BMJ Open

The effect of dexmedetomidine on postoperative nausea and vomiting in patients under general anesthesia: an updated meta-analysis of randomized controlled trials

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2022-067102
Article Type:	Original research
Date Submitted by the Author:	02-Aug-2022
Complete List of Authors:	Zhao, Weihong; Hebei General Hospital, Department of Anesthesiology Li, Jianli; Hebei General Hospital, Department of Anesthesiology Wang, Na; Hebei General Hospital, Department of Rheumatology Wang, Zhibin; The Fifth People's Hospital of Hengshui, Department of Anesthesiology Zhang, Meng; Hebei General Hospital, Department of Anesthesiology Zhang, Huanhuan; Hebei General Hospital, Department of Anesthesiology Liu, Meinv; Hebei General Hospital, Department of Anesthesiology He, Jinhua; Hebei General Hospital, Department of Anesthesiology Yu, Dongdong; Hebei General Hospital, Department of Anesthesiology
Keywords:	ANAESTHETICS, Adult anaesthesia < ANAESTHETICS, Adult surgery < SURGERY, Adverse events < THERAPEUTICS

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

The effect of dexmedetomidine on postoperative nausea and vomiting in patients under general anesthesia: an updated meta-analysis of randomized controlled trials

Weihong ZHAO, MD[1], Jianli LI, PhD[1], Na WANG, MD[2], Zhibin WANG, MD[3], Meng ZHANG, MD [1], Huanhuan ZHANG, MD [1], Meinv LIU, MD [1], Jinhua HE, MD [1], Dongdong YU, MD [1]

[1] Department of Anesthesiology, Hebei General Hospital, Shijiazhuang 050000, Hebei Province, China

[2] Department of Rheumatology, Hebei General Hospital, Shijiazhuang 050000, Hebei Province, China

[3] Department of Anesthesiology, The Fifth People's Hospital of Hengshui, Hengshui, 053000, Hebei Province, China.

Corresponding author and correspondence to:

Jianli Li, PhD.

Department of Anesthesiology, Hebei General Hospital,

Shijiazhuang, China

E-mail: hblijianli@163.com

Keywords: Dexmedetomidine, Perioperative period, Postoperative nausea and vomiting, Side effects, Meta-analysis

Word Counts

Main text: 2865 words (Excluding title page, references, figures and tables)

ABSTRACT

Objectives: To explore the effect of dexmedetomidine on postoperative nausea and vomiting in adult patients after general anesthesia.

Design: Systematic review and meta-analysis.

Data Sources: We searched the PubMed, the Web of Science, the Cochrane Library and Embase (January 1, 2000, to June 30, 2022) to find the relevant randomized controlled trials (RCTs) using the following search terms: dexmedetomidine and postoperative nausea and vomiting. All studies included the primary outcome of interest: the incidence of postoperative nausea and vomiting.

Data analysis: All the relevant data were performed by using RevManV.5.4. Heterogeneity was tested for each outcome, and random effect or fixed effect models were selected according to the level of heterogeneity.

Results: In total of 18 trials involving 2018 patients were involved in this meta-analysis. The incidence of postoperative nausea and vomiting in dexmedetomidine group was obviously lower than that in control group (odds ratio [OR] =0.49, 95% CI 0.36 to 0.67) and the perioperative opioid consumption in dexmedetomidine group was also decreased significantly (standard mean difference [SMD] = −1.04, 95% CI −1.53 to −0.54). Moreover, the length of hospitalization (SMD= −2.29, 95% CI −4.31 to −0.28) and the extubation time (SMD= −0.75, 95% CI −1.26 to −0.25) in dexmedetomidine group were shorter. Whereas, higher number of patients receiving dexmedetomidine occurred bradycardia (OR=1.60, 95% CI 1.13 to 2.27).

Conclusions: Dexmedetomidine can decrease the occurrence of postoperative nausea and vomiting in adult patients under general anesthesia and promote the recovery after surgery. However, dexmedetomidine may increase the occurrence of bradycardia.

PROSPERO registration number: CRD 42022341548

Strengths and limitations of this study

- This is an update meta-analysis of 18 published articles to investigate the effect of dexmedetomidine on postoperative nausea and vomiting in adult patients under general anesthesia.
- A thorough systematic review and meta-analysis provide confidence in the findings.
- The main limitation of this review is that varied quality and heterogeneity of included studies may limit the certainty of the findings of meta-analysis

INTRODUCTION

Postoperative nausea and vomiting (PONV), as a familiar negative events after operation, is known as nausea, vomiting, or retching within one day after operation(1), which may be due to the effect of anesthetics on the emetic control center in the medulla oblongata(2). The incidence of PONV is about 30% and even rising to 60%-80% in high-risk populations. PONV, an extreme poor medical experience for patients undergoing general anesthetic surgery, leads to many adverse influences including stomach discomfort, dehydration, water-electrolyte disorders, wound dehiscence, esophageal injury, reflux and aspiration, which extend the time of hospitalization and increase the medical costs(3). Fortunately, prophylactic antiemetic agents can decrease the happening of PONV, such as antihistamines, corticosteroids, dopamine antagonists, anticholinergics and 5-HT3 receptor antagonists. However, these drugs have some side effects including headache, restlessness, dry mouth, hypotension and cardiovascular complications, which limit its use in some cases(4). Therefore, exploring suitable drugs and methods to prevent and treat PONV is necessary.

Dexmedetomidine (DEX), as a new adrenal α2 receptor agonist with high selectivity, has

sedation, hypnosis and analgesia effects without respiratory depression, which is widely used in perioperative period. A previous study reported that DEX can decrease perioperative catecholamine release, maintain hemodynamic stability, reduce intraoperative analgesic and anesthetic requirements, and improve the quality of recovery(5). These characteristics have enabled DEX to be a multifunctional drug in the presentments of numerous negative events during anesthesia. There were two meta-analyses found that DEX significantly alleviated the postoperative pain intensity and decreased the opioid consumption(6; 7). For the last few years, the effect of DEX on PONV has attracted increasing attention from anesthesiologists. One clinical study has reported that postoperative administration of DEX, as patient-controlled analgesia (PCA) regimen, produced early antiemetic effects(8). Another research indicated that intravenous DEX could prevent the occurrence of PONV in adult patients after laparoscopic hysterectomy(9). While different results were observed in the similar articles(10; 11). Therefore, it is still disputed whether intraoperative use of DEX can ameliorate the occurrence of PONV in patients after general anesthesia.

As far as we know, no updated analysis of the data about the effect of DEX on PONV was performed during general anesthesia. Therefore, in order to obtain the most recent proof, we thoroughly evaluated the effect of intraoperative use of DEX on PONV in adult patients experiencing general anesthesia according to the results from the 18 randomized controlled trials (RCTs) in our meta-analysis. We hope these consequences will provide suggestions for anesthesiologists and surgeons to make better prevention plans in the future.

METHODS

Patient and public involvement

No patient involved.

Registration

This meta-analysis was conducted by following the criteria as outlined in the PRISMA guidelines(12) (Supplementary document 1). The meta-analysis was registered on PROSPERO (registry number: CRD 42022341548).

Search strategy

Two investigators independently searched for articles published in PubMed, the Web of Science, Embase, and the Cochrane Library without any restrictions. The basic search words included: ("Dex" OR "dexmedetomidine") AND ("PONV" OR "postoperative nausea and vomiting" OR "nausea" OR "vomiting" OR "nausea and vomiting" OR "postoperative emesis" OR "postoperative vomiting" OR "postoperative nausea"). The complete search strategy protocol was shown in Supplementary document 2. The literature search was updated on June 30, 2022.

Inclusion and exclusion criteria

The inclusion criteria: (1) RCTs; (2) Adult participants undergoing general anesthetic surgery; (3) The administration of DEX intraoperatively; (4) The outcomes in the included articles included nausea and vomiting; (5) DEX versus placebo or a single agent.

The exclusion criteria: (1) Reviews, abstracts, case reports or duplicates; (2) Drug/drugs (including DEX) versus combinational drugs; (3) Adult patients undergoing surgery under local or spinal-epidural anesthesia; (4) Full text not available.

