Comparison of ondansetron and tropisetron in preventing postoperative nausea and vomiting

A meta-analysis of randomized controlled trials

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ABSTRACT

الأهداف: لمقارنة فعالية عقار أوندانسيترون وعقار تروبيسيترون للوقاية من الغثيان والقيء بعد الجراحة (PONV).

المنهجية: أجرينا بحث في محركات البحث للدراسات السابقة لتحديد البحوث التي تقارن كفاءة عقار أوندانسيترون مع عقار التروبيسيترون في منع PONV. اشتملت التجارب المعشاة ذات الشواهد فقط التي تم تحديثها حتى يناير 2021م.

النتائج: اشتمل التحليل النهائي على 14 دراسة مجموع 1705 مريضًا وأشار إلى أن عقار أوندانسيترون كان أقل فعالية بنسبة 39% من عقار تروبيسيترون في منع القيء بعد الجراحة مع ارتفاع معدل حدوث الدوخة. ومع ذلك، لم يتم الكشف عن اختلاف كبير بين عقار أوندانسيترون و عقار تروبيسيترون في PONV والغثيان بعد الجراحة والعلاج المضاد للقيء والصداع.

الخلاصة: يتفوق عقار تروبيسترون على عقار أوندانسيترون في منع القيء بعد الجراحة.

Objectives: To compare the efficacy of prophylactic ondansetron and tropisetron for postoperative nausea and vomiting (PONV).

Methods: A literature search was performed to identify studies that compare the efficiency of ondansetron with that of tropisetron in preventing PONV. Only randomized controlled trials updated to January, 2021 were included.

Results: The final pooled analysis included 14 studies totaling 1705 patients and indicated that ondansetron was 39% less effective than tropisetron in preventing postoperative vomiting with a higher incidence of dizziness. However, no significant difference was detected between ondansetron and tropisetron in PONV, postoperative nausea, antiemetic treatment, and headache.

Conclusions: Tropisetron is superior to ondansetron in preventing postoperative vomiting.
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Keywords: meta-analysis, ondansetron, tropisetron, postoperative, antiemetic

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Postoperative nausea and vomiting (PONV) is a distressing side effect after anesthesia,[1] because it may cause some adverse effects such as deprivation of body fluids, electrolyte imbalance, delayed recovery, aspiration pneumonia, and decreased satisfaction of patients' after surgery.[2]

Prophylactic administration of 5-hydroxytryptamine-3 (5-HT3) receptor antagonists has been utilized as an effective method for preventing PONV. Comparative studies between different 5-HT3 antagonists for preventing PONV failed to show a clear advantage of a specific 5-HT3 antagonist.[3]

This meta-analysis was designed to determine the effect of two 5-HT3 receptor antagonists with different half-lives in preventing PONV, that is, the short-acting ondansetron versus the relatively long-acting tropisetron.

Methods. Two investigators (NW, RW) identified the eligible studies by searching PubMed, Web of Science, Cochrane Library, and Google Scholar, using "prevention," "nausea," "vomiting," "ondansetron," and

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"tropisetron" as search terms updated to January, 2021. Potential randomized controlled trials (RCTs) were identified by a systematic search of reference lists from related articles.

Inclusion criteria were: a RCT study; patients should have undergone operation; records of PONV-data; ondansetron or tropisetron administered prophylactically; and ondansetron and tropisetron comparison. On the other hand, none-english articles, animal studies, children studies, and published abstracts, meeting papers and letters were excluded.

The quality of the RCTs was separately evaluated by 2 investigators (JW, XS) utilizing the Cochrane Collaboration guidelines and Jadad improvement score.[4,5] Studies with Jadad improvement score of less than 4 were excluded.

Two independent investigators (YC, RW) extracted relevant data from the included studies. The primary outcome was PONV, while additional outcomes included the requirement of antiemetic treatment and the related complications. Any disagreement was solved by a third investigator.

Statistical analysis. Statistical calculations were conducted using Revman 5.3 (Cochrane Collaboration). The outcome was displayed as odds ratio (OR) with 95% confidence interval (CI). I^2 value was utilized to evaluate heterogeneity. If I^2 ≤50%, a fixed-effect model was peformed. Funnel plot and Egger test were utilized to assess publication bias. Statistical significance was $p<0.05$.

