

Efficacy of ginger for nausea and vomiting: a systematic review of randomized clinical trials

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Ginger (*Zingiber officinale*) is often advocated as beneficial for nausea and vomiting. Whether the herb is truly efficacious for this condition is, however, still a matter of debate. We have performed a systematic review of the evidence from randomized controlled trials for or against the efficacy of ginger for nausea and vomiting. Six studies met all inclusion criteria and were reviewed. Three on postoperative nausea and vomiting were identified and two of these suggested that ginger was superior to placebo and equally effective as metoclopramide. The pooled absolute risk reduction for the incidence of postoperative nausea, however, indicated a non-significant difference between the ginger and placebo groups for ginger 1 g taken before operation (absolute risk reduction 0.052 (95% confidence interval –0.082 to 0.186)). One study was found for each of the following conditions: seasickness, morning sickness and chemotherapy-induced nausea. These studies collectively favoured ginger over placebo.

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Ginger (*Zingiber officinale*) has been used for medicinal purposes since antiquity. In particular, it has been an important plant for the traditional Chinese and Indian pharmacopoeia. One of its indications has always been the treatment of nausea and vomiting. The aromatic, spasmolytic carminative and absorbent properties of ginger suggest that it has direct effects on the gastrointestinal tract.¹ German and European monographs on ginger are available^{2,3} and both list nausea/vomiting as indications. Recently, the US pharmacopoeia has approved ginger and powdered ginger monographs for inclusion in the National Formulary.⁴

The notion that ginger may be effective for nausea and vomiting is supported by several lines of evidence. Animal experiments suggest that ginger has antiemetic activity⁵ when nausea is induced by cisplatin⁶ or cyclophosphamide.⁷ Studies in healthy human volunteers suggest that ginger reduces experimentally induced nausea.^{8,9} Furthermore, non-randomized, non-placebo-controlled studies suggest an antiemetic effect in human patients.^{10,11} However, these data are insufficient to evaluate whether or not ginger is truly efficacious for clinical nausea and vomiting.

In this study, we have assessed the available evidence from randomized, controlled trials (RCT) for or against the efficacy of ginger for clinical nausea and vomiting.

Methods

Systematic literature searches were performed to identify all RCTs on ginger for nausea and vomiting. Computerized literature databases were Medline, Embase, Biosis, CISCOR (Research Council for Complementary Medicine, London) and the Cochrane Library (all from their respective inception to November 1997). The search terms used were ginger, *Zingiber officinale* and Ingwer (German term for *Zingiber officinale*). A manual search was performed using the bibliographies of studies and reviews located through the computer search and through scanning our own files. In addition, manufacturers of ginger preparations were asked to contribute published and unpublished material. No language restrictions were imposed.

Only double-blind, placebo-controlled RCTs of ginger monopreparations for nausea and vomiting were included. Studies on experimentally induced nausea or vomiting, or both, were excluded. All studies were assessed independently by both authors. Data were extracted in a standardized, predefined manner. The methodological quality of each study was assessed using the scoring system developed by Jadad and colleagues.¹² The authors met to agree consensus on the assessed data. Disagreements were settled by discussion.

Statistical combination of data was performed for studies on postoperative nausea. The incidence of postoperative nausea was defined as the common end-point and used to assess differences between treatment and control intervention. The absolute risk reduction and 95% confidence intervals were calculated using standard meta-analysis software (RevMan 3.01, Cochrane Collaboration). The number-needed-to-treat was calculated as the inverse of the absolute risk reduction.^{13 14}

Results

Six studies met all of our criteria and were reviewed.^{15–20} The assessment of methodological quality revealed a score of at least 3 of 5 points in the majority of studies. The studies related to four different clinical conditions: seasickness, morning sickness, chemotherapy-induced nausea and postoperative nausea. Most were conducted on postoperative nausea.^{18–20} Key data are summarized in Table 1.

Grøntved and colleagues¹⁵ studied 80 Danish cadets, allocated randomly to receive either one dose of ginger powder 1 g or placebo. Symptoms of seasickness were evaluated during the subsequent 4 h. Volunteers who received ginger powder suffered less seasickness compared with those who received placebo. The difference between ginger powder and placebo was statistically significant ($P < 0.05$) 4 h after receiving the medication.