Data extraction and analysis

All the information of the articles was collected independently by two researchers using standardized forms. Any problems were decided by a third author in order to discuss and reach an agreement. The corresponding data were collected: first author, type of surgery, publication year,

number of patients, administrations for patients, the incidence of PONV and bradycardia, the perioperative opioid consumption, the extubation time and the length of hospitalization. A standardized Excel file was used to save the extracted data.

Risk of bias assessment

In accordance with the Cochrane risk-of-bias tool, the risk of bias in the included articles were evaluated by two authors independently (Figure 1). According to the following criteria: bias from selection, performance, detection, attrition, reporting and other, we reviewed and scored each study as "high", "unclear", and "low".

Statistical analysis

We used the Review Manager 5.4 software to perform statistical analysis. For dichotomous data, we calculated odds ratios (ORs) with 95% confidence intervals (CIs). And we use standardized mean difference (SMD) and 95% CIs to analyze continuous outcomes. We used the *I*-square (I^2) test to evaluate the heterogeneity on included studies. A random effects model was chosen when $I^2 \geq 50\%$, otherwise a fixed effect model was selected. Funnel plots were used for quality assessment of bias. And the sensitivity analysis was performed for this meta-analysis involving at least 10 trials.

RESULTS

Study selection

The procedure of article screening, selection of articles, and the causes for exclusion were displayed in the flow diagram (Figure 2). The initial search included 2659 documents, and after taking out the duplicates and checking the abstracts and titles, 33 trials were considered potentially eligible. After carefully reading the full-text studies, 18 studies were eventually included.

Study characteristics

The main characteristics of the 18 articles were summed up in Table 1. 16 articles in the included articles investigated the efficacy of DEX compared to saline, 1 trial examined the efficacy of DEX compared to clonidine, and 1 trial compared to dexamethasone. The 18 articles in this meta-analysis were published from 2015 to 2021 with sample sizes varying from 19 to 334 participants and a total of 2018 patients.

Table 1: Characteristics of the included trials.

Author	Year	Number	Participants	Type of surgery	Administration	Nausea and Vomiting
Bakri	2015	43/43	Adults	Laparoscopic cholecystectomy	DEX/Dexa	9/12
Peng	2015	38/38	Adults	Craniotomy	DEX/Saline	16/28
Chen	2016	30/30	Adults	Laparoscopic resection of colorectal cancer	DEX/Saline	6/6
Bielka	2018	30/30	Adults	Laparoscopic cholecystectomy	DEX/Saline	2/8
Das	2018	50/50	Adults	Breast cancer surgery	DEX/Saline	2/8
Wu	2019	44/45	Adults	Laparoscopic radical prostatectomy	DEX/Saline	2/10
Bala	2019	30/30	Adults	Transsphenoidal Pituitary Surgery	DEX/Saline	2/6
Wu	2019	20/20	Adults	Cholangiojejunostomy or radical resection of tumor	DEX/Saline	1/3
Bakshi	2020	19/21	Adults	Robotic-assisted laparoscopic oncosurgeries	DEX/Saline	4/3
Chen	2020	39/38	Adults	Radical resection of gastric cancer	DEX/Saline	1/3
Asri	2020	21/21	Adults	Thoracic Surgery	DEX/Saline	0/5
Pi	2021	121/96	Adults	Thoracoscopic radical resection of lung cancer	DEX/Saline	0/1
Lu	2021	334/331	Adults	Abdominal Surgery	DEX/Saline	16/17
Bafna	2021	35/35	Adults	Endoscopic sinus surgery	DEX/Clonidine	4/1
Prashantha	2021	40/40	Adults	Laparoscopic cholecystectomy	DEX/Saline	5/14

Chen	2021	38/38	Adults	Thoracoscopic pulmonary segmentectomy	DEX/Saline	1/1
Yan	2021	50/50	Adults	Total Hip Arthroplasty	DEX/Saline	5/4
Chen	2021	40/40	Adults	Intestinal Surgery	DEX/Saline	1/6

Abbreviations: DEX, dexmedetomidine; Dexa, dexamethasone.

The association between DEX and PONV

All 18 trials involved the effect of DEX on the incidence of PONV. There was no heterogeneity between the articles (P<0.00001, I^2=26%, Fig. 3), so a fixed-effects model was be chosen. The consequences revealed that the occurrence of PONV in DEX group was lower than the control group (OR=0.49, 95% CI 0.36 to 0.67, Fig. 3), which indicated that DEX notably prevent the happening of PONV in adult patients after general anesthetic surgery.

The association between DEX and perioperative opioid consumption

8 studies assessed the effect of DEX on perioperative opioid consumption. Because of a high heterogeneity (P<0.00001, I^2=91%, Fig. 4), a random effect model was selected. The consequences of this meta-analysis indicated that the perioperative opioid consumption was lower in DEX group (SMD= −1.04, 95% CI −1.53 to −0.54, Fig. 4). Our results suggested that DEX decreased the perioperative opioid consumption significantly.

Other recovery outcomes

4 literatures including 200 patients involved the length of hospitalization. The study heterogeneity was high (P<0.00001, I^2=96%, Fig. 5), so a random effect model was selected. The consequence found that the length of hospitalization in DEX group was shorter (SMD= −2.29, 95% CI −4.31 to −0.28, Fig. 5). 4 trials including 292 subjects referred to the extubation time. A random effect model was chosen since the high heterogeneity (P=0.004, I^2=77%, Fig. 6). There was a shorter

time to extubation in DEX group (SMD= −0.75, 95% CI −1.26 to −0.25, Fig. 6). Therefore, meta-analysis of the 8 literatures indicated that DEX could accelerate the recovery of patients after anesthesia.

Side effects

8 trials described the incidence of bradycardia. A fixed effect model was selected considering the little heterogeneity (P=0.32, I^2=14%, Fig. 7). Compared to the control group, the number of participants developed bradycardia in the DEX group was higher (OR=1.60, 95% CI 1.13 to 2.27, Fig. 7). The consequences from this meta-analysis revealed that DEX may increase the occurrence of bradycardia.

Publication bias

Publication bias of literatures that included in our meta-analysis was assessed by funnel plots. No publication bias was found (Fig. 8). We removed each study one by one for sensitivity analysis and found that the results did not change (Supplementary document 3).

DISCUSSION

This present meta-analysis obviously showed that DEX is a potential effective agent for decreasing the incidence of PONV and promoting the recovery of adult patients undergoing general anesthetic surgery, but it might increase the incidence of bradycardia.

PONV is unsatisfactory experience and painful adverse event for patients, especially in the first day after surgery. Its incidence is approximately 30% and up to 80% without prevention(2; 13). Moreover, there may be some surgical types were associated with the high occurrence of PONV, especially in gynecological surgery, otolaryngology surgery and neurosurgery(4). There are many risk factors that can increase the incidence of PONV by 20% respectively in patients, including

anesthetic factors, surgical factors, female sex, non-smokers, and the medical history of motion sickness or/and PONV(14). These risk factors might also change with the premedication, anesthetic technique, postoperative management(15). Among the factors of anesthesia, general anesthesia is more likely to cause PONV compared with regional anesthesia(16). The pathophysiology process of PONV is very elusive. A study suggested that injuries from operation, anesthesia, visceral nerve stimulation, hypoxia, hypotension, and pain are the major irritants, which could trigger the vomiting response when they reach the cortical/thalamic, cerebellar and vestibular nuclei, and the chemoreceptor triggering band outside of the blood-brain barrier(17). Although there are multiple methods and drugs to prevent PONV in clinical practice, the efficacy of PONV prophylaxis remains unsatisfactory especially in high-risk patients(2).

