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Effect of herbal medicine on postoperative nausea and vomiting after laparoscopic surgery

A systematic review and meta-analysis

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Abstract

Background: Traditionally, herbal medicines have been used to alleviate nausea and vomiting; however, a comprehensive clinical evaluation for postoperative nausea and vomiting (PONV), especially after laparoscopic surgery, remains limited. This review aimed to evaluate the efficacy and safety of herbal medicine as an alternative therapy to prevent and manage nausea and vomiting after laparoscopic surgery compared with untreated, placebo, and Western medicine groups.

Methods: We searched 11 databases, including EMBASE, PubMed, and the Cochrane Library, to collect randomized controlled trials (RCTs) of herbal medicines on PONV after laparoscopic surgery on July 7, 2022. Two independent reviewers screened and selected eligible studies, extracted clinical data, and evaluated the quality of evidence using the Cochrane risk-of-bias tool. The primary outcome was the incidence of PONV, whereas the secondary outcomes included the frequency and intensity of PONV, symptom improvement time, antiemetic requirement frequency, and incidence of adverse events. Review Manager Version 5.3. was used for the meta-analysis.

Results: We identified 19 RCTs with 2726 participants comparing herbal medicine with no treatment, placebo, and Western medicine. The findings showed that compared with no treatment, herbal medicine demonstrated significant effects on vomiting incidence (risk ratio [RR] = 0.43, 95% confidence interval [CI] 0.32–0.57, $P < .00001$). Compared with placebo, herbal medicine revealed a significant effect on the severity of nausea 12 hours after laparoscopic surgery (standardized mean difference = –2.04, 95% CI –3.67 to –0.41, $P = .01$). Herbal medicines showed similar effects with Western medicine on the incidence of postoperative nausea (RR = 0.94, 95% CI 0.63–1.42, $P = .77$) and vomiting (RR = 0.68, 95% CI 0.25–1.84, $P = .45$). Furthermore, comparing the experimental group containing herbal medicine and control group excluding herbal medicine, adverse events were considerably lower in the group with herbal medicine (RR = 0.45, 95% CI 0.27–0.72, $P = .001$).

Conclusion: Herbal medicine is an effective and safe treatment for nausea and vomiting secondary to laparoscopic surgery. However, the number of studies was small and their quality was not high; thus, more well-designed RCTs are warranted in the future.

Abbreviations: CI = confidence interval, MD = mean difference, PONV = postoperative nausea and vomiting, RCT = randomized controlled trial, RoB = risk of bias, RR = risk ratio, SMD = standardized mean difference.

Keywords: botanical drug, herbal medicine, laparoscopic surgery, postoperative nausea and vomiting, systematic review

1. Introduction

Nausea and vomiting are common gastrointestinal manifestations that have numerous causes. They may arise from complex issues involving multiple organs, including the digestive system, secondary reactions to other conditions such as diabetes, or side effects of treatments such as chemotherapy.[1] Postoperative

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval is not required as this systematic review is a literature-based study that utilizes already published data, and no additional data is collected.

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nausea and vomiting (PONV) occurs frequently after surgical intervention, affecting approximately 25% to 30% of surgical patients.[2] The incidence of PONV varies depending on the type of surgery: abdominal surgery, gynecological surgery, and otolaryngological surgery, with high rates ranging from 50% to 70%.[3,4]

Abdominal surgery can broadly be classified into laparoscopic and open surgeries. Recently, laparoscopic surgery has become preferred over open surgery because of its reduced risk of infection, improved quality of life, and lower pain levels.[5,6] Despite these advantages, approximately 70% of patients undergoing laparoscopic surgery report experiencing PONV, which hinders postoperative recovery.[4] Delayed recovery after surgery prolongs the treatment period and increases the treatment costs, emphasizing the need for proactive measures to alleviate nausea and vomiting.[7] Current treatments, including antiemetic medications, are often administered preoperatively or postoperatively to relieve symptoms. Commonly used medications include 5-hydroxytryptamine type 3 receptor antagonists such as ondansetron and granisetron; dopamine antagonists such as prochlorperazine and metoclopramide; antihistamines such as diphenhydramine; and corticosteroids such as dexamethasone.[8] However, these drugs are not always effective and may lead to adverse effects, such as headache, constipation, elevated liver enzymes, increased blood glucose levels, and blood pressure changes.[9]

Various herbal medicines have been traditionally used to treat nausea and vomiting.[10] Particularly, fresh ginger (fresh rhizome of *Zingiber officinale Roscoe* [*Zingiberaceae*]) has been extensively studied for its effect on PONV. Previous reviews have analyzed the impact of ginger on nausea and vomiting associated with general surgery, indicating a lower incidence of PONV when ginger is consumed before surgery.[11,12] Previously reported controlled studies comparing ginger with a placebo in upper- and lower-extremity surgery, laparoscopic cholecystectomy, open surgery, and laparoscopic nephrectomy have also confirmed the efficacy of ginger in decreasing the incidence and intensity of PONV.[13–15] Some studies, however, suggest that ginger failed to demonstrate a significant effect on PONV.[16–18] Given these conflicting results, further research with diverse conditions, including intervention type, administration timing, and duration, is essential. Considering the characteristics of herbal medicine, which involves multiple components and targets and its clinical applicability,[19] exploring herbal formulations rather than single herbs may enhance the potential clinical utility of herbal medicine for PONV as an additional treatment option.

This study aimed to conduct a comprehensive review of the different types of herbal prescriptions used for PONV, including ginger, as well as the types of individual herbal components and frequency of use, to explore the overall effect size of herbal medicines and determine their role as complementary or alternative treatments to Western medicine. Additionally, we identified individual studies that caused heterogeneity and suggest future well-designed randomized controlled trials (RCTs) and guidelines for the use of herbal medicines. Particularly, among various surgical methods, we limited the patient group to laparoscopic surgery because it aligns with the recent trend in surgical techniques. Additionally, the pressure exerted on the abdominal organs during laparoscopic surgery itself may cause more nausea and vomiting.[5,20]

2. Methods

The protocol was registered in PROSPERO (CRD42022345749) during the pre-study stage (https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022345749), and a protocol paper has been published.[21] This study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines.[22] Ethical approval and patient consent were not required for this review because the aim was to analyze the results of previous trials in which participants had already consented to the study's purpose.

2.1. Inclusion and exclusion criteria

2.1.1. Patients. Patients who underwent laparoscopic surgery were included in the review regardless of the disease or surgical organ. However, those with other underlying conditions or causes of nausea and vomiting, such as pregnancy or chemotherapy, were excluded. No restrictions were placed on sex, age, or race.

2.1.2. Interventions. All formulations of orally administered herbal medicines, including powders, capsules, and decoctions, were included. We excluded all cases in which herbal medicine was administered by methods other than oral therapy, such as injections, enemas, and aromatherapy, and cases in which herbal medicine was combined with other complementary and alternative treatments, such as acupuncture and moxibustion. Orally administered herbal medicines did not impose any restrictions on dose, time, duration, or frequency of administration but were included only if the ingredients and dosages were clearly described in the text to the extent that they could be reproduced by readers.

To compare the effects of combination therapy on PONV with those of Western medicine alone, studies that included a combination of herbal and Western medicines were also included.

2.1.3. Control groups. The control groups compared with herbal medicine alone were the no treatment, placebo, and Western medicine groups. In cases where herbal and Western medicines were co-administered, this review included studies in which the same Western medicine was used in both the combination (experimental) and Western medicine monotherapy (control) groups.

2.1.4. Outcome measures. The primary outcome was the incidence of nausea and vomiting. Secondary outcomes included the frequency, duration, and intensity of each nausea and vomiting symptom; time of symptom onset and relief; frequency of antiemetic use; and occurrence of adverse events.

2.1.5. Study designs. This review included RCTs with eligible study designs and excluded animal studies, case reports, protocols, and reviews.

2.2. Search strategy

We searched 11 electronic databases on July 7, 2022, with no language restrictions. We searched 4 English-language databases (MEDLINE via PubMed, Embase, Cochrane Central Register of Controlled Trials, and Allied and Complementary Medicine Database), 5 Korean databases (Korean Studies Information Service System, National Digital Science Library, Korean Medical Database, KoreaMed, and Oriental Medicine Advanced Searching Integrated System), one Chinese-language database (China National Knowledge Infrastructure), and one Japanese-language database (Citation Information by Nii). We also searched the Clinical Research Information Service and ClinicalTrials.gov for additional unpublished data and manually searched the relevant gray literature using Google Scholar and OpenGrey.

We used expanded search terms for each database according to the patient and problem terms such as "Surgery, Laparoscopic," "Minimally Invasive Surgical Procedure," "Postoperative Nausea and Vomiting," "PONV," "Nausea," and "Vomiting" and intervention terms such as "Herbal medicine," "Phytomedicine," and "Medicine, Traditional."[21]

2.3. Study selection and data extraction

The retrieved articles were initially screened by 2 independent researchers (M.J.P. and N.-Y.H.) based on the inclusion criteria to determine whether they were eligible for this study based on the title and abstract. The articles were then categorized by secondary screening of the full text to determine their eligibility. The articles were collected and stored using EndNote 20 (Clarivate Analytics, Philadelphia, PA). Any disagreement between the 2 researchers regarding inclusion was mediated by a third researcher (J.K.).

Two researchers (M.J.P. and N.-Y.H.) independently collected and managed essential study data through a standardized data extraction form using Microsoft Office Excel 2019 (Microsoft Corp., Redmond, WA) in the selected article. A third researcher (J.K.) verified the collected data. The extracted data included basic information regarding the study and specific trial data, including study participants, interventions, and outcomes. The details included the first author, year of publication, type of surgery, number of patients, types, components, and dosages of interventions and controls, and timing and duration of administration. The results include outcome measures, statistical values, and safety information. To compensate for missing or unclear data, the corresponding authors were contacted via email.

2.4. Quality assessment

The quality of the included RCTs was evaluated using the Cochrane risk-of-bias (RoB) tool for randomized trials.[23] Two independent investigators (M.J.P. and N.-Y.H.) assessed the risk of bias in each study, and disagreements were resolved through a discussion with the assistance of a third investigator (J.K.). The 7 bias domains included random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and others. The response options for each item were categorized as low risk, high risk, or unclear risk.

2.5. Data analysis and synthesis

The data were integrated using Review Manager Version 5.3. (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). The results are presented as risk ratios (RR) with 95% confidence intervals (CIs) for dichotomous outcomes, such as the incidence of nausea, and mean difference (MD) or standardized mean difference (SMD) with 95% CIs for continuous outcomes, such as the intensity of nausea, depending on the heterogeneity of the outcome measures. If 2 or more RCTs were matched as methodologically similar and consistent, a quantitative synthesis was performed for the same outcome measure and presented as a forest plot; otherwise, narrative summaries and tables were used.

2.6. Sensitivity and subgroup analyses

Statistical heterogeneity between the studies was evaluated using the I^2-statistic in the meta-analysis. Heterogeneity was considered high if I^2 was greater than 50%, and a random-effects model was employed; otherwise, a fixed-effects model was used. In cases of high heterogeneity, we conducted a subgroup analysis based on the time interval between symptom observation and a sensitivity analysis by removing individual studies with poor methodological quality or outliers. Additionally, to assess their clinical utility, we tabulated the types and components of herbal prescriptions in the included studies.

2.7. Publication bias

To evaluate for publication bias, we reviewed the funnel plots when more than 10 studies were included in a meta-analysis of the same outcome indicators.

