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Review Article

Effects of Ramosetron on Nausea and Vomiting Following Spinal Surgery: A Meta-Analysis

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ABSTRACT

Background: Spinal surgery is associated with severe pain within the first few days after surgery. Opioids are commonly used to control postoperative pain, but these can lead to postoperative nausea and vomiting (PONV). Therefore, use of more effective and better-tolerated agents would be beneficial for these patients. Serotonin receptor antagonists, such as ramosetron, have been used to reduce PONV in patients receiving anesthesia.

Objective: We conducted a meta-analysis of published randomized controlled trials (RCTs) to compare the efficacy and tolerance of ramosetron to prevent PONV after spinal surgery.

Methods: Medline, Embase, Cochrane Library, and Science Citation Index databases were systematically searched for relevant RCT articles published between January 1979 and November 2020. Full text articles restricted to English language that described RCTs comparing the use of ramosetron with other serotonin antagonists to treat PONV following spinal surgery in adult patients were considered for meta-analysis. Two reviewers independently performed study selection, quality assessment, and data extraction of all articles. Differences were resolved by a third reviewer.

Results: The search identified 88 potentially relevant articles, of which only 3 met our selection criteria. Study drugs were administered at the end of spinal surgery in all 3 included articles. The meta-analysis revealed that ramosetron (0.3 mg) reduced the pain score (mean difference = −0.66; 95% CI −1.02 to −0.30), lowered the risk of PONV (risk ratio = 0.86; 95% CI, 0.76–0.97), and postoperative vomiting (risk ratio = 0.32; 95% CI, 0.17–0.60), and limited the use of rescue antiemetics (risk ratio = 0.66; 95% CI, 0.45–0.96) after spinal surgery. However, there were no significant differences in the incidence of postoperative nausea, the use of rescue pain medications, the number of rescue analgesics required, and the risk of discontinuation of patient-controlled analgesia between ramosetron and palonosetron (0.075 mg) or ondansetron (4 mg). There were no statistically significant differences in the risk of adverse events among the 3 medications.

Conclusions: This meta-analysis of 3 RCTs showed that ramosetron reduced the risk of PONV and POV, limited the use of rescue antiemetics, reduced the postoperative pain score, and did not increase the risk of discontinuing patient-controlled analgesia compared with palonosetron or ondansetron after spinal surgery in 3 RCTs. Therefore, this meta-analysis indicates that ramosetron is an effective and well tolerated antiemetic that can be used to prevent PONV following spinal surgery in adult patients. PROSPERO identifier: CRD42020223596 (*Curr Ther Res Clin Exp*. 2022; 83:XXX–XXX)

Introduction

Pain is the second most common complaint following surgery and general anesthesia. Adequate pain management in patients following spinal surgery facilitates early mobilization and expedites hospital discharge.[1] However, the perioperative use of anesthesia and analgesics for pain control is a major risk factor for postoperative nausea and vomiting (PONV). PONV is defined as any nau-

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sea, vomiting, or emesis in the postanesthesia care unit (PACU) or during the first 24 to 48 hours following surgery.[2,3] PONV is a distressing complication and can result in dehydration, electrolyte imbalance, acid–base imbalance, pulmonary aspiration, pneumothorax, hypoxia, suture rupture, wound dehiscence, bleeding, delay in the ability to resume oral intake, delayed postoperative recovery, and increased medical costs.[2,4]

Serotonin (5-hydroxytryptamine 3 [5-HT3]) receptor antagonists, such as ondansetron, granisetron, and dolasetron, are frequently used for PONV prophylaxis.[4,5] These antagonists have a considerably short duration of action and are thus commonly used in the immediate postoperative period, but they are less effective at preventing postoperative vomiting (POV) than postoperative nausea (PON).[6] Several meta-analyses have reported that an intravenous dose of the serotonin antagonist ramosetron (0.3 mg) has better efficacy and longer duration of action than other serotonin receptor antagonists after nonorthopedic surgery.[7,8] The incidence of PONV after orthopedic surgery is significantly reduced with antiemetic treatment.[2–4] Following joint surgery, ramosetron was shown to effectively reduce early PON or POV.[9–12] Palonosetron was also shown to reduce the total incidence of PONV in patients receiving fentanyl patient-controlled analgesia (PCA) after orthopedic surgery.[4] Some studies have found that ramosetron is more effective than palonosetron in reducing the severity of PONV after spinal surgery.[13,14] However, it is unclear whether or not ramosetron is superior to other serotonin antagonists in preventing PONV following spinal surgery. This meta-analysis was performed to investigate whether or not ramosetron is effective and well tolerated for preventing PONV after spinal surgery in adult patients.