Our meta-analysis found that DEX could notably decrease the happening of PONV in adult patients undergoing general anesthesia. DEX exerts the anxiolytic, sedative and analgesic effects by reducing the release of norepinephrine induced by α2 adrenergic receptors in the spinal cord and locus coeruleus. However, it could not result in excessive sedation or respiratory depression as the results of accumulation(18). Therefore, DEX was used as an appropriate short-acting sedative for patients under general anesthesia in perioperative period. Previous articles indicated that DEX reduced the occurrence of PONV, which were similar to our result. For instance, a study has reported that DEX administered could decrease the occurrence of PONV in patients experiencing intestinal surgery(19), another study discovered that intraoperative use of DEX could be a valid measure to prevent the PONV in patients after laparoscopic radical prostatectomy(20). But the mechanisms for the effect of DEX on PONV are still obscure. Previous articles reported DEX could decrease the occurrence of PONV by modulating 5-HT and dopamine release, suppressing the histamine-induced

expression of IL-6, and reducing sympathetic outflow and total catecholamine release(21; 22). So, one of the key mechanisms about the effect of DEX on PONV might be attributable to the regulation of neurotransmitters. It is well known to us that the amount of intraoperative opioid use directly influenced the frequency and degree of PONV(16). In our meta-analysis, we revealed that DEX could decrease the perioperative opioid consumption, which might explain the antiemetic effect of DEX.

DEX also can prevent perioperative stress response by regulating heart rate and blood pressure, which are the most common adverse events especially in patient with atrioventricular block or hypovolemia(23). In this meta-analysis, the incidence of perioperative bradycardia was increased in patients with DEX. Similar consequence was found in a meta-analysis of 3638 patients from 9 high-quality RCTs(24). Bradycardia may be due to presynaptic a-2 receptor stimulation by DEX, which results in decreasing norepinephrine release.

Nausea and vomiting are two distinguishing phenomena. A study has shown that DEX reduced early postoperative nausea but not vomiting in adult patients undergoing general anesthesia(25). However, nausea and vomiting usually coexist with patients, and the occurrence of postoperative vomiting (POV) or postoperative nausea (PON) clearly consistent with PONV, so a number of studies do not attempt to distinguish between these two variables(26-28). Therefore, we just explored the influence of DEX on PONV in this meta-analysis.

In fact, there have been two previous meta-analyses also reported that DEX could low the occurrence of PONV compared to the placebo group(15; 29). However, PONV has been rapidly developed and there are the increasing numbers of studies about it in the last few years. Therefore, an up-date meta-analysis is necessary to assess whether the consequences of newly updated or

published studies can alter the previous meta-analysis. Overall, DEX did decrease the occurrence of PONV and accelerated the recovery of adult patients after general anesthesia in this meta-analysis.

LIMITATIONS

There were several limitations to this meta-analysis. Firstly, the included articles did not give consistent doses of DEX, the influence of diverse doses of DEX on PONV in adult patients after general anesthesia needs to be further explored. Secondly, the severity degree of PONV was not quantified using a formal scale, so further study is required to explore the effect of DEX on different severity degree of PONV.

CONCLUSION

In a word, DEX can decrease the occurrence of PONV in adult patients who experiencing general anesthesia, and accelerate postoperative recovery. Thus, DEX can be used as an adjuvant drug for general anesthesia to prevent the development of PONV in clinical practice. However, it is essential to be vigilant the occurrence of bradycardia during surgery. The results of this meta-analysis may offer a new testimony to expand the clinical significance of DEX apart from its conventional usage for sedation and analgesia.

Author Contributions WZ and JL were involved in the conception and design of this meta-analysis. NW and ZW conducted the data extraction. HZ and ML contributed to statistical analysis. WZ analyzed the data and drafted the manuscript. JH, DY and MZ offered major comments and revised the manuscript. All authors have read and approved the manuscript.

Funding The work was supported by the Key Research and Development Program of Hebei Province (Grant No. 19277714D). The funding bodies had no role in the design of the study, and will have no role in the data collection, analysis, interpretation of data, and writing of the manuscript.

Ethics approval statement This study was a meta-analysis of previously published literatures, ethical approval was not necessary.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information.

ORCID Jianli Li: https://orcid.org/0000-0001-6867-7825

REFERENCES

1. Gao W, Zhang L, Han X, et al. 2022. Transcutaneous Electrical Acupoint Stimulation Decreases the Incidence of Postoperative Nausea and Vomiting After Laparoscopic Non-gastrointestinal Surgery: A Multi-Center Randomized Controlled Trial. *Front Med (Lausanne)* 9:766244. https://doi.org/10.3389/fmed.2022.766244
2. Gan TJ, Belani KG, Bergese S, et al. 2020. Fourth Consensus Guidelines for the Management of Postoperative Nausea and Vomiting. *Anesth Analg* 131:411-48. https://doi.org/10.1213/ane.0000000000004833
3. Ishikawa E, Iwamoto R, Hojo T, et al. 2022. Cross-sectional Study of PONV Risk Factors for Oral Surgery After Intubated General Anesthesia With Total Intravenous Anesthesia. *Anesth Prog* 69:18-23. https://doi.org/10.2344/anpr-68-03-12
4. Elvir-Lazo OL, White PF, Yumul R, et al. 2020. Management strategies for the treatment and prevention of postoperative/postdischarge nausea and vomiting: an updated review. *F1000Res* 9. https://doi.org/10.12688/f1000research.21832.1
5. Zhao Y, He J, Yu N, et al. 2020. Mechanisms of Dexmedetomidine in Neuropathic Pain. *Front Neurosci* 14:330. https://doi.org/10.3389/fnins.2020.00330
6. Adler AC, Daszkowski A, Tan JC, et al. 2021. The Association of Dexmedetomidine on Perioperative Opioid Consumption in Children Undergoing Adenotonsillectomy With and Without Obstructive Sleep Apnea. *Anesth Analg* 133:1260-8. https://doi.org/10.1213/ane.0000000000005410
7. Liu Y, Zhao G, Zang X, et al. 2021. Effect of dexmedetomidine on opioid consumption and pain control after laparoscopic cholecystectomy: a meta-analysis of randomized

controlled trials. *Wideochir Inne Tech Maloinwazyjne* 16:491-500. https://doi.org/10.5114/wiitm.2021.104197

8. Li HJ, Liu S, Geng ZY, et al. 2020. Adding dexmedetomidine to morphine-based analgesia reduces early postoperative nausea in patients undergoing gynecological laparoscopic surgery: a randomized controlled trial. *BMC Anesthesiol* 20:11. https://doi.org/10.1186/s12871-019-0928-y

9. Lee J, Hwang HW, Jeong JY, et al. 2022. The Effect of Low-Dose Dexmedetomidine on Pain and Inflammation in Patients Undergoing Laparoscopic Hysterectomy. *J Clin Med* 11. https://doi.org/10.3390/jcm11102802

10. Xie C, Zhang C, Sun H, et al. 2021. Effects of Dexmedetomidine on Postoperative Nausea and Vomiting in Adult Patients Undergoing Ambulatory Thyroidectomy: A Randomized Clinical Trial. *Front Med (Lausanne)* 8:781689. https://doi.org/10.3389/fmed.2021.781689

11. Yan C, Ti-jun D. 2021. Effects of Intraoperative Dexmedetomidine Infusion on Postoperative Delirium in Elderly Patients Undergoing Total Hip Arthroplasty. *International Surgery* 105:328-35. https://doi.org/10.9738/intsurg-d-17-00029.1

12. Page MJ, McKenzie JE, Bossuyt PM, et al. 2021. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *Syst Rev* 10:89. https://doi.org/10.1186/s13643-021-01626-4

13. Gloor Y, Czarnetzki C, Curtin F, et al. 2021. Genetic Susceptibility Toward Nausea and Vomiting in Surgical Patients. *Front Genet* 12:816908. https://doi.org/10.3389/fgene.2021.816908

14. Lu H, Zheng C, Liang B, et al. 2021. Mechanism and risk factors of nausea and vomiting after TACE: a retrospective analysis. *BMC Cancer* 21:513. https://doi.org/10.1186/s12885-021-08253-1

15. Liang X, Zhou M, Feng JJ, et al. 2015. Efficacy of dexmedetomidine on postoperative nausea and vomiting: a meta-analysis of randomized controlled trials. *Int J Clin Exp Med* 8:8450-71.