Results. The literature search identified 68 articles initially. After reading the abstracts, 42 studies were excluded. Of the 26 remaining studies, 14 articles were included in this meta-analysis after reviewing the full manuscript (Figure 1).[6-19] The characteristics of the 14 articles involving 1705 patients are summarized in Table 1. An overview of the risk of bias was shown in Figure 2.

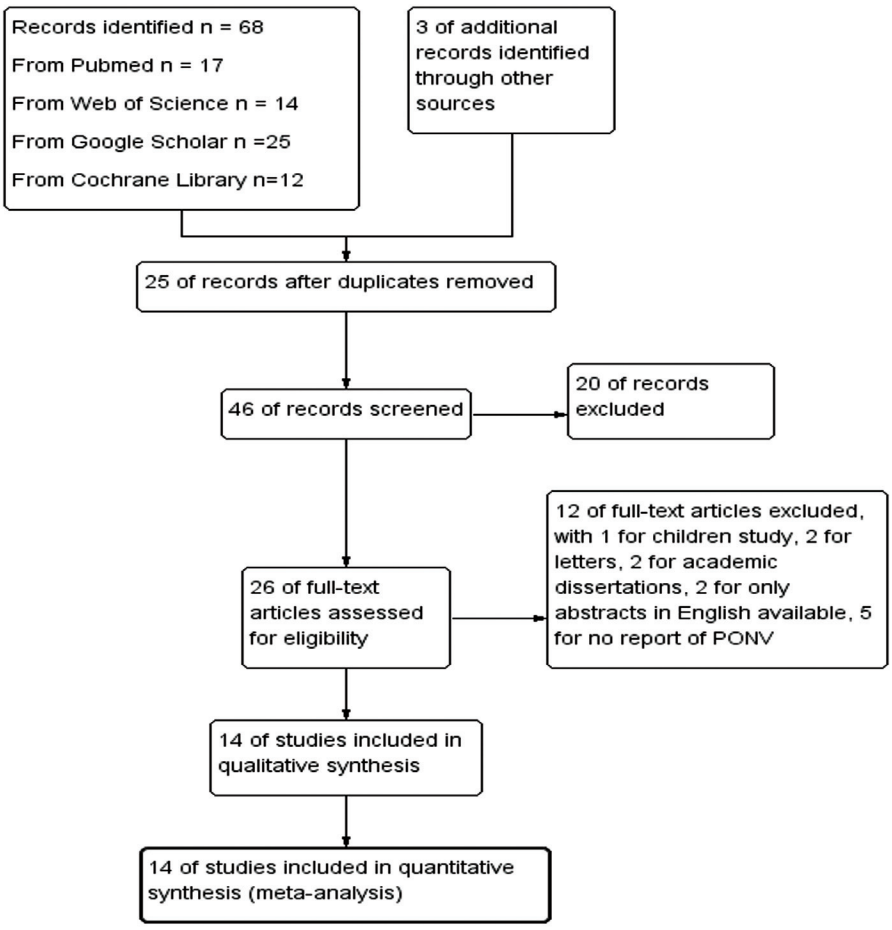

Figure 1 - Flow diagram of literature search.

Table 1 - Characteristics of the included studies.