3. Results

3.1. Study selection

A total of 687 articles were retrieved from 11 databases, and an additional 4 were identified through manual searches, resulting in a total of 691 articles for screening. Out of these, 45 articles were duplicates, leaving 646 for primary screening. After reviewing the titles and abstracts, 584 articles were excluded. Among them, 283 had poor overall relevance, 61 were not clinical trials, 36 had inappropriate patients, 203 had unsuitable interventions, and one could not be identified. The full text of the remaining 62 articles was then reviewed. Out of these, 43 were excluded: 7 did not enroll eligible patients, 25 had inappropriate or ambiguous interventions, 7 were not clinical trials, and 4 showed no relevance to the review purpose. The remaining 19 studies were selected, of which 17 were meta-analyzed and included a total of 2546 participants (Fig. 1).

3.2. Characteristics of the included studies

The details of the 19 articles included in the selection process are summarized in the table below (Table 1). All studies were RCTs, and the total number of patients included was 2726: 1367 in the treatment group and 1359 in the control group, with an average of 143 patients per study.

When categorized by the type of surgery, 1391 patients underwent laparoscopic cholecystectomy,[13,24,26,27,32,34,35,38] 1049 had gynecological laparoscopy,[16,17,25,28–31,33,36,37,39] 210 had laparoscopic appendectomy,[24,34,39] 43 had laparoscopic splenectomy,[24] 17 had laparoscopic hernia repair,[39] 3 had exploratory laparoscopy,[34] and 13 were unspecified.[24]

Regarding the study designs comparing the effects of the treatment and control groups, there were 14 two-arm studies, 4 three-arm studies,[16,29,36,37] and 1 four-arm study.[17]

Listing the detailed interventions compared, including duplicates, 5 studies compared herbal medicine to no intervention,[24–28] 10 studies compared herbal medicine to placebo,[13,16,17,29–33,36,37] 5 compared herbal medicine to Western medicine,[17,34–37] and 3 compared herbal–Western medicine combination treatment to Western medicine alone.[17,38,39]

The formation types of herbal medicines were categorized into capsules in 9 studies (ginger capsules),[13,16,17,29–32,35,36] decoctions in 7 (Chaihu-Shugan-San combined with Pingwei-San, He-Zhong-Yin, Shugan-Lidan-Tang, Tongfu-Xingqi-Tang, Xiangsha-Liujunzi-Tang, and reconciling-lifting-method-Tang),[24,26–28,34,38,39] and powders in 3 (Go-Rei-San, Hange-Shashin-To, and Jiawei-Pingwei-San).[25,33,37]

The types of Western medicines used in the comparison group were antiemetics in 2 studies (ondansetron and tropisetron),[35,39] gastrointestinal tract regulators and antispasmodics in 4 studies (metoclopramide and mosapride),[34,36–38] neuromuscular disorder-related drugs in one study (droperidol),[17] nonsteroidal anti-inflammatory drugs in one study (indomethacin),[34] and antidiarrheals in one study (loperamide).[38]

When categorized according to the dosing time of the herbal medicines, there were 10 studies in which herbal medicines were administered before surgery. In 7 studies,[13,16,30–32,35,36] herbal medicines were administered once 1 hour before surgery, and in the remaining 3 studies, herbal medicines were administered for 2 days before surgery,[24] 1 day before surgery,[25] and twice before surgery (the night before surgery and the morning of

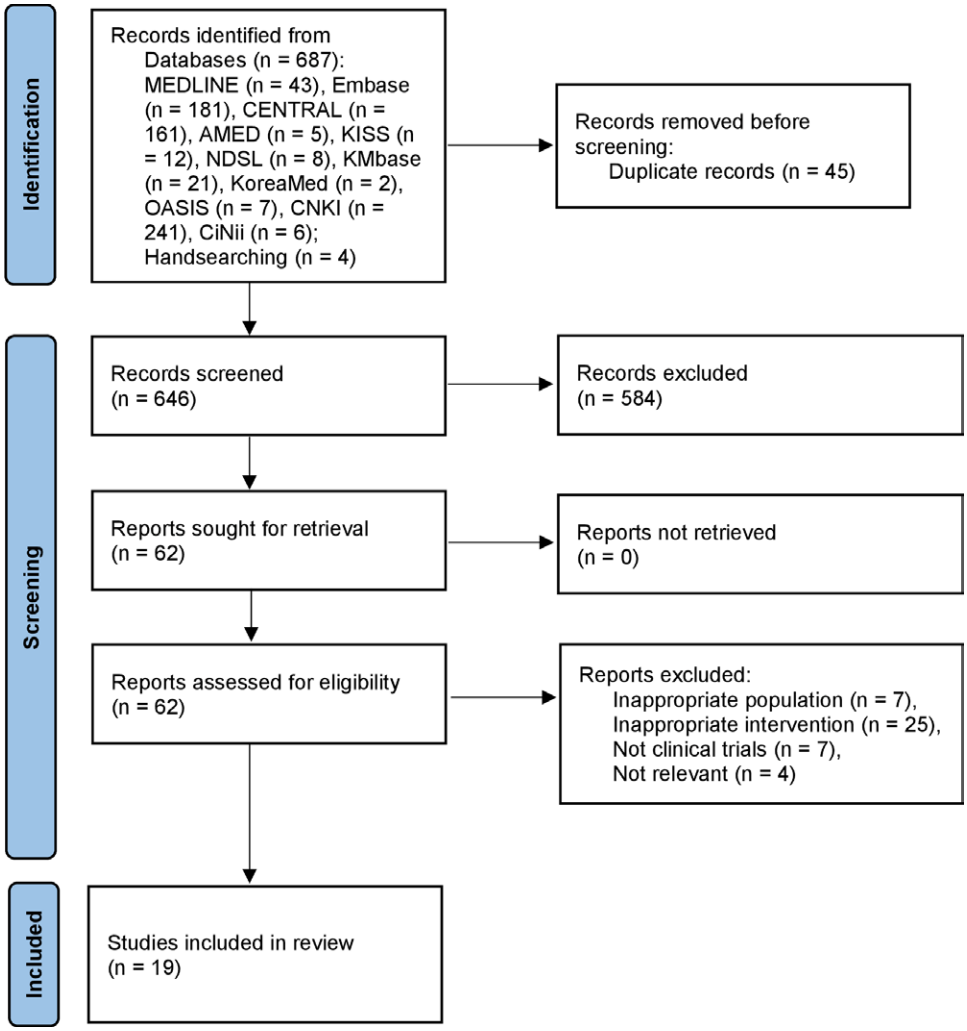

Figure 1. Flow diagram of the study selection process. AMED = Allied and Complementary Medicine Database, CENTRAL = Cochrane Central Register of Controlled Trials, CiNii = Citation Information by Nii, CNKI = China National Knowledge Infrastructure, KISS = Korean Studies Information Service System, KMbase = Korean Medical Database, NDSL = National Digital Science Library, OASIS = Oriental Medicine Advanced Searching Integrated System.

surgery).[33] In 6 studies,[26–28,37–39] herbal medicines were administered after surgery, and the duration varied from 1 to 21 days. In 3 cases,[17,29,34] the herbs were administered both before and after surgery.

3.3. Distribution of herbal medicine use

Nine studies used a single herb as an intervention, all of which used fresh ginger,[13,16,17,29–32,35,36] while the remaining 10 studies used a combination of 2 or more herbs. We reviewed the herbal information in studies that utilized combination formulations to examine the type and composition of the combinations (Table 2). Additionally, we investigate the type and frequency of use of the individual herbs included (Table 3). Of the 39 herbs in the 10 studies, Licorice root was the most frequently used (6 cases), followed by Bupleurum root, Scutellaria root, Pinellia tuber, Magnolia bark, and Peony root (5 cases each). Fresh ginger was the most frequently used as a single herb or in combination formulations across all studies (12 cases).

3.4. Risk of bias assessment

We assessed the risk of bias for the 19 RCTs included in the review using the RoB tool criteria, and the results are presented in Figures 2 and 3.

3.4.1. Random sequence generation. Six studies[13,25,28,29,31,32] were graded as low risk because randomization was properly performed using methods such as a random number table, computer random number generator, and block randomization. The remaining 13 studies were evaluated as unclear because the method of generating a random allocation sequence was not mentioned.

3.4.2. Allocation concealment. One study[25] mentioned the use of Internet-based central allocation; therefore, we considered allocation concealment to be appropriate and evaluated it as low risk. The remaining 18 studies were categorized as unclear because they either did not mention allocation concealment or did not present the appropriate envelope method.

3.4.3. Blinding of participants and personnel. Nine studies[13,16,17,29–33,36] were classified as low risk as they clearly described double blinding with the intervention using a placebo that was similar in appearance and taste to the actual drug (herbal or Western medicine) as a control. Ten studies were categorized as high risk because 5 of them[24–28] had a no treatment control group, which indicated that the researchers and participants could not be fully blinded. Additionally, 3 studies[34,35,37] used an injectable formulation of the intervention and 2 studies[38,39] compared the efficacy of a combination of herbal and Western medicines to Western medicine alone, which

Table 1

Characteristics of included studies.

First author Year	Type of surgery	Intervention (n)	Control (n)	Dosing time	Major outcomes (significance)	Adverse events
Gong 2007 [24]	1) Laparoscopic cholecystectomy 2) Laparoscopic appendectomy 3) Laparoscopic splenectomy 4) Others	He-Zhong-Yin decoction (100 mL) (500)	No intervention (500)	t.i.d. for 2 d before surgery	1) Incidence of vomiting ($P < .01$) 2) Frequency of vomiting ($P < .01$) 3) Duration of vomiting ($P < .01$)	Not reported
Kori 2013 [25]	Gynecological laparoscopy	Go-Rei-San powder (7.5 g) (49)	No intervention (50)	1 d before surgery	1) Incidence of vomiting; 0–3 h ($P < .01$) 0–24 h ($P < .01$) 2) Frequency of vomiting; 0–24 h ($P < .05$) 3) Severity of nausea; 0–3 h ($P < .001$) 0–24 h ($P < .01$)	None
Pei 2014 [26]	Laparoscopic cholecystectomy	Shugan-Lidan-Tang decoction (100 mL) (30)	No intervention (30)	t.i.d. for 7 d after surgery	1) Relieving time of NV ($P < .05$)	Not reported
Wang 2016 [27]	Laparoscopic cholecystectomy	Shugan-Lidan-Tang decoction (30)	No intervention (30)	b.i.d. for 1–3 wk after surgery	1) Incidence of NV; 6–24 h ($P < .05$)	$P < .05$; 1) discomfort in the right upper abdomen (1); C) discomfort in the right upper abdomen (2), poor appetite (3), anorexia (2), diarrhea (2)
Su 2022 [28]	Gynecological laparoscopy	Tongfu-Xingqi-Tang decoction (100 mL) (42)	No intervention (42)	t.i.d. or q.i.d. for 4 d, starting 6 h after surgery	1) Severity of NV; 0–12 h ($P < .05$)	None
Arfeen 1995 [16]	Gynecological laparoscopy	1) Ginger 0.5 g 1 cap and Placebo 1 cap (36) 2) Ginger 0.5 g 2 cap (36)	Placebo 2 cap (36)	1 h before surgery	1) Incidence of nausea; 0–3 h ($P > .05$) 2) Incidence of vomiting; 0–3 h ($P > .05$) 3) Distribution of nausea severity; 0–3 h ($P > .05$)	I1) flatulence and bloated feeling (1), heartburn (1); I2) severe heartburn (1) and nauseous (1) after swallowing the capsules, burping (1); C) feeling windy and burp (1)
Eberhart 2003 [29]	Gynecological laparoscopy	1) Ginger 0.1 g 1 cap and Placebo 1 cap (59) 2) Ginger 0.1 g 2 cap (57)	Placebo 2 cap (59)	-before surgery -3 h after surgery -6 h after surgery	1) Incidence of nausea; 0–3 h (not significant) 0–24 h (not significant) 2) Incidence of vomiting; 0–3 h (not significant) 0–24 h (not significant) 3) Use of antiemetics; 0–3 h (not significant) 0–24 h (not significant)	I1) flu-like symptoms (1), heartburn (1), respiratory symptoms (2), infection, requiring antibiotic treatment (3); I2) flu-like symptoms (1), heartburn (2), cardiovascular symptoms (2), infection, requiring antibiotic treatment (3); C) flu-like symptoms (1), infection, requiring antibiotic treatment (7), allergic reaction (1)