16. Poon YY, Ke TY, Hung KC, et al. 2021. Risk Factors of Postoperative Vomiting in the Eye of "Real-World Evidence"-Modifiable and Clinical Setting-Dependent Risk Factors in Surgical Trauma Patients. *J Pers Med* 11. https://doi.org/10.3390/jpm11050386

17. Konno D, Sugino S, Shibata TF, et al. 2022. Antiemetic effects of baclofen in a shrew model of postoperative nausea and vomiting: Whole-transcriptome analysis in the nucleus of the solitary tract. *CNS Neurosci Ther* 28:922-31. https://doi.org/10.1111/cns.13823

18. Zhang J, Yu Y, Miao S, et al. 2019. Effects of peri-operative intravenous administration of dexmedetomidine on emergence agitation after general anesthesia in adults: a meta-analysis of randomized controlled trials. *Drug Des Devel Ther* 13:2853-64. https://doi.org/10.2147/DDDT.S207016

19. Chen R, Kang Z, Wang Y, et al. 2021. The Anti-inflammatory Effect of Dexmedetomidine Administration on Patients Undergoing Intestinal Surgery: A Randomized Study. *Drugs R D* 21:445-53. https://doi.org/10.1007/s40268-021-00368-x

20. Wu S, Yao H, Cheng N, et al. 2019. Determining whether dexmedetomidine provides

a reno-protective effect in patients receiving laparoscopic radical prostatectomy: a pilot study. *Int Urol Nephrol* 51:1553-61. https://doi.org/10.1007/s11255-019-02171-9

21. Xu S, Hu S, Ju X, et al. 2021. Effects of intravenous lidocaine, dexmedetomidine, and their combination on IL-1, IL-6 and TNF-α in patients undergoing laparoscopic hysterectomy: a prospective, randomized controlled trial. *BMC Anesthesiol* 21:3. https://doi.org/10.1186/s12871-020-01219-z

22. Zhang W, Wang R, Li B, et al. 2022. The Effect of Dexmedetomidine on Postoperative Nausea and Vomiting in Patients Undergoing Thoracic Surgery-A Meta-Analysis of a Randomized Controlled Trial. *Front Surg* 9:863249. https://doi.org/10.3389/fsurg.2022.863249

23. Misra S, Behera BK, Mitra JK, et al. 2021. Effect of preoperative dexmedetomidine nebulization on the hemodynamic response to laryngoscopy and intubation: a randomized control trial. *Korean J Anesthesiol* 74:150-7. https://doi.org/10.4097/kja.20153

24. Lin C, Tu H, Jie Z, et al. 2021. Effect of Dexmedetomidine on Delirium in Elderly Surgical Patients: A Meta-analysis of Randomized Controlled Trials. *Ann Pharmacother* 55:624-36. https://doi.org/10.1177/1060028020951954

25. Geng ZY, Liu YF, Wang SS, et al. 2016. Intra-operative dexmedetomidine reduces early postoperative nausea but not vomiting in adult patients after gynaecological laparoscopic surgery: A randomised controlled trial. *Eur J Anaesthesiol* 33:761-6. https://doi.org/10.1097/eja.0000000000000491

26. Li B, Zhao Y, Liu X, et al. 2022. The Optimal Dose of Intraoperative Dexmedetomidine

for Antiemetic Effects of Post-operative Nausea and Vomiting in Patients Undergoing Elective Thoracic Surgery: A Retrospective Cohort Study. *Front Med (Lausanne)* 9:891096. https://doi.org/10.3389/fmed.2022.891096

27. Khan MA, Gupta A, Gupta N, et al. 2021. Efficacy of Palonosetron and Dexamethasone for Prevention of Post-operative Nausea and Vomiting in Female Patients Undergoing Laparoscopic Cholecystectomy: A Prospective Randomised Double-Blind Trial. *Turk J Anaesthesiol Reanim* 49:400-6. https://doi.org/10.5152/tjar.2021.191

28. Serpico VJ, Mone MC, Zhang C, et al. 2022. Preoperative multimodal protocol reduced postoperative nausea and vomiting in patients undergoing mastectomy with reconstruction. *J Plast Reconstr Aesthet Surg* 75:528-35. https://doi.org/10.1016/j.bjps.2021.09.059

29. Jin S, Liang DD, Chen C, et al. 2017. Dexmedetomidine prevent postoperative nausea and vomiting on patients during general anesthesia: A PRISMA-compliant meta analysis of randomized controlled trials. *Medicine (Baltimore)* 96:e5770. https://doi.org/10.1097/MD.0000000000005770

Figure legends

Figure 1: The risk of bias of included studies.

Figure 2: Flow diagram.

Figure 3: The total effect of dexmedetomidine on PONV.

Figure 4: Perioperative opioid consumption in dexmedetomidine and control group.

1 **Figure 5:** The effect of dexmedetomidine on the length of hospitalization.

2 **Figure 6:** The effect of dexmedetomidine on the extubation time.

3 **Figure 7:** Incidence of bradycardia in dexmedetomidine and control group.

4 **Figure 8:** The funnel plot.

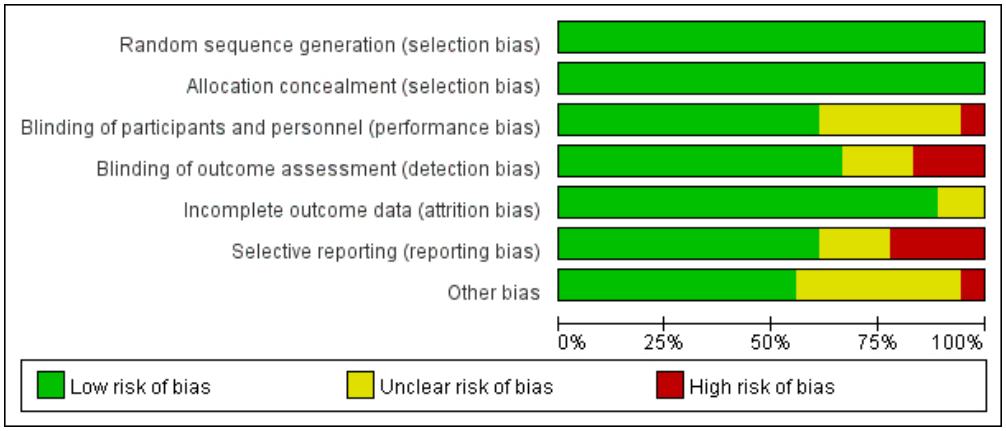

Figure 1: The risk of bias of included studies.

213x90mm (72 x 72 DPI)

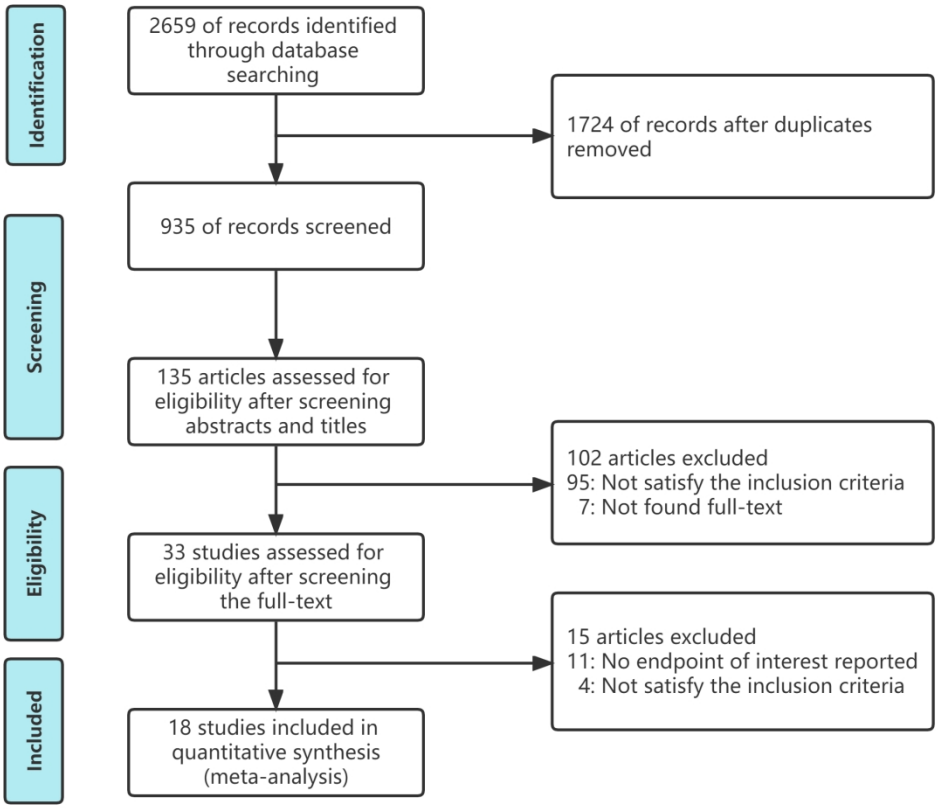

Figure 2: Flow diagram

735x638mm (72 x 72 DPI)

