Original Article

Effects of sevoflurane and propofol on postoperative nausea and vomiting in patients with colorectal cancer placed under general anesthesia: a systematic review and meta-analysis

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Background: This study sought to explore the effects of sevoflurane and propofol on postoperative nausea and vomiting (PONV) in patients with colorectal cancer (CRC). Sevoflurane inhalation anesthesia has the advantages of short induction time, stable hemodynamic, stable anesthesia maintenance and short recovery time, and its anesthetic effect is similar to that of propofol, so it is worthy of comparative analysis.

Methods: The PubMed, Cochrane, Web of Science, Embase, clinical research register and CQVIP databases were searched to retrieve the data of randomized controlled trials (RCTs) published between October 2000 and October 2021 on the effects of sevoflurane and propofol on nausea and vomiting after laparoscopic surgery in patients with CRC. Applying the inclusion criteria, the literature selection, data extraction, and quality evaluation assessments were carried out for the included articles. The I^2 test was used to evaluate the heterogeneity between the studies, and the meta-analysis was performed using RevMan 5.2.6 software provided by Cochrane.

Results: A total of 12 RCTs were included in this meta-analysis. There was statistically significant differences in changes in postoperative heart rate [odds ratio (OR) =3.55, 95% confidence interval (CI): 2.40, 5.27, P<0.00001, I^2=0%, Z=6.30], mean artery pressure (MAP) (OR =2.58, 95% CI: 2.04, 3.26, P<0.00001, I^2=58%, Z=7.87), the incidence of PONV (OR =1.73, 95% CI: 1.38, 2.17, P<0.00001, I^2=46%, Z=4.78), and the incidence of postoperative disturbance of consciousness (OR =2.09, 95% CI: 1.62, 3.07, P<0.00001, I^2=63%, Z=5.67) between the experimental group and the control group.

Conclusions: Combining anesthesia with sevoflurane and propofol had good prevention and treatment effects for PONV in patients with CRC who underwent a laparoscopy and had a moderate central sedation effect.

Keywords: Laparoscope; colorectal cancer (CRC); postoperative nausea and vomiting (PONV); sevoflurane; propofol

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Introduction

Postoperative complications are common in colorectal cancer (CRC) (1). With an incidence of 30–70% (2,3), postoperative nausea and vomiting (PONV) is one of the most common complications of general anesthesia. Due to pneumoperitoneum and other factors, the incidence of PONV in laparoscopic surgery is high, and it has been reported that the incidence of PONV may be as high as 50–70% (4). PONV seriously affects the postoperative feelings of patients, and even leads to the dehiscence of incisions, acid-based imbalances, aspiration, and other serious consequences (5). Thus, the prevention of PONV has become a major clinical concern. PONV occurs for variety of reasons, including as a result of general anesthesia, abdominal organ pulling, and surgery (especially laparoscopic surgery); however, carbon trioxide pneumoperitoneum is the main cause of PONV (6). The incidence of PONV is significantly higher in laparoscopic patients than non-laparoscopic patients. Thus, it is important to implement effective measures to reduce the incidence of PONV in laparoscopic abdominal surgery patients to prevent complications after body anesthesia and reduce the risks of surgery.

The causes and nerve conduction of nausea and vomiting are not identical. Nausea is a subjective sensation guided by simple neuro-mediators, which is difficult to simulate in animal models, but its mechanism is not fully understood. Vomiting is a stimulation reaction from the pharynx to the gastrointestinal tract chemoreceptor excitation area or senior cortical center, through a series of neurotransmitters, including norepinephrine, dopamine and 5-HT, to the vomiting center, through the excited motor nerve center, respiratory center, sports center and other nerve reflex formation, vomiting (7). PONV are related to the cost, safety and comfort of postoperative patients. In the eyes of patients, postoperative nausea and vomiting ranked first among the undesirable side effects. In minors, its incidence is highest. Because of obesity, postoperative anxiety, it may also be prolonged surgery makes its incidence increased. It is also associated with specific procedures (such as laparoscopy and abdominal surgery, head and neck surgery, middle ear surgery, strabismus surgery). Potent inhaled anesthetics have not been particularly valuable in altering the occurrence of PONV. Anesthesia that causes sympathetic nerve excitation can increase postoperative nausea and vomiting. Ether combined with opioids, for example, causes nausea and vomiting in more than 70 percent of children. The addition of nitrous oxide to volatile anesthetics can increase the occurrence of PONV, especially desflurane.