(*Continued*)

Table 1

(*Continued*)

First author Year	Type of surgery	Intervention (n)	Control (n)	Dosing time	Major outcomes (significance)	Adverse events
Pongrojpaw 2003 [30]	Gynecological laparoscopy	Ginger 0.5 g 2 cap (40)	Placebo 2 cap (40)	1 h before surgery	1) Incidence of nausea; 0–24 h ($P < .05$) 2) Incidence of vomiting; 0–24 h ($P > .05$) 3) Use of antiemetics; 0–24 h ($P > .05$) 4) Severity of nausea; 0 h (zero in both groups) 2 h ($P < .05$) 4 h ($P < .05$) 24 h ($P > .05$)	2 h ($P > .05$); I) abdominal discomfort (3); C) abdominal discomfort (5) 4 h ($P > .05$); I) abdominal discomfort (4); C) abdominal discomfort (7) 24 h ($P > .05$); I) abdominal discomfort (1); C) abdominal discomfort (6)
Apariman 2006 [31]	Gynecological laparoscopy	Ginger 0.5 g 3 cap (30)	Placebo 3 cap (30)	1 h before surgery	1) Incidence of vomiting; 0–2 h ($P > .05$) 2–6 h ($P > .05$) 2) Severity of nausea; 2 h ($P > .05$) 6 h ($P < .05$)	2 h ($P > .05$); 6 h ($P > .05$); abdominal discomfort, heartburn, flu-like symptoms, and insomnia
Bameshki 2018 [13]	Laparoscopic cholecystectomy	Ginger 0.25 g 2 cap (75)	Placebo 2 cap (75)	1 h before surgery	1) Incidence of vomiting; 0–2 h ($P < .05$) 2–4 h ($P > .05$) 4–6 h ($P > .05$) 6–12 h ($P < .05$) 2) Frequency of vomiting; 0–2 h ($P > .05$) 2–4 h ($P > .05$) 4–6 h ($P > .05$) 6–12 h ($P > .05$) 3) Severity of nausea; 2 h ($P < .05$) 4 h ($P > .05$) 6 h ($P > .05$) 12 h ($P < .05$)	Not reported
Albooghobeish 2018 [32]	Laparoscopic cholecystectomy	Ginger 0.5 g 2 cap and 0.25 g 1 cap (65)	Placebo 3 cap (65)	1 h before surgery	1) Incidence of vomiting; 0 h ($P < .001$) 0–2 h ($P < .001$) 2–6 h ($P < .001$) 6–12 h (none in both groups) 12–24 h (none in both groups) 2) Severity of nausea; 0 h ($P < .01$) 2 h ($P < .01$) 6 h ($P < .01$) 12 h ($P < .01$) 24 h ($P < .01$) 3) Use of antiemetics ($P < .01$)	Not reported

(*Continued*)

Table 1

(*Continued*)

First author Year	Type of surgery	Intervention (n)	Control (n)	Dosing time	Major outcomes (significance)	Adverse events
Kuwamura 2015 [33]	Gynecological laparoscopy	Hange-Shashin-To powder (2.5 g) (35)	Placebo (35)	-the night before surgery -the morning of surgery	1) Prevalence of nausea; 0 h ($P > .05$) 3 h ($P > .05$) 24 h ($P > .05$) 2) Severity of nausea; 0 h ($P > .05$) 3 h ($P > .05$) 24 h ($P > .05$)	None
Leng 2003 [34]	1) Laparoscopic cholecystectomy 2) Laparoscopic appendectomy 3) Exploratory laparoscopy	Reconciling-lifting-method-Tang decoction (100 mL) (32)	Indomethacin* 25 mg 1 T and Metoclopramide** 10 mg IM (32)	-b.i.d. for 2 d before surgery -b.i.d. for 2 d, starting 6 h after surgery *t.i.d. for 2 d before and after the surgery **the morning of the surgery and for 2 d after surgery	1) Incidence of vomiting; 0–8 h ($P < .01$) 8 h–1 d ($P < .01$) 1–2 d ($P < .01$)	Not reported
Soltani 2018 [35]	Laparoscopic cholecystectomy	Ginger 0.5 g 1 cap (50)	Ondansetron* 4 mg IV (50)	1 h before surgery *before completion of surgery	1) Frequency of vomiting; 0 h ($P > .05$) 0–2 h ($P < .01$) 2–4 h ($P > .05$) 4–8 h ($P > .05$) 8–16 h ($P > .05$) 16–24 h ($P > .05$) 2) Severity of nausea; 0 h ($P < .01$) 2 h ($P < .001$) 4 h ($P < .01$) 8 h ($P > .05$) 16 h ($P > .05$) 24 h ($P > .05$)	None
Phillips 1993 [36]	Gynecological laparoscopy	Ginger 0.5 g 2 cap (40)	1) Metoclopramide 5 mg 2 cap (40) 2) Placebo 2 cap (40)	1 h before surgery	1) Incidence of nausea 0–24 h ($P < .01$) 2) Incidence of vomiting 0–24 h ($P > .05$) 3) Use of antiemetics ($P < .05$)	$P > .05$; sedation, abnormal movement, itch, and visual disturbance
Li 2006 [37]	Gynecological laparoscopy	Jiawei-Pingwei-San powder (40)	1) Metoclopramide* 10 mg IM (40) 2) Normal saline* 2 mL IM (40)	b.i.d. for 1 d after surgery *after surgery	1) Incidence of NV; 0–8 h ($P > .05$) 8–24 h ($P < .05$)	Not reported
Liu 2021 [38]	Laparoscopic cholecystectomy	Chaihu-Shugan-San combined with Pingwei-San decoction (200 mL), Mosapride citrate* 5 mg 1 T, and Loperamide hydrochloride** 2 mg 1 cap (36)	Mosapride citrate* 5 mg 1 T and Loperamide hydrochloride** 2 mg 1 cap (36)	b.i.d. for 14 d after surgery *24 h before surgery **t.i.d. for 14 d, starting 6 h after surgery	1) Frequency of vomiting; 0–24 h ($P < .001$)	$P < .05$; I) post-cholecystectomy blocked dynamia (1), gallbladder hydrops (1); C) post-cholecystectomy blocked dynamia (2), gallbladder hydrops (3), hemobilia (2)

(*Continued*)

Table 1
(Continued)

First author Year	Type of surgery	Intervention (n)	Control (n)	Dosing time	Major outcomes (significance)	Adverse events
Zhu 2021 [39]	1) Gynecological laparoscopy 2) Laparoscopic hernia repair 3) Laparoscopic appendectomy	Xiangsha-Liujunzi-Tang decoction and Tropisetron hydrochloride* 5 mL IV (31)	Tropisetron hydrochloride* 5 mL IV (32)	b.i.d. as decoction (or 6–9 g as pills) for 3 d after surgery *for 3 d after surgery	1) Incidence of NV; 0–24 h ($P < .05$) 2) Severity of nausea ($P < .05$) 3) NV onset time ($P < .05$)	$P < .05$; I) headache (1), dizziness (1); C) headache (3), constipation (4), dizziness (2)
Visalyaputra 1998 [17]	Gynecological laparoscopy	1) Ginger 0.5 g 2 cap and Normal saline* 0.5 mL IV (27) 2) Ginger 0.5 g 2 cap and Droperidol* 1.25 mg IV (27)	1) Placebo 2 cap and Normal saline* 0.5 mL IV (28) 2) Placebo 2 cap and Droperidol* 1.25 mg IV (29)	-1 h before surgery -30 min before discharge *before surgery	1) Incidence of nausea; 0–24 h ($P > .05$) 2) Incidence of vomiting; 0–24 h ($P > .05$)	Not reported

b.i.d = bis in die, C = control, cap = capsule, I = Intervention, IM = intramuscular injection, IV = intravenous injection, NV = nausea and vomiting, q.i.d = quarter in die, T = tablet, t.i.d = ter in die.

suggested that there was a high risk of distortion in blinding participants and personnel to interventions that were clearly different in appearance.

3.4.4. Outcome assessment blinding. The assessment of outcome assessor blinding was categorized as low risk due to the presence of an outcome assessor who was blinded and described as independent and unaware of the type of intervention in 8 studies[13,16,17,25,32,33,35,36] and unclear in the remaining studies.

3.4.5. Incomplete outcome data. Fifteen of the 19 articles were evaluated as low risk because missing outcome data were either absent or very sparse in the experimental and control groups. Additionally, the reasons for withdrawal seemed unlikely to be associated with true outcomes, such as reasons for the surgery itself. The remaining 4 articles[16,17,34,35] were rated as unclear because they did not provide sufficient explanations for the number or reasons for withdrawals, impacting the balance between the 2 groups.

3.4.6. Selective reporting. Four studies[24,26,32,36] were categorized as high because they did not present all the outcomes described in the Methods section or reported outcomes that were not prespecified in the text. The remaining 15 studies were rated low as they appeared to cover all the outcomes described in the Methods section.

3.4.7. Other biases. When evaluating the inappropriate influence of funders, all studies were judged to be unclear due to insufficient descriptions of the funding source or the sponsor's role, making accurate assessment challenging.

3.5. Meta-analysis

3.5.1. Primary outcome: incidence of nausea and vomiting. This review evaluated the clinical efficacy of herbal medicines for PONV according to the incidence of nausea and vomiting, which represents the proportion of patients who experienced nausea and vomiting during a certain observation period after laparoscopic surgery among all participants. The outcome measures for nausea and vomiting differed between studies, with some measuring both nausea and vomiting symptoms simultaneously and others measuring either nausea or vomiting separately. In this review, to avoid ambiguous results, we analyzed the outcome measures for nausea and vomiting separately.

Furthermore, if more than one study was available for each period of symptom observation, the effect analysis was categorized. The reason for separating efficacy evaluations by time is that the incidence of PONV varies slightly over time, most notably within the first 24 hours after surgery and especially within the first 6 hours.[40–42] The more granular the observation time, the more precise is the efficacy analysis. Thus, we analyzed the efficacy by categorizing the common outcome assessment time.

3.5.1.1. Herbal medicine versus no treatment. 3.5.1.1.1. Incidence of vomiting. A total of 1099 patients from 2 RCTs were included in the analysis.[24,25] The herbal medicine treatment group had a significantly lower incidence of vomiting than the no treatment group (RR = 0.43, 95% CI 0.32–0.57, $P < .00001$), with low heterogeneity ($P = .36$, $I^2 = 0\%$) (Fig. 4).

3.5.1.2. Herbal medicine versus placebo.

3.5.1.2.1. Incidence of nausea.

3.5.1.2.1.1. Incidence of nausea 3 hours after surgery. To compare herbal medicine with placebo for the incidence of nausea 3 hours after surgery, a meta-analysis including 2 studies with a total of 283 patients found no significant difference in the incidence of nausea between the 2 groups (RR = 1.27, 95% CI 0.88–1.81, $P = .20$), with low heterogeneity ($P = .48$,

Table 2

Types and compositions of herbal prescriptions in the included studies.

