INTERVENTIONS FOR NAUSEA AND VOMITING IN EARLY PREGNANCY

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ABSTRACT

Background
Nausea and vomiting are the most common symptoms experienced in early pregnancy, with nausea affecting between 70 and 85% of women. About half of pregnant women experience vomiting.

Objectives
To assess the effects of different methods of treating nausea and vomiting in early pregnancy.

Search Strategy
We searched the Cochrane Pregnancy and Childbirth Group trials register (December 2002) and the Cochrane Central Register of Controlled Trials (The Cochrane Library, Issue 4, 2002).

Selection Criteria
Randomised trials of any treatment for nausea and/or vomiting in early pregnancy.

Data collection and analysis
Two reviewers assessed the trial quality and extracted the data independently.

Main Results
Twenty-eight trials met the inclusion criteria. For milder degrees of nausea and vomiting, 21 trials were included. These trials were of variable quality. Nausea treatments were: different antihistamine medications, vitamin B6 (pyridoxine), the combination tablet Debendox (Bendectin), P6 acupressure and ginger. For hyperemesis gravidarum, seven trials were identified testing treatments with oral ginger root extract, oral or injected corticosteroids or injected adrenocorticotropic hormone (ACTH), intravenous diazepam and acupuncture. Based on 12 trials, there was an overall reduction in nausea from anti-emetic medication (odds ratio 0.16, 95% confidence interval 0.08 to 0.33).

Reviewers' conclusions
Anti-emetic medication appears to reduce the frequency of nausea in early pregnancy. There is some evidence of adverse effects, but there is very little information on effects on fetal outcomes from randomised controlled trials. Of newer treatments, pyridoxine (vitamin B6) appears to be more effective in reducing the severity of nausea. The results from trials of P6 acupressure are equivocal. No trials of treatments for hyperemesis gravidarum show any evidence of benefit. Evidence from observational studies suggests no evidence of teratogenicity from any of these treatments.

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Jewell D, Young G Interventions for nausea and vomiting in early pregnancy (Cochrane Review). In: *The Cochrane Library*, Issue 4, 2003. Chichester, UK: John Wiley & Sons, Ltd.

BACKGROUND

Nausea and vomiting are the commonest symptoms consistently experienced in early pregnancy. Surveys report that nausea affects between 70% and 85% of pregnant women (Medalie 1957; Whitehead 1992; Gadsby 1993) and vomiting approximately 50% (Whitehead 1992; Gadsby 1993). Despite the popular name of 'morning sickness', only 17% of those with nausea experience it solely in the morning; for the others, it persists throughout the day (Whitehead 1992). It can also persist beyond the first trimester: in the Whitehead 1992 study, 13% of women reported it lasting beyond 20 weeks' gestation. Thirty-five per cent of women with paid employment lost time from work through nausea, and 26% lost time from housework (Gadsby 1993). Anecdotal evidence from members of the Cochrane Pregnancy and Childbirth Consumer Panel, who reviewed an earlier draft of this review, attest to the misery and serious disruption to everyday life that pregnant women can suffer from persistent nausea and vomiting. It is widely believed that the rate varies across different cultures but the perceived differences may be the result of different methodologies of reporting or different rates of referral to hospital (Fairweather 1968).

The aetiology is unknown although it has been suggested that it is a result of rising levels of human chorionic gonadotropin in the bloodstream. There is a consistent finding that nausea is less common in those women who subsequently experience miscarriages, and more common in twin pregnancies, but there are no other associations with pregnancy outcomes (Medalie 1957; Weigel 1989). Numerous treatments have been tried: Fairweather 1968 lists 30 that have been researched in addition to the traditional dietary interventions. It is also worth remembering that, up until quite recently, hyperemesis was a serious condition with a recorded mortality in the UK of three per million pregnancies for the years 1951 to 1960, compared with 159 per million in 1931 to 1940, and that termination of pregnancy was also widely practised when intravenous fluid replacement was less simple (Fairweather 1968).

OBJECTIVES

To assess the effectiveness of different methods of treating nausea and vomiting in early pregnancy.

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

All acceptably controlled trials of any treatments for nausea and/or vomiting in pregnancy, and for hyperemesis gravidarum.

Types of participants

Women suffering persistent nausea and/or vomiting in pregnancy where recruitment took place up to 20 weeks' gestation. All degrees of severity included, including trials of treatments for hyperemesis gravidarum.

Types of intervention

All interventions were included. Those identified by the search were as follows: for nausea and vomiting various antihistamine medications (dimenhydrinate, meclizine, buclizine, hydroxyzine, promethazine, thiethylperazine); the combination drug Bendectin (Debendox) containing doxylamine, dicyclomine and pyridoxine; vitamin B6 (pyridoxine); and acupuncture or acupressure. Acupressure is the application of pressure at an acupuncture point. It does not require needles and therefore can be administered by women themselves. The P6, or Neiguan point, is on the volar aspect of the wrist. Commercial products exist consisting of an elastic band holding a plastic disc to fit around the wrist. For hyperemesis gravidarum, trials were identified assessing treatment with powdered ginger root given orally, oral corticosteroids or adrenocorticotropic hormone (ACTH) injections, intravenous diazepam, oral ondansetron and acupuncture.

Types of outcome measures

Reduction in nausea and/or vomiting. Wherever possible, data were sought for numbers of women reporting substantial or complete relief from nausea. Some trials report continuous data. In two trials (Belluomini 1994; Smith 2000) results are reported using the Rhodes index. The Rhodes index consists of three subscales: nausea, vomiting (both with a range of 0 to 12) and retching (range 0 to 8). In two other trials (Sahakian 1991; Vutyavanich 1995) nausea was measured using a 10 cm visual analogue scale, graded 0 to 10. Where they were available, data on fetal outcomes and side-effects of medication were extracted.

SEARCH STRATEGY FOR IDENTIFICATION OF STUDIES

See: Cochrane Pregnancy and Childbirth Group search strategy

We searched the Cochrane Pregnancy and Childbirth Group trials register (December 2002).

The Cochrane Pregnancy and Childbirth Group's trials register is maintained by the Trials Search Co-ordinator and contains trials identified from:

1. quarterly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
2. monthly searches of MEDLINE;
3. handsearches of 30 journals and the proceedings of major conferences;
4. weekly current awareness search of a further 37 journals.

Details of the search strategies for CENTRAL and MEDLINE, the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service can be found in the 'Search strategies for identification of studies' section within the editorial information about the Cochrane Pregnancy and Childbirth Group.

