stated that the outcomes assessor was blinded or did not know to which group patients had been allocated; scored 'no' if paper or author stated there had not been blinded outcomes assessor; and scored 'not reported' if a blinded outcomes assessor was not mentioned in the paper, and the author could not be contacted.

Item 4. 'Dropouts and withdrawals accounted for?' scored 'yes' if both the reason and number dropping/withdrawing was presented; scored 'no' if the number randomized did not match the number analyzed, but there were no details provided about dropouts and withdrawals.

Item 5. 'Concealed allocation?' scored 'yes' if the trial used opaque envelopes sequentially numbered or if the allocator had to call a central number to receive the next allocation sequence once a patient had been enrolled in the trial. This item scored 'no' if a master list was generated ahead of time and held by the person allocating patients or if envelopes were used, but were not sequentially numbered. This is item scored 'not reported' if details were not provided in the paper, and the author could not be contacted.

Analysis

Relative risks (RRs) were calculated for dichotomous data based on the number randomized (intention-to-treat analysis) with a RR of one representing 'no effect' and less than one favoring acupuncture-point stimulation. Mantel-Haenszel methods were used for combining trials. Continuous data were analyzed on completers only, and no missing scores were imputed. To allow pooling across different nausea scales, standardized mean differences (SMDs) were calculated on nausea outcomes by dividing the differences between groups by the pooled standard deviation. Weighted mean differences (WMDs) were calculated for number of emetic episodes. For SMDs and WMDs, a point estimate of zero reflected 'no effect,' and less than zero favored acupuncture-point stimulation. Continuous outcome data were pooled using inverse variance methods.

Subgroup Analysis

Subgroup analysis was performed for each type of acupuncture-point stimulation. All acupuncture trials (electroacupuncture and manual acupuncture) were combined and then further analyzed by type of acupuncture (electroacupuncture or manual acupuncture). All acupressure trials were assessed together whether the acupressure stimulation was performed by the fingers or an acupressure band. All surface electrostimulation trials were assessed together, and these included those using a wristwatch-like device and those using surface electrodes attached to a TENS unit.

Sensitivity Analysis

Sensitivity analysis was conducted overall and within each subgroup for the following three items:

1) adequacy of allocation concealment versus inadequate or unclear allocation concealment,

2) sham vs nonsham control groups, and

3) state-of-the-art antiemetics versus non state-of-the-art antiemetics.

DESCRIPTION OF STUDIES

Initially, 14 trials were deemed eligible. One (Liu 1994) was excluded from pooling due to concerns by both reviewers that there was a high probability of bias. Two other trials (Lo 1998; Price 1991) were excluded because necessary data were not obtainable. Thus, the pooled analyses included 11 trials (N = 1247) (Dibble 2000; Dundee 1987; Dundee 1988; McMillan 1991; Noga 2002; Pearl 1999; Roscoe 2002; Roscoe 2003; Shen 2000; Streitberger 2003; Treish 2003). Data were provided by authors of eight of those studies (Dibble 2000; Noga 2002; Pearl 1999; Roscoe 2002; Roscoe 2003; Shen 2000; Streitberger 2003; Treish 2003).

Although there were no language restrictions, all included trials were published in English. Multiple publications of the same study were examined, but each study population was counted only once to avoid duplicates bias (Tramer 1997). All included studies were rated as having adequate acupuncture-point stimulation techniques. Adverse events were minimal and transient (Characteristics of Included Studies Table).

Twenty-two studies were excluded and data for those excluded can be found in the 'Characteristics of excluded studies' table (Aglietti 1990; Brown 1992; Dundee 1986; Dundee 1987a; Dundee 1987b; Dundee 1988a; Dundee 1990a; Dundee 1990b; Dundee 1990c; Dundee 1990d; Dundee 1990e; Dundee 1990f; Dundee 1991; King 1997; Liu 1994; Lo 1998; Pan 2000; Prance 1988; Price 1991; Saller 1986; Stannard 1989; White 1997).

METHODOLOGICAL QUALITY

We were able to obtain methodological quality details that were missing for eight of the 11 trials representing 1201 of the 1247 patients (Dibble 2000; Noga 2002; Pearl 1999; Roscoe 2002; Roscoe 2003; Shen 2000; Streitberger 2003; Treish 2003). Randomization was adequate in all trials for which details were available. A sham control was used in seven out of 11 trials and not in four out of the 11 trials. The outcomes assessor was reported to be blinded in seven of 11 trials and either unreported or not blinded in four out of the 11 trials. Reporting of dropouts or withdrawals was found to be adequate in all 11 trials. Of the 11 included trials, three scored 'not reported' for allocation concealment details; five were concealed, and three were unconcealed (Table 02).

A sensitivity analysis of allocation concealment did not show interaction effects (data not shown). There were no significant associations with outcomes (Table 04) with one exception: For electroacupuncture, uncertain or unconcealed trials were associated with a significant result favoring electroacupuncture for acute vomiting (P = 0.03), and concealed allocation was not.

Sensitivity analysis of sham-versus non-sham-controlled trials showed three patterns, but no interaction effects. First, there was

no significant association with outcomes for the majority of trials (Table 04). Secondly, all combined acupuncture trials (electroacupuncture plus manual acupuncture) or electroacupuncture trials alone showed significant or marginally significant results for acute vomiting regardless of whether a sham or non-sham control had been used. Third, the outcome of acute nausea was significantly or marginally significantly associated with findings favoring the treatment group for non-sham trials but not sham trials for all combined treatments and for electrostimulation. Also for acute nausea, non-sham acupressure trials were significantly associated with benefit, and there were no sham acupressure trials for acute nausea with which to make a comparison.

A sensitivity analysis according to antiemetic rating (consistent with ASCO guidelines or not) showed no interaction effects. However, in trials not using antiemetics consistent with ASCO guidelines, results were significant favoring the treatment group for acute vomiting whereas trials with ASCO-consistent or partially consistent antiemetics were not significantly associated with benefit for acute vomiting. However, antiemetic rating completely covaried with modality: all electroacupuncture trials gave antiemetics not ASCO consistent, and all other modalities (manual acupuncture, acupressure, electrostimulation) gave antiemetics that were either partially or totally ASCO consistent (Table 04).

RESULTS

Overall results (all modalities combined)

Acute vomiting

In the pooled results of the nine trials (N = 1214) (Dundee 1987; Dundee 1988; McMillan 1991; Noga 2002; Pearl 1999; Roscoe 2002; Roscoe 2003; Shen 2000; Streitberger 2003; Treish 2003) that evaluated acute vomiting, the incidence of acute vomiting in the acupuncture-point stimulation group was 22% (155/714) compared to 31% (154/500) among controls; (RR = 0.82; 95% confidence interval 0.69 to 0.99; P = 0.04) favoring acupuncture-point stimulation. The corresponding number needed to treat (NNT) was 11 (95% confidence interval seven to 25).

Acute nausea

The SMD (and 95% CI) of the seven trials (N = 896) (Dibble 2000; McMillan 1991; Pearl 1999; Roscoe 2002; Roscoe 2003; Streitberger 2003; Treish 2003) assessing acute nausea severity showed a trend towards significance favoring acupuncture-point stimulation (SMD = -0.11; 95% confidence interval -0.25 to 0.02; P = 0.10). Findings were dissimilar in sham-controlled trials (P = 0.78) versus nonsham trials (P = 0.08) (Table 04) for mean nausea severity though the test for interaction was nonsignificant (P = 0.5).

Delayed vomiting

Three trials (N = 757) (Pearl 1999; Roscoe 2003; Treish 2003) evaluated delayed vomiting episodes. All used ASCO-consistent antiemetics and noninvasive acupuncture-point stimulation, not acupuncture. There was no evidence of benefit for noninvasive acupuncture-point stimulation (WMD = 0.02; 95% confidence interval -0.13 to 0.17; P = 0.80) on mean number of delayed emetic episodes.

Delayed nausea

The five trials (N = 821) (Dibble 2000; Pearl 1999; Roscoe 2002; Roscoe 2003; Treish 2003) assessing delayed nausea all used ASCO-consistent or partially consistent antiemetics and noninvasive acupuncture-point stimulation, not acupuncture. There was no evidence of benefit for delayed mean nausea severity (SMD = 0.02; 95% confidence interval -0.16 to 0.13; P = 0.80).

Acupuncture: manual and electroacupuncture

Acute vomiting

The incidence of acute vomiting in the four pooled acupuncture trials (Dundee 1987; Dundee 1988; Shen 2000; Streitberger 2003) was 37% (35/95) in the acupuncture group and 60% (71/119) in controls. This was a significant reduction in the incidence of acute vomiting in the acupuncture group (RR = 0.74; 95% confidence interval 0.58 to 0.94; P = 0.01). NNT = 4.4 (95% confidence interval three to 11).

Findings were similar for incidence of acute vomiting in sham-controlled trials (RR = 0.74; 95% confidence interval 0.56 to 0.98; P = 0.04) (Table 04) versus nonsham trials (RR = 0.77; 95% confidence interval 0.59 to 1.00; P = 0.05). Three trials (Dundee 1988; Shen 2000; Streitberger 2003) used a sham-controlled arm, and the two largest trials (Shen 2000; Streitberger 2003) used a post treatment interview confirming that patients did not know to which treatment arm they had been allocated.

Manual acupuncture

One trial, the only manual acupuncture trial (Streitberger 2003), used partially ASCO-consistent antiemetics consisting of 5-HT_3 without steroids. The incidence of acute vomiting was 4/41 (10%) and 7/39 (18%) for treatment and controls, respectively, and this was not significant.

Electroacupuncture

The remaining three trials, all electroacupuncture trials, (Dundee 1987; Dundee 1988; Shen 2000) also used antiemetics, but none were ASCO consistent. The proportion of patients experiencing acute vomiting was lower for electroacupuncture 31/54 (57%) than controls 64/80 (80%) (RR = 0.76; 95% confidence interval 0.60 to 0.97; P = 0.02).

Acute nausea

Electroacupuncture

Of the three electroacupuncture trials, none measured acute nausea.

Manual acupuncture

The severity of acute nausea was measured only in the one manual acupuncture trial (Streitberger 2003). This showed no statistically

significant reduction (SMD = 0.02; 95% confidence interval -0.42 to 0.40; P = 0.9) in severity of acute nausea.

Delayed nausea and vomiting

No acupuncture trial had usable data on delayed nausea and vomiting. Although one trial (Shen 2000) did measure vomiting beyond the first day, that trial also administered chemotherapy on multiple days. Thus,it was impossible to discern whether vomiting beyond day 1 was acute or delayed. Therefore, this trial was classified as not having usable data for delayed vomiting.

Acupressure

Acute vomiting

All acupressure trials (N = 629) (Dibble 2000; Noga 2002; Roscoe 2003) used ASCO-consistent antiemetics. The proportion of patients experiencing acute vomiting were 17% (52/311) versus 20% (62/309) in acupressure and controls, respectively (RR = 0.83; 95% confidence interval 0.60 to 1.16; P = 0.3).

Acute nausea

Two nonsham acupressure trials (Dibble 2000; Roscoe 2003) had usable data on mean severity of acute nausea. The third trial (Noga 2002) had data on nausea duration and frequency, but not severity. Acupressure showed a protective effect for mean acute nausea severity (SMD = -0.19; 95% confidence interval -0.37 to -0.01; P = 0.04).