First author Year	Prescription; Dosage form; Dosage	Pharmaceutical manufacturer	Dose of individual components	Quality control	Chemical profile
Gong 2007 [24]	He-Zhong-Yin; Decoction; 100 mL, t.i.d.	NR	Dried root of *Bupleurum falcatum* L. [Apiaceae], 10 g; Dried root of *Scutellaria baicalensis* Georgi [Lamiaceae], 8 g; Dried root of *Paeonia lactiflora* Pall. [Paeoniaceae], 10 g; Dried unripe whole fruit of *Citrus trifoliata* L. [Rutaceae], 12 g; Dried bark of the trunk of *Magnolia obovata* Thunb. [Magnoliaceae], 10 g; Dried inner stem of *Phyllostachys nigra* (Lodd. ex Lindl.) Munro [Poaceae], 15 g; Dried ripe seed of *Prunus persica* (L.) Batsch [Rosaceae], 8 g; Dried ripe fruit of *Ziziphus jujuba* Mill. [Rhamnaceae], 10 g; Fresh rhizome of *Zingiber officinale* Roscoe [Zingiberaceae], 12 g; Dried tuber of *Pinellia ternata* (Thunb.) Makino [Araceae], denatured by ginger extract, 12 g; Steamed and dried root and rhizome of *Rheum officinale* Baill. [Polygonaceae], 12 g; Haematitum, 15 g; Dried capitulum of *Inula japonica* Thunb. [Asteraceae], 10 g	NR	NR
Kori 2013 [25]	Go-Rei-San; Extract granules; 7.5 g/d, NR	Tsumura & Co., Tokyo, Japan	Dried tuber of *Alisma plantago-aquatica subsp. orientale* (Sam.) Sam. [Alismataceae], 4 g; Dried rhizome of *Atractylodes lancea* (Thunb.) DC. [Asteraceae], 3 g; Dried sclerotium of *Polyporus umbellatus* (Pers.) Fries [Polyporaceae], 3 g; Dried sclerotium of *Poria cocos* (Schw.) Wolf. [Polyporaceae], 3 g; Dried bark of *Cinnamomum verum* J.Presl [Lauraceae], 1.5 g	NR	NR
Pei 2014 [26]	Shugan-Lidan-Tang; Decoction; 100 mL, t.i.d.	NR	Dried fruit of *Melia azedarach* L. [Meliaceae], 15 g; Dried root of *Bupleurum falcatum* L. [Apiaceae], 10 g; Dried root and rhizome of *Rheum officinale* Baill. [Polygonaceae], 10 g; Dried unripe whole fruit of *Citrus trifoliata* L. [Rutaceae], 5 g; Dried root of *Scutellaria baicalensis* Georgi [Lamiaceae], 10 g; Dried tuber of *Pinellia ternata* (Thunb.) Makino [Araceae], 10 g; Dried root of *Paeonia lactiflora* Pall. [Paeoniaceae], 10 g; Dried gizzard membrane of Gallus *gallus domesticus Brisson* [Phasianidae], 10 g; Fresh rhizome of *Zingiber officinale* Roscoe [Zingiberaceae], 15 g; Dried flower bud or flower of *Lonicera japonica* Thunb. [Caprifoliaceae], 15 g	NR	NR
Wang 2016 [27]	Shugan-Lidan-Tang; Decoction; NR, b.i.d.	NR	Dried ripe pericarp *Citrus reticulata* Blanco [Rutaceae], 10 g; Dried root of *Paeonia lactiflora* Pall. [Paeoniaceae], 20 g; Dried root of *Scutellaria baicalensis* Georgi [Lamiaceae], 10 g; Dried rhizome of *Atractylodes macrocephala* Koidz. [Asteraceae], 10 g; Dried gizzard membrane of *Gallus gallus domesticus Brisson* [Phasianidae], 10 g; Dried whole plant of *Lysimachia christinae* Hance [Primulaceae], 20 g; Dried root of *Dolomiaea costus* (Falc.) Kasana & A.K.Pandey [Asteraceae], 10 g; Dried root of *Bupleurum falcatum* L. [Apiaceae], 10 g; Dried immature fruit of *Citrus × aurantium* L. [Rutaceae], 10 g; Stir-baked root and rhizome of *Glycyrrhiza uralensis* Fisch. ex DC. [Fabaceae], 10 g; Dried rhizome of *Ligusticum officinale* (Makino) Kitag. [Apiaceae], 10 g	NR	NR
Su 2022 [28]	Tongfu-Xingqi-Tang; Decoction; 100 mL, t.i.d. or q.i.d.	NR	Dried ripe seed of *Raphanus raphanistrum subsp. sativus* (L.) Domin [Brassicaceae], 30 g; Dried rhizome of *Atractylodes macrocephala* Koidz. [Asteraceae], 25 g; Stir-baked immature fruit of *Citrus × aurantium* L. [Rutaceae], 15 g; Dried root and rhizome of *Rheum officinale* Baill. [Polygonaceae], 15 g; Dried bark of the trunk of *Magnolia obovata* Thunb. [Magnoliaceae], 10 g; Dried unripe pericarp of *Areca catechu* L. [Arecaceae], 10 g; Dried ripe seed of *Trichosanthes kirilowii* Maxim. [Cucurbitaceae], 10 g; Dried ripe fruit of *Wurfbainia villosa* (Lour.) Škorničk. & A.D.Poulsen [Zingiberaceae], powdered form dissolved in water, 6 g; Natrii sulfas, 5 g	NR	NR
Arfeen 1995 [16]	Ginger; Capsule; 1–2 cap, q.d.	Blackmores Ltd., Sydney, Australia	Fresh rhizome of *Zingiber officinale* Roscoe [Zingiberaceae], 0.5 g	NR	NR
Eberhart 2003 [29]	Ginger; Capsule; 1–2 cap, t.i.d.	NR	Fresh rhizome of *Zingiber officinale* Roscoe [Zingiberaceae], 0.1 g	NR	NR
Pongrojpaw 2003 [30]	Ginger; Capsule; 2 cap, q.d.	Khaolaor Laboratories Co., Ltd., Samut Prakan, Thailand	Fresh rhizome of *Zingiber officinale* Roscoe [Zingiberaceae], 0.5 g	NR	NR

(*Continued*)

Table 2

(*Continued*)

First author Year	Prescription; Dosage form; Dosage	Pharmaceutical manufacturer	Dose of individual components	Quality control	Chemical profile
Apariman 2006 [31]	Ginger; Capsule; 3 cap, q.d.	NR	Fresh rhizome of *Zingiber officinale* Roscoe [Zingiberaceae], 0.5 g	NR	NR
Bameshki 2018 [13]	Ginger; Capsule; 2 cap, q.d.	Goldaru Pharmaceutical Co., Isfahan, Iran	Fresh rhizome of *Zingiber officinale* Roscoe [Zingiberaceae], 0.25 g	NR	NR
Albooghobeish 2018 [32]	Ginger; Capsule; 3 cap, q.d.	Goldaru Pharmaceutical Co., Isfahan, Iran	Fresh rhizome of *Zingiber officinale* Roscoe [Zingiberaceae], 0.25–0.5 g	NR	NR
Kuwamura 2015 [33]	Hange-Shashin-To; Extract granules mixed with jelly; 2.5 g, q.d.	Tsumura & Co., Tokyo, Japan	Dried tuber of *Pinellia ternata* (Thunb.) Makino [Araceae], 5 g; Dried root of *Scutellaria baicalensis* Georgi [Lamiaceae], 2.5 g; Dried rhizome of *Zingiber officinale* Roscoe [Zingiberaceae], 2.5 g; Dried root and rhizome of *Glycyrrhiza uralensis* Fisch. ex DC. [Fabaceae], 2.5 g; Dried ripe fruit of *Ziziphus jujuba* Mill. [Rhamnaceae], 2.5 g; Dried root of *Panax ginseng* C.A.Mey. [Araliaceae], 2.5 g; Dried rhizome of *Coptis chinensis* Franch. [Ranunculaceae], 1.0 g	NR	NR
Leng 2003 [34]	Reconciling-lifting-method-Tang; Decoction; 100 mL, b.i.d.	NR	Dried root of *Codonopsis pilosula* (Franch.) Nannf. [Campanulaceae], 12 g; Dried rhizome of *Atractylodes macrocephala* Koidz. [Asteraceae], 15 g; Dried bark of the trunk of *Magnolia obovata* Thunb. [Magnoliaceae], 10 g; Dried root of *Bupleurum falcatum* L. [Apiaceae], 8 g; Dried root of *Paeonia lactiflora* Pall. [Paeoniaceae], 8 g; Dried root and rhizome of *Glycyrrhiza uralensis* Fisch. ex DC. [Fabaceae], 6 g	NR	NR
Soltani 2018 [35]	Ginger; Capsule; 1 cap, q.d.	Goldaru Pharmaceutical Co., Isfahan, Iran	Fresh rhizome of *Zingiber officinale* Roscoe [Zingiberaceae], 0.5 g	NR	NR
Phillips 1993 [36]	Ginger; Capsule; 2 cap, q.d.	Martindale Pharmaceuticals Ltd., Brentwood, UK	Fresh rhizome of *Zingiber officinale* Roscoe [Zingiberaceae], 0.5 g	NR	NR
Li 2006 [37]	Jiawei-Pingwei-San; Extracted granules; NR, b.i.d.	Jiangzhong Pharmaceutical Factory, Nanchang, China	Dried rhizome of *Atractylodes lancea* (Thunb.) DC. [Asteraceae], 8 g; Dried ripe pericarp *Citrus reticulata* Blanco [Rutaceae], 6 g; Dried root and rhizome of *Glycyrrhiza uralensis* Fisch. ex DC. [Fabaceae], 6 g; Dried root of *Dolomiaea costus* (Falc.) Kasana & A.K.Pandey [Asteraceae], 10 g; Dried bark of the trunk of *Magnolia obovata* Thunb. [Magnoliaceae], 10 g; Dried tuber of *Pinellia ternata* (Thunb.) Makino [Araceae], 10 g; Dried root of *Scutellaria baicalensis* Georgi [Lamiaceae], 10 g; Dried immature fruit of *Citrus × aurantium* L. [Rutaceae], 12 g; Dried rhizome of *Cyperus rotundus* L. [Cyperaceae], 12 g; Dried sclerotium of *Poria cocos* (Schw.) Wolf. [Polyporaceae], 15 g; Dried root of *Achyranthes bidentata* Blume [Amaranthaceae], 15 g	NR	NR
Liu 2021 [38]	Chaihu-Shugan-San combined with Pingwei-San; Decoction; 100 mL, b.i.d.	NR	Dried rhizome of *Atractylodes lancea* (Thunb.) DC. [Asteraceae], 15 g; Dried bark of the trunk of *Magnolia obovata* Thunb. [Magnoliaceae], 10 g; Dried ripe pericarp *Citrus reticulata* Blanco [Rutaceae], 10 g; Dried root of *Bupleurum falcatum* L. [Apiaceae], 10 g; Dried rhizome of *Ligusticum officinale* (Makino) Kitag. [Apiaceae], 10 g; Dried rhizome of *Cyperus rotundus* L. [Cyperaceae], 10 g; Dried immature fruit of *Citrus × aurantium* L. [Rutaceae], 10 g; Dried root of *Paeonia lactiflora* Pall. [Paeoniaceae], 10 g; Stir-baked root and rhizome of *Glycyrrhiza uralensis* Fisch. ex DC. [Fabaceae], 15 g	NR	NR
Zhu 2021 [39]	Xiangsha-Liujunzi-Tang; Decoction (NR, b.i.d.); Pills (6–9 g, NR).	NR	Dried root of *Panax ginseng* C.A.Mey. [Araliaceae], 3 g; Dried rhizome of *Atractylodes macrocephala* Koidz. [Asteraceae], 6 g; Dried sclerotium of *Poria cocos* (Schw.) Wolf. [Polyporaceae], 6 g; Stir-baked root and rhizome of *Glycyrrhiza uralensis* Fisch. ex DC. [Fabaceae], 2 g; Dried ripe pericarp *Citrus reticulata* Blanco [Rutaceae], 2.5 g; Dried tuber of *Pinellia ternata* (Thunb.) Makino [Araceae], denatured by ginger extract, 3 g; Dried root of *Dolomiaea costus* (Falc.) Kasana & A.K.Pandey [Asteraceae], 2 g; Dried ripe fruit of *Wurfbainia villosa* (Lour.) Škornič k. & A.D.Poulsen [Zingiberaceae], 2.5 g; Fresh rhizome of *Zingiber officinale* Roscoe [Zingiberaceae], 6 g	NR	NR
Visalyaputra 1998 [17]	Ginger; Capsule; 2 cap, b.i.d.	Faculty of Pharmacy, Mahidol University, Bangkok, Thailand	Fresh rhizome of *Zingiber officinale* Roscoe [Zingiberaceae], 0.5 g	NR	NR

b.i.d. = bis in die, cap = capsule, NR = not reported, q.i.d. = quarter in die, t.i.d. = ter in die.