PONV is the most common complication of anesthesia. Laparoscopic surgery is widely used in clinical settings but the incidence of nausea and vomiting is high (8). It is higher than that of non-laparoscopic surgery, which is mainly related to patient factors, anesthesia factors, the type and duration of surgery, and carbon dioxide pneumoperitoneum (9). Various inducing factors, such as acetylcholine, norepinephrine, 5-HT, and other transmitters, stimulate peripheral receptors and the vomiting center. Certain 5-HT3 receptor antagonists are widely used in the prevention and treatment of PONV (10), with the development of laparoscopic CRC surgery is increasingly promoted to take effective anti-emetic measures to prevent PONV has attracted more and more attention.

At present, there are some controversies about the effects of sevoflurane and propofol on the incidence of PONV, which may be related to the differences in pharmacological effects and water solubility of sevoflurane and propofol respectively.

Therefore, it is necessary to analyze this issue through systematic review meta-analysis in this study. We present the following article in accordance with the PRISMA reporting checklist (available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-783/rc).

Methods

Retrieval strategy

In this study, the PubMed, Cochrane, Web of Science, Embase, clinical research register and CQVIP databases were searched, and the retrieval time was limited from the initial construction time of the databases between October 2000 and October 2021. In addition, other methods, such as website, organization and citation searches, were employed to retrieve the relevant research articles. The key words used included “sevoflurane”, “propofol”, “rectal cancer”, and “nausea and vomiting” (see *Figure 1*).

Inclusion criteria

To be eligible for inclusion in this meta-analysis, the studies had to meet the following inclusion criteria: (I) report on a randomized controlled trial (RCT); (II) include subjects who had rectal cancer; (III) have the full text of the article available, and have the general basic data of the clinical