Delayed nausea and vomiting

Acupressure showed no protective effect for either delayed outcomes.

Noninvasive Electrostimulation

Acute vomiting

Four trials evaluated acute vomiting using noninvasive electrostimulation (Pearl 1999; Roscoe 2002; Roscoe 2003; Treish 2003) and all used ASCO-consistent or partially consistent antiemetics. The incidence of acute vomiting was 68/308 (22%) in the noninvasive electrostimulation group and 78/321 (24%) in controls. There was no protective effect by noninvasive electrostimulation.

Acute nausea

There was no protective effect observed among the five trials (McMillan 1991; Pearl 1999; Roscoe 2002; Roscoe 2003; Treish 2003) measuring mean acute nausea severity (SMD = -0.07; 95% confidence interval -0.23 to 0.10; P = 0.4). However, findings differed substantially for sham-controlled trials (SMD = -0.08;95% confidence interval -0.49 to 0.34; P = 0.72) versus nonsham trials (SMD = -0.13; 95% confidence interval -0.28 to 0.03; P = 0.10) for acute nausea (Table 04).

Delayed nausea and vomiting

There were no protective effects noted for either delayed vomiting or delayed nausea.

Given that individual noninvasive electrostimulation trials (McMillan 1991; Pearl 1999; Treish 2003) had reported beneficial effects, we explored possible explanations for the difference between their findings and ours. One paper (Pearl 1999) reported that benefits for delayed symptoms were evident on days two, three, and four, but not on day five after chemotherapy. However, we found no protective effects analyzing outcomes for each delayed day separately. The literature suggests acupuncture-point stimulation before chemotherapy is more effective than afterwards (McMillan 1991). However, we found no difference when prechemotherapy treatment was given (McMillan 1991; Roscoe 2002; Roscoe 2003; Treish 2003) versus when treatment was given after chemotherapy (Pearl 1999). We also found no difference between trials using Reliefbands (Pearl 1999; Roscoe 2002; Roscoe 2003; Treish 2003) versus other devices (McMillan 1991). One trial reported a gender effect with a significantly higher proportion of males than females reporting benefit (Roscoe 2003); however, there were too few males in the other trials to further examine this finding.

DISCUSSION

The pooled results of 11 RCTs evaluating acupuncture-point stimulation plus antiemetics for chemotherapy-induced nausea and vomiting showed a significant reduction in the proportion of patients experiencing acute vomiting. This is consistent with an early systematic review (Vickers 1996) and a subsequent meta-analysis (Lee 2004) both of which concluded that acupuncture-point stimulation reduces post-operative nausea and vomiting.

Acupuncture

We have found noteworthy differences according to modality. Stimulation using needles (manual acupuncture and electroacupuncture trials combined) reduced the proportion of patients experiencing acute vomiting, but did not reduce acute nausea severity. This finding is consistent with human studies showing that among P6 stimulation methods, acupuncture is the most effective method for treating chemotherapy-induced emesis (Dundee 1991a; McMillan 1991) and an animal study demonstrating antiemetic effects of acupuncture during chemotherapy (Lao 2003). No manual acupuncture or electroacupuncture trial in our study had usable data on delayed symptoms.

While our overall results showing the protective effects of needling stimulation for acute vomiting offer a 'proof of principle' of acupuncture's antiemetic effects, the implications for clinical practice are unclear. The electroacupuncture trials, which showed protective effects for both acute vomiting outcomes, did not give antiemetics that would be considered state-of-the-art by today's standards. By contrast, the one manual acupuncture trial that gave partially ASCO-consistent antiemetics showed no significant benefit for either acute vomiting outcome.

There are several possible explanations for these differences in the electroacupuncture versus manual acupuncture results. One explanation is that acupuncture simply might not offer anything

beyond what current drug regimens can offer due to a shared pathway of action. However, no direct evidence shows that 5-HT_3 antiemetics interfere with acupuncture effects.

A second explanation may be related to statistical power. For example, let us assume that acupuncture is associated with a relative risk of vomiting of 0.75, and the incidence of vomiting was 75% and 25% for patients being treated with suboptimal and state-of-the-art antiemetics, respectively. A trial of 200 patients would have a power of approximately 80% to detect the hypothesized treatment effect in patients receiving suboptimal antiemetics but only 15% in patients receiving state-of-the-art therapy. Indeed, the manual acupuncture (Streitberger 2003) control group event rate (18%) was very different than that in the largest electroacupuncture trial (82%) (Shen 2000).

A third explanation for different event rates in the two trials may be due to the proportion patients entered into the trial who were 'at risk' for vomiting based on a history of chemotherapy-induced vomiting. The history of vomiting with chemotherapy was 46% in the manual acupuncture control arm (Streitberger 2003) compared to 84% for one control arm and 62% in the other control arm of the largest electroacupuncture trial (Shen 2000).

Furthermore, there were notable dissimilarities in the acupuncture "dose" in these two trials. In the manual acupuncture trial, one point was stimulated until 'de qi' was elicited, and then needles were left in place for 20 minutes with no further stimulation. By contrast, the electroacupuncture trial stimulated two points (P6 and ST36) by passing an electrical current through the needles continuously for 20 minutes. The differences in treatment doses raise important research questions:
- is longer stimulation better than shorter duration of stimulation?
- is stimulation of more than one point more effective than one point?
- if 'yes' to these questions, is electroacupuncture preferred over manual acupuncture because of its ability to stimulate more than one point continuously?

Given this, what can a clinician tell a patient with refractory symptoms - the patient most likely to consider acupuncture? The clinician can relay what is known and leave it to the patient to decide: acupuncture is believed to be safe, has been shown effective in some patients, but there have been no clinical trials specifically examining refractory patients.

Acupressure

Acupressure showed a different effectiveness profile than acupuncture. Acupressure was effective for both mean and worst acute nausea severity in patients already receiving state-of-the-art antiemetics. Acupressure was not effective for acute vomiting, delayed nausea, or delayed vomiting. Given that nausea is highly subjective and neither trial used a sham control, we cannot say whether the reduction of acute nausea severity is a true finding or a function of performance bias in unblinded patients.

Sham-controlled trials of acupressure for other conditions support the anti-nausea effects of acupressure. Alkaissi *et al* found nine of ten sham-controlled, postoperative acupressure trials favored acupressure for early nausea (Alkaissi 2002). Belluomini *et al* reported morning sickness results similar to our chemotherapy results: acupressure reduced acute nausea but not acute vomiting (Belluomini 1994). Dundee and Yang found that acupressure, by itself, was not sufficient to prevent vomiting in chemotherapy patients, but could extend the duration of benefit of acupuncture (Dundee 1990a).

If our finding is correct, then acupressure offers a no-cost, convenient, self-administered intervention for chemotherapy patients to reduce acute nausea. However, placebo effects in nausea trials can be substantial (Jewell 2002). In our sensitivity analyses, only noninvasive electrostimulation permitted a comparison between sham and nonsham trials for acute nausea. This modality showed that nonsham controls tended towards significance whereas the sham-controlled trials did not, suggesting possible placebo effects in nonsham trials. Furthermore, patient expectation of benefit has been a significant predictor of reported benefit in a large unblinded trial (Roscoe 2003). Sham-controlled trials would be necessary to rule out the possibility that this result is a function of bias from nonblind studies.

Noninvasive electrostimulation

Noninvasive electrostimulation appeared to offer no benefit for any outcomes even though some individual trials reported benefits (McMillan 1991; Pearl 1999; Treish 2003). We were unable to identify a plausible source for this discrepancy. It may be due to aspects we could not explore in the data such as rescue medications, electrostimulation dose settings, or compliance with use. In two (McMillan 1991; Pearl 1999) of those trials, differences may be due data analysis methods. Both found benefit after comparing first and second chemotherapy cycles in crossover designs. We used only first-cycle data.

Acupuncture-point stimulation by any method was safe with only minimal and transient adverse events when they occurred at all. This is consistent with large, prospective studies demonstrating the safety of acupuncture (Ernst 2001; Lao 1996; MacPherson 1999).

Delayed symptoms remain a problem for many cancer patients (Dibble 2003; Dibble 2004), but noninvasive techniques (electrostimulation or acupressure) did not offer significant relief, and acupuncture delayed data were not available.

Limitations

The limitations of this review lie in the limitations of the primary studies. While methodological quality was generally high, two design issues limited our ability to interpret the data. One was the lack of a sham control in some of the studies making it difficult to interpret nausea scores, a subjective outcome. The other limitation as the lack of concurrent modern antiemetics in the electroacupunc-

ture studies making it impossible to assess whether acupuncture can offer adjunctive benefit on top of modern antiemetics. .

AUTHORS' CONCLUSIONS

Implications for practice

This review complements data on post-operative nausea and vomiting suggesting a biologic effect of acupuncture-point stimulation. Electroacupuncture has demonstrated benefit for chemotherapy-induced acute vomiting, but studies with state-of-the-art antiemetics as well as studies for refractory symptoms are needed to determine clinical relevance. Acupressure appears to reduce chemotherapy-induced acute nausea severity, though studies did not involve a placebo control. Noninvasive electrostimulation appears unlikely to have a clinically relevant impact when patients are given state-of-the-art pharmacologic antiemetic therapy. Neither electrostimulation nor acupressure offered significant relief for delayed symptoms, and acupuncture delayed data were not available. Acupuncture-point stimulation by any method is safe with minimal, transient, and rare side effects.

Implications for research

The most important research question emerging from this review is whether or not electroacupuncture combined with current antiemetics can offer additional benefit for those chemotherapy patients with refractory symptoms. Our review has raised the question of effective dose, e.g. whether stimulating more than one acupuncture-point and doing so continuously for 20 minutes can provide a greater effect that stimulating one point and leaving needles in place without continuous stimulation. These dosing questions should be examined in smaller dosing studies prior to a large trial.

Additionally, the existing literature provides some considerations for use in trial design:
(1) electroacupuncture is more effective when given before rather than after symptoms occur;
(2) electroacupuncture above 5 - 15Hz can be counterproductive, even exacerbating symptoms, so a lower electrical frequency is suggested (Dundee 1988a); and
(3) electroacupuncture antiemetic benefits last about eight hours (Dundee 1987). One study has demonstrated that combining electroacupuncture with subsequent acupressure can prolong electroacupuncture benefits (Dundee 1990a), and this combined-modality research could help address the inconvenience of the short duration of benefit with acupuncture.

The important research outcomes are acute and delayed nausea and vomiting. Therefore, a single-infusion chemotherapy regimen (rather than multiday) with a five-to seven-day follow up would be optimal to separate acute from delayed symptoms and assess acupuncture's relative impact on each. Use of a sham control is important, and the placebo needle (Streitberger 1998) would allow both real and sham treatments to use the same points and also to eliminate concerns about non-specific needling effects. If acupressure were added as a method to prolong treatment effects, a sham acupressure control would also be warranted.

POTENTIAL CONFLICT OF INTEREST

None known.

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REFERENCES

References to studies included in this review

Dibble 2000 *{published and unpublished data}*

Dibble S, Chapman J, Mack K, et al. Acupressure for nausea: results of a pilot study. *Oncology Nursing Forum* 2000;**27**(1):41–7.

Dundee 1987 *{published data only}*

* Dundee JW, Ghaly RG, Fitzpatrick KT, et al. Acupuncture to prevent cisplatin-associated vomiting. *Lancet* 1987;**1**:1083.