Fischer-Rasmussen and colleagues¹⁶ conducted a small crossover study in 27 women suffering from hyperemesis gravidarum. Patients received ginger powder 250 mg or placebo, four times daily for 4 days. Sickness was assessed using a symptom score. The results suggested a significantly ($P < 0.05$) greater symptomatic benefit after administration of ginger compared with placebo.

One RCT was identified for chemotherapy-induced nausea.¹⁷ Forty-one patients suffering from leukaemia were allocated randomly to one of two groups to receive either oral ginger or placebo, after administration of compazine i.v. The results suggested a significant (P value not reported) reduction in nausea in patients who received ginger compared with those who received placebo. This study has only been published as an abstract and crucial details were not reported.

Bone and colleagues¹⁸ studied 60 women before major gynaecological operations. Patients were allocated randomly to receive ginger 1 g, metoclopramide 10 mg or placebo as a single dose given with preoperative medication. The severity of postoperative nausea was assessed on a four-point scale. The incidence of nausea during the first 24 h after surgery was 28%, 30% and 51% in the ginger, metoclopramide and placebo groups, respectively. A statistically significant ($P < 0.05$) difference in favour of ginger compared with placebo was reported for the total number of incidents of nausea.

Phillips, Hutchinson and Ruggier¹⁹ randomized 120

women before laparoscopic surgery to one of three similar treatment groups. The medication was given 1 h before surgery and the incidence of nausea and vomiting was 21%, 27% and 41% in the ginger, metoclopramide and placebo groups, respectively. Significantly ($P = 0.006$) fewer patients with nausea were reported in the ginger group compared with the placebo group.

In a study by Arfeen and colleagues,²⁰ 108 women were allocated randomly to receive ginger 0.5 g, ginger 1 g or placebo before laparoscopic surgery. The incidence of nausea and vomiting was monitored 3 h after operation. There were no significant differences between groups.

Data from RCT on postoperative nausea^{18–20} were suitable for statistical pooling. The pooled absolute risk reduction for the incidence of postoperative nausea indicated a non-significant difference between the ginger group treated with ginger 1 g before operation and the placebo group (absolute risk reduction 0.052 (95% confidence interval -0.082 to 0.186)). These values indicate a point estimate of the number-needed-to-treat of 19 and a 95% confidence interval which also includes the possibility of no benefit.²¹

Discussion

The majority of the studies reported that ginger powder 1 g daily alleviated clinical nausea of diverse causes. One study on postoperative nausea,²⁰ however, showed no significant beneficial effects of ginger compared with placebo and, indeed, between doses of 0.5 g and 1 g of ginger powder. This study is also the most rigorous on this indication. The discrepancy between this negative outcome and the positive results from other RCT is not readily explicable.

There are only few data on the actions of ginger. Gingerols, in particular 6-gingerol, have been identified as the active ingredient of ginger, and are also responsible for its characteristic taste. There are several mechanisms which could explain the possible antiemetic effects of ginger. In an animal model, for instance, it was demonstrated that 6-gingerol enhanced gastrointestinal transport.²² This and other compounds of ginger have also been shown to have anti-hydroxytryptamine activity in isolated guinea pig ileum.^{23 24} Galanolactone, another constituent of ginger, is a competitive antagonist at ileal 5-HT₃ receptors.²⁴ Thus antiemesis could be brought about by effects on the gastric system through 5-HT₃ antagonism. This hypothesis is weakened by the results of a randomized, placebo-controlled, crossover study in human volunteers reporting that oral ingestion of powdered ginger root did not affect gastric emptying rate.²⁵ In contrast, effects on the central nervous system may be involved. This notion is strengthened by the finding that, in an animal model, oral 6-gingerol prevented vomiting in response to cyclophosphamide.⁷ A central effect is also implicated by studies reporting that ginger partly prevents motion sickness symptoms in healthy human volunteers.^{8–9} Another study investigating motion sickness, however, reported no effects of ginger on the vestibular and oculomotor system.²⁶

Table 1 Double-blind, randomized controlled trials of ginger for clinical nausea and vomiting