Materials and Methods

Search strategy and study selection

Our protocol is registered with PROSPERO (CRD42020223596). Two researchers independently performed a comprehensive literature search of Embase, Medline, Cochrane Library, and Science Citation Index databases for relevant articles published in English between January 1979 and November 2020. A basic search was performed using the following key words: (((((PONV) OR postoperative) OR postanesthetic) OR postanaesthetic) OR surgical)) AND ((((nausea) OR vomiting) OR emesis) OR retching) AND ((((lumbar surgery) OR spinal surgery) OR lumbar spine surgery) OR cervical surgery) AND ((ramosetron) OR (serotonin antagonist)). Relevant articles were further reviewed using the following study inclusion criteria: original research comparing ramosetron with another serotonin antagonists following spinal surgery in patients aged 18 years or older, randomized controlled trials (RCTs), studies in which ramosetron and a serotonin antagonist were administered intravenously, and availability of full text (detailed information).

Data extraction and quality assessment

Data from the studies were extracted by 2 reviewers (L.Y.Y. and C.X.B.). Differences were resolved by a third reviewer (Z.Z.C.). The following information was extracted from each article: author, year of publication, study design, number of patients, type of surgery, dose of ramosetron or an alternative serotonin antagonist, time of administration of the experimental drug, and definition of the postoperative period. The following results were extracted if reported: number of cases of PONV, PON, and POV in general and during different postoperative phases (PACU, postoperative 0 to 6 hours, 6 to 24 hours, 24 to 48 hours, and 48 to 72 hours), postoperative pain score, need for rescue antiemetics or rescue analgesics, and incidence of adverse effects related to study drugs, such as headache, dizziness, drowsiness, and cardiac events. If available, data on the ratio of relative risks and differences between treatment agents for categorical and continuous outcomes, respectively, were extracted from all publications. Categorical outcomes are reported as risk ratios (RRs) and their corresponding 95% CIs, and continuous outcomes are reported as weighted mean difference (MD). A P value < 0.05 was considered statistically significant.

Two authors (L.Y.Y. and C.X.B.) independently assessed the quality of the studies and assigned a numerical score between 0 and 7 as an estimated measure of the quality of the study (Table 1). The quality of the included studies was evaluated using the Newcastle-Ottawa scale (www.ohri.ca/programs/clinical_epidemiology/oxford.htm). The score considered study design, patient selection, randomization, assessment (grade) of nausea or/and vomiting, definition of outcomes, statistical method, and power analysis (0 being the weakest and 7 being the strongest). Differences were resolved by discussion and consensus. If disagreement persisted, all listed authors were consulted.

Statistical analysis

When 2 or more studies reported outcomes of interest, effect estimates were combined with meta-analyses in Review Manager version 5.3 (The Cochrane Collaboration, London, United Kingdom). Statistical heterogeneity between trials was evaluated using the Cochran χ^2 statistic and was considered significant when the P value was 0.1. When there was statistical heterogeneity, a random-effect model was used for analysis. In the absence of statistically significant heterogeneity, only the fixed-effect model was used.

To further test the robustness of the results, several sensitivity analyses were performed a priori. First, we evaluated whether or not the statistical method (random-effect model vs fixed-effect model) would influence the results. Second, we determined whether or not the quality of the publication (high or low quality) could influence the results of the meta-analysis. In addition, a subgroup analysis was performed according to different criteria (eg, high and low dose of the drug used). When the data were not presented in a manner that could be included in the meta-analysis or when only 1 study was identified for a given outcome, the results of individual studies are presented.

Results

Included studies

The literature search retrieved 88 potentially relevant articles from Embase, Medline, the Cochrane Library, and the Science Citation Index databases. After removing duplicate articles and reviews, 70 studies were eligible for inclusion in this meta-analysis (Figure 1). All abstracts from these publications were screened for ramosetron, PONV, and spinal surgery. Of the 70 studies, 52 studies did not administer ramosetron, 9 did not report postspinal surgery, 3 had patients younger than age 18 years, and 3 did not compare ramosetron with a serotonin antagonist in patients receiving spinal surgery. These studies were excluded from the analysis. The 3 remaining articles met the study criteria and were included in this meta-analysis.

Description of the included articles

Details of the included studies are presented in Table 2. The smallest study included 94 patients,[15] and the largest study included 296 patients.[13] Two studies compared ramosetron (0.3 mg) with palonosetron (0.075 mg),[13,14] whereas 1 study compared ramosetron with ondansetron (4 mg).[15] In all included articles, study drugs were administered at the end of spinal surgery. Song et al[13] administered the drug 20 minutes before the end of surgery

Table 1
Quality score of included studies.

