Research Article Open Access

Wenjie Zhou, Jie Zhou*

Clinical efficacy of 5-hydroxytryptamine 3 receptor antagonists in reducing propofol injection pain, postoperative nausea/vomiting and shivering: A meta-analysis

https://doi.org/10.1515/pteridines-2020-0003
received July 24, 2019; accepted January 2, 2020.

Abstract: Objective To investigate the clinical efficacy of 5-hydroxytryptamine 3 (5-HT_3) receptor antagonists in reducing propofol injection pain, postoperative nausea/vomiting, and shivering through pooling the available published data.

Methods Prospective randomized clinical studies relevant to 5-HT_3 receptor antagonists in reducing propofol injection pain published before June 2019 were identified from four electronic databases, Pubmed, the Cochrane central register of controlled trials, EMBASE and Wanfang. The incidence of propofol injection pain, postoperative nausea/vomiting, and shivering in patients after 5-HT_3 receptor antagonists were compared to relevant control groups by pooling the individual data through random or fixed-effect models. The publication bias was assessed by funnel plot and Egger's line regression test.

Results After screening, a total of 19 publications relevant to 5-HT_3 receptor antagonists in reducing propofol injection pain and prevention of postoperative nausea/vomiting or shivering were included for analysis. The pooled results demonstrated that 5-HT_3 receptor antagonists could significantly reduce the total propofol injection pain compared to placebo (RR=0.49, 95%CI:0.45-0.54, P<0.05). For mild propofol injection pain, there was no statistical difference between 5-HT_3 receptor antagonists and control groups (RR=1.07,95%CI:0.89-1.29, P>0.05). However, for moderate (RR=0.37, 95%CI: 0.31-0.46, P<0.05) and severe (RR=0.19, 95%CI:0.14-0.27, P<0.05) propofol injection pain, the incidence in 5-HT_3 receptor antagonists was significantly lower than that of control groups**.** The pooled results also indicated that incidence of postoperative nausea/vomiting (RR=0.28, 95%CI:0.17-0.44, P<0.05) and postoperative shivering (RR=0.33, 95%CI:0.23-0.48, P<0.05) were significantly reduced in 5-HT_3 receptor antagonists group compared to control group with a statistical difference.

Conclusion: In this meta-analysis, 5-HT_3 receptor antagonists effectively reduced propofol injection pain, postoperative nausea/vomiting, and shivering.

Keywords: 5-HT_3 receptor antagonists; propofol injection pain; postoperative nausea/vomiting; meta-analysis

Introduct]ion

Propofol is one of the most widely used clinical intravenous anesthetics with the advantages of rapid onset, complete recovery, no accumulation, and good controllability. However, local injection pain is a common adverse reaction, with an incidence rate of 28% to 90% in adults and 28% to 85% in children [1]. Propofol injection pain can cause obvious discomfort and distress to the patient, affecting blood pressure and heart rate [2-4].

The preventive effect of 5-HT_3 receptor antagonists (such as ondansetron, granisetron, and tropisetron) on nausea and vomiting after surgery had been confirmed by the previous publications [5, 6]. Compared with other antiemetic drugs, 5-HT_3 receptor antagonists have fewer side effects and no sedative and hypnotic effects. Several publications have shown that 5-HT_3 receptor antagonists can effectively prevent propofol injection pain compared to the placebo [7, 8]. In order to provide more reliable evidence for the clinical application of 5-HT3 receptor antagonists for reducing propofol injection pain, we performed this meta-analysis by pooling the available published data relevant to 5-HT_3 receptor antagonists on prevention propofol injection pain.

***Corresponding author: Jie Zhou,** Department of Anesthesiology, Lishui Central Hospital, Zhejiang Province 323000 PR China, E-mail: rzdp5u@163.com
Wenjie Zhou, Department of Anesthesiology, Lishui Traditional Chinese Medicine Hospital, Zhejiang Province 323000 PR China

Material and methods

Search Strategy

The publications were electronically searched according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement flow chart in the relevant databases (**Figure 1**). Prospective randomized clinical studies relevant to 5-hydroxytryptamine 3 receptor antagonists in reducing propofol injection pain published before June 2019 were systematically searched in the electronic databases of Pubmed, the Cochrane central register of controlled trials, EMBASE and Wanfang. The databases were searched using the following terms: propofol injection pain; 5-hydroxytryptamine 3 receptor antagonists/5-HT_3 receptor antagonists; ondansetron; granisetron; tropisetron; palonosetron; ramosetron. The search was confined to humans, and in either English or Chinese language only.

Data extraction and quality assessment

The data was extracted from each of the included studies by two independent reviewers and cross-checked. The general information such as named first author, publication date, sample size, 5-HT_3 receptor antagonist dosage, and administration in each study were extracted. The incidence of propofol injection pain, postoperative nausea/vomiting, and shivering were also extracted from each included publication.