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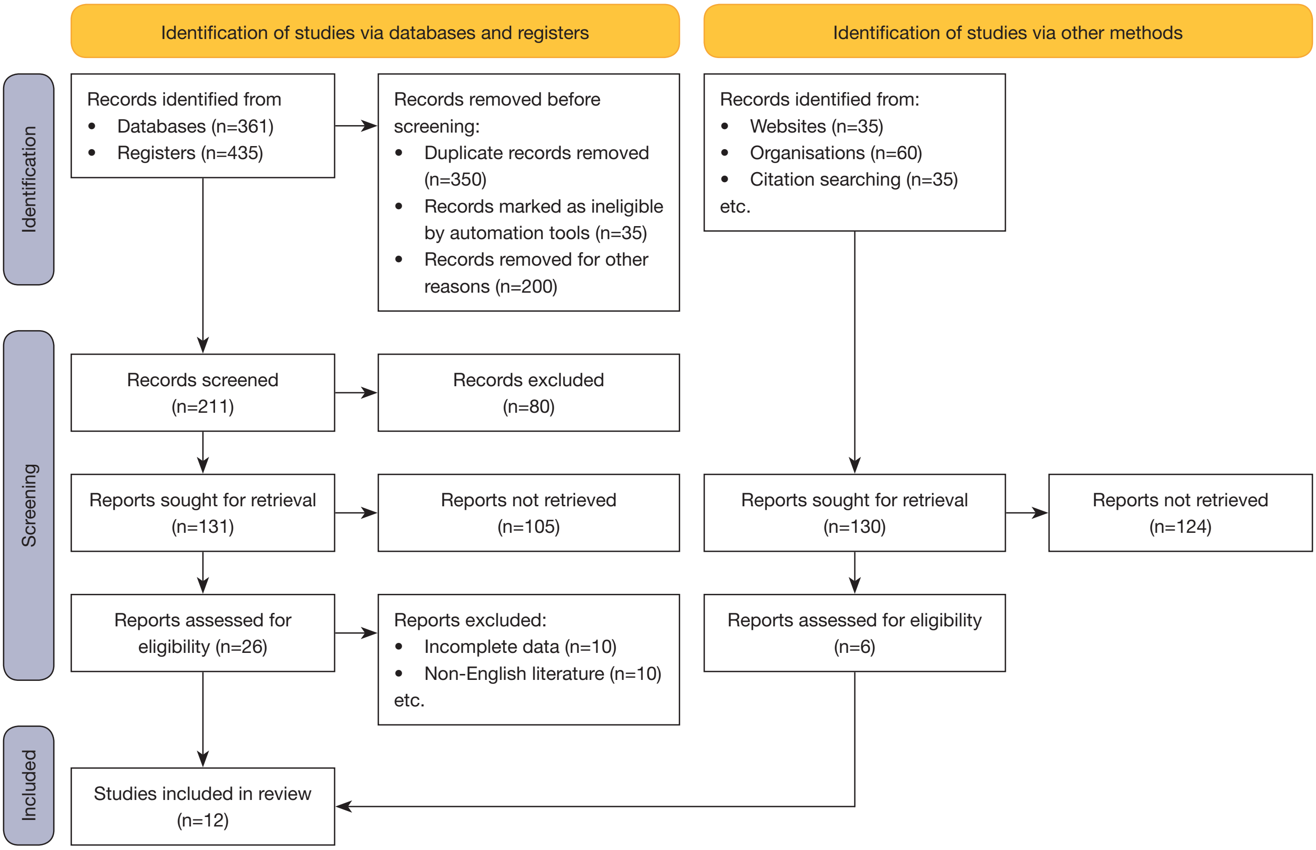

Figure 1 Flow chart of the literature screening.

patients available or directly available upon request; (IV) PICOS principle was adopted to clarify the criteria for the inclusion of patients. We used the PICOS principle to assist the logical framework or thinking in the construction of clinical research questions.

Exclusion criteria

Studies were excluded from this meta-analysis if they met any of the following exclusion criteria: (I) the data could not be extracted for the analysis; (II) the article concerned a case report, review, meta-analysis, etc.; (III) the subjects were non-human subjects or the study did not include a control group; (IV) the patients had mental disorders or did not cooperate with management; (V) the patients had a severe heart disease, malignant tumors, or severe infections.

Data extraction and collation

Data from the studies that met the above-mentioned criteria were extracted blindly. The following data were extracted: name of the first author, study area, year of publication of article, study design type, sample content (experimental group and control group), source of control group, thyroid function index data during pregnancy, odds ratio (OR) values for the influential factors, and 95% confidence intervals (CIs).

They were assessed according to the Cochrane Collaborative Network's risk of bias assessment criteria. The completeness of the results, data, and other sources of bias (e.g., selection bias). The quality assessments were made, and the studies were assessed as having, "low bias", "high bias", or "unclear" bias (if there was a lack of relevant information or bias uncertainty). All the evaluation results were input into RevMan 5.2.6 software to generate a risk of bias assessment map (see *Figure 2*).

Heterogeneity analysis

Stata 15 statistical software was used for the funnel plot analysis, and Egger's test was used to determine whether