First author (year of publication, country)	Study design	Patient selection	Randomization	Nausea or/and vomiting assessment	Definition of outcomes	Statistical tool	Power analysis	Total score
Choi[15] (2008, Republic of Korea)	1	1	1	1	1	1	1	7
Roh[14] (2014, Republic of Korea)	1	1	1	1	1	1	1	7
Song[13] (2017, Republic of Korea)	1	1	1	1	0	1	1	6

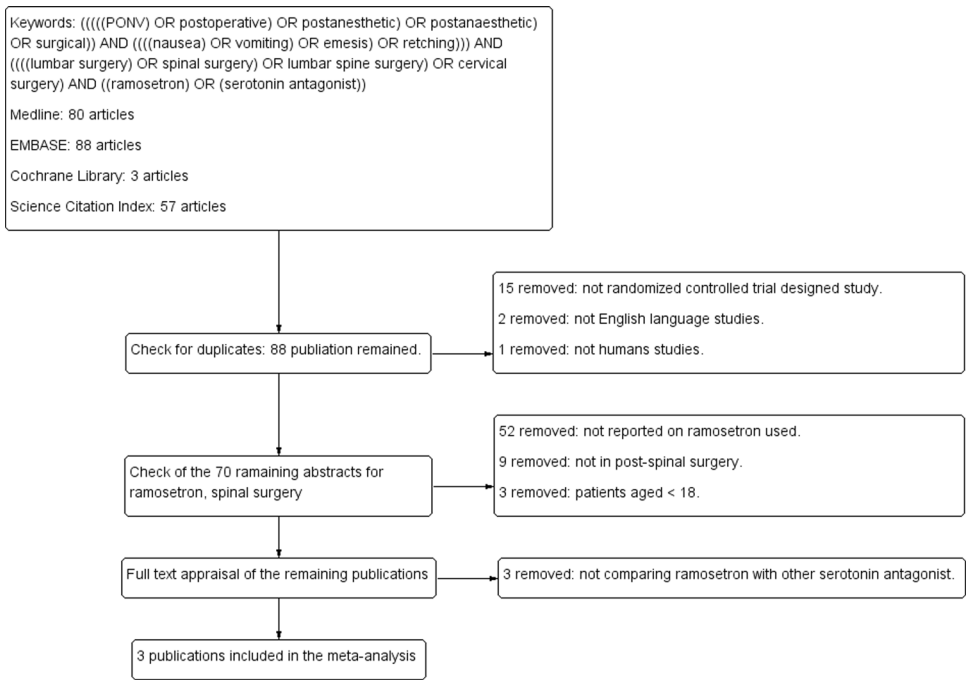

Figure 1. Study selection process.

and 24 hours after surgery; Roh et al[14] administered the drug 10 minutes before the end of surgery; and Choi et al[15] administered the drug at the end and 24 hours after surgery, but the specific time point at the end of surgery was not provided. The postoperative period was defined as 0 to 48 hours after surgery in 2 studies[13,15] and 0 to 72 hours in another.[14]

Outcomes of the pooled studies

Meta-analysis revealed that ramosetron significantly reduced the risk of PONV (RR = 0.86; 95% CI, 0.76–0.97; $P = 0.01$) (Figure 2A) and POV (RR = 0.32; 95% CI, 0.19–0.56; $P < 0.0001$) (Figure 2B). In the subgroup analysis, ramosetron reduced the risk of PONV (RR = 0.85; 95% CI, 0.74–0.99; $P = 0.03$) compared with palonosetron, but not compared with ondansetron. Treatment with ramosetron did not reduce the incidence of POV (24–48 hours: RR = 1.00; 95% CI, 0.21–4.87; $P = 1.00$; 48–72 hours: RR = 0.33; 95% CI, 0.01–8.08; $P = 0.50$) (Figure 2B), PON (total postoperative period: RR = 0.95; 95% CI, 0.74–1.22; $P = 0.69$; during PACU: RR = 0.78; 95% CI, 0.41–1.47; $P = 0.44$; 0–6 hours: RR = 1.02; 95% CI, 0.69–1.50; $P = 0.93$; 6–24 hours: RR = 0.95; 95% CI, 0.80–1.13; $P = 0.53$; 24–48 hours: RR = 0.72; 95% CI, 0.49–1.05; $P = 0.09$; 48–72 hours: RR = 2.00; 95% CI, 0.71–5.64; $P = 0.19$) (Figure 2C) compared with palonosetron or ondansetron. The pooled data showed that ramosetron significantly lowered the risk of POV during the first postoperative 24 hours (0–6 hours: RR = 0.17; 95% CI, 0.06–0.52; $P = 0.002$; 6–24 hours: RR = 0.41; 95% CI, 0.19–0.86; $P = 0.02$) and limited the use of rescue antiemetics (RR = 0.66; 95% CI, 0.45–0.96; $P = 0.03$) (Figure 3A).