Trials identified through the searching activities described above are given a code (or codes) depending on the topic. The codes are linked to review topics. The Trials Search Co-ordinator searches the register for each review using these codes rather than keywords.

In addition, we searched the Cochrane Central Register of Controlled Trials (The Cochrane Library, Issue 4, 2002) using the terms: Nausea or vomit* and Pregnan*.

METHODS OF THE REVIEW

Trials under consideration were evaluated for methodological quality and appropriateness for inclusion according to the prestated selection criteria, without consideration of their results. Individual outcome data were included in the analysis if they met the prestated criteria in 'Types of outcome measures'. Included trial data were processed as described in Clarke 2000.

All studies were read by both reviewers, who made independent assessments of quality of allocation concealment and who extracted data independently. Differences were resolved by discussion. When calculating odds ratios to quote in the text of the review, a fixed effects model has been used except where there is significant homogeneity between trials, when a random effects model is used.

DESCRIPTION OF STUDIES

See table of 'Characteristics of included studies'.

METHODOLOGICAL QUALITY

The quality of the studies reviewed here varies considerably. For instance, out of the 16 reports of placebo controlled trials of oral treatment for nausea, four (Cartwright 1951; Geiger 1959; McGuinness 1971; Vutyavanich 2001) state that the pills were in sealed bottles or envelopes. In three trials (Winters 1961; Diggory 1962; GP research gp 1963) allocation was by alternation, and in the remaining nine (Lask 1953; King 1955; Conklin 1958; Newlinds 1964; Erez 1971; GP research gp 1977; F-Rasmussen 1990; Sahakian 1991; Vutyavanich 1995) no information is given that would enable a judgement to be made about the method of randomisation. Similarly, three of the trials of acupressure do not state the precise method of randomisation (De Aloysio 1992; Belluomini 1994; O'Brien 1996). In Dundee 1988, women were described as allocated according to the day of the week on which they attended the hospital although, in a subsequent publication, (Dundee 1992) the authors state that the trial finished with patients randomised by weeks and not days. In Erez 1971, women were allocated to intervention or control groups in a ratio of 2:1, but no reason is given for this. In Knight 2001 allocation was by sealed opaque envelopes. In three trials for hyperemesis gravidarum, the interventions were injected preparations (Ylikorkala 1979; Sullivan 1996; Ditto 1999); in all three the method of randomisation was not stated. In Ylikorkala 1979 identical ampoules of adrenocorticotropic hormone (ACTH) or placebo injections were used; in Ditto 1999 and Sullivan 1996 it is not clear whether the nature of the treatment was concealed.

Women were recruited at different stages of their pregnancies. In the majority of studies where information is supplied, studies were limited to the first trimester. Such trials included Winters 1961, McGuinness 1971 and GP research gp 1977 (limited to the first 10 weeks' gestation), Lask 1953 (stated as being in early pregnancy), Erez 1971 (limited to the first two months' gestation) De Aloysio 1992 and Belluomini 1994. In Vutyavanich 1995, the entry period was up to 17 weeks' gestation; in Newlinds 1964, up to the end of the second trimester; in F-Rasmussen 1990, women were entered in the study up to 20 weeks' gestation; and in O'Brien 1996, up to 23 weeks' gestation. In Cartwright 1951, King 1955, Conklin 1958, Geiger 1959, Diggory 1962, GP research gp 1963, Dundee 1988 and Sahakian 1991, the stage of pregnancy during which recruitment took place is not stated. Similarly, there is very little information about the required severity of symptoms to justify invitation to participate in trials. The exceptions were: Winters 1961, where the women were entered with nausea two to three times daily; and Erez 1971 where women were entered with nausea and/or vomiting three times weekly for two weeks. The entry criteria for the trials of hyperemesis gravidarum were more clearly stated: in almost all cases (Ylikorkala 1979; F-Rasmussen 1990; Sullivan 1996; Safari 1998; Ditto 1999; Nelson-Piercy 2001) women were recruited where gestation was less than 16 weeks, with persisting vomiting unrelieved by hospital admission. In Sullivan 1996, Safari 1998, Ditto 1999 and Nelson-Piercy 2001, women had to have one or more additional features of ketonuria, weight loss or low serum potassium and the vomiting had to persist despite intravenous fluid replacement before they were recruited to the trial.

Given the nature of the problem under study, the outcome measures present no difficulty. Since it is a troublesome symptom, measuring symptomatic relief is the only valid measure, and there is unlikely to be any conflict between the choice made by women and their professional attendants. Failure of treatment has been assessed as those reporting little or no benefit of treatment, and the studies have used variable periods of observation. Unfortunately, only a minority of these studies provide any information on side effects (Cartwright 1951; Conklin 1958; Winters 1961; GP research gp 1963; Newlinds 1964; Erez 1971; McGuinness 1971) or fetal outcomes (Winters 1961; Erez 1971; Ylikorkala 1979); of those that did, some did not report findings on side effects or fetal outcomes in a form that could be included in a meta-analysis.

Because nausea is a problem that is worse in early pregnancy and frequently improves as pregnancy progresses, any trials using a crossover design must be treated with particular caution. In GP research gp 1977 and F-Rasmussen 1990, results have been taken only from the first treatment period. De Aloysio 1992 studied a combination of sham and real acupressure in a four sequence design. Here the results have been taken from the third period, the first in which one group had real acupressure to both wrists and the other group sham acupressure to both wrists. Hyde 1989, Evans 1993 and Bayreuther 1994 were all crossover studies in which no results were reported from the first treatment period, and all three have been accordingly excluded from the review.

Trials of acupressure also pose the specific problem regarding the choice of placebo, particularly when studying a problem such as nausea where the outcome measures are necessarily subjective. Dundee 1988 used two control groups, one using 'sham' acupressure at a point close to the elbow not

recognised as a standard acupuncture point, and one with no intervention at all. The results from both these groups have been combined as the control group in the meta-analysis. De Aloysio 1992 compared real treatment at the wrist provided by a band holding a plastic pointed device applying pressure to the P6 (Neiguan) point with sham acupressure provided by the same band with a blunted device. Belluomini 1994 compared real acupressure at the wrist with sham acupressure on the palm of the hand. O'Brien 1996 used three groups: comparing real acupressure at the wrist, with acupressure to a dummy point over the radius, and a control group receiving dietary advice only. Smith 2002 used four groups: traditional Chinese acupuncture, P6 acupuncture, sham acupuncture with needles inserted close to but not at traditional acupuncture points, and a control group given dietary advice and weekly contact with the research team. When true blinding of the experimental and placebo treatments is difficult then the dropout rate may have a strong influence on the result, and the completion rates of 57% (Dundee 1988) and 67% (Belluomini 1994) are regrettably low. Smith 2002 achieved completion rates of 95% at seven days and 80% (including 72% in the control group) at 26 days. Mamo 1995 has not been included in this review because the reporting is not adequate to judge the quality of the trial or the data reported.