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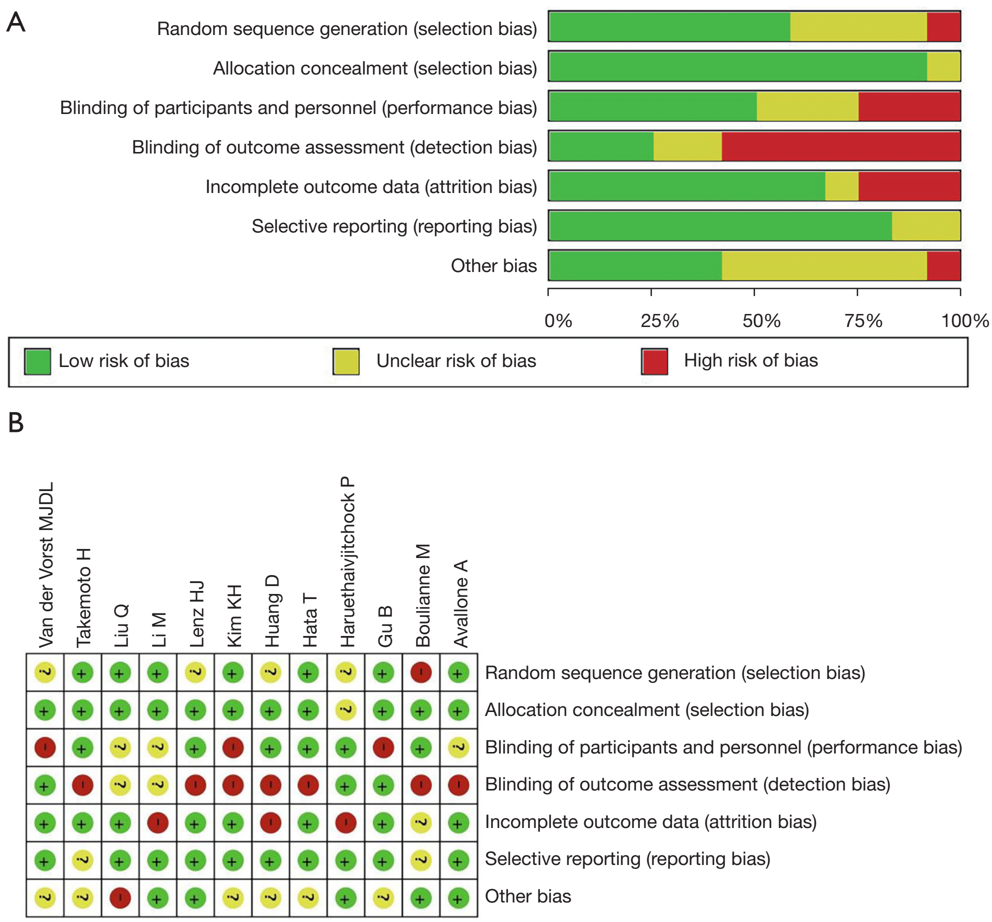

Figure 2 Literature quality evaluation chart. (A) Risk of bias graph; (B) risk of bias summary.

there was any publication bias in the included articles. If heterogeneity was observed, a subgroup analysis and sensitivity analysis were conducted to explore the source of the heterogeneity. If there was no significant statistical heterogeneity between the studies, the fixed-effects model was used for the pooled analysis. If there was significant statistical heterogeneity among the outcome index data, but there was no clinical heterogeneity, the random-effects model method was used to combine the data (see *Figure 3*).

Statistical analysis

The Cochrane Collaboration provided Review Manager 5.2 software (Cochrane Information Management System) for the statistical analysis. An χ^2 test (for which a P value <0.05 was set as the test level), a U test represented by a Z value, and a P value were used for the hypothesis tests, and an χ^2 test was used to test the heterogeneity of the articles.

Results

Literature retrieval results and included research characteristics

The PubMed, Cochrane, Web of Science, Embase, clinical research register and CQVIP databases were searched in this study. The retrieved articles then underwent a preliminary screening. Specifically, 2 researchers screened and reviewed the included articles by reading the abstract and the full text and eliminated duplicate articles or articles for which the relevant detection data could not be obtained, after which 32 articles remained. The 32 full-text articles were critically reviewed, and articles were excluded if they deviated from the content of this study or if there were multiple different reports on the same clinical study. The eligible articles were searched individually to prevent omissions. Ultimately, a total of 12 RCTs (11-22) were included in this study, and there is no obvious selection risk bias in this study (see *Table 1*).