I^2 = 0%). In both studies, ginger was administered to patients who underwent gynecological laparoscopy.[16,29]

3.5.1.2.1.2. Incidence of nausea 24 hours after surgery. A meta-analysis including 4 studies with a total of 390 patients found no significant difference in the incidence of nausea between the 2 groups 24 hours after surgery (RR = 0.79, 95% CI 0.56–1.12, P = .19), with high heterogeneity (P = .09, I^2 = 53%) (Fig. 5).[17,29,30,36]

3.5.1.2.2. Incidence of vomiting.

3.5.1.2.2.1. Incidence of vomiting 2 hours after surgery. A meta-analysis including 3 studies with a total of 340 patients demonstrated no significant difference in the incidence of vomiting between the 2 groups at 2 hours after surgery (RR = 0.38, 95% CI 0.12–1.25, P = .11), with high heterogeneity (P = .006, I^2 = 80%). Among them with ginger administered 1 hour before surgery, 2 studies included patients undergoing laparoscopic cholecystectomy[13,32] and 1 study had patients with gynecological laparoscopy.[31]

3.5.1.2.2.2. Incidence of vomiting 3 hours after surgery. A meta-analysis including 2 studies with a total of 283 patients revealed no significant difference in the incidence of vomiting between the 2 groups (RR = 1.40, 95% CI 0.85–2.30, P = .19), with low heterogeneity (P = .89, I^2 = 0%). In both studies, ginger was administered to patients who underwent gynecological laparoscopy.[16,29]

Table 3

Frequency of use of individual herbs.

Frequency	Latin name	Scientific name
12	*Zingiberis Rhizoma Recens*	*Zingiber officinale* Roscoe [Zingiberaceae]
6	*Glycyrrhizae Radix et Rhizoma*	*Glycyrrhiza uralensis* Fisch. ex DC. [Fabaceae]
5	*Bupleuri Radix*	*Bupleurum falcatum* L. [Apiaceae]
	Scutellariae Radix	*Scutellaria baicalensis* Georgi [Lamiaceae]
	Pinelliae Tuber	*Pinellia ternata* (Thunb.) Makino [Araceae]
	Magnoliae Cortex	*Magnolia obovata* Thunb. [Magnoliaceae]
	Paeoniae Radix	*Paeonia lactiflora* Pall. [Paeoniaceae]
4	*Atractylodis Rhizoma Alba*	*Atractylodes macrocephala* Koidz. [Asteraceae]
	Aurantii Fructus Immaturus	*Citrus × aurantium* L. [Rutaceae]
	Citri Unshius Pericarpium	*Citrus reticulata* Blanco [Rutaceae]

3.5.1.2.2.3. Incidence of vomiting 24 hours after surgery. A meta-analysis including 4 studies with a total of 390 patients demonstrated no significant difference in the incidence of vomiting between the 2 groups (RR = 0.81, 95% CI 0.45–1.49, P = .50), with low heterogeneity (P = .06, I^2 = 60%) (Fig. 6). All 4 studies administered ginger to patients who underwent gynecological laparoscopy.[17,29,30,36]

3.5.1.3. Herbal medicine versus Western medicine.

3.5.1.3.1. Incidence of nausea. A total of 136 patients from 2 RCTs were included in the meta-analysis. No significant difference was found in the incidence of nausea between the 2 groups (RR = 0.94, 95% CI 0.63–1.42, P = .77), and heterogeneity was low (P = .75, I^2 = 0%) (Fig. 7). Both studies administered ginger to patients undergoing gynecological laparoscopy, using metoclopramide[36] and droperidol[17] as a control.

3.5.1.3.2. Incidence of vomiting. A total of 200 patients from 3 RCTs were included in this meta-analysis.[17,34,36] No significant difference was found in the incidence of vomiting between the 2 groups (RR = 0.68, 95% CI 0.25 to 1.84, P = .45), and heterogeneity was high (P = .04, I^2 = 68%) (Fig. 8).

3.5.2. Secondary outcome: frequency of vomiting. To assess the clinical efficacy of herbal medicines for PONV, this review utilized the frequency of vomiting events, measured by the number of vomiting events per patient during the observation period following laparoscopic surgery.

3.5.2.1. Herbal medicine versus no treatment. A total of 1099 patients from 2 RCTs were included in the meta-analysis.[24,25] No significant difference was found in the number of vomiting events between the 2 groups (MD = –2.27, 95% CI – 5.63 to 1.09, P = .19), and heterogeneity was high (P < .00001, I^2 = 100%) (Fig. 9).

3.5.3. Secondary outcome: severity of nausea. This review assessed the clinical efficacy of herbal medicines for PONV based on the severity of nausea, referring to the subjective intensity experienced during the observation period following laparoscopic surgery. Assessment tools such as visual analog scale and numerical rating scale were employed. Additionally, when multiple study results were available, the effects were analyzed separately for each symptom observation period.

3.5.3.1. Herbal medicine versus placebo.

3.5.3.1.1. Severity of nausea 0 hour after surgery. A meta-analysis including 2 studies with a total of 200 patients revealed no significant difference in the severity of nausea between the 2

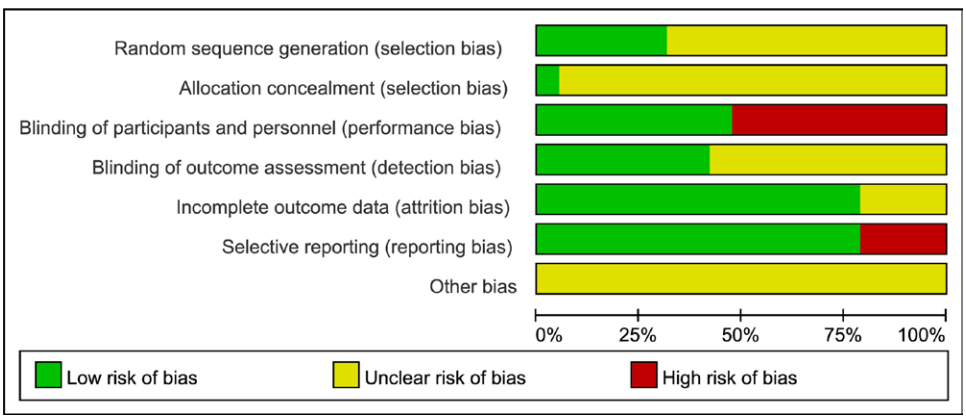

Figure 2. Risk of bias graph.

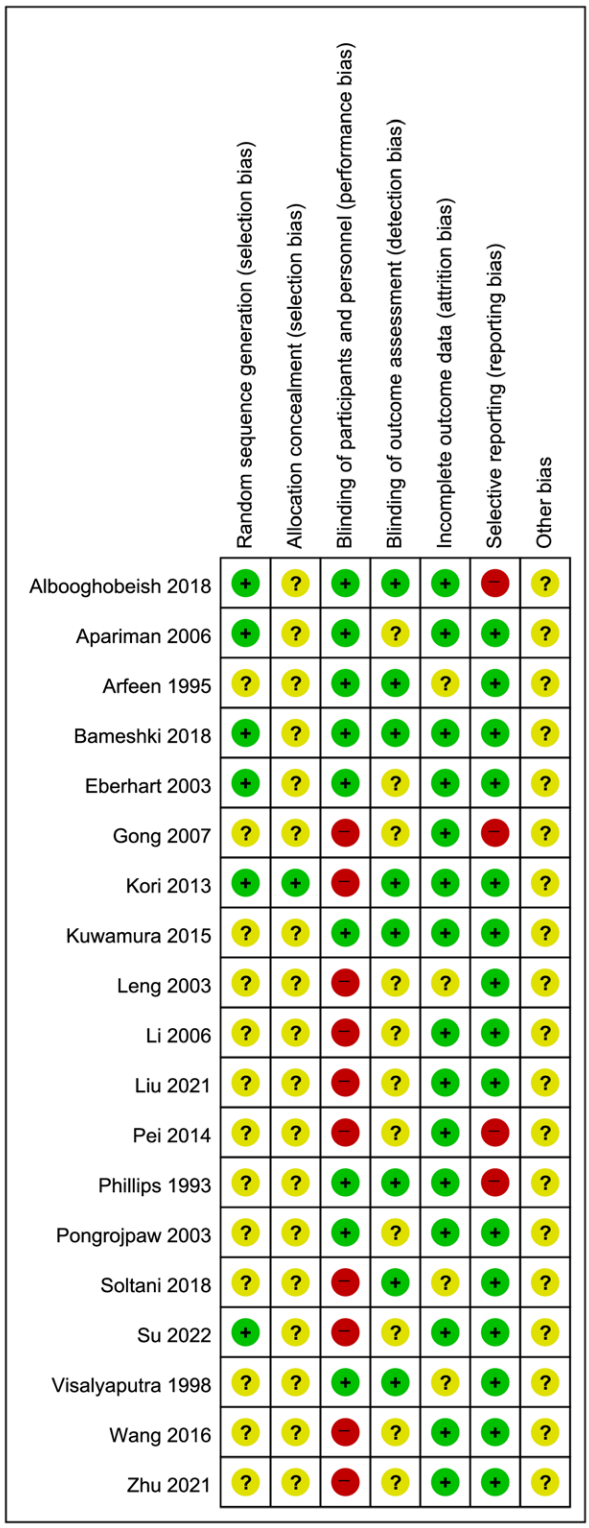

Figure 3. Risk of bias summary.

groups (SMD = −0.03, 95% CI −0.31 to 0.25, $P = .84$), with low heterogeneity ($P = .74$, $I^2 = 0\%$) (Fig. 10A).[32,33]

3.5.3.1.2. Severity of nausea 2 hours after surgery. A meta-analysis including 2 studies with 280 patients demonstrated no significant difference in the severity of nausea between the 2 groups (SMD = −1.21, 95% CI −2.94 to 0.53, $P = .17$), with high heterogeneity ($P < .00001$, $I^2 = 98\%$) (Fig. 10B).[13,32]

3.5.3.1.3. Severity of nausea 6 hours after surgery. A meta-analysis including 2 studies with a total of 280 patients demonstrated no significant difference in the severity of nausea between the 2 groups (SMD = −1.32, 95% CI −3.77 to 1.13, $P = .29$), with high heterogeneity ($P < .00001$, $I^2 = 99\%$) (Fig. 10C).[13,32]

3.5.3.1.4. Severity of nausea 12 hours after surgery. A meta-analysis including 2 studies with a total of 280 patients revealed that herbal medicine was more effective in reducing the intensity of nausea compared with placebo, which was significant (SMD = −2.04, 95% CI −3.67 to −0.41, $P = .01$), with high heterogeneity ($P < .00001$, $I^2 = 97\%$) (Fig. 10D).[13,32]

3.5.3.1.5 Severity of nausea 24 h after surgery. A meta-analysis including 2 studies with a total of 200 patients demonstrated no significant difference in the severity of nausea between the 2 groups (SMD = −0.84, 95% CI −2.11 to 0.43, $P = .19$), and the heterogeneity was high ($P < .00001$, $I^2 = 94\%$) (Fig. 10E). The studies administered ginger to patients undergoing laparoscopic cholecystectomy[32] and Hange-Shashin-To to those undergoing gynecological laparoscopy,[33] respectively.