Significant heterogeneity was observed in PON and POV during various postoperative phases among the pooled studies. Therefore, a random-effects model was used for these analyses. Pooled data analyses showed that ramosetron reduced the postoperative pain score (MD = −0.66; 95% CI, −1.02 to −0.30; $P = 0.0004$) postoperative time period analyses: (0–6 hours: MD = −0.61; 95% CI, −1.08 to −0.14; $P = 0.01$; 6–24 hours: MD = −0.70; 95% CI, −1.16 to −0.24; $P = 0.003$; 24–48 hours: MD = −1.20; 95% CI, −2.28 to −0.13; $P < 0.00001$; 48–72 hours: MD = −0.80; 95% CI, −1.33 to −0.27; $P = 0.003$) (Figure 3B). However, ramosetron did not reduce the PACU pain score (MD = 0.10; 95% CI, −0.33 to 0.53; $P = 0.65$) or use of rescue pain medications (MD = −9.43; 95% CI, −32.30 to 13.44; $P = 0.42$ (see Supplemental Figure 1A in the online version at doi:10.1016/j.curtheres.2022.100666) following spinal surgery. In addition, ramosetron did not increase the risk of PCA discontinuation (RR = 0.76; 95% CI, 0.41–1.40; $P = 0.38$) (see Supplemental Figure 1B in the online version at doi:10.1016/j.curtheres.2022.100666) or the use of rescue analgesics (RR = 0.90; 95% CI, 0.58–1.40; $P = 0.65$) (see Supplemental Figure 1C in the online version at doi:10.1016/j.curtheres.2022.100666) compared with other serotonin antagonists.

There were no statistically significant differences in the risk of total adverse events between the three medications (RR = 1.10; 95% CI, 0.80–1.51; $P = 0.54$) (see Supplemental Figure 2A in the online version at doi:10.1016/j.curtheres.2022.100666). Further-

Table 2
Characteristics of included studies.

First author (year of publication, country)	Surgery type	No. of patients	Age ± SD, y	Risk factors of PONV ± SD	Type of anesthesia	Treatment	Time of administration	Definition of postoperative period
Choi[15] (2008, Republic of Korea)	Lumbar spine	94	Group R 49 ± 9; group O 51 ± 11	≥3	General anesthesia	R (0.3 mg); O (4 mg)	End of surgery and 24 h after surgery	0–6 h, 6–24 h, and 24–48 h
Roh[14] (2014, Republic of Korea)	Lumbar spinal	196	Group R 49 ± 13; group P 49 ± 14	Group R 1.9 ± 0.6; Group P 1.9 ± 0.7	General anesthesia	R (0.3 mg); P (0.075 mg)	10 min before the end of surgery	Intervals of 0–6 h, 6 –24 h, 24–48 h, and 48–72 h
Song[13] (2017, Republic of Korea)	Cervical laminoplasty, cervical anterior interbody fusion, lumbar laminectomy, posterior lumbar interbody fusion, benign spinal cord tumor removal	296	Not provided	Not provided	General anesthesia	R (0.3 mg); P (0.075 mg)	20 min before the end of surgery and 24 h after surgery	Early (0–6 h) and late (6–48 h)

O = ondansetron; P = palonosetron; PONV = postoperative nausea and vomiting; R = ramosetron.

more, ramosetron had no effect on the incidence of headache (RR = 0.78; 95% CI, 0.44–1.41; $P = 0.41$) (see Supplemental Figure 2B in the online version at doi:10.1016/j.curtheres.2022.100666), dizziness (RR = 0.94; 95% CI, 0.59–1.49; $P = 0.78$) (see Supplemental Figure 2C in the online version at doi:10.1016/j.curtheres.2022.100666), or drowsiness (RR = 1.17; 95% CI, 0.78–1.75; $P = 0.45$) (see Supplemental Figure 2D in the online version at doi:10.1016/j.curtheres.2022.100666)). Roh et al[14] found no difference in the incidence of constipation, urinary retention ($P = 0.516$), or pruritus ($P = 1.000$) between ramosetron and palonosetron, and Song et al[13] reported no difference in the incidence of palpitation ($P > 0.999$).