First author (year), indication	Quality score ¹² (max 5)	Patient sample	Design	Treatment	Control	Duration of treatment	Outcome measure	Result	Comment
Grøntved ¹⁵ (1988), seasickness	4	80 cadets	2 parallel groups	Ginger powder 1 g	Placebo	One dose only	Symptom scores during 4 h after medication	Ginger superior to placebo but significant ($P < 0.05$) only after 4 h	5 subjects in the placebo group vomited 2 or more times, compared with none in the verum group
Fischer-Rasmussen ¹⁶ (1990), morning sickness	3	30 pregnant women with severe nausea	Cross-over, 2-day wash-out period	Ginger powder 4 × 250 mg daily	4 × placebo capsules daily	4 days	Symptom score	Significantly ($P = 0.035$) greater relief with ginger compared with placebo	3 drop outs; one spontaneous abortion occurred in the 12th week of gestation
Pace ¹⁷ (1987), chemotherapy-induced nausea	2	41 patients receiving chemotherapy (compazine) for leukaemia	2 parallel groups	Ginger (no further details)	Placebo (no further details)	2 days	Nausea symptoms	Significantly (P value not reported) less severe nausea in ginger compared with placebo group	Only published as an abstract, important details are missing
Bone ¹⁸ (1990), postoperative nausea	3	60 women after major gynaecological surgery	3 parallel groups	Ginger 1 g orally at time of premedication	Placebo or metoclopramide (10 mg)	One dose before operation	Incidence and severity of nausea	Incidence of nausea: 28% ginger, 51% placebo, 30% metoclopramide	Nausea was more severe in the placebo group throughout the 24-h observation period
Phillips ¹⁹ (1993), postoperative nausea	3	120 women after laparoscopic gynaecological surgery	3 parallel groups	Ginger powder 1 g	Placebo or metoclopramide (10 mg)	One dose 1 h before anaesthesia	Incidence of nausea and vomiting	Incidence rates were: 21% ginger, 41% placebo, 27% metoclopramide	No side-effects were observed; less patients from ginger group needed antiemetics subsequently
Arfeen ²⁰ (1995), postoperative nausea	4	108 women after laparoscopic gynaecological surgery	3 parallel groups	Ginger 0.5 or 1 g 1 h before surgery	Placebo	One dose before operation	Incidence of nausea and vomiting	No significant inter-group differences	Sample size determined by power calculation; there was a non-significant trend for high-dose ginger to increase nausea and vomiting

With a herb commonly used as a foodstuff and spice, one is inclined to assume that it is free of serious adverse effects. However, this can be a dangerous fallacy.²⁷ For instance, in doses taken with food, a spice may be safe, yet when taken in higher doses as a drug, this might not apply. There were no reports of adverse reactions to ginger compared with placebo in any of the above studies. The British Herbal Compendium documents no adverse effects of ginger.²⁸ The German monograph² warns that ginger should not be taken during pregnancy. The caution is based on data suggesting that ginger is mutagenic in several test systems.^{29–31} However, the situation is complex and antimutagenic effects have also been reported.³² Systematic studies of ginger or its constituents in mammalian cell cultures have not been reported. There is also no evidence that ginger is harmful when taken by pregnant women.¹⁶ However, in the light of suspicion of mutagenicity it seems wise to err on the side of caution.

Publication bias is of concern for all systematic reviews which may lead to a false positive overall result. It is known that negative studies tend to remain unpublished.³³ The literature relating to complementary medicine could be particularly distorted.³⁴ The data available are by no means beyond criticism. The outcome measures used in the above trials may be of debatable reliability, sample sizes are usually small and power calculations are mostly lacking.

Modern antiemetic agents include droperidol, the prokinetic metoclopramide and the 5-HT₃ receptor antagonist ondansetron.³⁵ The latter is superior to placebo and comparative studies demonstrated no significant differences compared with droperidol or metoclopramide.³⁶ In comparative studies of ginger and metoclopramide,^{18 19} no significant difference was found between treatments.

In summary, we found that ginger is a promising antiemetic herbal remedy, but the clinical data to date are insufficient to draw firm conclusions. Further rigorous studies are needed to establish whether ginger is efficacious for clinical nausea and vomiting.

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