Quality assessment

The methodological qualities of the included 19 publications were evaluated by two reviewers Wenjie Zhou & Jie Zhou independently by using the Cochrane Reviews Handbook 5.0. Six questionnaires, including randomization, allocation concealment, blinding, withdraw, free of selective reporting and other bias according were used in the quality evaluation analysis [9].

Statistical analysis

Stata12.0 software was used for data analysis. Dichotomous data such as propofol injection pain postoperative nausea and vomiting were expressed as a number and combined by the effect size of risk ratio (RR) with a 95% confidence interval (CI). Statistical heterogeneity across the included 19 studies was evaluated by the chi-square (χ^2) test [10], and the inconsistency was demonstrated through I^2[11]. The Egger's line regression test and funnel plots were applied for the evaluation of the publications [13].

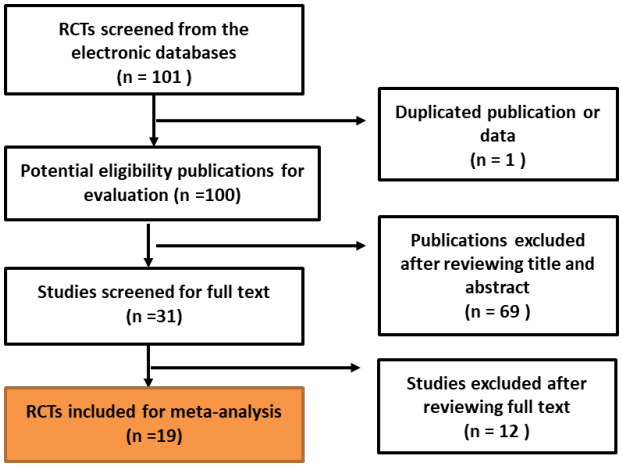

Figure 1: Flow diagram of the search strategy to identify relevant articles for inclusion.(RCTs, Randomized Controlled Trials).

Results

General characteristics of the included publications

A total of 19 publications [7, 8, 12-28] relevant to 5-HT_3 receptor antagonists in reducing propofol injection pain and prevention of postoperative nausea and vomiting or shivering were included in this study**.** Of the 19 studies, five 5-HT_3 receptor antagonists, ondansetron, granisetron, tropisetron, palonosetron, and ramosetron, were included for reducing propofol injection pain. The general characteristics of the included 19 publications were shown in **Table 1**.

The quality of the included studies

The methodological quality of the included 19 studies were assessed by six questionnaires including, randomization, allocation concealment, blinding, withdraw, free of selective reporting, and other bias according to the Cochrane Reviews Handbook 5.0. Generally, the methodological quality of the included 19 was of moderate risk of bias. The detailed quality results of each included study were demonstrated in **Table 2**.

Table 1: Study design and cohort characteristics of included studies.

First author	Year	No of subjects(5-HT3RA)/Control)	Administration		Operation	Induced anesthesia
			5-HT3RA	Control		
Arnbesh	1999	40/40	Ondansetron 4mg	0.9%NaCl 2mL	NA	Local venous reflux was blocked by ligation of forearm with tourniquet for 10 seconds followed by 5 mL pretreatment solution injected into vein, then tourniquet was loosened, and 25% of the amount of propofol was injected into vein (2.5 mg/kg) in 20 seconds.
Dubey	2003	50/50	Granisetron 2mg	0.9%NaCl 2mL	Laparoscopic surgery	Local venous reflux was blocked by ligation of forearm with tourniquet for 10 seconds followed by 5 mL pretreatment solution injected into vein, then tourniquet was loosened, and 25% of the amount of propofol was injected into vein (2.5 mg/kg) in 20 seconds.
Cao DH	2005	29/30	Ondansetron 4mg	0.9%NaCl 2mL	NA	Intravenous injection of 3 mL of pretreatment solution and 0.5 mL/s of propofol 180 mg after 30 seconds
Liu F	2006	31/31	Tropisetron 2mg	0.9%NaCl 2mL	NA	Intravenous injection of pretreatment solution 2 mL, 60 seconds followed by injection of 2 mg/kg propofol
Ma YS	2009	50/50	Granisetron 2mg	0.9%NaCl 3mL	Gynecological laparoscopy	Intravenous injection of 3 mL of pretreatment solution, release tourniquet after 1 minute, and inject propofol at a speed of 0.5 mL/s. Pain score was assessed when the dose was 0.5 mg/kg.
Xu XX	2010	30/30	Tropisetron 2mg	0.9%NaCl 2mL	NA	2 mL of pretreatment solution was injected intravenously, and 1.5-2 mg/kg of propofol was injected at a speed of 5 mg/s after 60 seconds.
Fu HQ	2010	100/100	Granisetron 2mg	0.9%NaCl 3mL	Laparoscopic cholecystectomy	Intravenous injection of 3 mL of pretreatment solution, release tourniquet after 1 minute, and inject propofol at a speed of 0.5 mL/s. Pain score was assessed when the dose was 0.5 mg/kg.
Liu QM	2011	30/30	Ondansetron 4mg	0.9%NaCl 3mL	Painless gastroscopy	3 mL of pretreatment solution was injected intravenously, and 1.5-2 mg/kg of propofol was injected at the speed of 0.5 mL/S after 30 seconds.
Yan YX	2011	60/60	Ondansetron 4mg	0.9%NaCl 2mL	Painless gastroscopy	Intravenous injection of 2 mL pretreatment solution and 60 seconds followed by injection of 2.5 mg/kg propofol
Lu H	2011	40/40	Ondansetron 4mg	0.9%NaCl 2mL	Painless gastroscopy	Intravenous injection of pretreatment solution 2 mL, 30 seconds followed by injection of 2mg/kg propofol

Continued **Table 1:** Study design and cohort characteristics of included studies.