RESULTS

Twenty-eight trials met the inclusion criteria. For nausea and vomiting, we have included trials testing various drugs (12 trials, 1557 women); vitamin B6 (two trials, 416 women); extract of ginger (one trial, 70 women) and acupuncture or acupressure (six trials, 1309 women). For hyperemesis we have included seven trials, 247 women. In most of the meta-analyses the trials show considerable heterogeneity, so a random effects model has been used when calculating summary statistics.

The analysis for all antiemetic drugs, using data from 12 trials, shows a beneficial reduction in the incidence of nausea with an odds ratio (OR) of 0.16 (95% confidence interval (CI) 0.08 to 0.33). The results suggest that the drugs tend to cause sleepiness, as would be expected by experience with their use outside pregnancy and childbirth: the odds ratio is 2.24, and the 95% confidence interval (1.05 to 4.75) does not include unity. As discussed above, the numbers of trials reporting effects on fetal outcomes are small, and the result is a statistic with wide confidence intervals, with no evidence of any significant effect. This analysis shows considerable heterogeneity between trials. This might be due to combining data from trials on different drugs, but the same is seen in two further analyses combining groups of drugs as antihistamines and phenothiazines. A third analysis of Bendectin (Debendox) combining data from three trials shows no significant heterogeneity. All three subgroup analyses shows similar magnitude of effect to the combined analysis.

Bendectin was a combination pill, specifically marketed for use in pregnancy, containing doxylamine and pyridoxine (vitamin B6). An older formulation also contained dicyclomine. Pyridoxine (vitamin B6) on its own has been tested in two trials (Sahakian 1991; Vutyavanich 1995). Here, there is no evidence of an effect on vomiting (OR 0.64, 95% CI 0.18 to 2.26) but the continuous data suggest effectiveness in reducing the severity of nausea. The two trials used very different doses of medication: Sahakian 1991, 75 mg daily, and Vutyavanich 1995, 30 mg daily. The two trials report similar effects on nausea score, but only Sahakian 1991 shows an effect on vomiting. It is possible that there is a dose response effect here, with the higher dose showing greater effect in those with worse symptoms. Unfortunately, there are not enough data to draw such conclusions with any confidence. The nature of the continuous data also makes it difficult to draw general conclusions, other than non-specific benefit, that can be applied to other populations.

One trial (Vutyavanich 2001) has compared ginger with placebo, each in capsule form, for nausea and vomiting in pregnancy, with 96% of women completing the trial. It reports benefit both for vomiting (OR 0.31, 95% CI 0.12 to 0.85) and for nausea (OR 0.06, 95% CI 0.02 to 0.21), and no adverse effects.

Six analyses are shown, illustrating the effects of acupuncture or P6 acupressure. The dichotomised data on morning sickness give odds ratios of 0.25 (95% CI 0.14 to 0.43) when compared with no treatment, and 0.35 (95% CI 0.12 to 1.06) when compared with sham or dummy acupuncture or acupressure. These effects are comparable to those obtained with drugs. Following concerns over the allocation process used in Dundee 1992 (see above), a sensitivity analysis was carried out excluding the data from Dundee 1992. This had only a marginal effect on the summary odds ratio (data not shown). Analysis of continuous data uses results from only two trials (Belluomini 1994; Smith 2002)

comparing acupuncture or acupressure with sham acupuncture or acupressure and produces a summary statistic where the 95% CI includes no effect in both cases. The same is true for the two analyses (one for nausea and one for vomiting) comparing acupuncture with a control group receiving no acupuncture, which uses data from Smith 2002. The data from O'Brien 1996 and Knight 2001 are not in a form that can be included in a meta-analysis. However, both trials achieved high rates of completion. Completion rates were 92.5% of those recruited completing the trial protocol in O'Brien 1996, and 80% in Knight 2001; otherwise, both these trials were conducted to a high standard. O'Brien 1996 showed no benefit of acupressure compared with either sham acupressure or no treatment. Knight 2001 conducted a careful trial using more traditional Chinese diagnosis with acupuncture at various points (always including the P6 point) compared with a form of sham acupuncture using pressure but no skin penetration, at points distant from traditional acupuncture points. This trial showed real acupuncture to have no greater effect than sham acupuncture.

Six analyses are shown of treatments for hyperemesis gravidarum, but only one (ACTH or steroids compared with placebo) contains more than a single trial. None of the studies shows evidence of benefit of intervention over control in the initial resolution of vomiting. Rates of resolution with placebo are high (Ylikorkala 1979; Ditto 1999). Any trials would have to be large to show any clinically important benefit at conventional levels of statistical significance. All of these trials are, by this standard, seriously underpowered. This conclusion is supported by the findings in the excluded N-of-1 trial (Magee 1996) where there was no difference between ascorbic acid and oral prednisolone. There is some indication that ginger may be beneficial but the results of this crossover trial are not easy to interpret (F-Rasmussen 1990). However, two trials showed that treatment, either with oral methylprednisolone (Safari 1998) or with intravenous diazepam (Ditto 1999) appeared to reduce the rate of readmission to hospital, and intravenous diazepam also reduced the length of stay in hospital (Ditto 1999). It is difficult to interpret these data given the absence of any patient-generated data on acceptability (for instance on the toleration of other effects of diazepam) and the small numbers in each case.

Randomised controlled trials tend only to give limited information on unwanted effects of treatments. A review article has attempted to quantify harms in this field by summarising the results of observational studies (Mazzotta 2000). This review finds no evidence of teratogenicity from treatment with Bendectin (data on 17,427 women taking the medication and 141,237 controls), antihistamines (4688 exposed women and 73,138 controls) or pyridoxine (458 exposed women and 911 controls).

DISCUSSION

Bendectin (Debendox) was widely prescribed to women for nausea in the first trimester and was the most commonly taken medication in pregnancy. However, in 1983 it was withdrawn from sale as a result of concern over possible teratogenic effects. Reviewing all studies to have reported on its teratogenicity, Bracken et al (Bracken 1989) concluded that the evidence provides no support for such fears, and the review by Mazzotta (Mazzotta 2000) confirms this view. Nevertheless, this preparation has been withdrawn, with the result that the only medications available are those where considerably less is known about their teratogenic potential.