Dundee 1988 *{published data only}*

Dundee J, Chaly R, Fitzpatrick K. Randomized comparison of the antiemetic effects of metoclopramide and electroacupuncture in cancer chemotherapy. *British Journal of Clinical Pharmacology* 1988;**25**(6):678–9.

McMillan 1991 *{published data only}*

* McMillan C, Dundee J. The role of transcutaneous electrical stimulation of neiguan anti-emetic acupuncture point in controlling sickness after cancer chemotherapy. *Physiotherapy* 1991;**77**:499–502.

Noga 2002 *{published and unpublished data}*

Noga S, Tolman A, Roman J, et al. Acupressure as an adjunct to pharmacologic control of nausea, vomiting and retching (N/V) during blood and marrow transplantation (BMT): a randomized, placebo-controlled, algorithm based study. Proceedings of the American Society of Clinical Oncology. 2002; Vol. 21:361a.

Pearl 1999 *{published and unpublished data}*

Pearl M, Fischer M, McCauley D, et al. Transcutaneous electrical nerve stimulation as an adjunct for controlling chemotherapy-induced nausea and vomiting in gynecologic oncology patients. *Cancer Nursing* 1999;**22**(4):307–11.

Roscoe 2002 *{published and unpublished data}*

Roscoe J, Morrow G, Bushunow P, et al. Acustimulation wristbands for the relief of chemotherapy-induced nausea. *Alternative Therapies in Health and Medicine* 2002;**8**(4):56–63.

Roscoe 2003 *{published and unpublished data}*

Roscoe J, Morrow G, Hickok J, et al. The efficacy of acupressure and acustimulation wrist band for the relief of chemotherapy-induced nausea and vomiting. *Journal of Pain and Symptom Management* 2003;**26**:731–42.

Shen 2000 *{published and unpublished data}*

Shen J, Wenger N, Glaspy J, et al. Electroacupuncture for control of myeloablative chemotherapy-induced emesis: A randomized controlled trial. *Journal of the American Medical Association* 2000;**284**(21):2755–61.

Streitberger 2003 *{published and unpublished data}*

Streitberger K, Friedrich-Rusi M, Bardenheuer H, et al. Effect of acupuncture compared with placebo-acupuncture at P6 as additional antiemetic prophylaxis in high-dose chemotherapy and autologous peripheral blood stem cell transplantation: A randomized controlled single-blind tri. *Clinical Cancer Research* 2003;**9**:2538–44.

Treish 2003 *{published and unpublished data}*

Treish I, Shord S, Valgus J, et al. Randomized double-blind study of the Reliefband as an adjunct to standard antiemetics in patients receiving moderately high to highly emetogenic chemotherapy. *Supportive Cancer Care* 2003;**8**:515–21.

References to studies excluded from this review

Aglietti 1990

Aglietti L, Roila F, Tonatao M, et al. A pilot study of metoclopramide, dexamethasone, diphenhydramine and acupuncture in women treated with cisplatin. *Cancer Chemotherapy and Pharmacology* 1990;**26**(3):239–40.

Brown 1992

Brown S, North D, Marvel MK, Fons R. Acupressure wrist bands to relieve nausea and vomiting in hospice patients: Do they work?. *American Journal of Hospice and Palliative Care* 1992;**9**(4):26–9.

Dundee 1986

Dundee JE, Chestnutt WN, Ghaly RG, Lynas AGA. Traditional Chinese acupuncture, a potential useful antiemetic?. *British Medical Journal* 1986;**293**:583–4.

Dundee 1987a

Dundee JW, Ghaly RG, Fitzpatrick KTJ. Optimising antiemesis in cancer chemotherapy. *British Medical Journal* 1987;**294**:179.

Dundee 1987b

Dundee JW, Lynas AGA, Ghaly RD. Alternative Medicine. *Anaesthesia* 1987;**42**:76–7.

Dundee 1988a

Dundee JW. Studies with acupuncture / acupressure as an antiemetic. *Acupuncture in Medicine* 1988;**5**:22–4.

Dundee 1990a

Dundee JW, Yang J. Prolongation of the antiemetic action of P6 acupuncture by acupressure in patients have cancer chemotherapy. *Journal of the Royal Society of Medicine* 1990;**83**(6):360–2.

Dundee 1990b

Dundee JW, Yang J. The emetic effects of cancer chemotherapy. *Comprehensive Therapy* 1990;**16**(11):58–63.

Dundee 1990c

Dundee JW, Yang J. Acupressure prolongs the antiemetic action of P6 acupuncture. *British Journal of Clinical Pharmacology* 1990;**29**:644p–5p.

Dundee 1990d

Dundee JW. Belfast experience with P6 acupuncture antiemesis. *Ulster Medical Journal* 1990;**59**(1):63–70.

Dundee 1990e

Dundee JW, McMillan CM. Clinical uses of P6 acupuncture antiemesis. *Acupuncture Electrotherapeutics and Research* 1990;**15**(3-4):211–5.

Dundee 1990f

Dundee JW, Yang J, Ghaly RG. Vomiting and chemotherapy. *Lancet* 1990;**335**:541.

Dundee 1991

Dundee JW, Yang J, McMillan C. Noninvasive stimulation of the P6 (Neiguan) antiemetic acupuncture point in cancer chemotherapy. *Journal of the Royal Society of Medicine* 1991;**84**(4):210–3.

King 1997

King CR. Nonpharmacologic management of chemotherapy-induced nausea and vomiting. *Oncology Nursing Forum* 1997;**24**(7 suppl):41–8.

Liu 1994

* Lui S, Chen Z, Hou J, et al. Magnetic disk applied on neiguan point for prevention and treatment of cisplatin-induced nausea and vomiting. *Journal of Traditional Chinese Medicine* 1994;**11**:181–3.

Lo 1998

Lo L. Effects of P6 Acupuncture on Acute and Delayed Nausea and Vomiting in Children Receiving Cancer Chemotherapy. Doctoral dissertation 1998.

Pan 2000

Pan XC, Morrison RS, Ness J, Fugh-Berman A, Leipzig RM. Complementary and alternative medicine in the management of pain, dyspnea, and nausea and vomiting near the end of life: A systematic review. *Journal of Pain and Symptom Management* 2000;**20**(5):374–87.

Prance 1988

Prance SE, Dresser A, Wood C, Fleming J, Aldridge J, Pietroni PC. Research on traditional Chinese acupuncture-science or myth? A review. *Journal of the Royal Society of Medicine* 1988;**81**(10):588–90.

Price 1991

Price H, Lewith G, Williams C. Acupuncture as an antiemetic in cancer chemotherapy. *Complementary Medicine Research* 1991;**5**:93–4.

Saller 1986

Saller R, Hellenbrecht D, Buhring M, Hess H. Enhancement of the antiemetic action of metoclopramide against cisplatin-induced emesis by transdermal electrical nerve stimulation. *Journal of Clinical Pharmacology* 1986;**26**:116–9.

Stannard 1989

Stannard D. Pressure prevents nausea. *Nursing Times* 1989;**85**(4):33–4.

White 1997

White PF. Are nonpharmacologic techniques useful alternatives to antiemetic drugs for prevention of nausea and vomiting?. *Anesthesia Analgesia* 1997;**84**(4):712–4.

References to studies awaiting assessment

Roscoe 2005

Roscoe JA, Matteson SE, Morrow GR, Hickok JT, Bushunow P, Griggs JJ. Acustimulation wrist bands are not effective for the control of chemotherapy-induced nausea in women with breast cancer. *Journal of Pain and Symptom Management* 2005;**29**:376–84.

References to ongoing studies

Dibble 2005

Dibble SL. Treating chemotherapy-induced nausea with acupressure. Grant #5RO1CA084014-03 funded by the National Cancer Institute Study in progress.

Additional references

Alkaissi 2002

Evertsson K, Johnson V, et al. P6 acupressure may relieve nausea and vomiting after gynecological surgery: an effectiveness study in 410 women. *Canadian Journal of Anesthesia* 2002;**49**(10):1034–9.

Anonymous 1996

Anonymous. Outcomes of cancer treatment for technology assessment and cancer treatment guidelines American Society of Clinical Oncology. *Journal of Clinical Oncology* 1996;**14**(2):671–9.

Anonymous 1998a

Anonymous. NIH Consensus Development Panel on Acupuncture. *Journal of the American Medical Association* 1998;**280**:1518–24.

Belluomini 1994

Belluomini J, Litt R, Lee K, Katz M. Acupressure for nausea and vomiting of pregnancy: A randomized, blinded study. *Obstetrics and Gynecology* 1994;**84**(2):245–8.

Campora 1994

Campora E, Giudici S, Merlini L, et al. Ondansetron and dexamethasone versus standard combination antiemetic therapy. A randomized trial for the prevention of acute and delayed emesis induced by cyclophosphamide-doxorubicin chemotherapy and maintenance of antiemetic effect. *American Journal of Clinical Oncology* 1994;**17**:522–6.

Dibble 2003

Dibble SL, Isreal J, Nussey B, et al. Delayed chemotherapy-induced nausea in women treated for breast cancer. *Oncology Nursing Forum* 2003;**30**(2):E40–7.

Dibble 2004

Dibble SL, Casey K, Nussey B, et al. Online exclusive: chemotherapy-induced vomiting in women treated for breast cancer. *Oncology Nursing Forum* 2004;**31**(1):E1–8.

Dundee 1988b

Dundee JW. Acupuncture as an antiemetic: studies of its use in postoperative vomiting, cancer chemotherapy and sickness of early pregnancy. *Complementary Medicine Research* 1988;**3**:2–14.

Dundee 1991a

Dundee JW, Yang J, McMillan C. Non-invasive stimulation of the P6 (Neiguan) antiemetic acupuncture point in cancer chemotherapy. *Journal of the Royal Society of Medicine* 1991;**84**:210–2.

Ernst 2001

Ernst E, White A. Prospective studies of the safety of acupuncture: a systematic review. *American Journal of Medicine* 2001;**110**(6):481–5.

Gralla 1999

Gralla R, Osoba D, Kris M, et al. Recommendations for the use of antiemetics: Evidence-based, clinical practice guidelines. *Journal of Clinical Oncology* 1999;**17**(9):2971–94.

Griffin 1996

Griffin A, Butow P, Coates A, et al. On the receiving end: V Patient perceptions of the side effects of chemotherapy in 1993. *Annals of Oncology* 1996;**7**:189–95.

Hesketh 1998

Hesketh P, Gralla R, du Bois A, et al. Methodology of antiemetic trials: response assessment, evaluation of new agents and definition of chemotherapy emotogenecity. *Supportive Care Cancer* 1998;**6**(3):221–7.

Hesketh 1999

Hesketh P. Defining the emoetogenicity of cancer chemotherapy regimens: Relevance to clinical practice. *Oncologist* 1999;**4**:191–6.

Ioannidis 2000

Ioannidis JP, Hesketh PJ, Lau J. Contribution of dexamethasone to control of chemotherapy-induced nausea and vomiting: a meta-analysis of randomized evidence. *Journal of Clinical Oncology* 2000;**18**(19):3409–22.

Jewell 2002
Jewell D, Young G. Interventions for nausea and vomiting in early pregnancy. In: *Cochrane Library*, 2, 2002. Oxford: Update Software.

Lao 1996
Lao L. Safety issues in acupuncture. *Journal of Alternative and Complementary Medicine* 1996;**2**(1):27–31.