First author	Year	No of subjects(5-HT3RA)/Control)	Administration		Operation	Induced anesthesia
			5-HT3RA	Control		
Zahedi	2011	45/45	Ondansetron 4mg	0.9%NaCl 2mL	Ophthalmic surgery	Local venous reflux was blocked by ligation of forearm with tourniquet for 10 seconds followed by 2 mL pretreatment solution injected into vein, then tourniquet was loosened, and injection of propofol 2 mg/kg.
Lee	2011	50/50	Ramosetron 0.3mg	0.9%NaCl 5mL		Injection of propofol 2 mg/kg
Shao LL	2011	5/50	Tropisetron 5mg	0.9%NaCl 2mL	NA	Pressure cuff sphygmomanometer to mean arterial pressure, intravenously injection pretreatment solution at 0.5 mL/s speed, loosen cuff after 1 minute, and injection propofol 1.5-2 mg/kg at 0.5 mL/s speed.
Singh	2011	25/25	Granisetron 2mg	0.9%NaCl 2mL	NA	Local venous reflux was blocked by ligation of forearm with tourniquet for 10 seconds followed by 5 mL pretreatment solution injected into vein, then tourniquet was loosened, and 25% of the amount of propofol was injected into vein (2.5 mg/kg) in 20 seconds.
Zhu M	2012	3/30	Ondansetron 4mg	0.9%NaCl 3mL	Painless artificial abortion	Intravenous injection of 3 mL of pretreatment solution, release tourniquet after 1 minute, and inject propofol at a speed of 0.5 mL/s. Pain score was assessed when the dose was 0.5 mg/kg.
Ahmed	2012	40/40	Granisetron 2mg	0.9%NaCl 2mL	NA	Intravenous injection of 2 mL of pretreatment solution and 60 seconds followed by injection of 2mg/kg propofol
Ryu	2014	40/40	Palonosetron75 μg	0.9%NaCl 2mL		Injection of propofol 2 mg/kg
Singh	2014	40/40	Ramosetron 0.3mg	0.9%NaCl 2mL		Injection of propofol 2.5 mg/kg
Alipour(1)	2014	56/56	Granisetron 2mg	0.9%NaCl 5mL		Injection of propofol 2.5 mg/kg
Alipour(2)	2014	56/56	Ondansetron 4mg	0.9%NaCl 5mL		Injection of propofol 2.5 mg/kg

NA, not applicable

Propofol injection pain incidence

In the aspect of general injection pain incidence, there was significant statistical heterogeneity across the 19 studies. Therefore, the data were pooled by random-effects methods. The pooled results demonstrated that the 5-HT_3 receptor antagonists could significantly reduce the total propofol injection pain compared to placebo (RR=0.49, 95%CI:0.45-0.54, P<0.05). For the different 5-HT_3 receptor antagonists ondansetron, granisetron, tropisetron, palonosetron, and ramosetron, the propofol injection pain incidence was also statistically significantly reduced (Pall<0.05), **Figure 2**.

Table 2: The general quality of the included 19 studies.

Author	Year	Randomization	Allocation concealment	Blinding	Withdraw	Free of selective reporting	Other bias
Liu QM	2011	Unclear	Unclear	Unclear	No	Unclear	Unclear
Zhu M	2012	Unclear	Unclear	Yes	No	Unclear	Unclear
Yan YX	2011	Unclear	Unclear	Yes	No	Unclear	Unclear
Lu H	2011	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Cao DH	2005	Unclear	Unclear	Yes	No	Unclear	Unclear
Ma YS	2009	Yes	Unclear	Yes	No	Yes	Unclear
Fu HQ	2010	Unclear	Unclear	No	No	Yes	Unclear
Liu F	2006	Yes	Unclear	Yes	Unclear	Yes	Unclear
Shao LL	2011	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Xu XX	2010	Unclear	Unclear	Unclear	No	Unclear	Unclear
Singh	2011	Yes	Yes	Yes	No	Yes	Unclear
Arnbesh	1999	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Ahmed	2012	Yes	Yes	Yes	No	Unclear	Unclear
Dubey	2003	Yes	Yes	Yes	No	Unclear	Unclear
Zahedi	2011	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Ryu	2014	Yes	Unclear	Unclear	Unclear	Unclear	Unclear
Singh	2014	Yes	Unclear	Unclear	Unclear	Unclear	Unclear
Lee	2011	Yes	Unclear	Yes	Unclear	Unclear	Unclear
Alipour	2014	Yes	Unclear	Yes	No	Unclear	Unclear