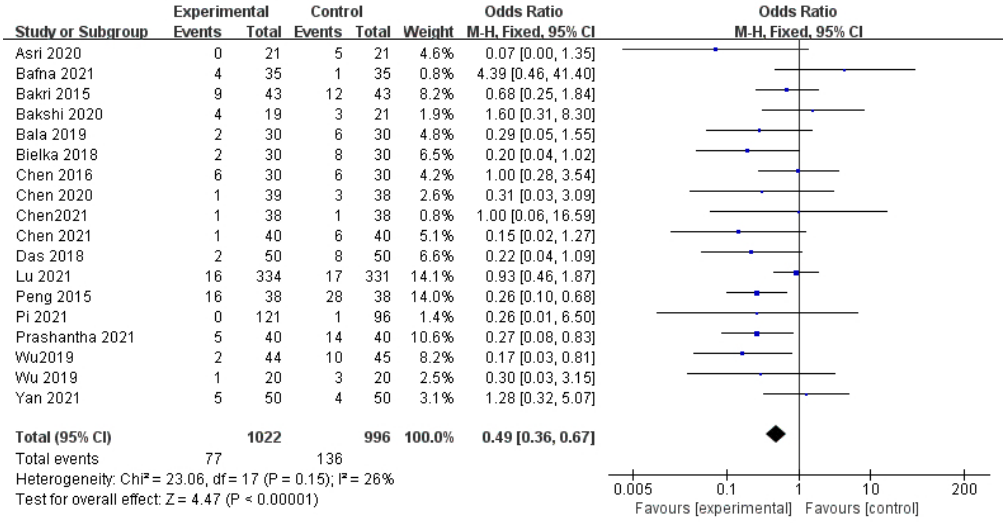

Figure 3: The total effect of dexmedetomidine on postoperative nausea and vomiting.

277x146mm (72 x 72 DPI)

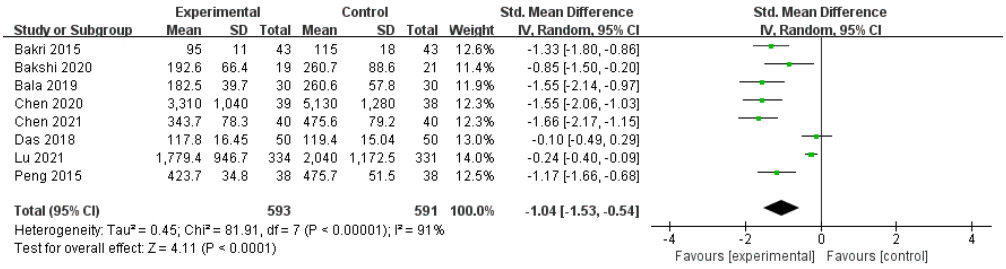

Figure 4: Perioperative opioid consumption in dexmedetomidine and control group.

311x84mm (72 x 72 DPI)

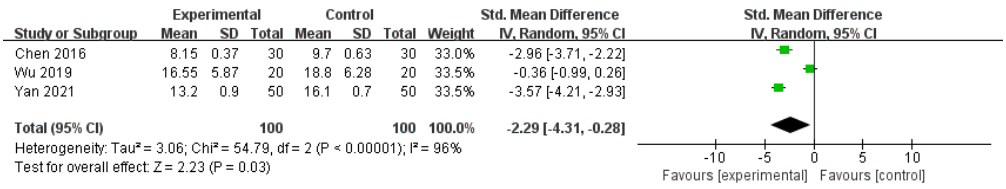

Figure 5: The effect of dexmedetomidine on the length of hospitalization.

300x56mm (72 x 72 DPI)

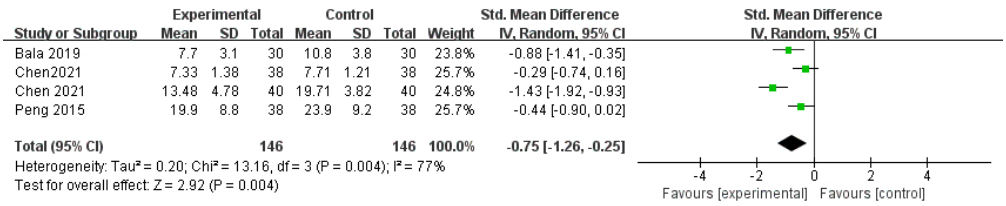

Figure 6: The effect of dexmedetomidine on the extubation time.

300x62mm (72 x 72 DPI)

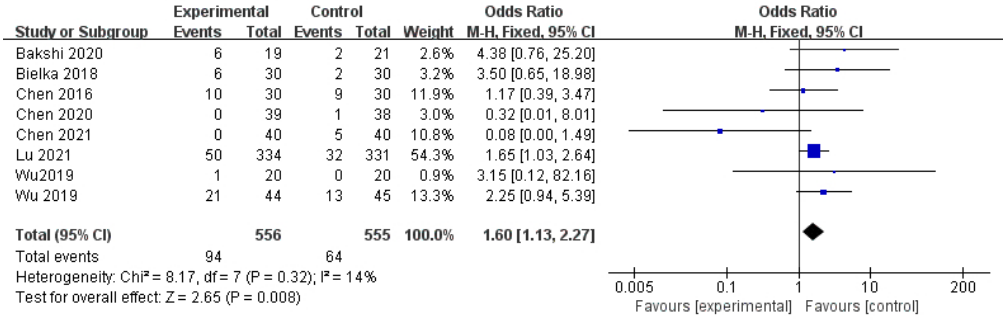

Figure 7: Incidence of bradycardia in dexmedetomidine and control group.

277x90mm (72 x 72 DPI)

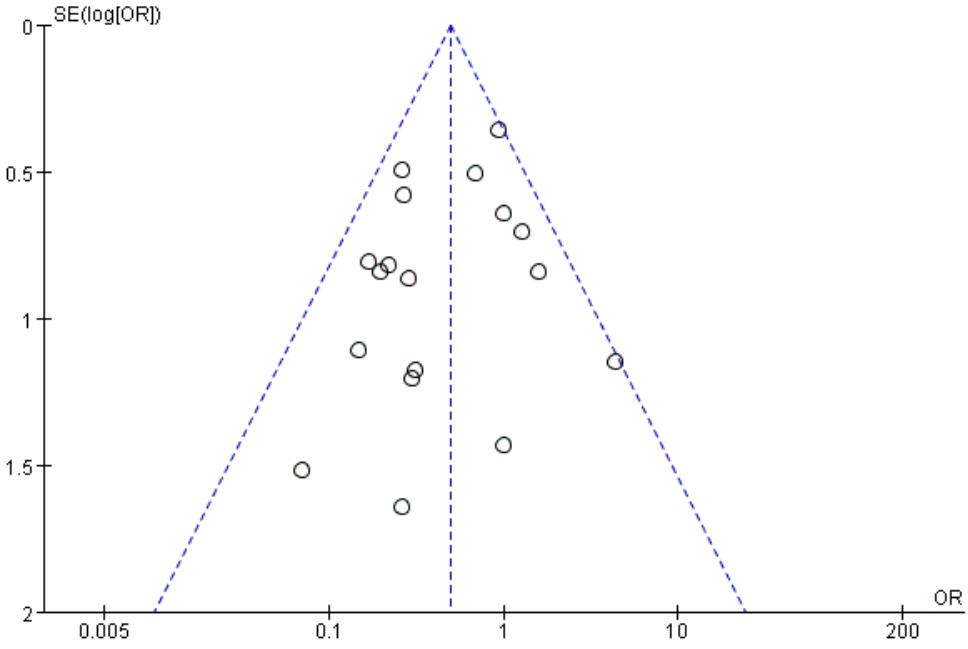

Figure 8: The funnel plot

211x141mm (72 x 72 DPI)