3.5.4. Secondary outcome: use of antiemetics. This review evaluated the clinical efficacy of herbal medicines for PONV based on the number of patients experiencing severe nausea and vomiting during the observation period after laparoscopic surgery, necessitating the use of additional antiemetics.

3.5.4.1. Herbal medicine versus placebo. A total of 465 patients from 4 RCTs were included in the analysis.[29,30,32,36] No significant difference was found in the use of antiemetics between the 2 groups (RR = 0.38, 95% CI 0.10–1.40, $P = .15$), and heterogeneity was high ($P < .0001$, $I^2 = 88\%$) (Fig. 11).

3.6. Safety evaluation: incidence of adverse events

Eleven RCTs involving 971 patients reported cumulative incidences of adverse events.[16,25,27–31,33,35,38,39] No adverse events were reported in 4 of these studies.[25,28,33,35] The patients in the experimental group, including herbal medicines, experienced adverse events such as abdominal discomfort, heartburn, headache, and dizziness. A meta-analysis of the included studies revealed a difference in the incidence of adverse events between the 2 groups, with a significantly lower occurrence in the herbal medicine group (RR = 0.45, 95% CI 0.27–0.72, $P = .001$) and low heterogeneity ($P = .17$, $I^2 = 34\%$) (Fig. 12).

3.7. Publication bias

We assessed publication bias through a funnel plot of 11 articles related to adverse events, comparing experimental (containing herbal medicine) and control (without herbal medicine) groups. Our determination was that publication bias was low since no asymmetry was noted in the distribution of data points (Fig. 13).

4. Discussion

The pathophysiology of PONV remains unclear; however, it is believed to be influenced by a variety of factors, including patient characteristics, anesthetic factors, and the type of surgery.[43] Surgical procedures, such as long operating times and the use of analgesics, along with specific types like laparoscopy and laparotomy, can affect PONV.[44] Among the various surgical types, laparoscopic surgery was selected for this study due to its increasing prevalence in recent years,[5] and the compression of the gastrointestinal tract caused by the inflation of the abdomen with carbon dioxide during laparoscopy may lead to intestinal ischemia. This, coupled with the release of serotonin,

makes patients more susceptible to nausea and vomiting.[20,45] As many as half of patients experience PONV after laparoscopic surgery,[46] which can result in additional issues such as dehydration, electrolyte imbalance, and in severe cases, aspiration pneumonia.[47]

Compared with patients without PONV, those with PONV experience longer hospital stays, additional treatment costs, and a poorer quality of life.[7,48] Specifically, postoperative recovery room time is prolonged by 30%, from an average of 3 to 4 hours. Additionally, the presence of PONV adds approximately 14% to the cost of care, increasing from approximately $730 to $830 in 2020.[48] Despite these impacts, the management of PONV has received relatively minimal attention compared to pain and infection control in postoperative care.

Current medications for the prevention and treatment of PONV primarily consist of 5-hydroxytryptamine type 3 receptor antagonists, which interfere with neurotransmitter action.[18] However, these drugs are not always effective and are known to cause side effects such as changes in blood pressure and extrapyramidal disorders.[9] Furthermore, treatment guidelines that can be consistently applied to all patients remain unclear due to the variety of clinical situations and conditions.

Due to these obstacles, conventional treatments are limited, and there is a need for the development of new therapies or the research and clinical application of alternative medicine. Existing clinical trials and analytical studies primarily focus on ginger,[7,12,49] whose components and actions have been shown to suppress nausea and vomiting.[50] Ginger's gingerols, shogaols, sesquiterpenes, and monoterpenes interfere with acetylcholine and serotonin action, increasing gastrointestinal motility and effectively treating nausea and vomiting. Additionally, as ginger acts directly in the gastrointestinal tract, it does not cause central nervous system side effects observed with other medications.[51] Consequently, several studies have reported the efficacy of ginger in treating nausea and vomiting in pregnant women and managing nausea and vomiting as side effects of chemotherapy and various surgical procedures.[11,52,53] Nevertheless, we found no studies that conducted systematic reviews or meta-analyses to determine the overall efficacy of herbal medicines for PONV in laparoscopic surgery, a scenario frequently encountered in clinical practice.

As mentioned earlier, there is a growing interest in laparoscopic surgery in the surgical field, and patients prefer this surgical method. However, the benefits of laparoscopic surgery in the context of PONV have not been clearly emphasized, and its prevention and treatment are essential. Therefore, in this study, we collected published RCTs on laparoscopic surgery and herbal medicine and conducted a systemic review by integrating the efficacy of each comparative intervention method via a meta-analysis.

Five studies[24–28] compared herbal medicine with no treatment, and two efficacy indicators were meta-analyzed: incidence and frequency of vomiting. The incidence of vomiting was significantly lower in the herbal medicine group than in the no treatment group. The herbal medicines used in these studies, He-Zhong-Yin decoction[24] and Go-Rei-San powder,[25] were administered to the patients for prophylactic purposes before surgery.

Ten studies compared herbal medicine to a placebo,[13,16,17,29–33,36,37] and 4 efficacy endpoints were meta-analyzed: incidence of nausea and vomiting, severity of nausea,

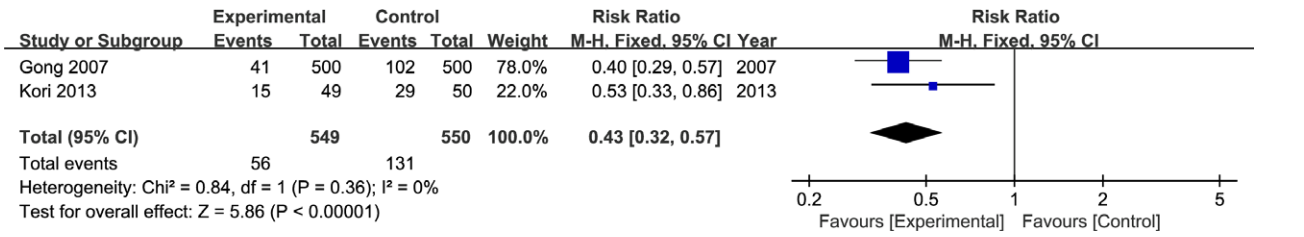

Figure 4. Forest plot of the comparison for the incidence of vomiting between herbal medicine and no treatment.

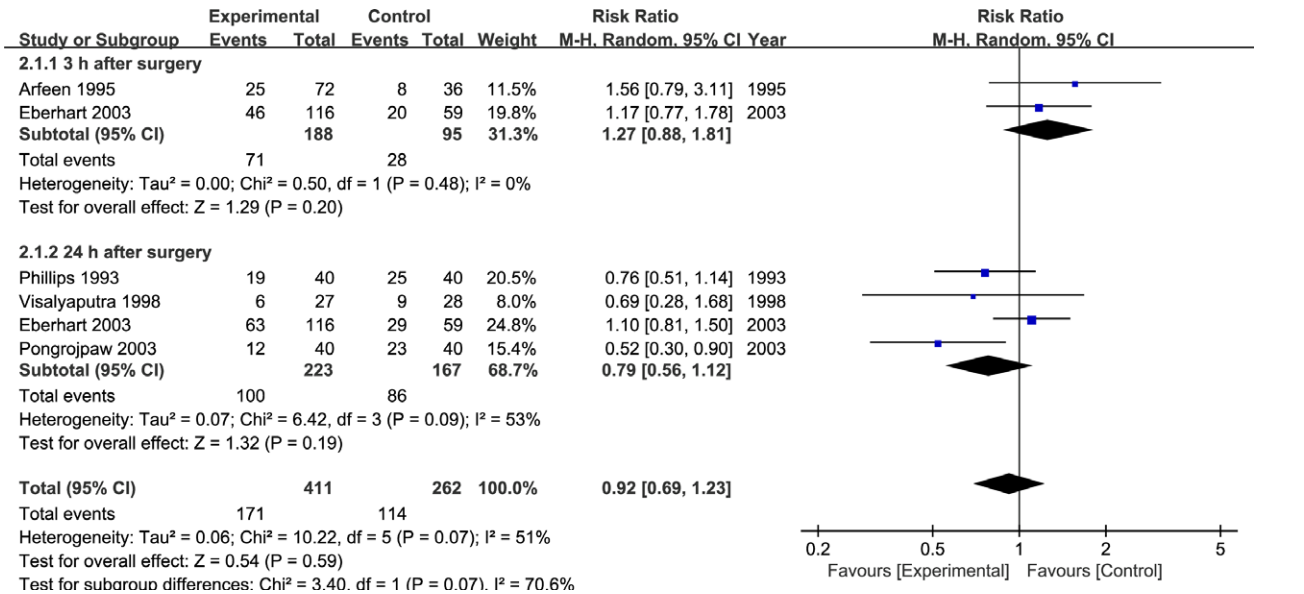

Figure 5. Forest plot of the comparison for the incidence of nausea between herbal medicine and placebo.

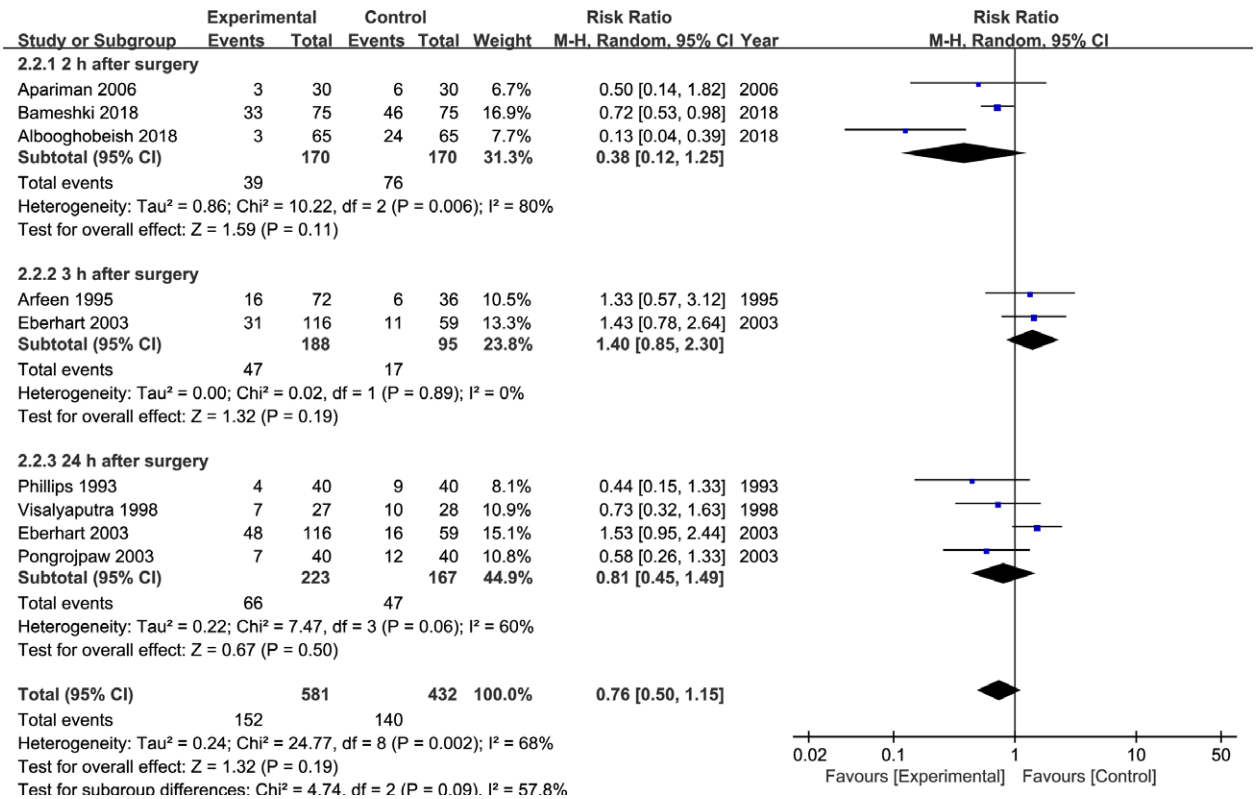

Figure 6. Forest plot of the comparison for the incidence of vomiting between herbal medicine and placebo.