Propofol injection pain degree analysis

According to the pain degree, we performed a subgroup analysis for mild, moderate, and severe propofol injection pain comparing incidence between 5-HT_3 receptor antagonists and control groups. For mild propofol injection pain, there was no statistical difference between 5-HT_3 receptor antagonists and control groups (RR=1.07, 95%CI:0.89-1.29, P>0.05). However, for moderate (RR=0.37, 95%CI:0.31-0.46, P<0.05) and severe (RR=0.19, 95%CI:0.14-0.27, P<0.05) propofol injection pain, the incidence in 5-HT_3 receptor antagonists was significantly lower than that of control groups, **Figure 3.**

Postoperative nausea/vomiting and shivering

There was no statistical heterogeneity in the aspects of postoperative nausea/vomiting and shivering; therefore the data was combined through fixed-effect model. The pooled results indicated that incidence of postoperative nausea/vomiting (RR=0.28, 95%CI:0.17-0.44, P<0.05) and postoperative shivering (RR=0.33, 95%CI:0.23-0.48, P<0.05) was significantly reduced in the 5-HT_3 receptor antagonists group compared to the control group with a statistical difference, **Figure 4**.

Publication bias evaluation

A funnel plot was used to evaluate publication bias for 5-HT_3 receptor antagonists in reducing propofol injection pain. The funnel plot was asymmetric at the bottom, and Egger's line regression test also demonstrated significant publication bias (t=-7.53, P<0.05), Figure 5.