Lao 2003
Lao L, Zhang G, Wong R, et al. The effect of electroacupuncture as an adjunct on cyclophosphamide-induced emesis in ferrets. *Pharmacology and Biochemical Behavior* 2003;**74**(3):691–9.

Lee 2004
Lee A, Done ML. Stimulation of the wrist acupuncture point P6 for preventing postoperative nausea and vomiting. In: *The Cochrane Database of Systematic Reviews*, 3, 2004. Chichester: John Wiley and Sons, Ltd.

Love 1989
Love R, Leventhal H, Easterling D, et al. Side effects and emotional distress during cancer chemotherapy. *Cancer* 1989;**63**(3):604–12.

MacPherson 1999
MacPherson H. How safe is acupuncture? Developing the evidence on risk. *Journal of Alternernative and Complementary Medicine* 1999; **5**(3):223–4.

Oettle 2001
Oettle H, Riess H. Treatment of chemotherapy-induced nausea and vomiting. *Journal of Cancer Research in Clinical Oncology* 2001;**127**: 340–5.

Osoba 1997
Osoba D, Zee B, Warr D, et al. Effect of postchemotherapy nausea and vomiting on health-related quality of life. The Quality of Life and Symptom Control Committees of the National Cancer Institute of Canada Clinical Trials Group. *Supportive Care Cancer* 1997;**5**: 307–13.

Roscoe 2000
Roscoe J, Morrow G, Hickok J, et al. Nausea and vomiting remain a significant clinical problem: trends over time in controlling chemotherapy-induced nausea and vomiting in 1413 patients treated in community clinical practices. *Journal of Pain and Symptom Management* 2000;**20**(2):113–21.

Stewart 1999
Stewart D, Dahrouge S, Coyle D, et al. Costs of treating and preventing nausea and vomiting in patients receiving chemotherapy. *Journal of Clinical Oncology* 1999;**7**(1):344–51.

Streitberger 1998
Streitberger K, Kleinhenz L. Introducing a placebo needle into acupuncture research. *Lancet* 1998;**1**:88–91.

Tramer 1997
Tramer M, Reynolds D, Moore R, et al. Impact of covert duplicate publication on meta-analysis: a case study. *BMJ* 1997;**315**(7109): 635–40.

Vickers 1996
Vickers AJ. Can acupuncture have specific effects on health? A systematic review of acupuncture antiemesis trials. *Journal of the Royal Society of Medicine* 1996;**6**:303–11.

References to other published versions of this review

Ezzo 2005
Ezzo J, Vickers AJ, Richardson MA, Allen C, Dibble SL, Issell B, et al. Acupuncture-point stimulation for chemotherapy-induced nausea and vomiting. *Journal of Clinical Oncoloy* 2005;**23**:7188–98.

* *Indicates the major publication for the study*

TABLES

Characteristics of included studies

Study	Dibble 2000
Methods	Parallel design.
Participants	17 (17 evaluable) breast cancer patients.
Interventions	TREATMENT: Antiemetics + acupressure applied by the patient to P6 and ST36 for maximum of three minutes. Each point was held in the morning and then as needed throughout the day. CONTROL: Antiemetics only
Outcomes	Acute nausea. Delayed nausea.
Notes	No AE's*
Allocation concealment	A – Adequate

Characteristics of included studies (*Continued*)

Study	**Dundee 1987**
Methods	Crossover design (within cycle).
Participants	10 (10 evaluable) testicular cancer inpatients with prior history of emesis or nausea, or both, with chemotherapy.
Interventions	TREATMENT: Antiemetics + electroacupuncture administered to P6 until "de qi" elicited. Each patient had five or six treatments over three days, only one of which was the sham point. At least eight hours elapsed between successive treatments. CONTROL: Antiemetics + sham point in right elbowatments over three days, only one of which was the sham point. At least eight hours elapsed between successive treatments. CONTROL: Antiemetics + sham point in right elbow.
Outcomes	Acute vomiting.
Notes	No AE's*
Allocation concealment	B – Unclear

Study	**Dundee 1988**
Methods	Parallel design.
Participants	20 (20 evaluable) consecutive cancer patients having their first course of chemotherapy (mixed cancers).
Interventions	TREATMENT: Antiemetics + low frequency electroacupuncture (10 Hz applied for five minutes prior to or soon after the beginning of chemo) "de qi" elicited. CONTROL: Antiemetics only.
Outcomes	Acute vomiting
Notes	No AE's*
Allocation concealment	B – Unclear

Study	**McMillan 1991**
Methods	Crossover.
Participants	16 (16 evaluable) cancer inpatients receiving chemotherapy for five consecutive days; history of emesis or nausea, or both, with prior chemotherapy.
Interventions	TREATMENT: Antiemetics + TENS stimulation of P6 prior to chemotherapy for five minutes followed by stimulation for five minutes every two hours when awake for five days. CONTROL: Antiemetics only.
Outcomes	Acute vomiting. Acute nausea.
Notes	No AE's*
Allocation concealment	B – Unclear

Study	**Noga 2002**
Methods	Parallel.
Participants	120 (110 evaluable) hematologic cancer patients.
Interventions	TREATMENT: Antiemetics + SeaBand (acupressure band) at P6 worn for 24 hours postchemotherapy. CONTROL: Antiemetics + SeaBand at sham point.
Outcomes	Acute vomiting. Acute nausea. Delayed vomiting.

	Delayed nausea.
Notes	AE's: Some discomfort noted with elastic bands; no problem with Velcro bands.
Allocation concealment	C – Inadequate

Study	**Pearl 1999**
Methods	Crossover.
Participants	42 (32 evaluable) gynecologic cancer patients receiving single-infusion chemotherapy.
Interventions	TREATMENT: Antiemetics + ReliefBand (TENS) stimulation at P6 worn continuously for seven days (except during bathing) beginning at discharge from the hospital. CONTROL: AE + Sham ReliefBands at P6 worn continuously for seven days (except during bathing) beginning at discharge.
Outcomes	Acute vomiting. Acute nausea. Delayed vomiting. Delayed nausea.
Notes	Transient rash at electrode site in two patients.
Allocation concealment	C – Inadequate

Study	**Roscoe 2002**
Methods	Crossover.
Participants	42 (38 evaluable) breast, lung, ovarian, colorectal cancer patients who reported moderate or greater levels of nausea after first course of chemotherapy.
Interventions	TREATMENT: Antiemetics + ReliefBand (TENS) worn prior to chemo and for as long as helpful. CONTROL1: Antiemetics + sham Reliefand. CONTROL 2: Antiemetics only.
Outcomes	Acute nausea. Delayed nausea.
Notes	AE assessment not reported.
Allocation concealment	A – Adequate

Study	**Roscoe 2003**
Methods	Parallel.
Participants	747 (700 evaluable) cancer patients receiving initial doxorubicin or cisplatin therapy.
Interventions	TREATMENT1: Antiemetics + SeaBand (bilateral acupressure) or TREATMENT2: Antiemetics + Relief-Band (single acustimulation) worn for five days except when necessary to remove to avoid immersion in water. CONTROL: Antiemetics only.
Outcomes	Acute vomiting. Acute nausea. Delayed vomiting. Delayed nausea.
Notes	Three reports of skin irritation at electrode site.
Allocation concealment	D – Not used

Study	Shen 2000
Methods	Parallel.
Participants	104 (104 evaluable) breast cancer inpatients receiving high-dose chemotherapy with prior history of emesis or nausea, or both.
Interventions	TREATMENT: Antiemetics + Low frequency electroacupuncture (2-10 Hz for 20 min applied two hours before chemo everyday for five days) at P6 and ST36; "de qi" elicited. CONTROL 1: Antiemetics + Sham acupuncture: Needles inserted superficially, no manipulation at into LU7 and GB34 delivered under the same conditions as experimental group but with no electrical current; no "de qi". CONTROL 2: Antiemetics only.
Outcomes	Acute vomiting.
Notes	One patient felt electrical shock; one patient with peripheral neuropathy had aggravation of tingling.
Allocation concealment	A – Adequate

Study	Streitberger 2003
Methods	Parallel.
Participants	80 patients (80 evaluable) with mixed cancers
Interventions	TREATMENT: Manual acupuncture at P6 30 minutes prior to first application of chemotherapy and the day after. Needle stimulation until "de qi" occured and then remained in place for 20 min without additional stimulation. CONTROL: Noninvasive placebo acupuncture at same point.
Outcomes	Acute vomiting. Acute nausea.
Notes	AE assessment not reported.
Allocation concealment	A – Adequate

Study	Treish 2003
Methods	Parallel.
Participants	49 (37 evaluable) cancer patients with mixed cancers.
Interventions	TREATMENT: Antiemetics + ReliefBand worn for five days except when necessary to remove to avoid immersion in water. CONTROL: Antiemetics + sham Reliefband.
Outcomes	Acute vomiting. Acute nausea. Delayed vomiting. Delayed nausea.
Notes	No AE's*
Allocation concealment	C – Inadequate

AE=adverse events. Note: Trials that say "No AE's" mean that the trial assessed AE's, and there were none. "AE assessment not reported" = it is not clear whether there were no AE's or they were just not reported as there was no mention of assessing AE's in the paper.

Characteristics of excluded studies

Study	Reason for exclusion
Aglietti 1990	Randomization not stated.

Characteristics of excluded studies (*Continued*)

Brown 1992	No control group.
Dundee 1986	Postoperative sickness only.
Dundee 1987a	No control group.
Dundee 1987b	No patient data.
Dundee 1988a	Review.
Dundee 1990a	Not randomized.
Dundee 1990b	Review.
Dundee 1990c	Not randomized.
Dundee 1990d	Postoperative symptoms only.
Dundee 1990e	Review.
Dundee 1990f	No patient data.
Dundee 1991	No control group.
King 1997	Review.
Liu 1994	Received a high probabilty of bias rating by both review authors.
Lo 1998	Data not obtainable for pooling.
Pan 2000	Review.
Prance 1988	Review.
Price 1991	Data not usable for pooling.
Saller 1986	Randomization not stated.
Stannard 1989	Not randomized.
White 1997	Review.