REVIEWER'S CONCLUSIONS

Implications for practice

Most of the drugs listed in this review have been shown to be more effective than placebo in reducing nausea and vomiting. Of the drugs listed, Pyridoxine (Vitamin B6) 10 to 25 mg three times a day is the least likely to cause side-effects. According to standard therapeutic practice, it would seem wise to start treatment with the lower dose. The most recent evidence that fresh ginger root is beneficial is encouraging. The authors of this single paper (Vutyavanich 2001) caution that the active ingredient in ginger is not known and the composition may vary widely according to different regions of origin and postharvesting factors. The evidence on P6 acupuncture or acupressure is mixed. It has not been shown to be clearly more effective than sham or dummy acupressure, or than standard dietary and lifestyle advice. Rest and small amounts of carbohydrate, such as biscuits, are widely believed to be helpful.

Implications for research

The previous version of this review (CDSR 2003) specifically requested research on ginger (now answered in the single trial by Vutyavanich 2001) and large scale follow-up studies to assess possible harmful effects (now answered in the review by Mazzotta 2000). Trials of treatment for hyperemesis will continue to be difficult, from a combination of rarity and the high rate of resolution through routine treatment with intravenous fluids, presumably the result of correcting ketosis.

ACKNOWLEDGEMENTS

None.

POTENTIAL CONFLICT OF INTEREST

None known.

TABLES

Characteristics of included studies

Study	**Belluomini 1994**
Methods	Method of randomisation not stated.
Participants	Pregnant women with nausea with or without vomiting, and 12 weeks' gestation or less by completion of the study. 90 women entered in trial; 60 completed, 30 in each arm.
Interventions	Experimental treatment of P6 acupressure (point on anterior surface of wrist), control treatment of acupressure applied to a sham point on palmar surface of hand proximal to 5th metacarpal, each applied for 10 minutes, four times a day for 7 days.
Outcomes	Nausea and vomiting scores at end of treatment, measured by two subscales of Rhodes index, each graded 0-12.
Notes	Note high rate of dropout. Some percentages reported on effects on vomiting within each group who were vomiting at the outset, but what the denominator is in these cases is not clear.
Allocation concealment	C
Study	**Carlsson 2000**
Methods	Numbered envelopes.
Participants	40 women admitted with hyperemesis not responding to conventional outpatient therapy. Not stated if participants were all ketotic. 19 women received deep acupuncture first (17 completed); 21 women superficial acupuncture first (16 competed).
Interventions	Crossover treatment of active (deep) acupuncture at P6 point compared with placebo (superficial) acupuncture and lateral side of forearm, both given for 30 minutes, 3 times a day.

Outcomes	Persistent vomiting on day 3 (ie only results from first period used).
Notes	Some concern over randomisation, since active group in first period has worse nausea scores on VAS at baseline.
Allocation concealment	A
Study	**Cartwright 1951**
Methods	Identical tablets in sealed containers in traditional double-blind design.
Participants	Unclear: women described as having nausea with or without vomiting. 77 women randomised, 39 to treatment, 38 to control. All competed.
Interventions	Dimenhydrinate (Dramamine) 100 mg twice daily and similar placebo twice daily.
Outcomes	Persisting nausea.
Notes	Side-effect reported of sleepiness in 20.5% of experimental group; 10.5% of placebo group.
Allocation concealment	A
Study	**Conklin 1958**
Methods	Allocation to different treatment groups described as arbitrary.
Participants	58 women attending outpatient department with nausea and vomiting severe enough to warrant treatment but mild enough not to need admission to hospital. 40 in treatment groups, 18 in placebo groups. All completed.
Interventions	Active treatment of buclizine 50 mg, with or without vitamin B12 25 mcg, or buclizine alone 25 mg or meclizine 25 mg with pyridoxine 50 mg. Control tablets of placebo or vitamin B12 25 mcg. All given twice daily for 7 days.
Outcomes	Not having 'marked improvement' or 'complete relief' of symptoms in the course of therapy.
Notes	Note that there were 6 treatment groups in all. Side-effects reported: drowsiness in 7 out of 15 on buclizine; 3 out of 11 on placebo.
Allocation concealment	C
Study	**De Aloysio 1992**
Methods	Randomisation stated to be according to a table of random numbers.
Participants	60 women at 7-12 weeks' gestation, with nausea and vomiting who had not received antiemetic treatment for at least 3 days before admission to the trial. 30 women in acupressure group (26 completed); 30 in placebo group (28 completed).
Interventions	Active treatment P6 acupressure applied as a band attached to the wrist applying pressure to the P6 point. Placebo treatment was a similar band with the point blunted, not exerting pressure on the P6 point. Complex design in which each type of band was put on each wrist in sequence. Date for meta-analysis taken from third phase when one group had active treatment to both wrists and the other placebo treatment to both wrists, for 72 hours (26 in treatment group, 28 in control group).
Outcomes	Morning sickness.
Notes	
Allocation	C

concealment	
Study	**Diggory 1962**
Methods	Women assigned 'in sequence' to one of four groups.
Participants	Women attending antenatal clinic complaining of nausea or vomiting. Number originally recruited not stated. Outcome data available on 76 women in treatment groups, 34 in placebo group.
Interventions	Group 1: diet sheet only (details not stated). Groups 2, 3 and 4 all received diet sheet with tablets. Group 2 placebo tablets, group 3 meclizine 25 mg in the morning and 50 mg at night; group 4 meclizine 25 mg and 50 mg at night with pyridoxine 50 mg in the morning and 100 mg at night. Data from group given diet sheet alone (n = 29) excluded from meta-analysis.
Outcomes	Nausea.
Notes	
Allocation concealment	C
Study	**Ditto 1999**
Methods	Randomisation stated to be according to a random number table.
Participants	50 women at < 16 weeks' gestation, with persistent nausea and vomiting for a week with one or more of: ketones in the urine, weight loss > 5% since onset of symptoms, serum potassium < 3.4 mmol. 25 women in diazepam group; 25 in IV fluid only group - all 50 completed.
Interventions	All women given IV fluids, with either diazepam 10 mg twice daily IV followed by 5 mg twice daily for a week or no added IV drugs and oral placebo tablets twice daily for a week.
Outcomes	Treatment failure by day 2, defined as vomiting more than 5 times a day. Secondary outcomes were a reduction in nausea score; length of hospital stay; readmission rate.
Notes	
Allocation concealment	B
Study	**Dundee 1988**
Methods	Randomised by day of attendance; later on by week.
Participants	350 women attending hospital antenatal clinic. 119 women in real acupressure group (58 completed); 112 in dummy acupressure group (60 completed); 119 in control group (83 completed).
Interventions	3 groups: real acupressure (pressure applied to P6 point); sham acupressure (pressure applied to point close to right elbow) - both for 5 minutes every 4 hours on 4 successive mornings - and control group without treatment and asked only to complete record form.
Outcomes	Severe or troublesome morning sickness over 4 days. Data available for 119 women in P6 acupressure group; 112 in dummy acupressure and 119 in control group.
Notes	The method of randomisation is clearly unsatisfactory. It could have been subverted by professionals ensuring patients were seen on particular days of the week, or by patients asking for this to be arranged. We are seeking further