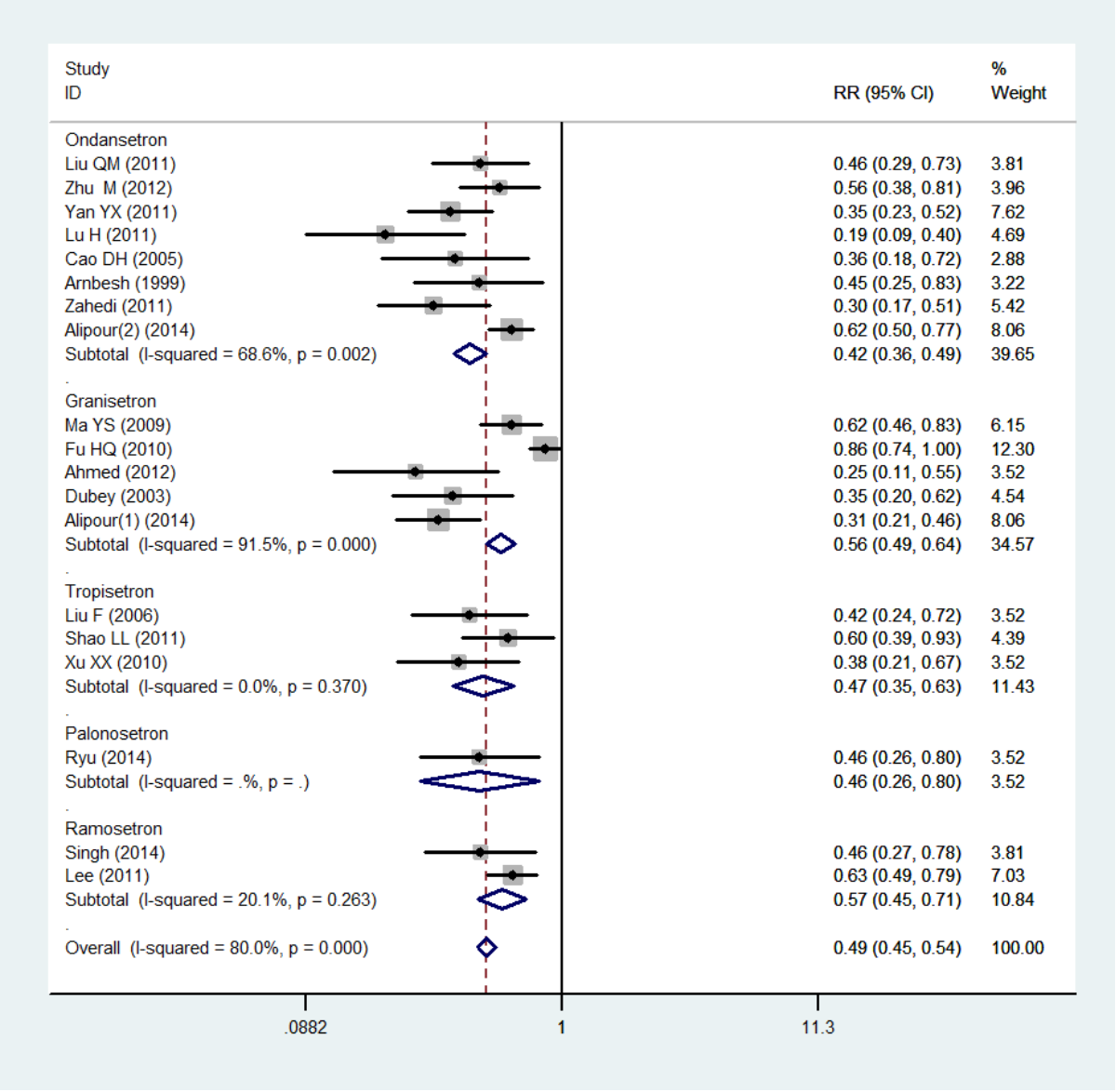

Figure 2: A forest plot of the propofol injection pain incidence between 5-hydroxytryptamine 3 receptor antagonists and control groups. (RR, risk ratio).

Discussion

In the present work, we systematically searched and reviewed electronic databases and included a total of 19 studies relevant to 5-HT_3 receptor antagonists in reducing propofol injection pain. The general methodical quality of the included 19 individual studies was moderate. The combined results indicated that 5-HT_3 receptor antagonists could effectively reduce moderate and severe propofol injection pain, postoperative nausea/vomiting, and shivering. Injection pain is a common side effect in the clinical use of propofol [2, 29]. Among the 33 low-mortality clinical anesthesia problems, anesthesiologists ranked propofol injection pain as seventh according to the importance and incidence. The clinical manifestation of propofol injection pain is a burning pain at the injection site when propofol is injected intravenously, however, the mechanism has yet to be elucidated [30].

5-HT_3 receptor antagonists have a central antiemetic effect, which can effectively reduce the possibility of reflux and aspiration caused by intravenous anesthetics, and have fewer other adverse reactions [31-33]. Therefore, 5-HT_3 receptor antagonists, including ondansetron, granisetron, tropisetron, palonosetron, and ramosetron,