ADDITIONAL TABLES

Table 01. Search strategies other than Medline

Search strategies

Embase 1980 to 2005 Week 25
Search Strategy:
1. ACUPUNCTURE/ (7062)
2. Transcutaneous Nerve Stimulation/ (2001)
3. (acupuncture$ or acupoint$ or meridian$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (9515)
4. alternative medicine.mp. or Alternative Medicine/ (7760)
5. (electroacupuncture or electro-acupuncture).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (1124)
6. moxibustion.mp. (168)
7. chinese medicine/ (3920)
8. (acupressure or "traditional chinese medicine" or "relief band$" or bioband$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (1535)
9. ("transcutaneous electric$ nerve stimulation" or "transdermal electric$ nerve stimulation").mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (774)

Table 01. Search strategies other than Medline (*Continued*)

Search strategies

10. tens.ti. (275)
11. tens.ab. (2613)
12. or/1-11 (23232)
13. VOMITING/ (46464)
14. NAUSEA/ (54834)
15. "NAUSEA AND VOMITING"/ (3139)
16. (nausea or vomiting).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (86215)
17. Chemotherapy Induced Emesis/ (1446)
18. (emesis or antiemetic$ or anti-emetic$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (10915)
19. Antiemetic Agent/ (5084)
20. or/13-19 (89177)
21. Antineoplastic Agent/ (60911)
22. (antineoplastic$ or cytotoxic$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (211089)
23. chemo$.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (274675)
24. exp NEOPLASM/ (1137931)
25. (neoplasm$ or cancer$ or tumour$ or tumor$ or carcinoma$ or "marrow transplant$").mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (1145326)
26. CISPLATIN/ or CISPLATIN.mp. (57462)
27. or/21-26 (1533562)
28. 12 and 20 and 27 (222)
29. random$.ti,ab. (276682)
30. factorial$.ti,ab. (5625)
31. (crossover$ or cross over$ or cross-over$).ti,ab. (31816)
32. placebo$.ti,ab. (85820)
33. (doubl$ adj blind$).ti,ab. (68837)
34. (singl$ adj blind$).ti,ab. (5801)
35. assign$.ti,ab. (79553)
36. allocat$.ti,ab. (25073)
37. volunteer$.ti,ab. (79737)
38. CROSSOVER PROCEDURE.sh. (16269)
39. DOUBLE-BLIND PROCEDURE.sh. (55961)
40. RANDOMIZED CONTROLLED TRIAL.sh. (95693)
41. SINGLE BLIND PROCEDURE.sh. (5342)
42. or/29-41 (485772)
43. ANIMAL/ or NONHUMAN/ or ANIMAL EXPERIMENT/ (2799332)
44. HUMAN/ (4921945)
45. 44 and 43 (353280)
46. 43 not 45 (2446052)
47. 42 not 46 (425555)
48. 28 and 47 (47)
49. from 48 keep 1-47 (47)

PsycINFO <1967 to June Week 2 2005>Search Strategy:

1. ACUPUNCTURE/ (486)
2. (acupuncture or acupoint$ or meridian$).mp. [mp=ttle, abstract, subject headings, table of contents, key concepts] (1081)
3. alternative medicine$.mp. [mp=title, abstract, subject headings, table of contents, key concepts] (1095)

Table 01. Search strategies other than Medline (*Continued*)

Search strategies

4. (electroacupuncture or electro-acupuncture).mp. [mp=title, abstract, subject headings, table of contents, key concepts] (103)
5. moxibustion.mp. [mp=title, abstract, subject headings, table of contents, key concepts] (10)
6. "traditional chinese medicine".mp. [mp=title, abstract, subject headings, table of contents, key concepts] (84)
7. ("relief bands" or bioband$).mp. [mp=title, abstract, subject headings, table of contents, key concepts] (0)
8. ("transcutaneous electric$ nerve stimulation" or "transdermal electric$ nerve stimulation").mp. [mp=title, abstract, subject headings, table of contents, key concepts] (135)
9. tens.ti. or tens.ab. (256)
10. or/1-9 (2416)
11. (nausea or vomiting).mp. [mp=title, abstract, subject headings, table of contents, key concepts] (2861)
12. NAUSEA/ (354)
13. VOMITING/ (567)
14. (emises or antiemetic$ or anti-emetic$).mp. [mp=title, abstract, subject headings, table of contents, key concepts] (209)
15. exp ANTIEMETIC DRUGS/ (2988)
16. or/11-15 (5860)
17. (antineoplastic$ or cytotoxic$).mp. [mp=title, abstract, subject headings, table of contents, key concepts] (593)
18. chemo$.mp. [mp=title, abstract, subject headings, table of contents, key concepts] (3010)
19. exp NEOPLASMS/ (12547)
20. (neoplasm$ or cancer$ or tumour$ or tumor$ or carcinoma$ or "marrow transplant$").mp. [mp=title, abstract, subject headings, table of contents, key concepts] (17107)
21. or/17-20 (20079)
22. 10 and 16 and 21 (6)
23. from 22 keep 1-6 (6)
Papas Database and CCTR (Cochrane Controlled Trials Registry) Search strategy
((acupuncture or acupressure or TENS or "trancutaneous electric nerve stimulation" or "transdermal electric* nerve stimulation" or acupoint* or meridian$ or electroacupuncture or electro-acupuncture or moxibustion or "relief bands") AND (nausea or vomiting or emesis or antiemetic* or anti-emetic*) AND (antineoplastic* or cytotoxic or chemo* or neoplasm* or cancer* or tumour* or tumor* or carcinoma* or "marrow transplant*" or cisplatin))
Bibliographies from retrieved articles were searched for additional studies. ASCO conference abstracts were searched 2002-2004.

Table 02. Methodological quality of included studies

Study	Random adequate	Concealment adequate	Sham control	Asses'r blind stated	Dropouts accounted
Dibble 2000	yes	yes (called a central number)	no	no	yes
Dundee 1987	not reported	not reported	yes	not reported	yes
Dundee 1988	not reported	not reported	no	yes	yes
McMillan 1991	not reported	not reported	no	not reported	yes
Noga 2002	yes	no (master list held in house-PC)	yes	no	yes
Pearl 1999	yes	no (mater list held in house)	yes	yes	yes
Roscoe 2002	yes	yes (opaque env, numbered)	yes	yes	yes

Table 02. Methodological quality of included studies (*Continued*)

Study	Random adequate	Concealment adequate	Sham control	Asses'r blind stated	Dropouts accounted
Roscoe 2003	yes	yes (call central office-PC)	no	yes	yes
Shen 2000	yes	yes	yes	yes	yes
Streitberger 2003	yes	yes	yes	yes	yes
Treish 2003	yes	no (master list-PC)	yes	yes	yes

Table 03. Chemotherapy and antiemetic regimens and ratings

Study	Chemotherapy used	Chemotherapy rating.	Antiemetics used....	Antiemetic rating
Dibble 2000	cyclophosphamide, methotrexate, flurouracil, or doxorubicin	moderate / high emetogenicity	ondansetron, dexamethasone, granistron, proclorperazine, lorazepam	ASCO consistent
Dundee 1987	cisplatin	high emetogenicity	metoclopramide, prednisolone	ASCO not consistent
Dundee 1988	not specified	not specified	metoclopramide	ASCO not consistent
McMillan 1999	cisplatin, cyclophosphamide	high emetogenicity	ondansetron	ASCO partially consistent
Noga 2002	high-dose chemotherapy with stem cell transplantation, cyclophosphamide	high emetogenicity	ondansetron, dexamethasone, proclorperazine, lorazepam, metoclopramide	ASCO consistent
Pearl 1999	cisplatin	high emetogenicity	ondansetron, dexamethasone, proclorperazine, lorazepam	ASCO consistent
Roscoe 2002	doxorubicin, others	moderate / high emetogenicity	ondansetron, granistron	ASCO partially consistent
Roscoe 2003	cisplatin, doxorubicin	high emetogenicity	ondansetron, dexamethasone	ASCO consistent
Shen 2000	high-dose chemotherapy with stem cell transplant, cisplatin, cyclophosphamide	high emetogenicity	proclorper-azine,lorazepam, meto-clopramide, droperidol, diphenhydramine	ASCO not consistent
Streitberger 2003	high-dose chemotherapy with stem cell transplant, melphalan, others	high emetogenicity	ondansetron, metoclopramide, triflupromazine	ASCO partially consistent
Treish 2003	high-dose chemotherapy with stem cell	high emetogenicity	ondansetron, dexamethasone,	ASCO consistent

Table 03. Chemotherapy and antiemetic regimens and ratings (*Continued*)

Study	Chemotherapy used	Chemotherapy rating.	Antiemetics used....	Antiemetic rating
	transplant, cisplatin, cyclophosphamide, others		proclorperazine	

Table 04. Sensitivity analysis results

Type of acupuncture	Acute vomiting	Acute nausea	Delayed vomiting	Delayed nausea
All modalities				
Concealment adequate	RR 0.84 (0.69, 1.03) (N = 241)	SMD -0.11 (-0.26, 0.03) (N = 812)	WMD -0.03 (-0.20, 0.14) (N = 689)	SMD 0.00 (-0.16, 0.15) (N = 753)
Concealment inadequate or unknown	RR 0.74 (0.48, 1.15) (N = 973)	SMD -0.15 (-0.58, 0.29) (N = 84)	WMD 0.16 (-0.13, 0.45) (N = 68)	SMD -0.19 (-0.67, 0.30) (N = 68)
Sham control	RR 0.81 (0.62, 1.05) (N = 399)	SMD -0.04 (-0.24, 0.26) (N = 174)	WMD 0.16 (-0.13, 0.45) (N = 68)	SMD -0.10 (-0.51, 0.31) (N = 94)
No sham control	RR 0.84 (0.68, 1.04) (N = 866)	SMD -0.14 (-0.29, 0.02) (N = 735)	WMD -0.03 (-0.20, 0.14) (N = 689)	SMD -0.04 (-0.17, 0.14) (N = 740)
Modern antiemetics	RR 0.88 (0.67, 1.09) (N = 1080)	No comparison data	No comparison data	No comparison data
Older antiemetics	RR 0.76 (0.60, 0.97) (N = 134)			
Acupuncture only				
Concealment adequate	RR 0.54 (0.17, 1.71)	No comparison data	No data	No data
Concealment inadequate or unknown	RR 0.76 (0.60, 0.97)			
Sham control	RR 0.74 (0.56, 0.98)			
No sham control	RR 0.77 (0.59, 1.00)			
Modern antiemetics	RR 0.88 (0.67, 1.09)			
Older antiemetics	RR 0.76 (0.60, 0.97)			
Manual Acupuncture				
Concealment adequate	No comparison data	No comparison data	No data	No data
Concealment inadequate or unknown				
Sham control				
No sham control				
Modern antiemetics				
Older antiemetics				
Electroacupuncture				
Concealment adequate	RR 0.86 (0.68, 1.09) (N = 104)	No data	No data	No data
Concealment inadequate or unknown	RR 0.41 (0.18, 0.92) (N = 30)			
Sham control	RR 0.79 (0.61, 1.02) (N = 80)			
No sham control	RR 0.77 (0.59, 1.00) (N = 91)			
Modern antiemetics	NA			
Older antiemetics				
Acupressure				

Table 04. Sensitivity analysis results (*Continued*)

Type of acupuncture	Acute vomiting	Acute nausea	Delayed vomiting	Delayed nausea
Concealment adequate	RR 0.82 (0.58, 1.15) (N = 500)	No comparison data	No comparison data	No comparison data
Concealment inadequate or unknown	RR 1.00 (0.31, 3.28) (N = 120)			
Sham control	RR 1.00 (0.31, 3.28) (N = 120)			
No sham control	RR 0.82 (0.58, 1.15) (N = 500)			
Modern antiemetics	No comparison data			
Older antiemetics				
Noninvasive electrostimulation	RR 0.90 (0.65, 1.25) (N = 538)	SMD -0.06 (-0.24, 0.12) (N = 484)	WMD -0.03 (-0.20, 0.14) (N = 689)	SMD 0.06 (-0.12, 0.23) (N = 501)
Concealment adequate	RR 0.87 (0.49, 1.55) (N = 91)	SMD -0.15 (-0.58, 0.29) (N = 84)	WMD 0.16 (-0.13, 0.45) (N = 68)	SMD -0.19 (-0.67, 0.30) (N = 68)
Concealment inadequate or unknown	RR 0.89 (0.52, 1.52) (N = 119)	SMD -0.08 (-0.49, 0.34) (N =94)	WMD 0.16 (-0.13, 0.45) (N = 68)	SMD -0.10 (-0.51, 0.31) (N = 94)
Sham control	RR 0.87 (0.65, 1.15) (N = 524)	SMD -0.13 (-0.28, 0.03) (N = 718)	WMD -0.03 (-0.20, 0.14) (N = 689)	SMD 0.04 (-0.12, 0.19) (N = 723)
No sham control	No comparison data	No comparison data	No comparison data	No comparison data
Modern antiemetics				
Older antiemetics				

Legend:
No comparison data = all studies in that group have the same characteristic (i.e., all used modern antiemetics) so sensitivity analysis of modern versus older antiemetics could not be done.
No data = no studies exist on that outcome.