Supplementary document 1

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	2-3
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	3
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	3
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	3,Supplementary document 2
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	3,Supplementary document 2
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	3
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	3-4
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (eg. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	3-4
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	4
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	4
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	6
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Table 1
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data	4

Section and Topic	Item #	Checklist item	Location where item is reported
		conversions.	
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	4
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	4
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	4
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	4
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	4
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	4
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	4
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	4
Study characteristics	17	Cite each included study and present its characteristics.	4
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	6, Figure 8
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	5
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	5-6
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	5-6
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	5-6
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Supplementary document 3
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	6
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	-
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	6
	23b	Discuss any limitations of the evidence included in the review.	8

Section and Topic	Item #	Checklist item	Location where item is reported
	23c	Discuss any limitations of the review processes used.	8
	23d	Discuss implications of the results for practice, policy, and future research.	8
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	-
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	-
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	-
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Title page
Competing interests	26	Declare any competing interests of review authors.	Title page
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Title page

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: http://www.prisma-statement.org/

Supplementary document 2: The search strategy

Pubmed

Search: (DEX[Title/Abstract]) OR (("Dexmedetomidine"[Mesh]) OR (Dexmedetomidine[Title/Abstract])) AND (("Postoperative Nausea and Vomiting"[Mesh]) OR ((((((((((PONV[Title/Abstract]) OR (Nausea[Title/Abstract] AND Vomiting, Postoperative[Title/Abstract])) OR (Vomiting, Postoperative[Title/Abstract])) OR (Postoperative Emesis[Title/Abstract])) OR (Postoperative Vomiting[Title/Abstract])) OR (Emesis, Postoperative[Title/Abstract])) OR (Emeses, Postoperative[Title/Abstract])) OR (Postoperative Emeses[Title/Abstract])) OR (Postoperative Nausea[Title/Abstract])) OR (Nausea, Postoperative[Title/Abstract])))

Embase

- #1 Dexmedetomidine
- #2 'mpv-1440':ab,ti OR 'mpv 1440':ab,ti OR 'mpv1440':ab,ti OR 'precedex':ab,ti OR 'dexmedetomidine hydrochloride':ab,ti OR 'hydrochloride, dexmedetomidine':ab,ti
- #3 #1 OR #2
- #4 postoperative AND nausea AND vomiting
- #5 'ponv':ab,ti OR 'nausea and vomiting, postoperative':ab,ti OR 'vomiting, postoperative':ab,ti OR 'postoperative emesis':ab,ti OR 'postoperative vomiting':ab,ti OR 'emesis, postoperative':ab,ti OR 'emeses, postoperative':ab,ti OR 'postoperative emeses':ab,ti OR 'postoperative nausea':ab,ti OR 'nausea, postoperative':ab,ti
- #6 #4 OR #5
- #7 #3 AND #6

Cochrane

- #1 Dexmedetomidine
- #2 (MPV-1440):ti,ab,kw OR (MPV 1440):ti,ab,kw OR (MPV1440):ti,ab,kw OR (Precedex):ti,ab,kw OR (Dexmedetomidine Hydrochloride):ti,ab,kw OR (Hydrochloride, Dexmedetomidine):ti,ab,kw
- #3 #1 OR #2
- #4 Postoperative nausea and vomiting
- #5 (PONV):ti,ab,kw OR (Nausea and Vomiting, Postoperative):ti,ab,kw OR (Vomiting, Postoperative):ti,ab,kw OR (Postoperative Emesis):ti,ab,kw OR (Postoperative Vomiting):ti,ab,kw OR (Emesis, Postoperative):ti,ab,kw OR (Emeses, Postoperative):ti,ab,kw OR (Postoperative Emeses):ti,ab,kw OR (Postoperative Nausea):ti,ab,kw OR (Nausea, Postoperative):ti,ab,kw
- #6 #4 OR #5
- #7 #3 AND #6

Supplementary document 3: The sensitivity analysis of effect of dexmedetomidine on PONV

Study	Odds Ratio	95% CI
Omitting Asri 2020	0.51	[0.37, 0.70]
Omitting Bafna 2021	0.46	[0.33, 0.63]
Omitting Bakri 2015	0.47	[0.34, 0.66]
Omitting Bakshi 2020	0.47	[0.34, 0.64]
Omitting Bala 2019	0.50	[0.36, 0.69]
Omitting Bielka 2018	0.51	[0.37, 0.70]
Omitting Chen 2016	0.47	[0.34, 0.65]
Omitting Chen 2020	0.49	[0.36, 0.68]
Omitting Chen2021	0.49	[0.35, 0.67]
Omitting Chen 2021	0.51	[0.37, 0.70]
Omitting Das 2018	0.51	[0.37, 0.70]
Omitting Lu 2021	0.42	[0.29, 0.60]
Omitting Peng 2015	0.53	[0.38, 0.73]
Omitting Pi 2021	0.49	[0.36, 0.68]
Omitting Prashantha 2021	0.52	[0.37, 0.72]
Omitting Wu2019	0.52	[0.38, 0.71]
Omitting Wu 2019	0.49	[0.36, 0.68]
Omitting Yan 2021	0.46	[0.34, 0.64]
Random effects model	**0.48**	**[0.32, 0.73]**

BMJ Open

The effect of dexmedetomidine on postoperative nausea and vomiting in patients under general anesthesia: an updated meta-analysis of randomized controlled trials

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2022-067102.R1
Article Type:	Original research
Date Submitted by the Author:	27-Dec-2022
Complete List of Authors:	Zhao, Weihong; Hebei General Hospital, Department of Anesthesiology Li, Jianli; Hebei General Hospital, Department of Anesthesiology Wang, Na; Hebei General Hospital, Department of Rheumatology Wang, Zhibin; The Fifth People's Hospital of Hengshui, Department of Anesthesiology Zhang, Meng; Hebei General Hospital, Department of Anesthesiology Zhang, Huanhuan; Hebei General Hospital, Department of Anesthesiology Liu, Meinv; Hebei General Hospital, Department of Anesthesiology He, Jinhua; Hebei General Hospital, Department of Anesthesiology Yu, Dongdong; Hebei General Hospital, Department of Anesthesiology
Primary Subject Heading:	Anaesthesia
Secondary Subject Heading:	Anaesthesia, Surgery
Keywords:	ANAESTHETICS, Adult anaesthesia < ANAESTHETICS, Adult surgery < SURGERY, Adverse events < THERAPEUTICS

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

The effect of dexmedetomidine on postoperative nausea and vomiting in patients under general anesthesia: an updated meta-analysis of randomized controlled trials

Weihong ZHAO, MD[1], Jianli LI, PhD[1], Na WANG, MD[2], Zhibin WANG, MD[3], Meng ZHANG, MD [1], Huanhuan ZHANG, MD [1], Meinv LIU, MD [1], Jinhua HE, MD [1], Dongdong YU, MD [1]

[1] Department of Anesthesiology, Hebei General Hospital, Shijiazhuang 050000, Hebei Province, China

[2] Department of Rheumatology, Hebei General Hospital, Shijiazhuang 050000, Hebei Province, China

[3] Department of Anesthesiology, The Fifth People's Hospital of Hengshui, Hengshui, 053000, Hebei Province, China.