Publication bias and sensitivity analyses

The funnel plot showing PON as an end point indicates the presence of publication bias (see Supplemental Figure 3 in the online version at doi:10.1016/j.curtheres.2022.100666)). This bias could be attributed to the following factors. First, the postoperative periods were divided differently in the 3 articles. Roh et al[14] evaluated the pain score in the PACU and at postoperative intervals of 0 to 6 hours, 6 to 24 hours, 24 to 48 hours, and 48 to 72 hours; Choi et al[15] subdivided the postoperative phase into 3 time periods (0 to 6 hours, 6 to 24 hours, and 24 to 48 hours), and Song et al[13] divided the postoperative phase into early (0 to 6 hours) and late (6 to 48 hours). Second, surgery in the study by Song et al[13] included lumbar spinal surgery, as well as cervical and benign spinal cord tumor operations; the other 2 studies included only lumbar surgery.[14,15] (Results of sensitivity analyses were similar regardless of the effect model applied (Table 3).

Discussion

This meta-analysis of only three RCTs found that ramosetron was associated with a lower risk of PONV, POV, and the use of rescue antiemetics compared with palonosetron or ondansetron following spinal surgery. The analysis also demonstrated that ramosetron was effective at reducing the postoperative pain score and did not increase the risk of PCA discontinuation or postoperative adverse events compared with palonosetron or ondansetron after spinal surgery in adult patients. No significant differences were found in the incidence of PON, the use of rescue analgesics, or the number of pain medications required between ramosetron and palonosetron or ondansetron.

Ramosetron has a significantly higher binding affinity for 5-HT3 receptors and a slower receptor dissociation rate than the conventional serotonin receptor antagonist ondansetron. As a result, ramosetron is a more potent antagonist. In contrast, palonosetron has a higher binding affinity (>30-fold) for the 5-HT3 receptor compared with ramosetron or ondansetron.[16,17] Because of the short half-life of most 5-HT3 receptor antagonists, these medications are typically administered at the end of surgery. Tong et al[2,18] administered ramosetron or ondansetron at the end of the surgery, but palonosetron at the beginning to manage PONV. However, because the length of spinal surgery is not constant, administration of 5-HT3 receptor antagonists before or at the beginning of surgery is not necessarily effective for preventing PONV. Thus, in this meta-analysis only studies that administered antiemetics at the end of spinal surgery were included.

Compared with regional anesthesia, general anesthesia is associated with a higher incidence of PONV and a greater use of opioids to control postoperative pain following spinal surgery. Elvir-Lazo et al[2] reported that the risk of PONV increases by 60% with every additional 30 minutes of surgical procedures. The highest incidence of PONV occurs within the first days after surgery.[19] In our analysis, ramosetron lowered the risk of PONV compared with palonosetron or ondansetron, which could be attributed to ramosetron being administered postoperatively rather than preoperatively. Our analysis also showed a lower risk of POV during the first 24 hours of postoperative care, but not after 24 hours. Unlike the results of POV, there were no differences in PON in any of the postoperative periods, which could be partially attributed to the qualitative assessment of nausea rather than the quantitative measurement of PON. Although POV is generally assessed as a dichotomous variable of “yes” or “no,” PON can be assessed according to severity (mild-moderate-severe) on a Likert or visual analog scale. The method used is clinically important, because “mild nausea” may not require any rescue antiemetics, whereas moderate-to-severe nausea often does, making this a more relevant method in clinical practice from the patient’s perspective.

It is well known that spinal surgery is associated with severe pain within the first few days after surgery, and that this pain is often managed with opioids.[14] Multimodal analgesics have been proposed to effectively reduce postoperative pain, but these agents can prolong gastric emptying time and possibly contribute to abdominal complications, such as emesis, after spinal surgery.[20] Certain types of surgeries (eg, neurosurgery, abdominal, ophthalmic,