Author/ year	Dosage	Jadad improvement score	Sample size O/T	Patient characteristics/ surgical setting	Administration time	PONV measurement tool	Observing time (hours)	Outcomes measures
Aydin et al[6] 2019	Ondansetron 8 mg; Tropisetron 5 mg	7	55/55	18-65 years, ASA: I-II; Middle ear surgery; General anesthesia	During skin closure	Visual analog score 0-3	48	a, b, c, d, e
Jokela et al[7] 2002	Ondansetron 16 mg; Tropisetron 5 mg	7	60/60	O: 51±13 years; T: 49±14 years; ASA: I-III; female; Thyroid or parathyroid surgery; General anesthesia	Orally 1 hour before the operation	Yes or no	24	a, b, c, d, e, f
Quan et al[8] 2007	Ondansetron 4mg; Tropisetron 5mg	5	120/118	18-75 years, ASA: I-II; Elective surgery	Before induction of anesthesia	Yes or no	24	a, b, c
Ekinci et al[9] 2011	Ondansetron 4mg; Tropisetron 2.5mg	7	20/20	20-72 years, ASA: I-II; female; Total abdominal hysterectomy General Anesthesia	5 min after induction of anesthesia	Visual analog score 0-3	24	a, d, e, f
Sarvela et al[10] 2006	Ondansetron 8 mg; Tropisetron 5 mg	5	30/28	33±5 years; female; Elective cesarean section; Spinal-epidural anesthesia	5 min after delivery	Numerical rating score 0-10 >3	24	a, d
Scholz et al[11] 1998	Ondansetron 4 mg; Tropisetron 2 mg	6	271/296	18-75 years, ASA: I-III; abdominal and non-abdominal (ENT, eye, breast) surgery General anesthesia	3 min before induction of anesthesia	Yes or no	24	a, d, e
Naguib et al[12] 1996	Ondansetron 4 mg; Tropisetron 5 mg	5	29/25	21-68 years, ASA: I-II; Elective laparoscopic cholecystectomy; General anesthesia	10 min before induction of anesthesia	Yes or no	24	a
Koivuranta et al[13] 1999	Ondansetron 8 mg; Tropisetron 5 mg	6	45/43	≥18 years; ASA: I-III; Gynecological laparotomy; General anesthesia	At the end of surgery	Visual analog score 0-3	24	a, b, c, d, e, f
Wang et al[14] 2002	Ondansetron 8mg; Tropisetron 3mg	4	30/30	No mention Elective surgery; General anesthesia	At the end of surgery	Visual analog score 0-3	24	a, d
Wei et al[15] 1999	Ondansetron 4mg; Tropisetron 5mg	4	30/30	21-72 years, ASA: I-II; Elective abdominal surgery; General anesthesia	10 min before induction of anesthesia	Visual analog score 0-3	24	a, c
Paech et al[16] 2003	Ondansetron 4 mg; Tropisetron 2 mg	7	36/42	O: 48.3±12.2 years; T: 49.4±14.1 years; female; Major open abdominal gynecological surgery General anesthesia combined with epidural anesthesia	After induction of anesthesia	Visual analog score 0-3	24	b, c, d
Tsui et al[17] 1999	Ondansetron 4 mg; Tropisetron 5 mg	6	39/37	≤65 years; ASA: I-III; female; Gynecological laparotomy General anesthesia	Immediately before induction of anesthesia	Visual analog score 0-3	24	b, c, d
Geng et al[18] 2009	Ondansetron 8mg; Tropisetron 5mg	4	48/48	18-60 years, ASA: I-II; female; Gynecological laparotomy; General anesthesia	30 min before completion of surgery	Yes or no	24	b, c, d, f
Argiriadou et al[19] 2002	Ondansetron 4mg; Tropisetron 5mg	7	29/31	O: 43.9±13.6 years; T: 47.9±16.7 years; ASA: I-II; Elective laparoscopic cholecystectomy; General anesthesia	At anesthesia induction	Visual analog score 0-5	12	c, d, e

RCT: randomized controlled trial, ASA: American Society of Anesthesiologists, PONV: postoperative nausea and vomiting, O: Ondansetron, T: Tropisetron, a: The incidence of PONV, b: The incidence of PON, c: The incidence of POV, d: The incidence of antiemetic treatment, e: The incidence of headache, f: The incidence of dizziness