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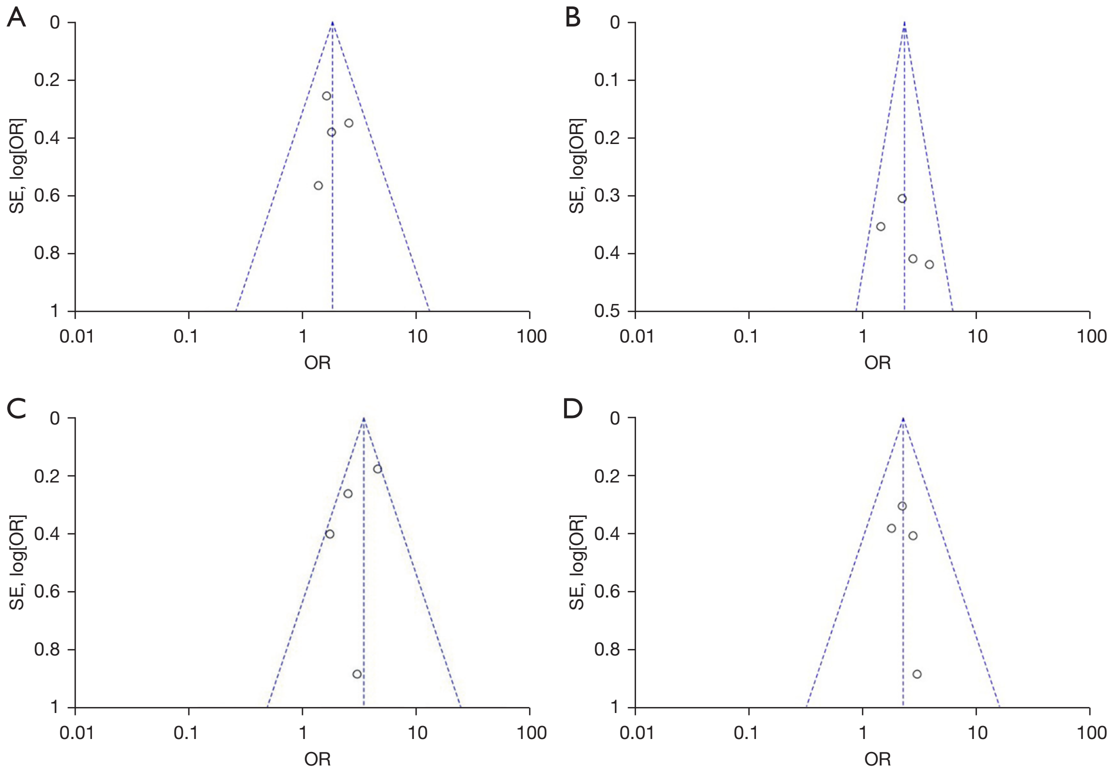

Figure 3 Funnel plot of publication bias in the articles on (A) postoperative heart rate variability; (B) MAP; (C) the incidence of PONV; and (D) the incidence of postoperative disturbance of consciousness. MAP, mean artery pressure; PONV, postoperative nausea and vomiting; OR, odds ratio; SE, standard error.

Table 1 Basic clinical features of the 12 articles included in our study

Study	Age (mean ± standard deviation)	Gender (male), %	Experimental group (N)	Control group (N)	NOS score	Research type
Kim KH 2017	63.71±2.2	41.25	40/60	20/60	8	RCT
Takemoto H 2017	65.65±3.4	69.12	75/120	45/120	7	RCT
Hata T 2021	63.12±4.5	45.72	244/386	142/386	8	RCT
van der Vorst MJDL 2021	62.15±4.5	44.12	100/189	89/189	8	RCT
Avallone A 2021	62.85±1.4	51.89	21/30	9/30	8	RCT
Li M 2021	64.36±1.2	63.45	133/233	100/233	7	RCT
Liu Q 2020	62.62±2.2	78.10	40/70	30/70	9	RCT
Lenz HJ 2017	62.61±3.0	48.75	30/56	26/56	9	RCT
Huang D 2020	67.25±4.5	59.23	45/80	35/80	7	RCT
Haruethaivijitchock P 2020	68.22±5.2	56.22	15/25	10/25	8	RCT
Gu B 2021	61.35±1.1	53.16	68/100	32/100	8	RCT
Boulianne M 2020	61.25±1.0	66.34	38/62	24/62	8	RCT

NOS, Newcastle-Ottawa Scale; RCT, randomized controlled trial.