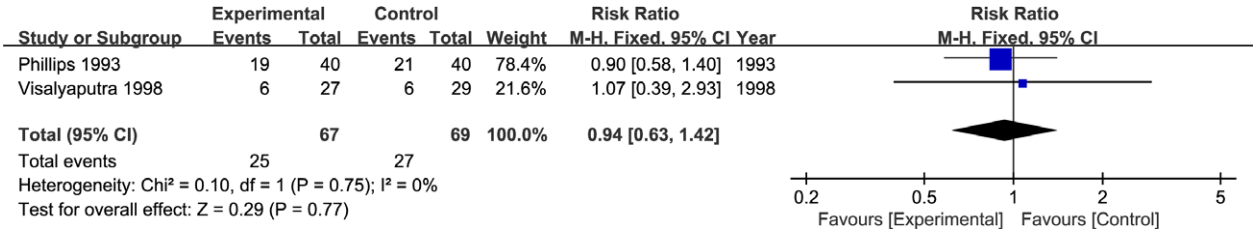

Figure 7. Forest plot of the comparison for the incidence of nausea between herbal medicine and Western medicine.

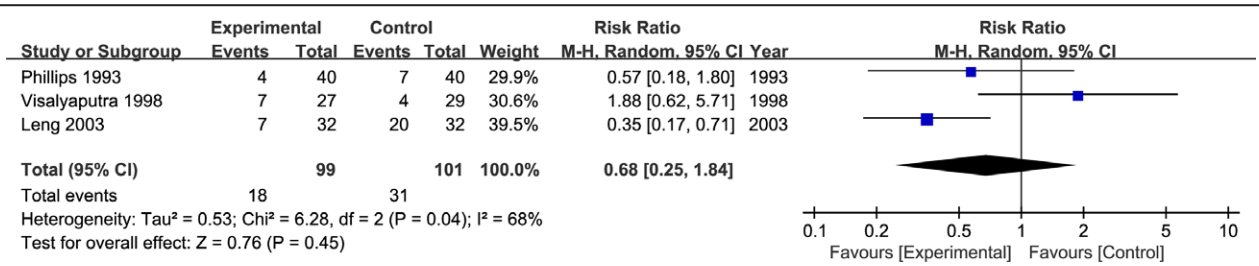

Figure 8. Forest plot of the comparison for the incidence of vomiting between herbal medicine and Western medicine.

and use of antiemetics. The results collectively demonstrated a significant effect of herbal medicine on reducing the intensity of nausea compared with placebo at 12 hours postoperatively. Both studies,[13,32] included in the meta-analysis of the severity of nausea 2 hours/6 hours/12 hours after surgery involved patients undergoing laparoscopic cholecystectomy, with ginger administered 1 hour preoperatively. However, different doses of ginger were used, i.e., 1.25[32] and 0.5 g[13] of ginger, leading to high heterogeneity. In the meta-analysis of the incidence of nausea 24 hours after surgery and incidence of vomiting 24 hours after surgery, all 4 studies administered ginger to patients undergoing gynecological laparoscopy.[17,29,30,36] In a sensitivity analysis, excluding one study[29] using 0.3 to 0.6 g of ginger reduced heterogeneity from 53% to 0%, and the remaining 3 studies[17,30,36] had a total ginger dose of 1 to 2 g. Regarding the incidence of vomiting 2 hours after surgery, excluding one study using 0.5 g of ginger[13] from the meta-analysis of the 3 studies[13,31,32] reduced heterogeneity from 80% to 61%. The total dose of ginger was 1.25[32] and 1.5 g,[31] suggesting that the ginger dose used in the trials may have contributed to the difference in efficacy and increased heterogeneity.

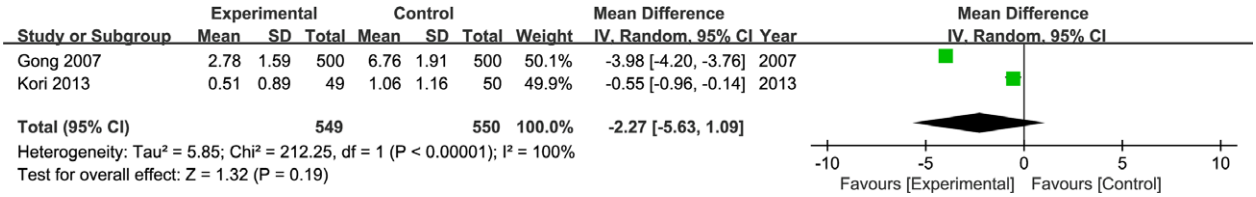

Figure 9. Forest plot of the comparison for the frequency of vomiting between herbal medicine and no treatment.

Similarly, regarding the secondary outcome of the use of antiemetics, a high heterogeneity of 88% was noted, which reduced to 65% when excluding one study that used a total dose of 0.3 to 0.6 g of ginger[29] compared to the other 3 studies[30,32,36] using 1 to 1.25 g of ginger. One study administered ginger to patients undergoing laparoscopic cholecystectomy,[32] and 3 other studies used ginger for patients undergoing gynecological laparoscopy.[29,30,36] Excluding this study reduces the heterogeneity to 78%.[32] Differences in the type of surgery and patients' sex may affect the results' heterogeneity, as a previous study reported a sex difference in the incidence of PONV, explaining that hormonal changes during a woman's menstrual cycle may increase PONV risk, resulting in a 2- to 4-fold higher incidence of PONV in women compared with men.[54]

Five studies compared herbal medicines to Western medicines,[17,34–37] and 2 efficacy indicators were meta-analyzed: incidence of nausea and vomiting. The meta-analysis demonstrated similar effects on the incidence of nausea and vomiting, with no significant differences between herbal and Western medicines. Regarding the incidence of vomiting, of the 3 studies included in the meta-analysis, two used metoclopramide,[34,36] and one used droperidol as a control.[17] The heterogeneity was reduced to 0% when the study using droperidol was excluded.[17] The type of drug used as a control in the clinical trials may have contributed to the differences in efficacy and increased heterogeneity.

Three studies compared a combination of herbal and Western medicines to Western medicine alone.[17,38,39] However, similar outcome measures were not evaluated, preventing a meta-analysis. Despite this limitation, each study confirmed the efficacy of herbal–Western medicine combination treatment. One study analyzed the frequency of vomiting episodes in a combination group receiving herbal medicine (Chaihu-Shugan-San combined with Pingwei-San) and prokinetics (mosapride citrate and loperamide hydrochloride) versus a Western-medicine-alone group. They found a significant reduction in the number of vomiting episodes in the combination group ($P < .001$).[38] Another study analyzed PONV onset time, severity of nausea, and incidence of PONV in a combination group (Xiangsha-Liujunzi-Tang and Tropisetron) compared with a Western-medicine-alone group.[39] All outcomes favored the combination arm ($P < .05$).

The meta-analysis showed no significant difference in the incidence of adverse events between the herbal and placebo groups. Additionally, as there were fewer adverse events in the herbal treatment and combination treatment groups than in the no-treatment and Western-medicine-alone groups, it can be concluded that herbal medicine can be a safe treatment for PONV. It is also suggested that herbal medicine in combination treatment can mitigate the adverse events caused by Western medicine.

In this study, our aim was to objectively determine the efficacy and safety of herbal medicine in the treating nausea and vomiting after laparoscopic surgery. We concluded that herbal medicine can be used effectively and safely to reduce the incidence of PONV, especially the intensity of nausea 12 hours after surgery. However, there are several limitations. Firstly, the included RCTs were of low quality and subject to several risks of bias. More than half of the studies did not blind the participants or researchers by using visually distinguishable interventions. While the Cochrane risk-of-bias tool was utilized, discrepancies among reviewers and subjectivity in bias assessment may lead to inconsistencies. To bolster reliability, ensuring consensus among reviewers through training and calibration exercises can mitigate subjective bias in risk evaluation. Secondly, although we tried to maintain consistency in the intervention methods by limiting them to orally administered drugs in the herbal medicine category, there was heterogeneity in the composition, dose, and timing of administration. The number of comparable studies using combination treatments as treatment groups or Western medicines as controls was insufficient. Finally, there were limited subgroup analyses to address the high heterogeneity. There are clinical heterogeneities due to patient characteristics, concomitant medications, or surgical techniques. To enhance, upcoming research endeavors might explore employing sophisticated statistical techniques customized to tackle diversity, such as random-effects models or subgroup analyses focusing on patient attributes, interventions, or outcomes. Furthermore, we believe that these gaps should be addressed in the future with more rigorously designed RCTs comparing the same interventions, employing strict double-blinding, randomization, and allocation concealment, and minimizing the risk of bias to enhance the foundation of evidence and improve the dependability of conclusions. In forthcoming studies, it is crucial to prioritize thorough data reporting and transparency to mitigate the influence of missing data on the overall analysis. Additionally, to evaluate and generalize the treatment effect of interventions more objectively, there should be increased activation of prospective observational studies and large-scale registry studies in this field, both qualitatively and quantitatively. It is necessary to conduct clinical trials using single herbal medicine and investigate more effective combinations of herbal medicines through methodologies such as network analysis based on updated quantitative data from recent research. Moreover, research on the active ingredients and pharmacokinetics of single and combined herbal medicines, as well as ginger, should be conducted to suggest prescription formulations likely to produce better results and be employed clinically. In this study, we only included RCTs that specified each component of the herbal prescriptions and presented the full prescription information in the text, minimizing heterogeneity among prescription interventions and ensuring clarity and consistency. To address the overestimation of treatment effects due to publication bias, researchers should proactively seek out gray literature and unpublished studies. Additionally, they should consider incorporating research in languages other than English and Chinese to mitigate language bias. In future research, to address geographical bias, researchers should strive for a diverse representation of geographic locations in their studies, while also contemplating the adoption of standardized outcome measures to facilitate comparisons among studies. These efforts may help produce reproducible and unbiased research results not only in East Asia but also in other countries that use herbal medicine.