ANALYSES

Comparison 01. ACUPUNCTURE-POINT STIMULATION (ALL TYPES) VERSUS CONTROL (ALL TYPES)

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 ACUTE VOMITING. MAIN RESULTS: PROPORTION VOMITING IN FIRST 24 HOURS (ALL PATIENTS)	9	1214	Relative Risk (Fixed) 95% CI	0.82 [0.69, 0.99]
02 ACUTE NAUSEA. MAIN RESULTS. MEAN NAUSEA SEVERITY IN FIRST 24 HOURS	7	896	Standardised Mean Difference (Fixed) 95% CI	-0.11 [-0.25, 0.02]
03 DELAYED VOMITING: MAIN RESULTS: MEAN NUMBER OF VOMITING EPISODES DAY 2 THROUGH 5-7	3	757	Weighted Mean Difference (Fixed) 95% CI	0.02 [-0.13, 0.17]

04 DELAYED NAUSEA. MAIN RESULTS. MEAN NAUSEA SEVERITY DAY TWO THROUGH DAYS FIVE TO SEVEN	5	821	Standardised Mean Difference (Fixed) 95% CI	-0.02 [-0.17, 0.12]

Comparison 02. ACUPUNCTURE (MANUAL AND ELECTROACUPUNCTURE TRIALS COMBINED) VS. CONTROL

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 ACUTE VOMITING. MAIN RESULTS: PROPORTION VOMITING IN FIRST 24 HOURS	4	214	Relative Risk (Fixed) 95% CI	0.74 [0.58, 0.94]
02 ACUTE NAUSEA. MAIN RESULTS. MEAN NAUSEA SEVERITY IN FIRST 24 HOURS	1	80	Standardised Mean Difference (Fixed) 95% CI	0.02 [-0.42, 0.46]

Comparison 03. ELECTROACUPUNCTURE VS CONTROL

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 ACUTE VOMITING. MAIN RESULTS: PROPORTION VOMITING IN FIRST 24 HOURS	3	134	Relative Risk (Fixed) 95% CI	0.76 [0.60, 0.97]

Comparison 04. MANUAL ACUPUNCTURE VS CONTROL

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 ACUTE VOMITING. MAIN RESULTS: PROPORTION VOMITING IN FIRST 24 HOURS	1	80	Relative Risk (Fixed) 95% CI	0.54 [0.17, 1.71]
02 ACUTE NAUSEA. MAIN RESULTS. MEAN NAUSEA SEVERITY IN FIRST 24 HOURS	1	80	Standardised Mean Difference (Fixed) 95% CI	0.02 [-0.42, 0.46]

Comparison 05. ACUPRESSURE VS CONTROL

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 ACUTE VOMITING. MAIN RESULTS: PROPORTION VOMITING IN FIRST 24 HOURS	2	620	Relative Risk (Fixed) 95% CI	0.83 [0.60, 1.16]
02 ACUTE NAUSEA. MAIN RESULTS. MEAN NAUSEA SEVERITY IN FIRST 24 HOURS	2	474	Standardised Mean Difference (Fixed) 95% CI	-0.19 [-0.38, -0.01]

03 DELAYED VOMITING: MAIN RESULTS: MEAN NUMBER OF VOMITING EPISODES DAY 2 THROUGH 5-7	1	463	Weighted Mean Difference (Fixed) 95% CI	-0.07 [-0.25, 0.11]
04 DELAYED NAUSEA. MAIN RESULTS. MEAN NAUSEA SEVERITY DAY 2 THROUGH DAYS 5-7	2	485	Standardised Mean Difference (Fixed) 95% CI	-0.05 [-0.23, 0.13]

Comparison 06. NONINVASIVE ELECTROSTIMULATION VS CONTROL

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 ACUTE VOMITING. MAIN RESULTS: PROPORTION VOMITING IN FIRST 24 HOURS	4	629	Relative Risk (Fixed) 95% CI	0.90 [0.67, 1.19]
02 ACUTE NAUSEA. MAIN RESULTS. MEAN NAUSEA SEVERITY IN FIRST 24 HOURS	5	568	Standardised Mean Difference (Fixed) 95% CI	-0.07 [-0.23, 0.10]
03 DELAYED VOMITING: MAIN RESULTS: MEAN NUMBER OF VOMITING EPISODES DAY 2 THROUGH 5-7	3	527	Weighted Mean Difference (Fixed) 95% CI	0.06 [-0.11, 0.22]
04 DELAYED NAUSEA. MAIN RESULTS. MEAN NAUSEA SEVERITY DAY 2 THROUGH DAYS 5-7	4	569	Standardised Mean Difference (Fixed) 95% CI	0.03 [-0.14, 0.19]

INDEX TERMS

Medical Subject Headings (MeSH)

*Acupuncture Points; Antiemetics [therapeutic use]; Antineoplastic Agents [*adverse effects]; *Electroacupuncture; Nausea [chemically induced; *therapy]; Randomized Controlled Trials; Vomiting [chemically induced; *therapy]

MeSH check words

Humans

COVER SHEET

Title Acupuncture-point stimulation for chemotherapy-induced nausea or vomiting

Authors Ezzo JM, Richardson MA, Vickers A, Allen C, Dibble SL, Issell BF, Lao L, Pearl M, Ramirez G, Roscoe JA, Shen J, Shivnan JC, Streitberger K, Treish I, Zhang G

Contribution of author(s) Jeanette Ezzo, MPH, PhD, contributed to the concept and design of the study, extracted methodological quality items from published reports, wrote manuscripts, cross checked biostatistics, conducted Revman analyses, and oversaw the details of the review process.
Andrew Vickers, PhD, contributed to the concept and design of the study, contributed to the statistical analyses, extracted methodological quality items from published reports,

wrote portions of the manuscript, provided ongoing input throughout the process on the methodological decisions pertaining to the manuscript, and approved the final manuscript.
Mary Ann Richardson, DrPH, provided input in the concept and design of the study, oversaw all searches for studies, wrote and edited drafts, oversaw administrative details of review, extracted data on the study details of each study, participated in all decisions of the paper, initiated contact with primary authors of included studies, and approved the final manuscript.
Claire Allen provided ongoing feedback on the wording of concepts that would be understandable to consumers/patients. She offered ideas on interpretation of study results in consumer friendly language. She also contributed to the concept and design of the study and approved the final manuscript.
Suzanne L. Dibble, RN, DNSc, contributed to the concept and design of the study, provided data for the statistical pooling, provided linkages to the nausea and vomiting literature for assistance in interpretation of results, and approved the final manuscript.
Brian Issell, MD, contributed to the concept and design of the study, extracted chemotherapy data from the papers, provided expertise into the classification of chemotherapy regimens (i.e. high, moderate, low emetogenicity), and antiemetic regimens (ASCO consistent or not), provided guidance on the interpretation of the data, and approved the final manuscript.
Lixing Lao, PhD, LAc, contributed to the concept and design of the study, provided expertise in the evaluation of the acupuncture-point treatments, provided input on the interpretation of results, and approved the final manuscript.
Michael Pearl, MD, contributed to the concept and design of the study, provided data for the statistical pooling, provided additional information on the methodological details of his trial, and approved the final manuscript.
Gilbert Ramirez, DrPH, contributed to the concept and design of the study, provided technical assistance in statistical analysis including calculation of the numbers needed to treat, provided input on interpretation of results, and approved the final manuscript.
Joseph A. Roscoe, PhD, contributed to the concept and design of the study, provided data for the statistical pooling, provided wording in synthesizing and interpreting data, provided input on interpreting the lack of statistical significance of electrostimulation trials, provided additional information on the methodological details of his two trials, and approved the final manuscript.
Joannie Shen, MD, MPH, PhD, contributed to the concept and design of the study, provided data for the statistical pooling, provided additional information on the methodological details of her trial, and approved the final manuscript.
Jane Shivan, MScN, RN, AOCN, contributed to the concept and design of the study, provided data for the statistical pooling, provided additional information on the methodological details of her trial, and approved the final manuscript.
Konrad Streitberger, MD, contributed to the concept and design of the study provided data for the statistical pooling, provided additional information on the methodological details of his trial, provided input on the interpretation of results, and approved the final manuscript.
Grant Zhang, PhD, LAc, contributed to the concept and design of the study, provided expertise in the evaluation of the acupuncture-point treatments, provided input in the interpretation of results, and approved the final manuscript.

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Review first published	2006/2
Date of most recent amendment	23 May 2006
Date of most recent SUBSTANTIVE amendment	21 February 2006
What's New	Information not supplied by author

Date new studies sought but none found	Information not supplied by author
Date new studies found but not yet included/excluded	Information not supplied by author
Date new studies found and included/excluded	Information not supplied by author
Date authors' conclusions section amended	Information not supplied by author
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Editorial group code	HM-SYMPT

GRAPHS AND OTHER TABLES

Analysis 01.01. Comparison 01 ACUPUNCTURE-POINT STIMULATION (ALL TYPES) VERSUS CONTROL (ALL TYPES), Outcome 01 ACUTE VOMITING. MAIN RESULTS: PROPORTION VOMITING IN FIRST 24 HOURS (ALL PATIENTS)

Review: Acupuncture-point stimulation for chemotherapy-induced nausea or vomiting

Comparison: 01 ACUPUNCTURE-POINT STIMULATION (ALL TYPES) VERSUS CONTROL (ALL TYPES)

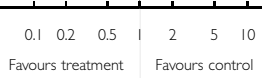
Outcome: 01 ACUTE VOMITING. MAIN RESULTS: PROPORTION VOMITING IN FIRST 24 HOURS (ALL PATIENTS)

Study	Acupoint Stimulation n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dundee 1987	2/7	3/3		2.7	0.29 [0.09, 0.92]
Dundee 1988	3/10	6/10		3.8	0.50 [0.17, 1.46]
Noga 2002	5/60	5/60		3.2	1.00 [0.31, 3.28]
Pearl 1999	6/21	7/21		4.4	0.86 [0.35, 2.12]
Roscoe 2002	3/14	5/28		2.1	1.20 [0.33, 4.31]
Roscoe 2003	97/498	57/249		48.3	0.85 [0.64, 1.14]
Shen 2000	26/37	55/67		24.9	0.86 [0.68, 1.09]
Streitberger 2003	4/41	7/39		4.6	0.54 [0.17, 1.71]
Treish 2003	9/26	9/23		6.1	0.88 [0.42, 1.84]
Total (95% CI)	714	500		100.0	0.82 [0.69, 0.99]

Total events: 155 (Acupoint Stimulation), 154 (Control)