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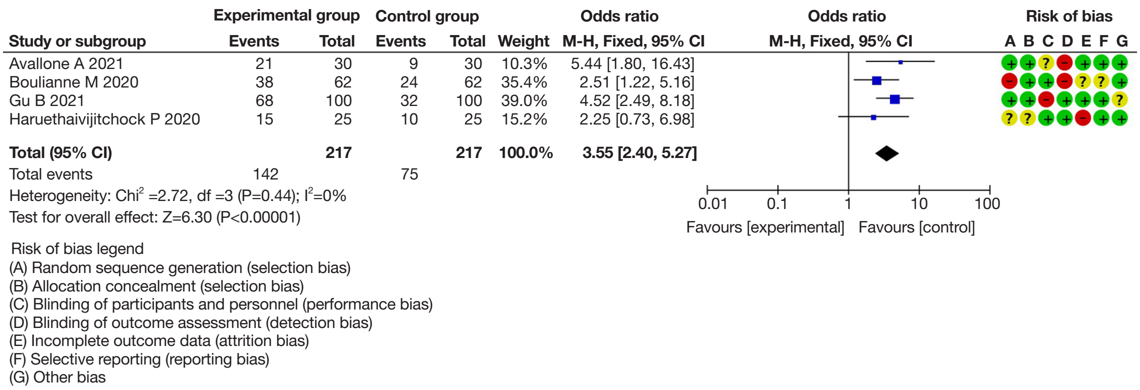

Figure 4 Meta-analysis of changes in the postoperative heart rates between the 2 groups. M-H, Mantel-Haenszel; CI, confidence interval.

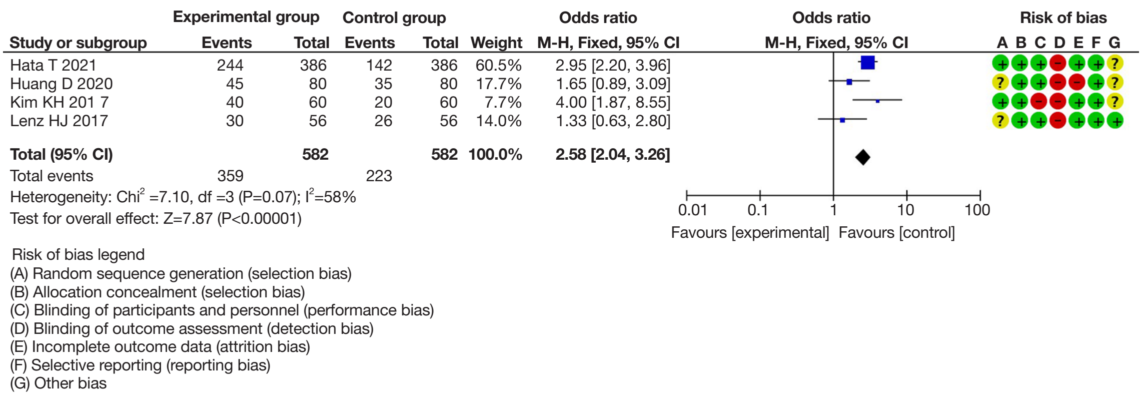

Figure 5 Meta-analysis of MAP between the 2 groups. M-H, Mantel-Haenszel; CI, confidence interval; MAP, mean artery pressure.