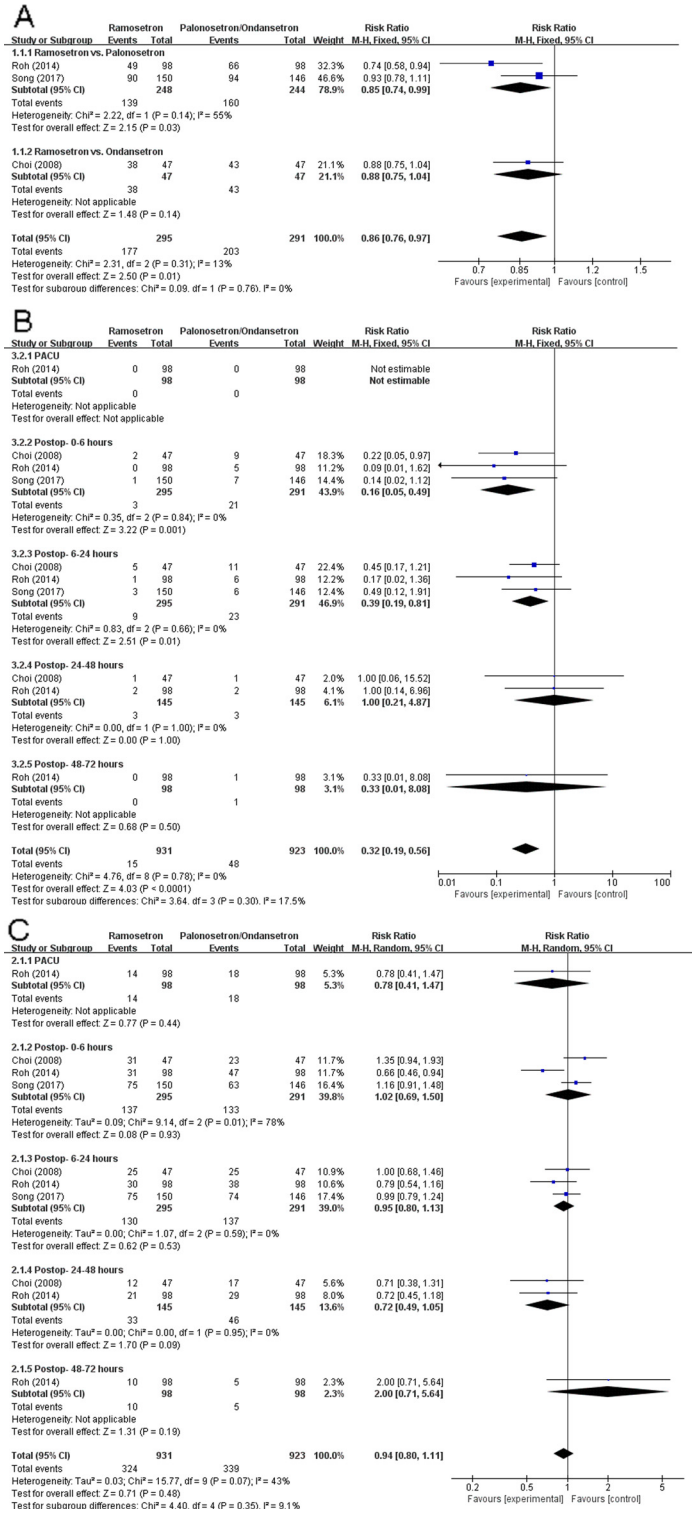

Figure 2. (A) Forrest plot of postoperative nausea and vomiting. (B) Forrest plot of postoperative vomiting. (C) Forrest plot of postoperative nausea.

oral, and maxillofacial surgeries) have a higher incidence of PONV, possibly due to prolonged exposure to general anesthesia and higher opioid use.[21,22] Multimodal analgesics have become increasingly popular to prevent postoperative pain, but these analgesics are frequently accompanied by critical complications, such as PONV, during the postoperative period.[18] Moreover, PONV can be exacerbated with the combined use of anesthesia and analgesics. This meta-analysis found that administration of ramosetron reduced the risk of PONV and POV, and limited the use of rescue antiemetics, as well as reduced the pain score compared with palonosetron or ondansetron during the postoperative period. However, there were no differences in PCA discontinuation, number of rescue analgesics required, or rescue pain medications administered after spinal surgery.

The most commonly noted complications in the included studies were headache, dizziness, and drowsiness. Our analysis showed that ramosetron was not associated with a significant increase in these 3 adverse effects compared with palonosetron or on-