	information from the authors of the study to find out whether it happened. We feel that such subversion is unlikely. It does, however, potentially introduce a differential placebo effect between intervention and control groups. We have included in the meta-analysis a sensitivity analysis which excludes the data from this study. For purposes of data, the dummy acupressure and control group data have been added together. Trial noted a larger number of dropouts from the P6 group. If analysed on intention to treat the difference between 'real' and 'dummy' acupressure disappeared.
Allocation concealment	C
Study	**Erez 1971**
Methods	Method of randomisation not stated. 2:1 allocation.
Participants	150 women in first two months of pregnancy attending antenatal clinic of naval hospital, reporting recurrent nausea and had vomited at least 3 times per week for 2 weeks. 100 women in active group, 50 in placebo group (all completed in each group).
Interventions	Hydroxyzine 25 mg (100 women) or placebo (50 women), twice daily for 3 weeks.
Outcomes	No relief from symptoms.
Notes	Equal numbers of miscarriages in two groups. 7 reported drowsiness in hydroxyzine group.
Allocation concealment	C
Study	**F-Rasmussen 1990**
Methods	Randomisation not detailed.
Participants	30 women initially recruited before 20 weeks' gestation, with vomiting severe enough to result in admission to hospital. 3 excluded in initial assessment period; 27 available for assessment (14 in treatment group, 13 in control group).
Interventions	Powdered ginger root, 250 mg or placebo tablets of lactose, each four times daily for 4 days.
Outcomes	Based on a scoring system to measure relief from symptoms.
Notes	Crossover trial, with results taken only from the first treatment period. At end of second period, women asked to state a preference for one or other treatment. 70.4% preferred ginger, 14.8% placebo, and 14.8% unable to state a preference.
Allocation concealment	C
Study	**GP research gp 1963**
Methods	Alternate allocation treatment or control.
Participants	76 women (40 in treatment group, 36 in control group). No other details (eg parity, age) given. All completed.
Interventions	Meclozine and pyridoxine to experimental group; pyridoxine alone to control group. Doses of each not stated, treatment for 1 week.
Outcomes	Nausea, assessed one week after starting treatment.
Notes	Side-effects reported more commonly in experimental group (21% compared with 11%). 20% of all cases on active treatment reported sleepiness, compared with 6%

	of those in placebo group.
Allocation concealment	C
Study	**GP research gp 1977**
Methods	Crossover trial. Method for deciding first treatment not stated.
Participants	56 women recruited with nausea and/or vomiting in the first 10 weeks' gestation. 28 in active group (26 completed); 28 in placebo group (26 completed).
Interventions	Debendox (dicyclomine, doxylamine and pyridoxine) with extra 10 mg pyridoxine, compared with placebo with extra 10 mg pyridoxine. Both given as 2 tablets at night, with instructions to take extra tablet in the morning if symptoms persist.
Outcomes	Results taken from first treatment period only. Numbers reporting nausea at the end of the first week used in meta-analysis; from 24 in treatment group, 26 in control group.
Notes	Results inferred from table where the total numbers of patient days are reported.
Allocation concealment	B
Study	**Geiger 1959**
Methods	Pills in sealed envelopes. Randomisation not otherwise stated.
Participants	110 women, no other details supplied. 53 women in Bendectin group (52 completed); 57 in placebo group (all completed).
Interventions	Bendectin tablets or placebo, 2 at night. If no better after 2-3 days to add further tablets each morning.
Outcomes	Numbers with persisting nausea, out of 52 women in treatment group, 57 in control group. Time of assessment not stated.
Notes	
Allocation concealment	A
Study	**King 1955**
Methods	Method of randomisation not stated.
Participants	Numbers and details of participants recruited to trial not stated. Data available on 60 in active group; 40 in placebo group.
Interventions	Meclizine tablets or placebo given for three days, dose not stated.
Outcomes	Failure of treatment, meaning no change in symptoms while taking the tablets. Data reported on 60 in treatment group, 40 in control group.
Notes	Interesting approach on the part of the investigator. Told the women that the tablets were new, and very expensive. This might have the effect of enhancing any placebo effect.
Allocation concealment	C
Study	**Knight 2001**
Methods	Sealed envelopes.
Participants	55 women attending single hospital in SW of England, at 6-10 weeks' gestation

	complaining of nausea with or without vomiting. 28 women in intervention group (22 completed); 27 in control group (22 completed).
Interventions	Real acupuncture, according to traditional Chinese diagnosis (but always including acupuncture at P6 point), compared with sham treatment using blunt cocktail sticks taped not at acupuncture points. Treatments given twice weekly for one week then weekly for two weeks.
Outcomes	Nausea assessed on VAS (measured 0-100), three days after first treatment.
Notes	Well conducted trial. For instance missing values all included assuming no change. 4 sets of results in study, each 3 days after treatment, all showed no difference between groups.
Allocation concealment	A
Study	**Lask 1953**
Methods	Method of randomisation not stated.
Participants	Women specifically complaining of vomiting in early pregnancy. Data reported on 120 women, 60 in each group.
Interventions	Active treatment of either mepyramine 100 mg or promethazine 25 mg, or control of lactose tablets, each to be taken one at night for three nights.
Outcomes	No improvement in symptoms.
Notes	Not clear in this trial how many or who received either of the active preparations.
Allocation concealment	C
Study	**McGuinness 1971**
Methods	Tablets in sealed bottles, randomisation not otherwise stated.
Participants	Women complaining of nausea or vomiting in the first trimester of gestation. Total number randomised not reported. Data available on 41 women in active group; 40 in placebo group.
Interventions	Debendox tablets (combination of dicyclomine, doxylamine and pyridoxine), or lactose tablets as placebo, 2 each night for 14 nights.
Outcomes	Failure of symptoms to improve on medication, using a 5 point grading scale. Data reported on 81 women, 41 in treatment group, 40 in control group.
Notes	Side-effects reported: in Debendox group 12 out of 41, 29% (a total of 8 reporting feeling tired, weak, lack of energy or drowsiness); in placebo group 6 in 40, 15% (3 reporting tiredness or sleepiness).
Allocation concealment	A
Study	**Nelson-Piercy 2001**
Methods	Computer generated allocation stratified by study centre, packs issued by hospital pharmacy.
Participants	25 women admitted with hyperemesis (ketonuria on admission), dependent on IV fluids for at least one week (first admission) or 24 hours (second or subsequent admission). 13 women in intervention group (12 completed), 12 in placebo group (all completed).
Interventions	Oral prednisolone 20 mg or placebo tablets, twice daily for one week. Experimental