Changes in the postoperative heart rate

The heterogeneity test of the included 12 RCTs that examined postoperative heart rate change showed that the heterogeneity of the studies was small enough to allow a meta-analysis to be conducted of the selected articles using a fixed-effects model. After the meta-analysis, forest plots were drawn of the postoperative heart rate changes of the 4 included articles, which showed that there was a statistical difference between the postoperative heart rate changes of the experimental and control groups (OR =3.55, 95% CI: 2.40, 5.27, P<0.00001, I^2=0%, Z=6.30; see *Figure 4*).

Mean artery pressure (MAP)

The heterogeneity test of the included 12 RCTs that examined MAP showed that the heterogeneity of the studies was small enough to allow a meta-analysis to be conducted of the selected articles using a fixed-effects model. After the meta-analysis, forest plots were drawn of the MAP of the 4 included articles, which showed there was a statistical difference in the MAP between the experimental and control groups [OR =2.58, 95% CI: 2.04, 3.26, P<0.00001, I^2=58%, Z=7.87] (see *Figure 5*).

Incidence of PONV

The heterogeneity test of the included 12 RCTs that examined the incidence of PONV showed that the heterogeneity of the studies was small enough to allow a meta-analysis to be conducted of the selected articles using a fixed-effects model. After the meta-analysis, forest plots were drawn of the incidence of PONV of the 4 included articles, with the rhombus plot away from the vertical line, which showed that there was a statistical difference in the incidence of PONV between the experimental and control groups (OR =1.73, 95% CI: 1.38, 2.17, P<0.00001, I^2=46%, Z=4.78; see *Figure 6*).

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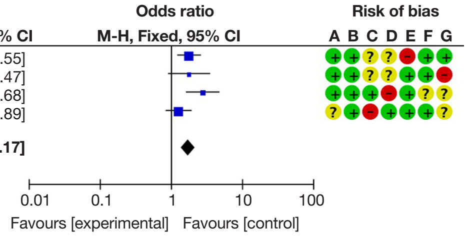
Study or subgroup	Experimental group Events	Experimental group Total	Control group Events	Control group Total	Weight	Odds ratio M-H, Fixed, 95% CI
Li M2021	133	233	100	233	37.5%	1.77 [1.23, 2.55]
Liu Q 2020	40	70	30	70	11.2%	1.78 [0.91, 3.47]
Takemoto H 2016	75	120	45	120	14.7%	2.78 [1.65, 4.68]
Van der Vorst MJDL 2020	100	189	89	189	36.6%	1.26 [0.84, 1.89]
Total (95% CI)		**612**		**612**	**100.0%**	**1.73 [1.38, 2.17]**
Total events	348		264			

Heterogeneity: Chi^2 =5.51, df =3 (P=0.14); I^2=46%
Test for overall effect: Z=4.78 (P<0.00001)

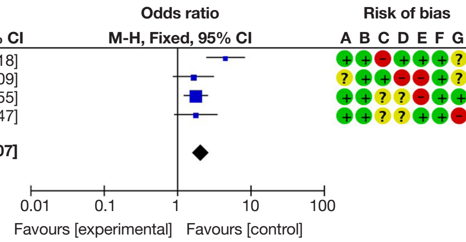


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Figure 6 Meta-analysis of the incidence of PONV between the 2 groups. M-H, Mantel-Haenszel; CI, confidence interval; PONV, postoperative nausea and vomiting.

Study or subgroup	Experimental group Events	Experimental group Total	Control group Events	Control group Total	Weight	Odds ratio M-H, Fixed, 95% CI
Gu B 2021	68	100	32	100	12.6%	4.52 [2.49, 8.18]
Huang D 2020	45	80	35	80	18.8%	1.65 [0.89, 3.09]
Li M 2021	133	233	100	233	52.8%	1.77 [1.23, 2.55]
Liu Q 2020	40	70	30	70	15.8%	1.78 [0.91, 3.47]
Total (95% CI)		**483**		**483**	**100.0%**	**2.09 [1.62, 3.07]**
Total events	286		197			

Heterogeneity: Chi^2 =8.02, df =3 (P=0.05); I^2=63%
Test for overall effect: Z=5.67 (P<0.00001)



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Figure 7 Meta-analysis of the incidence of postoperative disturbance of consciousness between the 2 groups. M-H, Mantel-Haenszel; CI, confidence interval.