Corresponding author and correspondence to:

Jianli Li, PhD.

Department of Anesthesiology, Hebei General Hospital,

Shijiazhuang, China

E-mail: hblijianli@163.com

Keywords: Dexmedetomidine, Perioperative period, Postoperative nausea and vomiting, Side effects, Meta-analysis

Word Counts

Main text: 2907 words (Excluding title page, references, figures and tables)

ABSTRACT

Objectives: To explore the effect of dexmedetomidine on postoperative nausea and vomiting in adult patients after general anesthesia.

Design: Systematic review and meta-analysis.

Eligibility criteria for selecting studies: Randomized controlled trials comparing the efficacy of dexmedetomidine with placebo or a single drug on postoperative nausea and vomiting in adult patients after general anesthesia.

Data Sources: We searched the PubMed, the Web of Science, the Cochrane Library and Embase (January 1, 2000, to June 30, 2022) to select the relevant randomized controlled trials (RCTs).

Data analysis: All the relevant data were analyzed by using RevManV.5.4. Heterogeneity was tested for each outcome, and random effect or fixed effect models was selected according to the level of heterogeneity. The primary outcome was the incidence of postoperative nausea and vomiting. The second outcomes were the incidence of bradycardia, perioperative opioid consumption, extubation time and the length of hospitalization.

Results: In total of 18 trials involving 2018 patients were included in this meta-analysis. Notably, 15 updated studies were not involved in the previous meta-analysis. The incidence of postoperative nausea and vomiting in dexmedetomidine group was lower than that in control group (odds ratio [OR] =0.49, 95% CI 0.36 to 0.67) and the perioperative opioid consumption in dexmedetomidine group was also decreased significantly (standard mean difference [SMD] = −1.04, 95% CI −1.53 to −0.54). Moreover, the length of hospitalization (SMD= −2.29, 95% CI −4.31 to −0.28) and the extubation time (SMD= −0.75, 95% CI −1.26 to −0.25) in dexmedetomidine group were shorter. Whereas, more number of patients receiving dexmedetomidine occurred bradycardia (OR=1.60, 95%

CI 1.13 to 2.27).

Conclusions: Dexmedetomidine could decrease the occurrence of postoperative nausea and vomiting in adult patients under general anesthesia and promote the recovery after surgery. However, dexmedetomidine might increase the occurrence of bradycardia.

PROSPERO registration number: CRD 42022341548

Strengths and limitations of this study

- An up-to-date assessment of the effectiveness of dexmedetomidine on postoperative nausea and vomiting.
- We excluded studies that DEX compared with opioids agents in our meta-analysis to eliminate the effect of opioids on postoperative nausea and vomiting.
- The main limitation of this review was that varied quality and heterogeneity of included studies might affect the certainty of meta-analysis.

INTRODUCTION

Postoperative nausea and vomiting (PONV), as a familiar negative events after operation, is known as nausea, vomiting, or retching within one day after operation, which may be due to the effect of anesthetics on the emetic control center in the medulla oblongata[1]. The incidence of PONV is about 30% and even rising to 60%-80% in high-risk populations. PONV, an extreme poor medical experience for patients undergoing general anesthetic surgery, leads to many adverse influences including stomach discomfort, dehydration, water-electrolyte disorders, wound dehiscence, esophageal injury, reflux and aspiration, which extend the time of hospitalization and increase the medical costs[2]. Fortunately, prophylactic antiemetic agents could decrease the happening of PONV. However, these drugs produce some side effects including headache,

restlessness, dry mouth, hypotension and cardiovascular complications, which limit their use in some cases[3]. Therefore, exploring suitable drugs and methods to prevent and treat PONV is necessary.

Dexmedetomidine (DEX), as a new adrenal α2 receptor agonist with high selectivity, has sedation, hypnosis and analgesia effects without respiratory depression, which is widely used in perioperative period. These characteristics have enabled DEX to be a multifunctional drug in the presentments of numerous negative events during anesthesia. For the last few years, the effect of DEX on PONV attracted increasing attention from anesthesiologists. One clinical study reported that postoperative administration of DEX, as patient-controlled analgesia (PCA) regimen, produced early antiemetic effects[4]. Another research indicated that intravenous DEX could prevent the occurrence of PONV in adult patients after laparoscopic hysterectomy[5]. While different results were observed in the similar articles[6; 7]. Therefore, it is still disputed whether intraoperative use of DEX can ameliorate the occurrence of PONV in patients after general anesthesia.

As far as we know, no updated analysis of the data about the effect of DEX on PONV was performed during general anesthesia. Therefore, in order to obtain the most recent proof, we thoroughly evaluated the effect of intraoperative use of DEX on PONV in adult patients experiencing general anesthesia according to the results from the 18 randomized controlled trials (RCTs) in our meta-analysis.

METHODS

Patient and public involvement

No patient involved.

Registration

This meta-analysis was prepared by following the criteria as outlined in the PRISMA guidelines[8] (Supplementary document 1). The meta-analysis was registered on PROSPERO (registry number: CRD 42022341548).

Search strategy

Two investigators independently searched for articles published in PubMed, the Web of Science, Embase, and the Cochrane Library. The complete search strategy protocol was shown in Supplementary document 2. In order to ensure the contemporary practice, the literature was searched from January 1, 2000 to June 30, 2022.

Inclusion and exclusion criteria

The inclusion criteria were in accordance with PICO[9]:

Patients: Adult participants undergoing general anesthetic surgery;

Intervention: received a single or continuously-administered intravenous dose of intraoperative DEX;

Comparison: received a single or continuously-administered intravenous injection of placebo or comparator;

Outcomes: the incidence of PONV and bradycardia, the perioperative opioid consumption, the extubation time and the length of hospitalization.

The reviews, abstracts, case reports or duplicates were excluded. Additionally, some RCTs meeting the following criteria were also excluded (1) Drug/drugs (including DEX) versus combinational drugs; (2) DEX compared with opioids agents; (3) Adult patients undergoing surgery under local or spinal-epidural anesthesia; (4) Full text not available.

Data extraction and analysis

All information of the articles was collected independently by two researchers using standardized forms. Any problems were decided by a third author in order to discuss and reach an agreement. The corresponding data were collected: first author, type of surgery, publication year, number of patients, administrations for patients, the incidence of PONV and bradycardia, the perioperative opioid consumption, the extubation time and the length of hospitalization. A standardized Excel file was used to save the extracted data. And all the data were pooled together. Studies were excluded when the primary outcome was not clearly reported with quantifiable data or it was not possible to extract and calculate the appropriate data from the published results.

Risk of bias assessment

In accordance with the Cochrane risk-of-bias tool[10], the risk of bias in the included articles were evaluated by two authors independently (Figure 1). According to the following criteria: bias from selection, performance, detection, attrition, reporting and other, we reviewed and scored each study as "high", "unclear", and "low".

Statistical analysis

We used the Review Manager 5.4 software to perform statistical analysis. For dichotomous data, we calculated odds ratios (ORs) with 95% confidence intervals (CIs). And when the outcome was expressed using varied approaches, we used standardized mean difference (SMD) and 95% CIs to analyze the continuous data. We used the *I*-square (I^2) test to evaluate the heterogeneity of included studies. A random effects model was chosen when $I^2 \geq 50\%$, otherwise a fixed effect model was selected. Funnel plots were used for quality assessment of bias. And the sensitivity analysis was performed by removing these studies and observing the consistency for this meta-analysis involving at least 10 trials.

RESULTS

Study selection

The procedure of article screening, selection of articles, and the causes for exclusion were displayed in the flow diagram (Figure 2). The initial search included 2659 documents, and after taking out the duplicates and checking the abstracts and titles, 33 trials were considered potentially eligible. After carefully reading the full-text studies, 18 studies were eventually included, of which 15 studies were new articles appearing after the previously published meta-analyses.