	group: if still vomiting after 72 hours changed to equivalent hydrocortisone IV.
Outcomes	Persistent vomiting at one week. Also numbers readmitted.
Notes	Clinicians blinded to study medication.
Allocation concealment	A
Study	**Newlinds 1964**
Methods	Method of randomisation not stated.
Participants	225 pregnant women recruited, complaining of nausea in first and second trimester. 112 in active group (93 completed); 113 in control group (87 completed). Women not included in analysis because: not returning for assessment, not taking tablets, or transfer to another hospital).
Interventions	Active treatment of thiethylperazine (Torecan) 10 mg, or placebo pills of lactose, each three times a day for 28 days.
Outcomes	Poor response to treatment or unclassified after 28 days' treatment. Data recorded on 93 women in treatment group, 87 in control group.
Notes	Side-effects reported in 12 out of 93 women in experimental group (4 reports of drowsiness) and 10 out of 87 in control group (3 reports of drowsiness). In published report it states: "the patients were not told they were taking part in a trial".
Allocation concealment	C
Study	**O'Brien 1996**
Methods	Block randomisation, details not stated.
Participants	161 women primarily recruited through newspaper advertisements; gestation range 4-23 weeks, mean 10 weeks. 54 women in acupressure group, 53 in placebo group; 54 in control group. 149 completed the study, distribution of dropouts between groups not reported.
Interventions	Three groups: acupressure applied at the P6 point, both wrists (experimental group, n = 54); acupressure applied to a dummy point at the wrist, over the radius (placebo group, n = 53); and a control group given dietary advice only (n = 54). Interventions took place for 3 days.
Outcomes	Rhodes score completed twice daily for the duration of the study.
Notes	Women in all three groups reported significant decreases in nausea, and there was no difference between the three groups in either nausea or vomiting.
Allocation concealment	C
Study	**Safari 1998**
Methods	Randomisation by computer generated random numbers. Tablets in sealed containers.
Participants	40 women, gestation < 16 weeks, with persistent vomiting, ketones in the urine and weight loss, where the vomiting did not resolve with intravenous fluid replacement. 20 women in methylprednisolone group (17 completed); 20 in promethazine group (18 completed).
Interventions	Methylprednisolone orally, 16 mg 3 times a day for 3 days, tapering to nil over 2

	weeks, or promethazine 25 mg 3 times a day for 2 weeks.
Outcomes	Resolution of vomiting within 2 days of starting treatment; readmission to hospital within 2 weeks of starting treatment.
Notes	
Allocation concealment	A
Study	**Sahakian 1991**
Methods	Method of randomisation not stated.
Participants	Entry criteria not stated. 74 women recruited. 59 completed study, 31 in treatment group, 28 in control group.
Interventions	Vitamin B6 tablets, 25 mg or placebo tablets, each three times daily for 3 days.
Outcomes	Women continuing to vomit after 3 days of therapy. Also nausea assessed on a 10 cm VAS, graded 0-10. Data used in meta-analysis used mean change in VAS, measured in cm, averaged out for 3 days of therapy.
Notes	
Allocation concealment	A
Study	**Smith 2002**
Methods	Block randomisation, details not otherwise stated.
Participants	Women at less than 14 weeks' gestation, n = 593. 148 women in traditional acupuncture group (135 at day 7); 148 in P6 group (138 at day 7); 148 in sham acupuncture group (134 at day 7); 149 in no acupuncture control group (127 at day 7).
Interventions	A four arm trial comparing: traditional Chinese acupuncture; P6 acupuncture; sham acupuncture (needles inserted into an area close to but not on acupuncture points); and no acupuncture; this last group given standard advice on diet and lifestyle, and contacted by telephone weekly during trial. Note that the acupuncture received by women in the traditional acupuncture group always included acupuncture at the P6 point. Treatments given twice weekly for first week, then weekly for a further three weeks.
Outcomes	Nausea and vomiting subscales of Rhodes scales (graded 0-12) completed on day 7.
Notes	For the purposes of the meta-analysis, only data from the P6 acupuncture group have been included. More data have been requested from the author.
Allocation concealment	D
Study	**Sullivan 1996**
Methods	Participants randomised by the pharmacy. Medications supplied so that they could not be identified.
Participants	30 women admitted with hyperemesis gravidarum. Hyperemesis was defined as requiring two of the following: 2.25 kg weight loss; ketonuria; hypokalaemia (K < 3.0 mmol) or hyponatraemia (Na < 134 mmol) requiring intravenous replacement; positive serum test for acetone; more than two visits to the obstetric emergency department for hyperemesis requiring intravenous hydration or promethazine suppositories. 15 women in each group, all 30 completed.