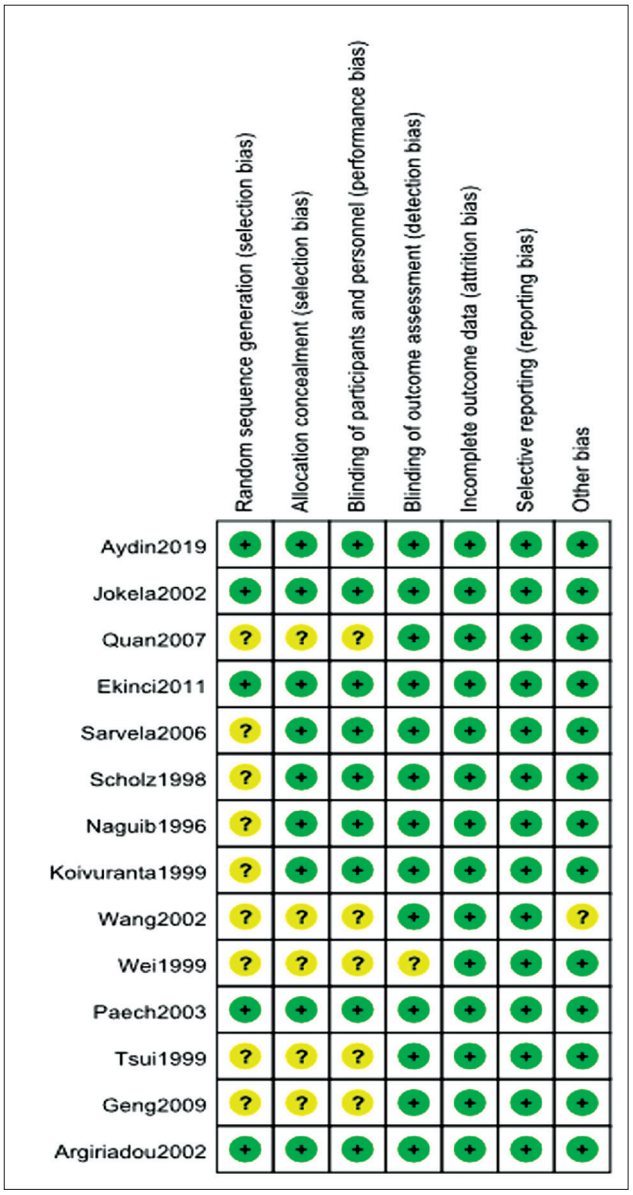

Figure 2 - Risk of bias summary.