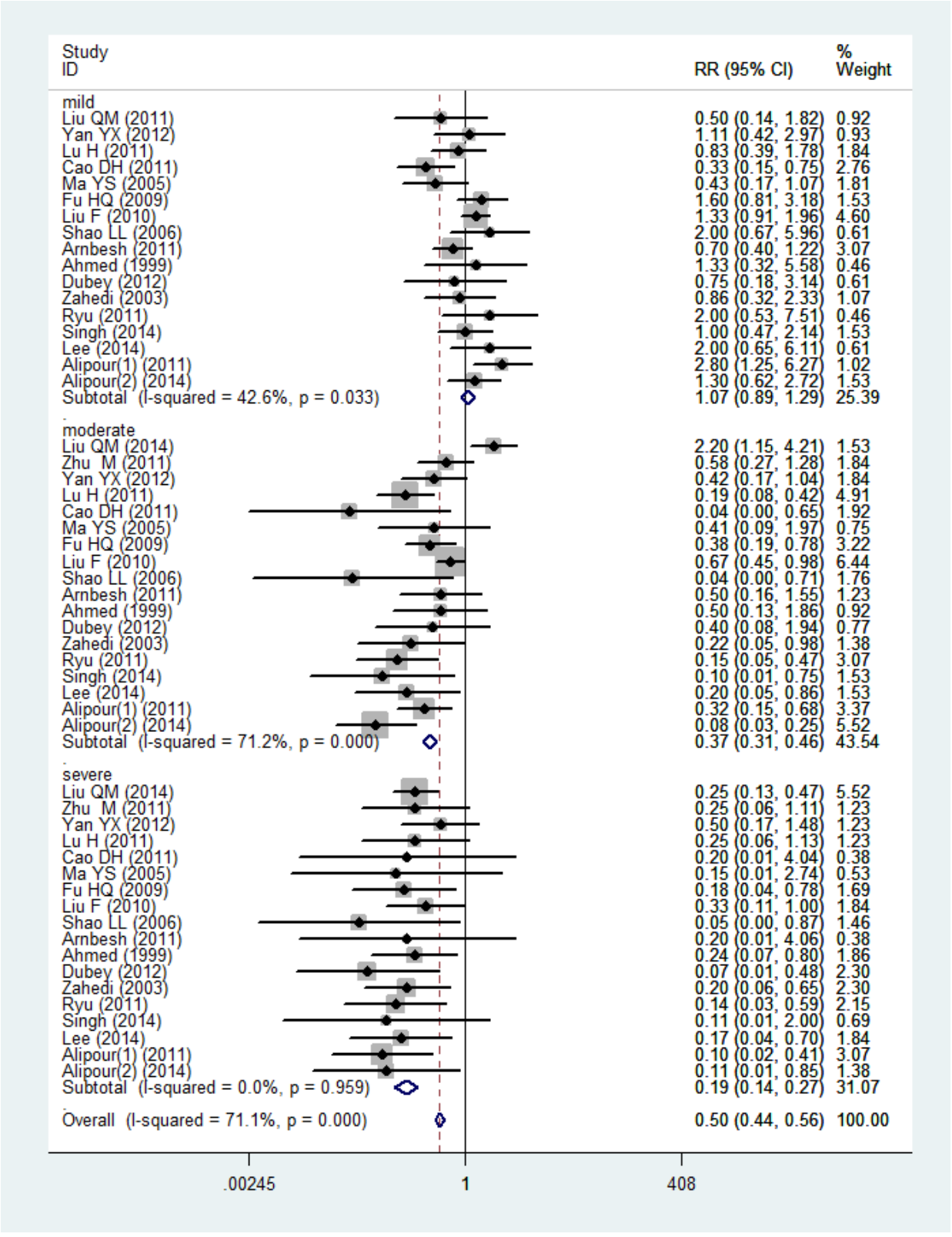

Figure 3: A forest plot of the propofol injection pain incidence between 5-hydroxytryptamine 3 receptor antagonists and control groups according to the pain degree. (RR, risk ratio).

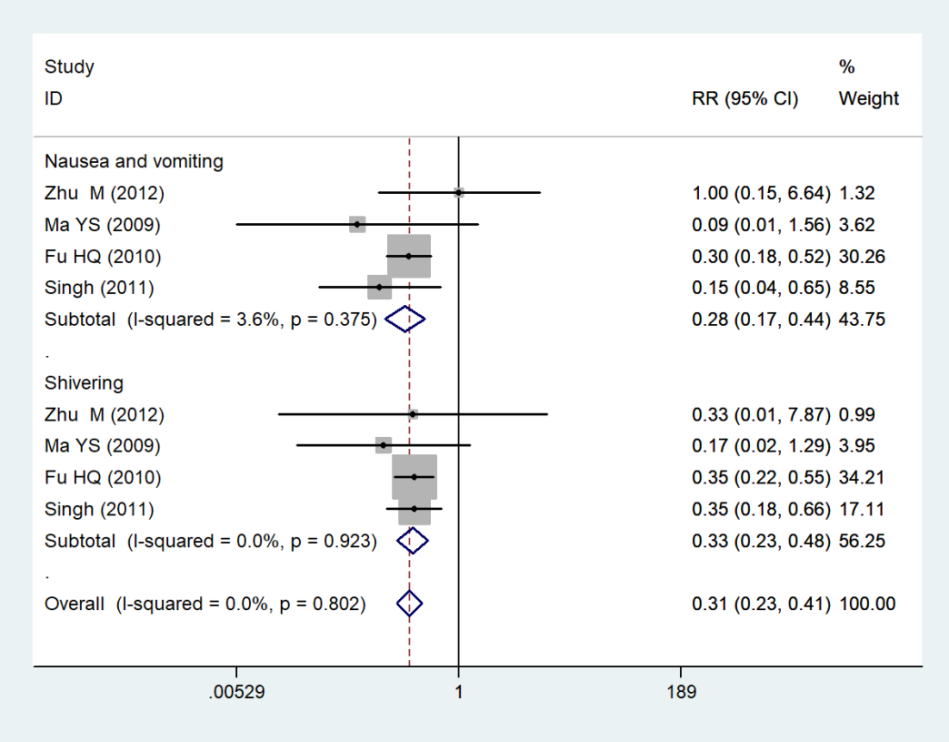

Figure 4: A forest plot of postoperative nausea/vomiting and shivering incidence between 5-hydroxytryptamine 3 receptor antagonists and control groups according to the pain degree. (RR, risk ratio).

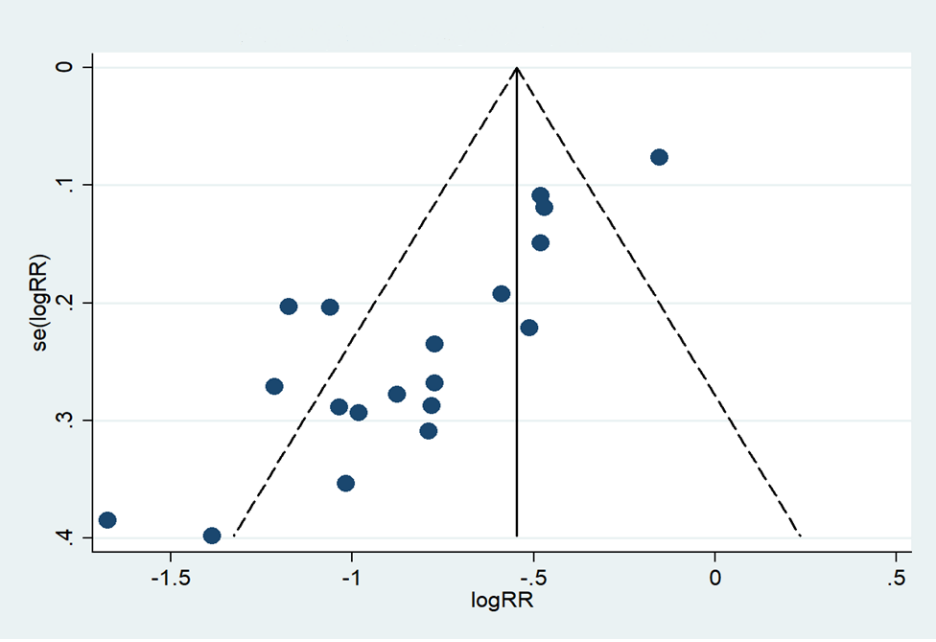

Figure 5: A funnel plot was used to evaluate the publication bias for 5-hydroxytryptamine 3 receptor antagonists in reducing propofol injection pain. (SE, standard error; RR, risk ratio).

have better application prospects than lidocaine and opioids. Clinically, 5-HT_3 receptor antagonists are mainly used to prevent nausea and vomiting after anesthesia with good clinical efficacy [34-36].