5. Conclusions

This systematic review demonstrates the efficacy and safety of herbal medicines in reducing the incidence and intensity of

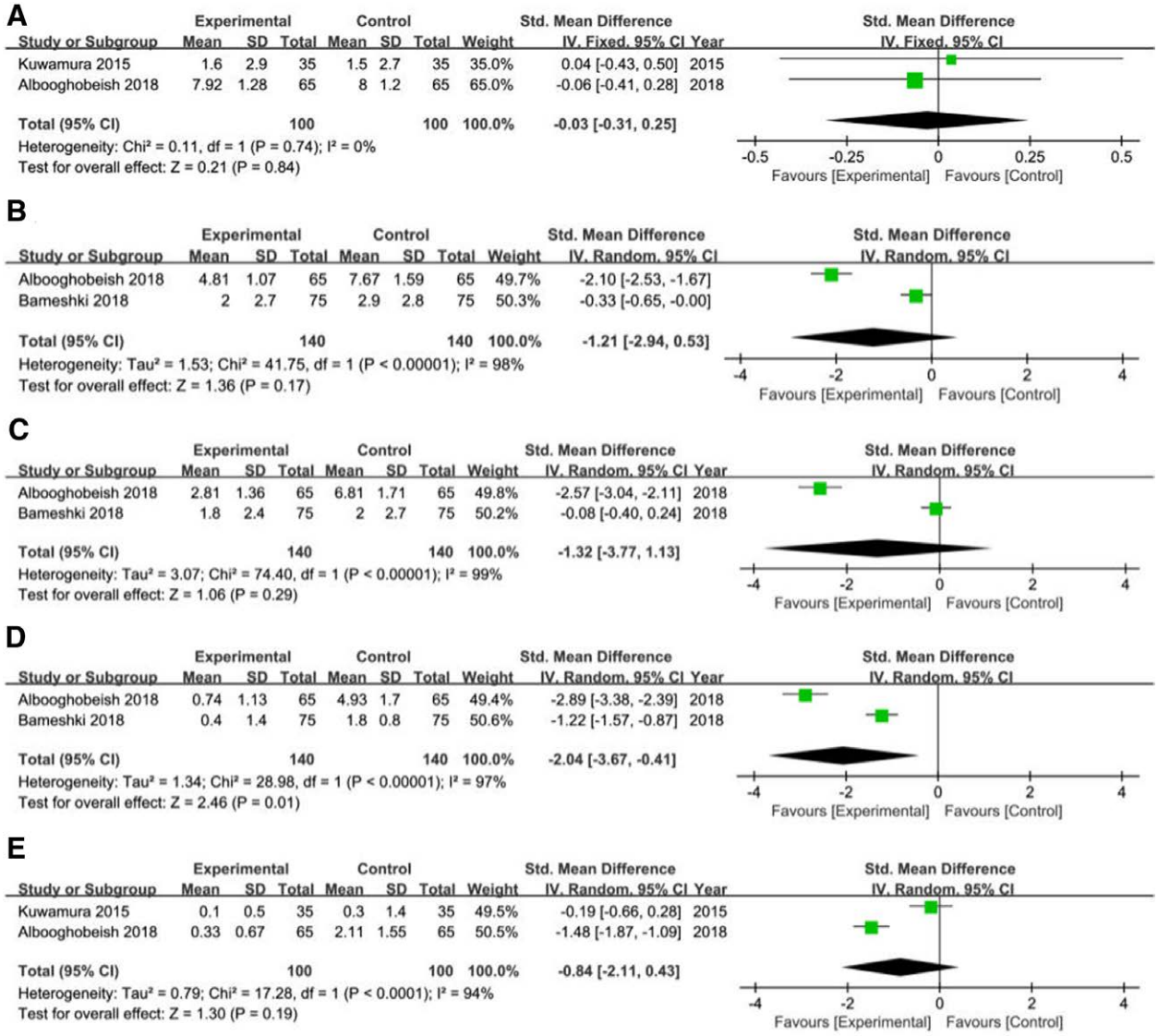

Figure 10. Forest plot of the comparison for the severity of nausea between herbal medicine and placebo; (A) 0 hour, (B) 2 hours, (C) 6 hours, (D) 12 hours, and (E) 24 hours after surgery.

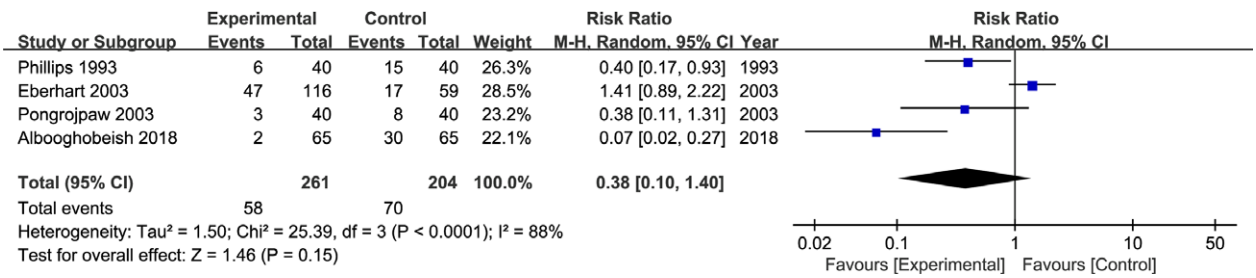

Figure 11. Forest plot of the comparison for the use of antiemetics between herbal medicine and placebo.

nausea and vomiting following laparoscopic surgery. The significance of this study lies in its effort to update the results of recent RCTs, aiming to enhance the clinical utility of herbal medicines for PONV. This expansion goes beyond the scope of existing studies, which had been limited to a single herbal medicine, ginger, to include complex herbal preparations with high clinical utility. This was achieved through extensive database searches encompassing various countries closely related to traditional herbal medicine. Additionally, the study specifically focused on laparoscopic surgery, a method currently performed frequently among various surgical techniques. The choice to concentrate on laparoscopic surgery is particularly relevant, considering its high incidence of PONV, and aligns with the latest clinical practices. Despite the relatively small number of studies, the results revealed significant benefits of herbal medicines for PONV across outcome measures. Further RCTs should be conducted to explore groups that were not identified in this study, including the complementary effects of combination therapy.

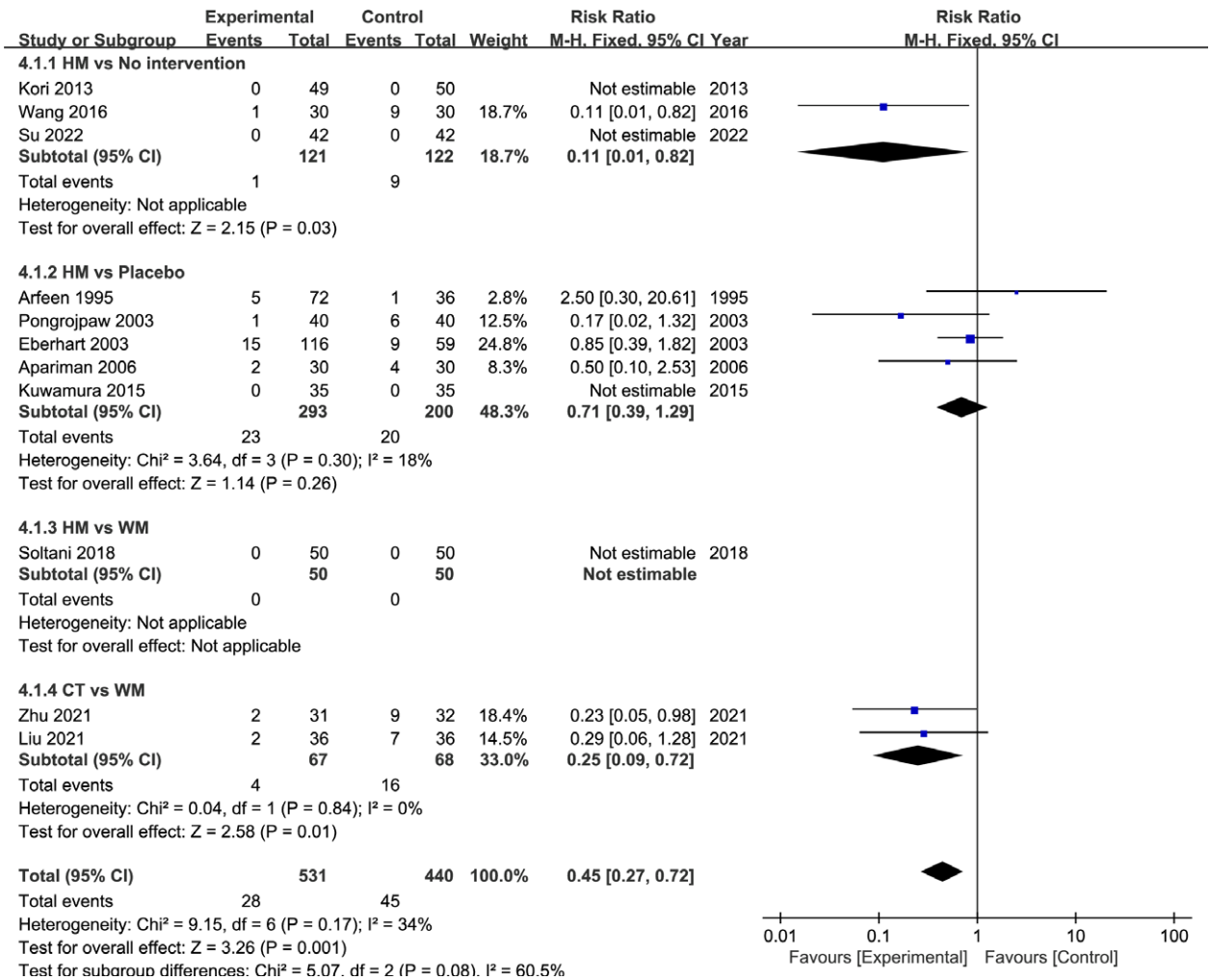

Figure 12. Forest plot of the comparison for the incidence of adverse events between the experimental and control groups. CT = combination therapy, HM = herbal medicine, WM = Western medicine.

Author contributions

Conceptualization: Na-Yeon Ha, Mu-Jin Park.
Data curation: Na-Yeon Ha, Mu-Jin Park.
Formal analysis: Na-Yeon Ha, Mu-Jin Park.
Methodology: Seok-Jae Ko, Jae-Woo Park, Jinsung Kim.
Writing – original draft: Na-Yeon Ha, Mu-Jin Park.
Writing – review & editing: Seok-Jae Ko, Jae-Woo Park, Jinsung Kim.

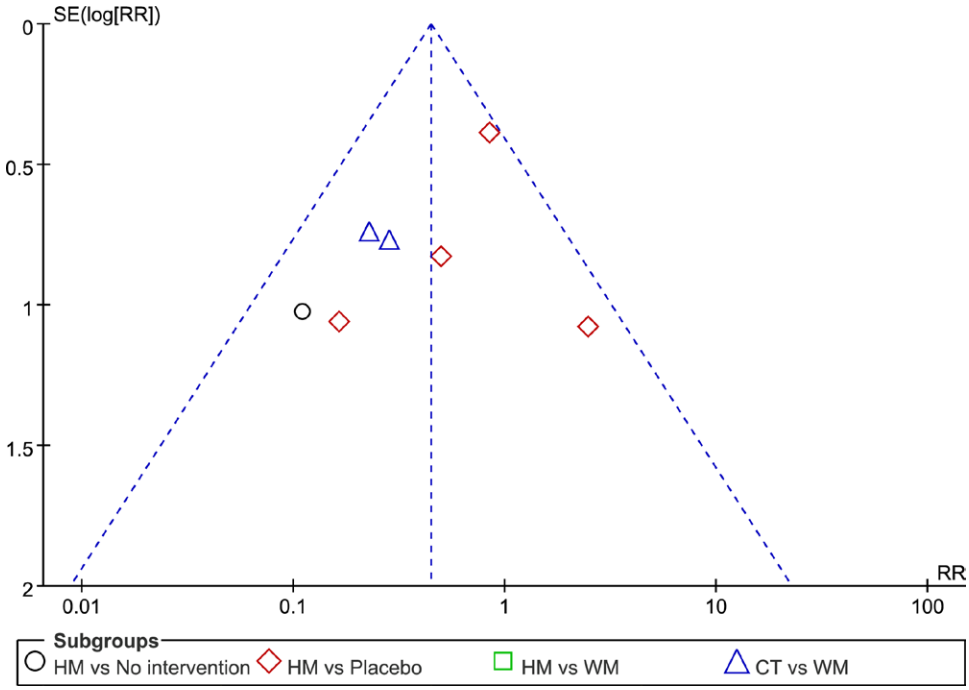

Figure 13. Funnel plot of the comparison for the incidence of adverse events between the experimental and control groups. CT = combination therapy, HM = herbal medicine, WM = Western medicine.

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