Test for heterogeneity chi-square=5.10 df=8 p=0.75 I^2 =0.0%

Test for overall effect z=2.07 p=0.04



Analysis 01.02. Comparison 01 ACUPUNCTURE-POINT STIMULATION (ALL TYPES) VERSUS CONTROL (ALL TYPES), Outcome 02 ACUTE NAUSEA. MAIN RESULTS. MEAN NAUSEA SEVERITY IN FIRST 24 HOURS

Review: Acupuncture-point stimulation for chemotherapy-induced nausea or vomiting

Comparison: 01 ACUPUNCTURE-POINT STIMULATION (ALL TYPES) VERSUS CONTROL (ALL TYPES)

Outcome: 02 ACUTE NAUSEA. MAIN RESULTS. MEAN NAUSEA SEVERITY IN FIRST 24 HOURS

Study	Treatment		Control		Standardised Mean Difference (Fixed)	Weight	Standardised Mean Difference (Fixed)
	N	Mean(SD)	N	Mean(SD)	95% CI	(%)	95% CI
Dibble 2000	8	1.75 (2.66)	9	2.75 (1.39)		2.0	-0.46 [-1.42, 0.51]
McMillan 1991	8	1.00 (0.76)	8	1.12 (0.65)		2.0	-0.16 [-1.14, 0.82]
Pearl 1999	15	1.87 (1.06)	16	1.37 (0.81)		3.7	0.52 [-0.20, 1.24]
Roscoe 2002	13	2.62 (1.46)	25	2.86 (1.53)		4.2	-0.16 [-0.83, 0.52]
Roscoe 2003	451	2.09 (1.53)	226	2.27 (1.55)		74.1	-0.12 [-0.28, 0.04]
Streitberger 2003	41	0.61 (0.83)	39	0.59 (0.94)		9.8	0.02 [-0.42, 0.46]
Treish 2003	19	0.71 (0.56)	18	2.33 (3.12)		4.2	-0.72 [-1.38, -0.05]
Total (95% CI)	555		341			100.0	-0.11 [-0.25, 0.02]

Test for heterogeneity chi-square=6.99 df=6 p=0.32 I^2 =14.2%

Test for overall effect z=1.63 p=0.1

Analysis 01.03. Comparison 01 ACUPUNCTURE-POINT STIMULATION (ALL TYPES) VERSUS CONTROL (ALL TYPES), Outcome 03 DELAYED VOMITING: MAIN RESULTS: MEAN NUMBER OF VOMITING EPISODES DAY 2 THROUGH 5-7

Review: Acupuncture-point stimulation for chemotherapy-induced nausea or vomiting

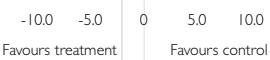
Comparison: 01 ACUPUNCTURE-POINT STIMULATION (ALL TYPES) VERSUS CONTROL (ALL TYPES)

Outcome: 03 DELAYED VOMITING: MAIN RESULTS: MEAN NUMBER OF VOMITING EPISODES DAY 2 THROUGH 5-7

Study	Treatment		Control		Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	N	Mean(SD)	N	Mean(SD)	95% CI	(%)	95% CI
Pearl 1999	15	0.36 (0.60)	16	0.08 (0.15)		22.8	0.28 [-0.03, 0.59]
Roscoe 2003	456	0.35 (0.88)	233	0.38 (1.20)		73.4	-0.03 [-0.20, 0.14]
Treish 2003	19	0.53 (0.83)	18	1.11 (1.44)		3.8	-0.58 [-1.34, 0.18]
Total (95% CI)	490		267			100.0	0.02 [-0.13, 0.17]

Test for heterogeneity chi-square=5.35 df=2 p=0.07 I^2 =62.7%

Test for overall effect z=0.26 p=0.8



Analysis 01.04. Comparison 01 ACUPUNCTURE-POINT STIMULATION (ALL TYPES) VERSUS CONTROL (ALL TYPES), Outcome 04 DELAYED NAUSEA. MAIN RESULTS. MEAN NAUSEA SEVERITY DAY TWO THROUGH DAYS FIVE TO SEVEN

Review: Acupuncture-point stimulation for chemotherapy-induced nausea or vomiting

Comparison: 01 ACUPUNCTURE-POINT STIMULATION (ALL TYPES) VERSUS CONTROL (ALL TYPES)

Outcome: 04 DELAYED NAUSEA. MAIN RESULTS. MEAN NAUSEA SEVERITY DAY TWO THROUGH DAYS FIVE TO SEVEN

Study	Treatment N	Treatment Mean(SD)	Control N	Control Mean(SD)	Standardised Mean Difference (Fixed) 95% CI	Weight (%)	Standardised Mean Difference (Fixed) 95% CI
Dibble 2000	8	2.04 (1.76)	9	3.64 (0.68)		1.9	-1.17 [-2.22, -0.12]
Pearl 1999	15	1.87 (0.83)	16	1.62 (0.76)		4.2	0.31 [-0.40, 1.02]
Roscoe 2002	13	2.78 (1.42)	25	3.03 (1.62)		4.6	-0.16 [-0.83, 0.51]
Roscoe 2003	465	2.30 (1.30)	233	2.26 (1.40)		84.5	0.03 [-0.13, 0.19]
Treish 2003	19	2.23 (2.08)	18	3.67 (2.49)		4.8	-0.62 [-1.28, 0.05]
Total (95% CI)	520		301			100.0	-0.02 [-0.17, 0.12]

Test for heterogeneity chi-square=9.04 df=4 p=0.06 I² =55.8%

Test for overall effect z=0.28 p=0.8

Analysis 02.01. Comparison 02 ACUPUNCTURE (MANUAL AND ELECTROACUPUNCTURE TRIALS COMBINED) VS. CONTROL, Outcome 01 ACUTE VOMITING. MAIN RESULTS: PROPORTION VOMITING IN FIRST 24 HOURS

Review: Acupuncture-point stimulation for chemotherapy-induced nausea or vomiting

Comparison: 02 ACUPUNCTURE (MANUAL AND ELECTROACUPUNCTURE TRIALS COMBINED) VS. CONTROL

Outcome: 01 ACUTE VOMITING. MAIN RESULTS: PROPORTION VOMITING IN FIRST 24 HOURS

Study	All Acupuncture n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dundee 1987	2/7	3/3		7.4	0.29 [0.09, 0.92]
Dundee 1988	3/10	6/10		10.6	0.50 [0.17, 1.46]
Shen 2000	26/37	55/67		69.3	0.86 [0.68, 1.09]
Streitberger 2003	4/41	7/39		12.7	0.54 [0.17, 1.71]
Total (95% CI)	95	119		100.0	0.74 [0.58, 0.94]

Total events: 35 (All Acupuncture), 71 (Control)

Test for heterogeneity chi-square=4.82 df=3 p=0.19 I² =37.8%

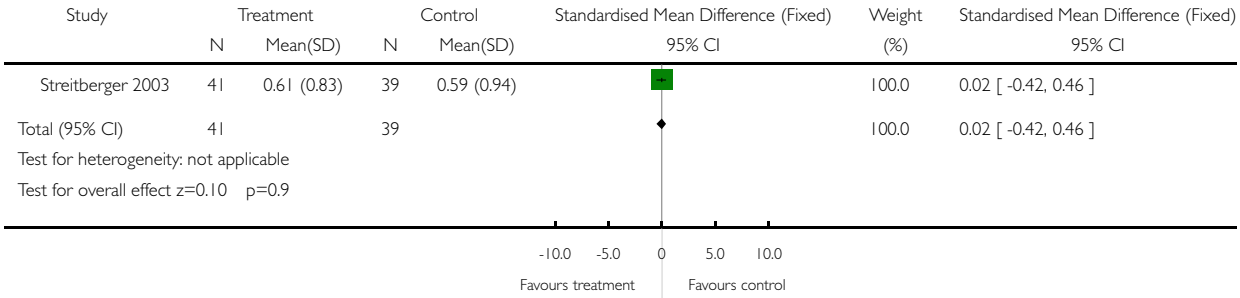
Test for overall effect z=2.47 p=0.01

Analysis 02.02. Comparison 02 ACUPUNCTURE (MANUAL AND ELECTROACUPUNCTURE TRIALS COMBINED) VS. CONTROL, Outcome 02 ACUTE NAUSEA. MAIN RESULTS. MEAN NAUSEA SEVERITY IN FIRST 24 HOURS

Review: Acupuncture-point stimulation for chemotherapy-induced nausea or vomiting

Comparison: 02 ACUPUNCTURE (MANUAL AND ELECTROACUPUNCTURE TRIALS COMBINED) VS. CONTROL

Outcome: 02 ACUTE NAUSEA. MAIN RESULTS. MEAN NAUSEA SEVERITY IN FIRST 24 HOURS

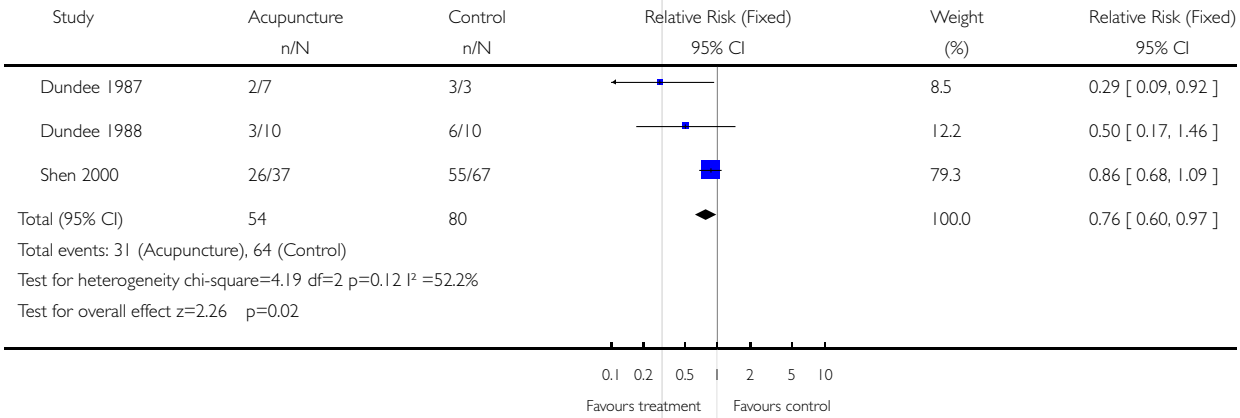


Analysis 03.01. Comparison 03 ELECTROACUPUNCTURE VS CONTROL, Outcome 01 ACUTE VOMITING. MAIN RESULTS: PROPORTION VOMITING IN FIRST 24 HOURS

Review: Acupuncture-point stimulation for chemotherapy-induced nausea or vomiting

Comparison: 03 ELECTROACUPUNCTURE VS CONTROL

Outcome: 01 ACUTE VOMITING. MAIN RESULTS: PROPORTION VOMITING IN FIRST 24 HOURS



Analysis 04.01. Comparison 04 MANUAL ACUPUNCTURE VS CONTROL, Outcome 01 ACUTE VOMITING. MAIN RESULTS: PROPORTION VOMITING IN FIRST 24 HOURS

Review: Acupuncture-point stimulation for chemotherapy-induced nausea or vomiting

Comparison: 04 MANUAL ACUPUNCTURE VS CONTROL

Outcome: 01 ACUTE VOMITING. MAIN RESULTS: PROPORTION VOMITING IN FIRST 24 HOURS

Study	Manual Acupuncture n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Streitberger 2003	4/41	7/39		100.0	0.54 [0.17, 1.71]
Total (95% CI)	41	39		100.0	0.54 [0.17, 1.71]
Total events: 4 (Manual Acupuncture), 7 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.04 p=0.3					