Incidence of postoperative disturbance of consciousness

The heterogeneity test of the included 12 RCTs that examined the incidence of postoperative disturbance of consciousness showed that the heterogeneity of the studies was small enough to allow a meta-analysis to be conducted of the selected articles using a fixed-effects model. After the meta-analysis, forest plots were drawn made of the incidence of postoperative conscious disturbance of the 4 included articles, with the rhombus plot away from the vertical line, which showed that there was a statistical difference in the incidence of the postoperative conscious disturbance between the experimental and control groups (OR =2.09, 95% CI: 1.62, 3.07, P<0.00001, I^2=63%, Z=5.67; see *Figure 7*).

Discussion

Proper fasting before surgery is recommended to prevent vomiting and regurgitation during or after surgery, and to prevent aspiration, lung infection, and suffocation (23). However, surgery patients may experience fluid quantity insufficiency, and after the operation may experience thirst, dizziness, fatigue, nausea, and other symptoms (24). Oral and pharyngeal suction and extubation under shallow anesthesia often cause nausea and vomiting. The tracheal catheter should be removed as soon as possible after spontaneous breathing recovery by patients (25). After extubation, the placement of the oropharyngeal airway should be avoided where possible to avoid excessive stimulation to the pharynx, such as repeated attraction (26). The extubation of patients with a full stomach and intestinal obstructions should be performed with caution to prevent nausea, vomiting, aspiration, and suffocation. As hypoxemia and hypotension can also cause nausea and vomiting, patients' respiratory and circulatory functions should be maintained

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throughout and after surgery (27). Oxygen inhalation is an important measure in the treatment of hypoxemia, but the etiological treatment is more important, such as airway obstruction to open the airway and increase tidal volume is the most important. The high incidence of PONV in abdominal surgery may be related to local tissue ischemia and the release of 5-HT from gastrointestinal tissues caused by surgical compression (28). Oxygen inhalation can improve the hypoxia state, thus preventing the release of 5-HT. However, it has also been reported that a high concentration of oxygen inhalation does not effectively reduce the incidence of PONV (29). Hypotension should also be treated with blood transfusion, fluid rehydration, and vasoactive drugs (30).

Despite great developments in anesthesia and anesthesia technology, PONV is still a common complication of surgery with anesthesia. PONV is not only painful for patients, it is also prone to result in poor wound healing, esophageal injury, water and electrolyte disorders, and other complications, thus increasing the length of hospital stay of patients, resulting in increased medical costs. PONV generally occurs within 24 h of surgery, and most frequently occurs within 2 h of surgery, but also occasionally occurs within 48 h of surgery (31). The incidence of PONV is affected by individual factors, the type and duration of the surgery, the anesthetic drugs and methods, preoperative anxiety, and other factors. Different incidence rates have been reported in different articles; however, the incidence rate of PONV is generally about 20–30%. As patients' demands for comfort after anesthesia and surgery continue to increase, great concern about this issue has been generated.

As a common gastrointestinal tumor, CRC is treated with surgical therapy, chemotherapy, radiotherapy, immunotherapy, and targeted therapy. For CRC patients, various gastrointestinal symptoms after anesthesia can directly affect the efficacy or even end chemotherapy in advance, resulting in a poor prognosis (32). As the most common adverse reaction of the gastrointestinal tract after CRC chemotherapy, chemotherapy induced nausea and vomiting (CINV) may result in a series of serious consequences; for example, patients' nutritional status may deteriorate, their body microenvironment may change, and their emotional adverse responses may require treatment. The treatments for CINV include anti-emetic drugs, traditional Chinese medicine, external treatment of traditional Chinese medicine, and a combination of Chinese and Western medicine. 5-HT receptor antagonists and neurokinin-1 receptor antagonists can treat the nausea and vomiting of patients after chemotherapy; however, the effects are not good for delayed type nausea and vomiting.

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Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-783/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-783/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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