Interventions	10 mg ondansetron IV every 8 hours, or 50 mg promethazine IV every 8 hours for 48 hours.
Outcomes	Those with persistent vomiting after 48 hours.
Notes	Days of hospitalisation and doses of medication similar in two groups. More women in promethazine group had side effect of sedation. Note: described as a pilot study.
Allocation concealment	A
Study	**Vutyavanich 1995**
Methods	By random numbers.
Participants	342 women attending antenatal clinic at Maharaj Nakorn Chiang Mai Hospital in Thailand, who had attended the clinic for the first time at less than 17 weeks' gestation. 173 initially allocated to treatment group, 169 to control group. Data reported on 169 women in treatment group and 167 in control group.
Interventions	Identical looking tablets of pyridoxine 10 mg or placebo three times a day for 5 days.
Outcomes	Number of vomiting episodes. Severity of nausea graded using a visual analogue scale, graded 0-10, during 5 days of study. Data used in meta-analysis used mean change in VAS, measured in cm, averaged out for 5 days of therapy.
Notes	Pyridoxine brought about a greater reduction in mean nausea scores than the placebo.
Allocation concealment	A
Study	**Vutyavanich 2001**
Methods	Sealed opaque envelopes. Clinicians blind to study. allocation.
Participants	70 women before 17 weeks gestation, with nausea, with or without vomiting. 32 in intervention group, all completed, 38 in placebo group, 35 completed.
Interventions	Ginger capsules, 250 mg or equivalent placebo capsules, each four times daily for 4 days.
Outcomes	Vomiting or failure to improve after 4 days.
Notes	Description of active treatment: fresh ginger root chopped and baked, then ground and weighed and packed into capsules.
Allocation concealment	D
Study	**Winters 1961**
Methods	Alternate allocation to pills or placebos.
Participants	394 women 4-12 weeks' gestation, with nausea 2-3 times daily. 199 in treatment group, 195 in control group. All women completed.
Interventions	2 components of the trial. Either trimethobenzamide 200 mg 1 hour before meals and at bedtime compared with placebo, or trimethobenzamide 300 mg with 25 mg pyridoxine compared with placebo, both three times daily for 10 days.
Outcomes	Persisting nausea or worse.
Notes	Stated (but data not supplied) that there was no difference between the two groups in side-effects and no disturbance of labour or fetal outcome.

Allocation concealment	C
Study	**Ylikorkala 1979**
Methods	Injections given in numbered ampoules, randomisation not otherwise stated.
Participants	32 women admitted to hospital with vomiting, where the vomiting did not stop spontaneously after 2 days stay. 16 women in each group, all completed.
Interventions	Daily intramuscular injections of 0.5 mg synthetic ACTH or placebo for 4 days.
Outcomes	Persistence of vomiting during hospital stay.
Notes	Note that rates of readmission, spontaneous abortion, preterm labour and birthweight of fetuses are the same in both groups. In the introduction to this trial the authors state that there is no dysfunction in the pituitary-adrenal axis in hyperemesis and levels of ACTH and cortisol are higher in hyperemesis than in normal pregnancy. Rationale for the trial is the ACTH had been used for this condition for 20 years at the time the trial was done.
Allocation concealment	A

ACTH: adrenocorticotropic hormone
IV: intravenous
SW: south west
VAS: visual analogue scale

Characteristics of excluded studies

Study	Reason for exclusion

	women participating. Results only given at the end of study as subjective impression whether acupressure had helped or not. This data are considered too subjective to be included in a review.
Luz 1987	Trial to assess the effect of bromopride on nausea and vomiting during pregnancy registered on Oxford Database of Perinatal Trials. Recruitment and follow up recorded as complete - December 1980. Numerous letters to the author to obtain unpublished data or learn what had become of this trial, the latest in January 2001, have not been answered.
Magee 1996	An N of 1 trial. Well conducted trial on a single patient with hyperemesis gravidarum treated with oral prednisolone 50 mg daily or ascorbic acid 100 mg daily, in a double blind crossover design. The patient felt better on ascorbic acid but there were no differences in the scores of nausea or vomiting.
Mamo 1995	Trial of acupressure bands. Women in placebo group given counselling and dietary advice. Total number of women in trial = 38. 11% in intervention group received anti-emetic drugs compared with 37% in group B. Trial excluded because no details of randomisation, dropouts or the denominators in the two study groups.
Norheim 2001	Trial comparing acupressure wristbands with placebo wristbands for nausea and vomiting in pregnant women at 8 to 12 weeks' gestation (n = 97). Insufficient data in published report concerning numbers of participants randomised to and withdrawing from the different groups. The authors of this Cochrane Review are requesting further data from the authors.
Steele 2001	Trial comparing acupressure wristbands with placebo wristbands for nausea and vomiting in pregnant women at less than 13 weeks' gestation (n = 138). The trial reported significantly less frequency and severity of nausea and vomiting in the active treatment group. However, the paper presents three separate but related problems: (1) Randomisation was by participants picking out from a box packets containing either active or placebo bands, together with instructions for use. Since active bands had a plastic button and placebo bands did not, it may have been possible to feel through the packing whether the bands were active or not. A considerable imbalance in the numbers in each group (85 in active group, 53 in placebo group) supports a strong suspicion that the randomisation may have been being subverted. (2) The participants in the placebo group were offered active bands at the end of the study period. (3) The data were analysed using one-tailed tests. Concerns that (2) and (3) suggest that the investigators held a strong prior belief about the effectiveness of acupressure wristbands. This, combined with the concerns over randomisation, makes the findings unreliable.
Weiner 1990	Trial to evaluate the efficacy of promethazine versus metoclopramide in the treatment of hyperemesis gravidarum, registered on Oxford Database of Perinatal Trials. Numerous letters to the author to obtain unpublished data or learn what had become of this trial, the latest in January 2001, have not been answered.
Werntoft 2001	Three arm trial comparing: acupressure wristbands correctly placed over the P6 point; the same wristbands incorrectly placed; no treatment. Data collected on 60 women. However, it appears that 80 were randomised, and unknown numbers in each group withdrew. The authors of the Cochrane Review are requesting further information from the authors concerning numbers in each group.

n: number

Characteristics of ongoing studies

Study	**Smith 2000b**
title	
Participants	Pregnant women, at less than 16 weeks' gestation, with nausea, dry retching, or vomiting, and not clinically dehydrated at the time of trial entry.

Participants	Pregnant women, at less than 16 weeks' gestation, with nausea, dry retching, or vomiting, and not clinically dehydrated at the time of trial entry.
Interventions	Ginger, compared with vitamin B6.
Outcomes	Rhodes index of nausea and vomiting: SF36 to measure quality of life.
Starting date	July 2000.
Contact information	Caroline Smith, Clinical Trials Unit, Department of Obstetrics and Gynaecology, University of Adelaide, SA 5006, Australia. Email: caroline.anne.smith@adelaide.edu.au tel: +61 8 82047565.
Notes	

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** Indicates the major publication for the study*

GRAPHS

To view a graph or table, click on the outcome title of the summary table below.

To view graphs using MetaView, click on the "Show metaview" link at the top of the graph.