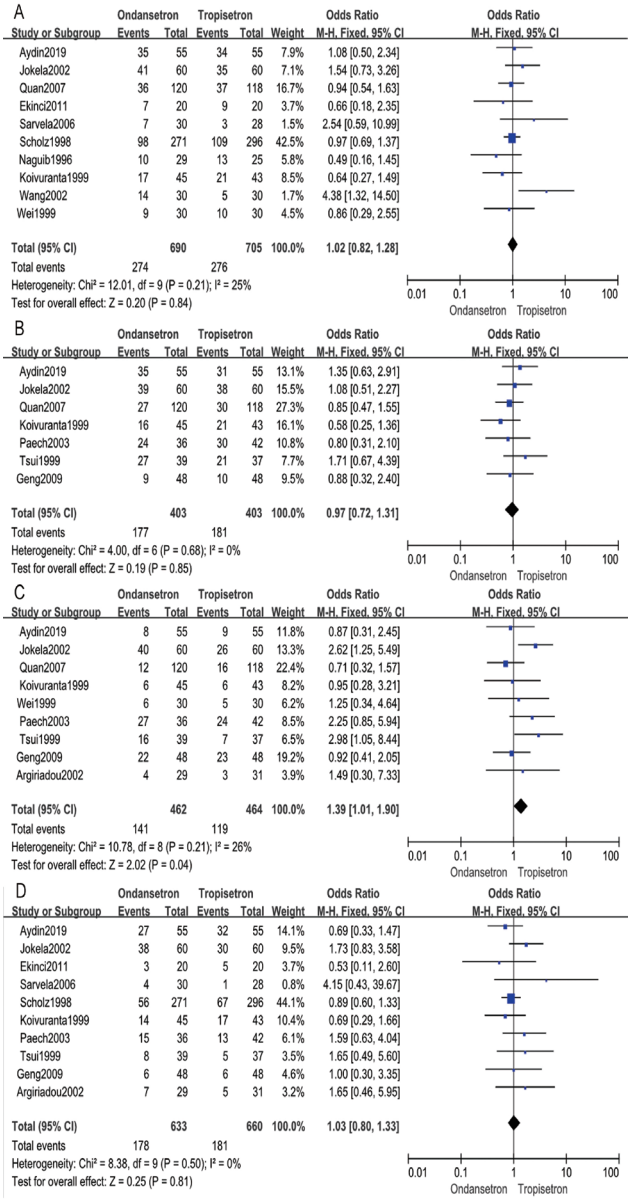

Figure 3 - Forest plot comparing between ondansetron and tropisetron: **A)** postoperative nausea and vomiting; **B)** postoperative nausea; **C)** postoperative vomiting; **D)** antiemetic treatment.

As shown in Figure 3, 10 studies involving 1395 patients reported the incidence of PONV. The effect of ondansetron and tropisetron was equal in preventing PONV (OR: 1.02; 95% CI: 0.82-1.28; p=0.84; I^2=25%) (Figure 3A).[6-15]

Postoperative nausea (PON) was assessed in 7 studies including 806 patients.[6-8,16-18] Meanwhile, postoperative vomiting (POV) was reported in 9 studies including 926 patients.[6-8,13,15-19] This meta-analysis indicated no difference in PON between ondansetron and tropisetron (OR: 0.97; 95% CI: 0.72–1.31; p=0.85; I^2=0%) (Figure 3B). Ondansetron was 39% less effective than tropisetron in preventing POV (OR: 1.39; 95% CI: 1.01-1.90; p=0.04; I^2=26%) (Figure 3C).

Antiemetic treatment. Antiemetic treatment was reported in 10 studies including 1293