In addition to anti-nausea and vomiting effects, 5-HT_3 receptor antagonists can prevent propofol injection pain according to the previously published studies. Its effect on reducing propofol injection may be related to its antagonism of peripheral 5-HT_3 receptors and blockade of Na+ channels in nerve cells, or possibly due to the activation of endorphin IV receptors [37]. Previous experiments in rats have shown that ondansetron can block Na+ channels in brain neurons, and its local anesthetic effect is approximately 15 times that of lidocaine.

In conclusion

Based on the present publications, our meta-analysis demonstrated that 5-HT_3 receptor antagonists could effectively reduce propofol injection pain, postoperative nausea/vomiting, and shivering. However, there are several limitations in our present work, which should be taken into consideration when interpreting our results. Firstly, only publications written in English or Chinese were included; Secondly, significant publication bias was found in the present meta-analysis; Thirdly, the general methodology quality was not high. Therefore, well designed multicenter prospective randomized clinical trials relevant to 5-HT3 receptor antagonists in reducing propofol injection pain and prevention of postoperative nausea and vomiting are needed to further verify our findings.

Conflict of interest: Authors state no conflict of interest

References

1. Agarwal A, Ansari MF, Gupta D, Pandey R, Raza M, Singh PK, et al. Pretreatment with thiopental for prevention of pain associated with propofol injection. Anesth Analg. 2004 Mar;98(3):683–6.
2. Desousa KA. Pain on propofol injection: causes and remedies. Indian J Pharmacol. 2016 Nov-Dec;48(6):617–23.
3. Auerswald K, Pfeiffer F, Behrends K, Burkhardt U, Olthoff D. [Pain on injection with propofol]. Anasthesiol Intensivmed Notfallmed Schmerzther. 2005 May;40(5):259–66.
4. Tan CH, Onsiong MK. Pain on injection of propofol. Anaesthesia. 1998 May;53(5):468–76.
5. Eberhart LH, Morin AM, Bothner U, Georgieff M. Droperidol and 5-HT3-receptor antagonists, alone or in combination, for prophylaxis of postoperative nausea and vomiting. A meta-analysis of randomised controlled trials. Acta Anaesthesiol Scand. 2000 Nov;44(10):1252–7.
6. Loewen PS, Marra CA, Zed PJ. 5-HT3 receptor antagonists vs traditional agents for the prophylaxis of postoperative nausea and vomiting. Can J Anaesth. 2000 Oct;47(10):1008–18.
7. Qimin L, Jianmin Z, Xiaoyin Z, Lidan X. Clinical study of Ondansetron Combined with Low Dose Sufentanil in Preventing Injection Pain of Propofol. Strait Pharmaceutical Journal; 2011. pp. 114–5.
8. Ming Z. A comparative study of ondansetron and lidocaine in the prevention of propofol injection pain. Shanxi Medical Journal; 2012. pp. 263–5.
9. Zafarmand MH, van der Schouw YT, Grobbee DE, de Leeuw PW, Bots ML. The M235T polymorphism in the AGT gene and CHD risk: evidence of a Hardy-Weinberg equilibrium violation and publication bias in a meta-analysis. PLoS One. 2008 Jun;3(6):e2533.
10. DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials. 1986 Sep;7(3):177–88.
11. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ. 2003 Sep;327(7414):557–60.
12. Ambesh SP, Dubey PK, Sinha PK. Ondansetron pretreatment to alleviate pain on propofol injection: a randomized, controlled, double-blinded study. Anesth Analg. 1999 Jul;89(1):197–9.
13. Dubey PK, Prasad SS. Pain on injection of propofol: the effect of granisetron pretreatment. Clin J Pain. 2003 Mar-Apr;19(2):121–4.
14. Cao D, Ding J, Wang M, Zhou Z. Comparison of lidocaine and ondansetron for the prevention of pain on injection of propofol. Xiandai Yiyao Weisheng. 2005:2578–9.
15. Liu F, Ge H, Zhou R. Preventive effect of tropisetron on intravenous pain induced by propofol. Zhongguo Yiyuan Yaoxue Zazhi. 2006:192–3.
16. Ma Y, Lin X, Zhou J. Effects of Granisetron/Lidocaine Combination on Propofol Injection-induced Pain: A Double-blind Randomized Clinical Trial. Journal of Sichuan University 2009:536-538.
17. Fu H. Clinical Efficacy of Granisetron Combined with Lidocaine pretreatment in Minimizing Propofol Injection Pain and Vomiting. China Pharmacy; 2010. pp. 1476–8.
18. Tu X. The Prevention for Injection Pain with Several Method. Hebei Med. 2010:847–9.
19. Singh DK, Jindal P, Singh G. Comparative study of attenuation of the pain caused by propofol intravenous injection, by granisetron, magnesium sulfate and nitroglycerine. Saudi J Anaesth. 2011 Jan;5(1):50–4.
20. Shao L, Lv H, Tian A, Liu Y, Wu Q. Effect of Combination of Tropisetron and Lidocaine on Propofol Injection induced Pain. Chinese Journal of Hemorheology. 2011;284-286:336.
21. Yan Y, Mou Z, Wu Z. Prevention and treatment of propofol injection pain by hypothermia, ondansetron and lidocaine alone or in combination. Chinese Community Doctors; 2011. p. 175.
22. Lu H. Preventive effect of intravenous ondansetron on propofol injection pain. Journal of Mudanjiang Medical University 2011:39-40.