Analysis 04.02. Comparison 04 MANUAL ACUPUNCTURE VS CONTROL, Outcome 02 ACUTE NAUSEA. MAIN RESULTS. MEAN NAUSEA SEVERITY IN FIRST 24 HOURS

Review: Acupuncture-point stimulation for chemotherapy-induced nausea or vomiting

Comparison: 04 MANUAL ACUPUNCTURE VS CONTROL

Outcome: 02 ACUTE NAUSEA. MAIN RESULTS. MEAN NAUSEA SEVERITY IN FIRST 24 HOURS

Study	Manual Acupuncture N	Mean(SD)	Control N	Mean(SD)	Standardised Mean Difference (Fixed) 95% CI	Weight (%)	Standardised Mean Difference (Fixed) 95% CI
Streitberger 2003	41	0.61 (0.83)	39	0.59 (0.94)		100.0	0.02 [-0.42, 0.46]
Total (95% CI)	41		39			100.0	0.02 [-0.42, 0.46]
Test for heterogeneity: not applicable							
Test for overall effect z=0.10 p=0.9							

Analysis 05.01. Comparison 05 ACUPRESSURE VS CONTROL, Outcome 01 ACUTE VOMITING. MAIN RESULTS: PROPORTION VOMITING IN FIRST 24 HOURS

Review: Acupuncture-point stimulation for chemotherapy-induced nausea or vomiting

Comparison: 05 ACUPRESSURE VS CONTROL

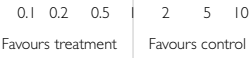
Outcome: 01 ACUTE VOMITING. MAIN RESULTS: PROPORTION VOMITING IN FIRST 24 HOURS

Study	Acupressure n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Noga 2002	5/60	5/60		8.0	1.00 [0.31, 3.28]
Roscoe 2003	47/251	57/249		92.0	0.82 [0.58, 1.15]
Total (95% CI)	311	309		100.0	0.83 [0.60, 1.16]

Total events: 52 (Acupressure), 62 (Control)

Test for heterogeneity chi-square=0.10 df=1 p=0.75 I^2 =0.0%

Test for overall effect z=1.09 p=0.3



Analysis 05.02. Comparison 05 ACUPRESSURE VS CONTROL, Outcome 02 ACUTE NAUSEA. MAIN RESULTS. MEAN NAUSEA SEVERITY IN FIRST 24 HOURS

Review: Acupuncture-point stimulation for chemotherapy-induced nausea or vomiting

Comparison: 05 ACUPRESSURE VS CONTROL

Outcome: 02 ACUTE NAUSEA. MAIN RESULTS. MEAN NAUSEA SEVERITY IN FIRST 24 HOURS

Study	Acupressure N	Acupressure Mean(SD)	Control N	Control Mean(SD)	Standardised Mean Difference (Fixed) 95% CI	Weight (%)	Standardised Mean Difference (Fixed) 95% CI
Dibble 2000	8	1.75 (2.66)	9	2.75 (1.39)		3.5	-0.46 [-1.42, 0.51]
Roscoe 2003	231	1.99 (1.47)	226	2.27 (1.55)		96.5	-0.19 [-0.37, 0.00]
Total (95% CI)	239		235			100.0	-0.19 [-0.38, -0.01]

Test for heterogeneity chi-square=0.29 df=1 p=0.59 I^2 =0.0%

Test for overall effect z=2.11 p=0.03

Analysis 05.03. Comparison 05 ACUPRESSURE VS CONTROL, Outcome 03 DELAYED VOMITING: MAIN RESULTS: MEAN NUMBER OF VOMITING EPISODES DAY 2 THROUGH 5-7

Review: Acupuncture-point stimulation for chemotherapy-induced nausea or vomiting

Comparison: 05 ACUPRESSURE VS CONTROL

Outcome: 03 DELAYED VOMITING: MAIN RESULTS: MEAN NUMBER OF VOMITING EPISODES DAY 2 THROUGH 5-7

Study	Acupressure N	Acupressure Mean(SD)	Control N	Control Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Roscoe 2003	230	0.31 (0.73)	233	0.38 (1.20)		100.0	-0.07 [-0.25, 0.11]
Total (95% CI)	230		233			100.0	-0.07 [-0.25, 0.11]

Test for heterogeneity: not applicable

Test for overall effect z=0.76 p=0.4

Analysis 05.04. Comparison 05 ACUPRESSURE VS CONTROL, Outcome 04 DELAYED NAUSEA. MAIN RESULTS. MEAN NAUSEA SEVERITY DAY 2 THROUGH DAYS 5-7

Review: Acupuncture-point stimulation for chemotherapy-induced nausea or vomiting

Comparison: 05 ACUPRESSURE VS CONTROL

Outcome: 04 DELAYED NAUSEA. MAIN RESULTS. MEAN NAUSEA SEVERITY DAY 2 THROUGH DAYS 5-7

Study	Acupressure N	Acupressure Mean(SD)	Control N	Control Mean(SD)	Standardised Mean Difference (Fixed) 95% CI	Weight (%)	Standardised Mean Difference (Fixed) 95% CI
Dibble 2000	8	2.04 (1.76)	9	3.64 (0.68)		2.9	-1.17 [-2.22, -0.12]
Roscoe 2003	235	2.24 (1.31)	233	2.26 (1.40)		97.1	-0.01 [-0.20, 0.17]
Total (95% CI)	243		242			100.0	-0.05 [-0.23, 0.13]

Test for heterogeneity chi-square=4.48 df=1 p=0.03 I^2 =77.7%

Test for overall effect z=0.53 p=0.6

Analysis 06.01. Comparison 06 NONINVASIVE ELECTROSTIMULATION VS CONTROL, Outcome 01 ACUTE VOMITING. MAIN RESULTS: PROPORTION VOMITING IN FIRST 24 HOURS

Review: Acupuncture-point stimulation for chemotherapy-induced nausea or vomiting

Comparison: 06 NONINVASIVE ELECTROSTIMULATION VS CONTROL

Outcome: 01 ACUTE VOMITING. MAIN RESULTS: PROPORTION VOMITING IN FIRST 24 HOURS

Study	Electrostimulation n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Pearl 1999	6/21	7/21		9.1	0.86 [0.35, 2.12]
Roscoe 2002	3/14	5/28		4.3	1.20 [0.33, 4.31]
Roscoe 2003	50/247	57/249		74.1	0.88 [0.63, 1.24]
Treish 2003	9/26	9/23		12.5	0.88 [0.42, 1.84]
Total (95% CI)	308	321		100.0	0.90 [0.67, 1.19]

Total events: 68 (Electrostimulation), 78 (Control)

Test for heterogeneity chi-square=0.22 df=3 p=0.97 I^2 =0.0%

Test for overall effect z=0.76 p=0.4

Analysis 06.02. Comparison 06 NONINVASIVE ELECTROSTIMULATION VS CONTROL, Outcome 02 ACUTE NAUSEA. MAIN RESULTS. MEAN NAUSEA SEVERITY IN FIRST 24 HOURS

Review: Acupuncture-point stimulation for chemotherapy-induced nausea or vomiting

Comparison: 06 NONINVASIVE ELECTROSTIMULATION VS CONTROL

Outcome: 02 ACUTE NAUSEA. MAIN RESULTS. MEAN NAUSEA SEVERITY IN FIRST 24 HOURS

Study	Electrostimulation N	Mean(SD)	Control N	Mean(SD)	Standardised Mean Difference (Fixed) 95% CI	Weight (%)	Standardised Mean Difference (Fixed) 95% CI
McMillan 1991	8	1.00 (0.76)	8	1.12 (0.65)		2.8	-0.16 [-1.14, 0.82]
Pearl 1999	15	1.87 (1.06)	16	1.37 (0.81)		5.3	0.52 [-0.20, 1.24]
Roscoe 2002	13	2.62 (1.46)	25	2.86 (1.53)		6.1	-0.16 [-0.83, 0.52]
Roscoe 2003	220	2.19 (1.59)	226	2.27 (1.55)		79.5	-0.05 [-0.24, 0.13]
Treish 2003	19	0.71 (1.56)	18	2.33 (3.12)		6.2	-0.65 [-1.31, 0.02]
Total (95% CI)	275		293			100.0	-0.07 [-0.23, 0.10]

Test for heterogeneity chi-square=5.64 df=4 p=0.23 I^2 =29.0%

Test for overall effect z=0.80 p=0.4

Analysis 06.03. Comparison 06 NONINVASIVE ELECTROSTIMULATION VS CONTROL, Outcome 03 DELAYED VOMITING: MAIN RESULTS: MEAN NUMBER OF VOMITING EPISODES DAY 2 THROUGH 5-7

Review: Acupuncture-point stimulation for chemotherapy-induced nausea or vomiting

Comparison: 06 NONINVASIVE ELECTROSTIMULATION VS CONTROL

Outcome: 03 DELAYED VOMITING: MAIN RESULTS: MEAN NUMBER OF VOMITING EPISODES DAY 2 THROUGH 5-7

Study	Electrostimulation		Control		Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	N	Mean(SD)	N	Mean(SD)	95% CI	(%)	95% CI
Pearl 1999	15	0.36 (0.60)	16	0.08 (0.15)		28.2	0.28 [-0.03, 0.59]
Roscoe 2003	226	0.39 (1.01)	233	0.38 (1.20)		67.0	0.01 [-0.19, 0.21]
Treish 2003	19	0.53 (0.83)	18	1.11 (1.44)		4.7	-0.58 [-1.34, 0.18]
Total (95% CI)	260		267			100.0	0.06 [-0.11, 0.22]

Test for heterogeneity chi-square=4.84 df=2 p=0.09 I^2 =58.7%

Test for overall effect z=0.69 p=0.5

Analysis 06.04. Comparison 06 NONINVASIVE ELECTROSTIMULATION VS CONTROL, Outcome 04 DELAYED NAUSEA. MAIN RESULTS. MEAN NAUSEA SEVERITY DAY 2 THROUGH DAYS 5-7

Review: Acupuncture-point stimulation for chemotherapy-induced nausea or vomiting

Comparison: 06 NONINVASIVE ELECTROSTIMULATION VS CONTROL

Outcome: 04 DELAYED NAUSEA. MAIN RESULTS. MEAN NAUSEA SEVERITY DAY 2 THROUGH DAYS 5-7

Study	Electrostimulation		Control		Standardised Mean Difference (Fixed)	Weight	Standardised Mean Difference (Fixed)
	N	Mean(SD)	N	Mean(SD)	95% CI	(%)	95% CI
Pearl 1999	15	1.87 (0.83)	16	1.62 (0.76)		5.4	0.31 [-0.40, 1.02]
Roscoe 2002	13	2.78 (1.42)	25	3.03 (1.62)		6.1	-0.16 [-0.83, 0.51]
Roscoe 2003	230	2.36 (1.30)	233	2.26 (1.40)		82.3	0.07 [-0.11, 0.26]
Treish 2003	19	2.23 (2.05)	18	3.67 (2.49)		6.2	-0.62 [-1.28, 0.04]
Total (95% CI)	277		292			100.0	0.03 [-0.14, 0.19]

Test for heterogeneity chi-square=4.81 df=3 p=0.19 I^2 =37.6%

Test for overall effect z=0.35 p=0.7