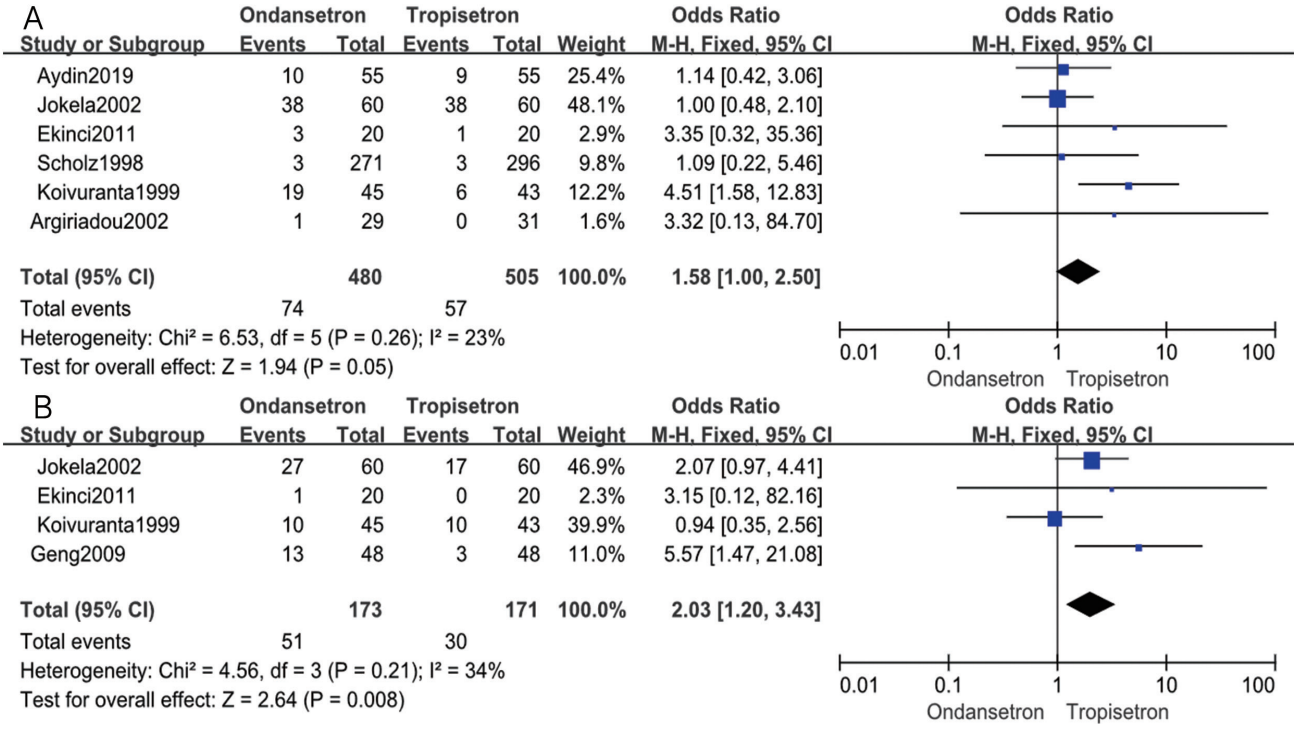

Figure 4 - Forest plot of comparison of the side effects experienced by patients receiving ondansetron and tropisetron treatment: **A)** headache and **B)** dizziness.

patients.[6,7,9-11,13,16-19] The difference in antiemetic treatment was not statistically significant between ondansetron and tropisetron (OR: 1.03; 95% CI: 0.80-1.33; p=0.81; I^2 = 0%) (Figure 3D).

Complications. Headache was evaluated in 6 studies involving 985 patients.[6,7,9,11,13,19] As displayed in Figure 4A, ondansetron compared to tropisetron tended to have higher incidence of headache; however, it wasn't statistically significant (OR: 1.58; 95% CI: 1.00-2.50; p=0.05; I^2=23%). On the other hand, dizziness was evaluated in 4 studies involving 344 patients.[7,9,13,18] As shown in Figure 4B, ondansetron had 103% higher incidence of dizziness than that with tropisetron (OR: 2.03; 95% CI: 1.20-3.43; p=0.008; I^2=34%).

Publication bias. The funnel plot of PONV was asymmetrical. However, Egger test did not reveal significant difference in PONV (p=0.501).

Discussion. Previous systematic review has shown that 5-HT3 receptor antagonists could prevent PONV.[20] The mechanism may be that they can block vagal nerves which trigger the emetic reflex.[21] Ondansetron is the original member of this class with a short elimination half-life, and its effect is confirmed in many studies of different patient populations. Tropisetron is also a potent 5-HT3 receptor antagonist with longer elimination half-life than that of ondansetron. It is produced by systematic methyl substitution of the serotonin molecules.[22] It is still a matter of significant interest to compare the efficacy and side-effect profiles of the short-acting ondansetron and the relatively long-acting tropisetron prophylactically given to patients of both genders undergoing surgery.

The present meta-analysis indicated that tropisetron was more effective than ondansetron in preventing POV, and prophylactic ondansetron and tropisetron had similar incidence of PONV, incidence of PON, and antiemetic efficacy in adults.

We note a difference in the half-life time of ondansetron (T1/2 = 3.2 hours) and tropisetron (T1/2 = 7.3–8 hours), which is probably related to the lower percentage of patients who experienced POV in the tropisetron group.[23] It indicates that prophylactic tropisetron can provide a more long-standing antiemetic coverage after surgery. However, tropisetron does not reduce the incidence of PONV and PON, and

requirement for antiemetic treatment, as compared to that with ondansetron.

Furthermore, tropisetron causes fewer side effects than ondansetron. Compared with ondansetron, tropisetron can decrease the incidence of dizziness. Additionally, tropisetron tends to increase the incidence of headache; however, this difference was not statistically significant. If more RCTs are included and more patients are involved, tropisetron may be shown to be more effective. Nonetheless, we were able to demonstrate in this meta-analysis that tropisetron can more effectively prevent POV with a lower incidence of dizziness than ondansetron.

Several potential limitations associated with these results should be mentioned. First, 2 of the included RCTs had relatively small sample sizes, which might influence the credibility of the conclusion. Second, there were some clinical differences between the included studies: dosages and the administration routes of the study drugs in the included RCTs vary, which may affect the reliability of pooling effects. Finally, the optimal dosages of ondansetron and tropisetron were the remaining question, which need further attention.

In conclusion, tropisetron is superior to ondansetron in preventing POV. It is 39% more effective than ondansetron in preventing POV with a lower incidence of dizziness.

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