23. Zahedi H, Maleki A, Rostami G. Ondansetron pretreatment reduces pain on injection of propofol. Acta Med Iran. 2012;50(4):239–43.
24. Ahmed A, Sengupta S, Das T, Rudra A, Iqbal A. Pre-treatment with intravenous granisetron to alleviate pain on propofol injection: A double-blind, randomized, controlled trial. Indian J Anaesth. 2012 Mar;56(2):135–8.
25. Ryu HB, Kim SJ. Analgesic effects of palonosetron in the intravenous propofol injection. Korean J Anesthesiol. 2014 Feb;66(2):99–104.
26. Lee KH, Rim SK, Lee JY, Lee SY, Lee SN, Lee EJ, et al. Effects of pretreatment with intravenous palonosetron for propofol-remifentanil-based anesthesia in breast and thyroid cancer surgery: a double-blind, randomized, controlled study. Korean J Anesthesiol. 2014 Jul;67(1):13–9.
27. Alipour M, Tabari M, Alipour M. Paracetamol, ondansetron, granisetron, magnesium sulfate and lidocaine and reduced propofol injection pain. Iran Red Crescent Med J. 2014 Mar;16(3):e16086.
28. Singh D, Jagannath S, Priye S, Shivaprakash, Kadli C, Reddy D. Prevention of propofol injection pain: comparison between lidocaine and ramosetron. J Anaesthesiol Clin Pharmacol. 2014 Apr;30(2):213–6.
29. Wang W, Wu L, Zhang C, Sun L. Is propofol injection pain really important to patients? BMC Anesthesiol. 2017 Feb;17(1):24.
30. Lee JH, Jung SY, Kim MH, Cho K. The effect of dexmedetomidine on propofol injection pain. Korean J Anesthesiol. 2014 Dec;67 Suppl:S30–1.
31. Singh PM, Borle A, Panwar R, Makkar JK, McGrath I, Trikha A, et al. Perioperative antiemetic efficacy of dexamethasone versus 5-HT3 receptor antagonists: a meta-analysis and trial sequential analysis of randomized controlled trials. Eur J Clin Pharmacol. 2018 Oct;74(10):1201–14.
32. Kim KI, Lee DE, Cho I, Yoon JH, Yoon SS, Lee HS, et al. Effectiveness of palonosetron versus other serotonin 5-HT3 receptor antagonists in triple antiemetic regimens during multiday highly emetogenic chemotherapy. Ann Pharmacother. 2012 Dec;46(12):1637–44.
33. Gamse R. Antiemetic action of 5-HT3 receptor antagonists: review of preclinical and clinical results with ICS 205-930. Cancer Treat Rev. 1990 Sep;17(2-3):301–5.
34. Lin SJ, Hatoum HT, Buchner D, Cox D, Balu S. Impact of 5-HT3 receptor antagonists on chemotherapy-induced nausea and vomiting: a retrospective cohort study. BMC Health Serv Res. 2012 Jul;12(1):215.
35. Smith HS, Cox LR, Smith EJ. 5-HT3 receptor antagonists for the treatment of nausea/vomiting. Ann Palliat Med. 2012 Jul;1(2):115–20.
36. Du Q, Zhai Q, Zhu B, Xu XL, Yu B. Economic evaluation of 5-HT3 receptor antagonists in combination with dexamethasone for the prevention of 'overall' nausea and vomiting following highly emetogenic chemotherapy in Chinese adult patients. J Oncol Pharm Pract. 2017 Sep;23(6):403–12.
37. Fakhfouri G, Rahimian R, Dyhrfjeld-Johnsen J, Zirak MR, Beaulieu JM. 5-HT3 Receptor Antagonists in Neurologic and Neuropsychiatric Disorders: The Iceberg Still Lies beneath the Surface. Pharmacol Rev. 2019 Jul;71(3):383–412.