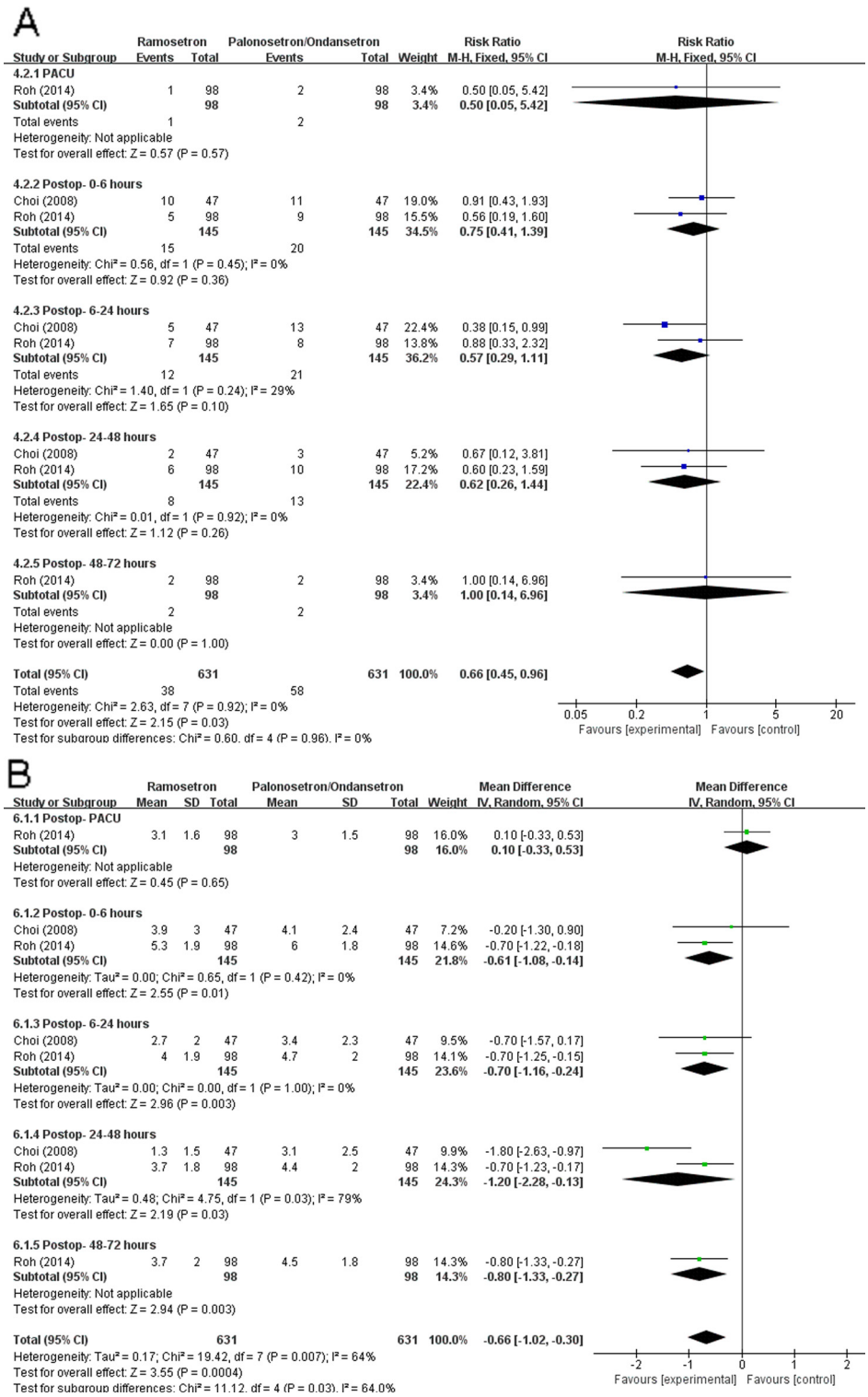

Figure 3. (A) Forrest plot of rescue antiemetics. (B) Forrest plot of postoperative pain score.

dansetron after spinal surgery. These findings are consistent with those of Roh et al[14] who reported no considerable differences in other adverse events, including constipation, urinary retention, and pruritus, and Song et al[13] who reported no differences in palpitation. Evidence also suggests that 5-HT3 receptor antagonists can increase the risk of cardiac injury in patients receiving chemotherapy.[23] Adverse events associated with these medications include decreased heart rate and a prolonged QT interval.[24] None of the included studies in this meta-analysis reported severe cardiac adverse events, such as PR interval prolongation, fatal arrhythmias, or sudden cardiac death.

This meta-analysis has some limitations that should be noted. First, the numbers of RCTs and patients analyzed in our study were relatively small as our literature search was restricted to English language studies that included adult patients. These limitations may have led to selection bias. Further, the ethnicity of the patients was restricted to only Asians. This is an important consideration for future studies because ethnicity can influence the

Table 3
Sensitivity analysis of outcomes.