01 All antiemetic medication compared with placebo				
Outcome title	No. of studies	No. of participants	Statistical method	Effect size

01 Effect on nausea	12	1505	Odds Ratio (Random) 95% CI	0.16 [0.08, 0.33]
02 Effect on drowsiness or sleepiness	4	343	Odds Ratio (Random) 95% CI	2.24 [1.05, 4.75]
03 Effect on miscarriage or neonatal loss	1	161	Odds Ratio (Random) 95% CI	0.96 [0.32, 2.87]
04 Effect on fetal abnormality	1	161	Odds Ratio (Random) 95% CI	0.31 [0.03, 3.07]
02 Bendectin (Debendox) compared with placebo				
Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Effect on nausea	3	240	Odds Ratio (Random) 95% CI	0.23 [0.07, 0.70]
03 Antihistamines compared with placebo				
Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Effect on nausea	6	571	Odds Ratio (Random) 95% CI	0.20 [0.06, 0.63]
04 Phenothiazines compared with placebo				
Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Effect on nausea	2	300	Odds Ratio (Random) 95% CI	0.09 [0.00, 1.88]
05 Vitamin B6 compared with placebo				
Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Effect on vomiting	2	392	Odds Ratio (Random) 95% CI	0.64 [0.18, 2.26]
02 Improvement in nausea score	2	395	Weighted Mean Difference (Random) 95% CI	-0.99 [-1.47, -0.51]
06 Ginger compared with placebo				
Outcome title	No. of studies	No. of participants	Statistical method	Effect size

01 Effect on vomiting	1	67	Odds Ratio (Random) 95% CI	0.31 [0.12, 0.85]
02 Effect on nausea	1	67	Odds Ratio (Random) 95% CI	0.06 [0.02, 0.21]
03 Effect on miscarriage	1	67	Odds Ratio (Random) 95% CI	0.34 [0.03, 3.49]
07 Acupuncture or acupressure, compared with sham or dummy acupuncture or acupressure				
Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Effect on morning sickness	2	285	Odds Ratio (Random) 95% CI	0.35 [0.12, 1.06]
02 Effect on vomiting score	2	332	Weighted Mean Difference (Random) 95% CI	-0.31 [-0.76, 0.14]
03 Effect on nausea score	2	332	Weighted Mean Difference (Random) 95% CI	-0.57 [-1.41, 0.26]
08 Acupuncture or acupressure compared with no treatment				
Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Effect on morning sickness	1	238	Odds Ratio (Random) 95% CI	0.25 [0.14, 0.43]
02 Effect on vomiting score	1	265	Weighted Mean Difference (Random) 95% CI	-0.30 [-0.79, 0.19]
03 Effect on nausea score	1	265	Weighted Mean Difference (Random) 95% CI	-0.70 [-1.45, 0.05]
09 Adrenocorticotropic hormone or steroids versus placebo for hyperemesis gravidarum				
Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Effect on persistent vomiting within 4 days of treatment	2	56	Odds Ratio (Random) 95% CI	1.96 [0.39, 9.93]
02 Effect on subsequent readmission to hospital	2	56	Odds Ratio (Random) 95% CI	0.53 [0.14, 1.95]

03 Effect on spontaneous abortion	1	32	Odds Ratio (Random) 95% CI	1.00 [0.06, 17.51]
10 Ginger versus placebo for hyperemesis gravidarum				
Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Improvement in hyperemesis symptom score	1	27	Weighted Mean Difference (Random) 95% CI	-3.15 [-7.22, 0.92]
11 Diazepam versus placebo for hyperemesis gravidarum				
Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Effect on persistence of vomiting	1	50	Odds Ratio (Random) 95% CI	0.64 [0.10, 4.19]
02 Effect on readmission with recurrent symptoms	1	50	Odds Ratio (Random) 95% CI	0.13 [0.01, 1.19]
03 Effect on length of stay in hospital	1	50	Weighted Mean Difference (Random) 95% CI	-1.10 [-2.07, -0.13]
12 Methylprednisolone versus promethazine for hyperemesis gravidarum				
Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Effect on persistence of vomiting	1	40	Odds Ratio (Random) 95% CI	1.59 [0.24, 10.70]
02 Effect on subsequent readmission to hospital	1	35	Odds Ratio (Random) 95% CI	0.07 [0.00, 1.38]
13 Ondansetron versus promethazine for hyperemesis gravidarum				
Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Effect on persistence of vomiting	1	30	Odds Ratio (Random) 95% CI	0.29 [0.03, 3.12]
14 Acupuncture or acupressure for hyperemesis gravidarum				
Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Effect on persistent vomiting	1	33	Odds Ratio (Random) 95% CI	0.23 [0.05, 1.03]

COVER SHEET

Title	**Interventions for nausea and vomiting in early pregnancy**
Reviewer(s)	**Jewell D, Young G**
Contribution of reviewer(s)	**Both reviewers read the papers and agreed extraction and interpretation of data. David Jewell was responsible for all data entry and writing the review.**
Issue protocol first published	Information not available
Issue review first published	1996/4
Date of most recent amendment	Information not available
Date of most recent SUBSTANTIVE amendment	03 August 2003
Most recent changes	December 2002: We have added five new trials (Carlsson 2000; Knight 2001; Nelson-Piercy 2001; Smith 2002a; Vityavanich 2001), included papers on hyperemesis (Sullivan 1995; Safari 1998; Ditto 1999) and excluded a new paper (Evans 1993) on sensory afferent stimulation for nausea.
Date new studies sought but none found	Information not supplied by reviewer
Date new studies found but not yet included/excluded	Information not supplied by reviewer
Date new studies found and included/excluded	01 December 2002
Date reviewers' conclusions section amended	Information not supplied by reviewer
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SOURCES OF SUPPORT

External sources of support

- No sources of support supplied

Internal sources of support

- University of Bristol UK

SYNOPSIS

Drugs do help sickness in early pregnancy, but acupressure and ginger may work with no side effects

Many women have sickness and vomiting in early pregnancy. Women with persistent vomiting may need to be given extra fluids. Many drugs have been tried. Antihistamines work well but are likely to make women feel sleepy. One widely used pill (Debendox/Bendectin) using an antihistamine combined with vitamin B6 was withdrawn after its use was linked to limb defects in babies; but this was not confirmed by later research. Vitamin B6 (pyridoxine) on its own may work but the evidence is not very strong. Acupressure (sea bands) could help, so may ginger, and more research is now being done.

Index Terms

Medical Subject Headings (MeSH)
Antiemetics [therapeutic use]; Nausea [prevention & control]; Pregnancy Complications [prevention & control]; Pregnancy Trimester, First ; Pregnancy Trimester, Second ; Vomiting [prevention & control]
Mesh check words: Female Human Pregnancy