Outcome	Analysis method	Fixed-effect model (95% CI)	Random-effect model (95% CI)
Postoperative nausea and vomiting	RR	0.86 (0.76 to 0.97)	0.87 (0.77 to 0.98)
Postoperative nausea	RR	0.94 (0.84 to 1.06)	0.94 (0.80 to 1.11)
PACU	RR	0.78 (0.41 to 1.47)	0.78 (0.41 to 1.47)
0-6 h	RR	1.02 (0.85 to 1.21)	1.02 (0.69 to 1.50)
6-24 h	RR	0.93 (0.78 to 1.11)	0.95 (0.80 to 1.13)
24-48 h	RR	0.72 (0.49 to 1.05)	0.72 (0.49 to 1.05)
48-72 h	RR	2.00 (0.71 to 5.64)	2.00 (0.71 to 5.64)
Postoperative vomiting	RR	0.32 (0.19 to 0.56)	0.36 (0.21 to 0.64)
PACU	RR	Not estimated	Not estimated
0-6 h	RR	0.17 (0.06 to 0.52)	0.17 (0.06 to 0.52)
6-24 h	RR	0.41 (0.19 to 0.86)	0.41 (0.19 to 0.86)
24-48 h	RR	1.00 (0.21, to 4.87)	1.00 (0.21 to 4.87)
48-72 h	RR	0.33 (0.01 to 8.08)	0.33 (0.01 to 8.08)
Rescue antiemetic	RR	0.66 (0.45 to 0.96)	0.67 (0.45 to 0.98)
PACU	RR	0.50 (0.05 to 5.42)	0.50 (0.05 to 5.42)
0-6 h	RR	0.75 (0.41 to 1.39)	0.77 (0.42 to 1.42)
6-24 h	RR	0.57 (0.29 to 1.11)	0.58 (0.26 to 1.29)
24-48 h	RR	0.62 (0.26 to 1.44)	0.62 (0.26 to 1.44)
48-72 h	RR	1.00 (0.14 to 6.96)	1.00 (0.14 to 6.96)
Patient-controlled analgesia discontinuation	RR	0.76 (0.41 to 1.40)	0.76 (0.41, 1.40)
Pain score	MD	−0.58 (−0.79 to −0.37)	−0.66 (−1.02 to −0.30)
PACU	MD	0.10 (-0.33 to 0.53)	0.10 (−0.33 to 0.53)
0-6 h	MD	−0.61 (−1.08 to −0.14)	−0.61 (−1.08 to −0.14)
6-24 h	MD	−0.70 (−1.16 to −0.24)	−0.70 (-1.16 to −0.24)
24-48 h	MD	−1.02 (−1.47 to −0.57)	−1.20 (-2.28 to −0.13)
48-72 h	MD	−0.80 (−1.33 to −0.27)	−0.80 (-1.33 to −0.27)
Rescue analgesics	RR	0.97 (0.85 to 1.12)	0.90 (0.58 to 1.40)
Rescue pain medications	MD	−2.63 (−8.46 to 3.21)	−9.43 (−32.30 to 13.44)
Adverse events	RR	1.10 (0.80 to 1.51)	1.08 (0.72 to 1.61)
Headache	RR	0.78 (0.44 to 1.41)	0.80 (0.44 to 1.44)
Dizziness	RR	0.94 (0.59 to 1.49)	0.95 (0.60 to 1.51)
Drowsiness	RR	1.17 (0.78 to 1.75)	1.17 (0.78 to 1.76)

MD = mean difference; PACU = postanesthesia care unit; RR = relative risk.

risk of PONV,[25,26] and there have been reports that genetic factors in certain ethnicities can either protect against PONV, predispose individuals to motion sickness, or influence those who have had a previous surgery with PONV. And there are also pharmacogenetic differences between Asian and non-Asian patients.[25,26] Secondly, postoperative pain was only measured using a pain score without distinguishing resting pain from nonresting pain. The degree of pain can differ depending on the activity of the individual and therefore must be considered when assessing pain severity. Further studies are needed to address these limitations and better understand the value of ramosetron following spinal surgery.

Conclusions

This meta-analysis of 3 RCTs showed that ramosetron reduced the risk of PONV and POV, limited the use of rescue antiemetics, reduced the postoperative pain score, and did not increase the risk of PCA discontinuation compared with palonosetron or ondansetron after spinal surgery in 3 RCTs. No significant differences between ramosetron and either palonosetron or ondansetron were found with regard to the incidence of PON, use of rescue pain medications, or rescue analgesics required. Therefore, this meta-analysis indicates that ramosetron is an effective and well-tolerated antiemetic that could be used to prevent PONV following spinal surgery in adult patients.

Conflicts of Interest

The authors have indicated that they have no conflicts of interest regarding the content of this article.

CRediT authorship contribution statement

Yiyun Lin: Conceptualization, Data curation, Formal analysis, Methodology, Software, Writing – original draft. **Sun Tiansheng:** Conceptualization, Supervision. **Zhang Zhicheng:** Data curation, Formal analysis, Software. **Chen Xiaobin:** Data curation, Formal analysis, Methodology, Software, Writing – review & editing. **Li Fang:** Methodology, Supervision.

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L. Yiyun contributed to conceptualization, data curation, formal analysis, methodology, software, and writing (original draft); S. Tiansheng contributed to conceptualization and supervision;

Z. Zhicheng contributed to data curation, formal analysis, and software; C. Xiaobin contributed to data curation, formal analysis, methodology, software, and writing (review and editing); and L. Fang contributed to methodology and supervision.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.curtheres.2022.100666.

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