Study characteristics

The main characteristics of the 18 articles were summed up in Table 1. 16 articles in the included studies investigated the efficacy of DEX compared to saline, 2 trials examined the efficacy of DEX compared to clonidine and dexamethasone, respectively. The 18 articles including a total of 2018 patients in this meta-analysis were published from 2015 to 2021 with sample sizes varying from 19 to 334 participants.

Table 1: Characteristics of the included trials.

Author	Year	Age (yr)		Gender male/female	Sample size	Type of surgery	Administration mode	Comparisons	Numbers of Nausea and/or vomiting DEX/Control	Scale used for assessing PONV
		DEX	Control							
Bakri [11]	2015	31.1 ± 2.4	32.3 ± 2.1	15/71	43/43	Laparoscopic cholecystectomy	1μg/kg DEX IV	8 mg Dexa IV	9/12	A visual analogue scale (VAS) of 0–100 mm, 0 score meant no nausea, while 100 score meant the worst imaginable nausea
Peng [12]	2015	42.3±10.8	43.5 ±11.1	33/43	38/38	Craniotomy	Continuous infusion of DEX 0.5μg/kg/h IV	Equal volume of saline	16/28	0, absent; 1, nausea not requiring treatment; 2, nausea requiring treatment; and 3, vomiting.
Chen [13]	2016	56.67±2.705	60.17±1.644	29/31	30/30	Laparoscopic resection of colorectal cancer	Loading dose 1μg /kg DEX, continuous infusion of 0.3μg /kg/h IV	Equal volume of saline	6/6	Verbal rating scale scores. 0: no, 1–3: mild, 4–6: moderate, 7–10: severe
Bielka [14]	2018	55 (49–61)	53 (49–66)	7/53	30/30	Laparoscopic cholecystectomy	Continuous infusion of DEX 0.5μg/kg/h IV	Equal volume of saline	2/8	NR
Das[15]	2018	50.74±9.05	47.92±8.08	NR	50/50	Breast cancer surgery	Continuous infusion of DEX 0.6μg/kg/h IV	Equal volume of saline	2/8	NR
Wu[16]	2019	67	69	NR	NR	Laparoscopic radical prostatectomy	Loading dose 1μg /kg DEX, continuous infusion of 0.5μg /kg/h IV	Equal volume of saline	2/10	NR
Bala [17]	2019	37.2 ± 11.0	41 ± 13.4	33/27	30/30	Transsphenoidal Pituitary Surgery	Loading dose 1μg /kg DEX, continuous infusion of 0.5μg /kg/h IV	Equal volume of saline	2/6	NR
Wu[18]	2019	55.00±5.07	54.85±4.96	25/15	20/20	Cholangiojejunostomy or resection of tumor	Loading dose 0.5μg /kg DEX, continuous infusion of 0.5μg /kg/h IV	Equal volume of saline	1/3	NR
Bakshi [19]	2020	51.8 ±12	47.2 ±13	14/26	19/21	Robotic-assisted laparoscopic oncosurgeries	Loading dose 1μg /kg DEX, continuous infusion of 0.2μg /kg/h IV	Equal volume of saline	4/3	NR
Chen [20]	2020	42.68±7.59	43.35±6.82	41/36	39/38	Radical resection of gastric cancer	Loading dose 0.6μg /kg DEX, continuous infusion of 0.4μg /kg/h IV	Equal volume of saline	1/3	NR
Asri [21]	2020	51 ± 12	46 ± 16	32/10	21/21	Thoracic Surgery	Continuous infusion of DEX 0.3μg/kg/h IV	Equal volume of saline	0/5	NR

Table 1: Characteristics of the included trials.

Author	Year	Age (yr)		Gender male/female	Number	Type of surgery	Administration mode	Comparisons	Numbers of PONV DEX/Control DEX/Control	Scale used for assessing PONV
		DEX	Control							
Pi[22]	2021	42.15±1.34	41.88±1.56	162/55	121/96	Thoracoscopic radical resection of lung cancer	Loading dose 0.4μg /kg DEX, continuous infusion of 0.2μg /kg/h IV	Equal volume of saline	0/1	NR
Lu[23]	2021	70.1 ±5.8	70.4 ±6.5	445/230	344/331	Abdominal Surgery	Loading dose 0.5μg /kg DEX, continuous infusion of 0.2μg /kg/h IV	Equal volume of saline	16/17	10-point rating scale 0: no PONV and 10: maximal PONV
Bafna[24]	2021	27.23+7.75	27.49+8.68	38/32	35/35	Endoscopic sinus surgery	Loading dose 1μg /kg DEX, continuous infusion of 1μg /kg/h IV	Loading dose 2μg /kg clonidine, continuous infusion of 1μg /kg/h IV	4/1	NR
Prashantha [25]	2021	37.73 ± 7.24	35.63 ± 12.61	19/61	40/40	Laparoscopic cholecystectomy	DEX IV	Saline IV	5/14	NR
Chen[26]	2021	55.93 ± 11.14	55.64 ± 10.81	41/35	38/38	Thoracoscopic pulmonary segmentectomy	0.6μg/kg DEX infusion from 10 min before induction	Equal volume of saline	1/1	NR
Yan[7]	2021	73.2 ± 5.8	72.7 ± 4.3	42/58	50/50	Total Hip Arthroplasty	Continuous infusion of DEX 0.3μg/kg/h IV	Equal volume of saline	5/4	NR
Chen[27]	2021	50.76 ± 8.32	51.07 ± 9.43	44/36	40/40	Intestinal Surgery	Loading dose 1μg /kg DEX, continuous infusion of 0.4μg /kg/h IV	Equal volume of saline	1/6	NR

Abbreviations: DEX: dexmedetomidine; Dexa: dexamethasone; NR: not reported.

The association between DEX and PONV

All 18 trials involved the effect of DEX on the incidence of PONV. There was no heterogeneity between the articles (P<0.00001, I^2=26%, Fig. 3), so a fixed-effects model was be chosen. The consequences revealed that the occurrence of PONV in DEX group was lower than the control group (OR=0.49, 95% CI 0.36 to 0.67, Fig. 3), which indicated that DEX notably prevent the happening of PONV in adult patients after general anesthetic surgery.

The association between DEX and perioperative opioid consumption

8 studies assessed the effect of DEX on perioperative opioid consumption. Because of a high heterogeneity (P<0.00001, I^2=91%, Fig. 4), a random effect model was selected. The consequences of this meta-analysis indicated that the perioperative opioid consumption was lower in DEX group (SMD= −1.04, 95% CI −1.53 to −0.54, Fig. 4). Our results suggested that DEX decreased the perioperative opioid consumption significantly.

Other recovery outcomes

4 literatures including 200 patients involved the length of hospitalization. The study heterogeneity was high (P<0.00001, I^2=96%, Fig. 5), so a random effect model was selected. The consequence found that the length of hospitalization in DEX group was shorter (SMD= −2.29, 95% CI −4.31 to −0.28, Fig. 5). 4 trials including 292 subjects referred to the extubation time. A random effect model was chosen since the high heterogeneity (P=0.004, I^2=77%, Fig. 6). There was a shorter time to extubation in DEX group (SMD= −0.75, 95% CI −1.26 to −0.25, Fig. 6). Therefore, meta-analysis of the 8 literatures indicated that DEX could accelerate the recovery of patients after anesthesia.

Side effects

8 trials described the incidence of bradycardia. A fixed effect model was selected considering the little heterogeneity (P=0.32, I^2=14%, Fig. 7). Compared to the control group, the number of participants developed bradycardia in the DEX group was higher (OR=1.60, 95% CI 1.13 to 2.27, Fig. 7). The consequences from this meta-analysis revealed that DEX might increase the occurrence of bradycardia.

Risk of bias

Publication bias of literatures including the incidence of PONV in our meta-analysis was assessed by funnel plots, and no publication bias was found (Fig. 8). We removed each study one by one for sensitivity analysis and found that the results did not change (Supplementary document 3).

DISCUSSION

This present meta-analysis showed that DEX is a potential effective agent for decreasing the incidence of PONV and promoting the recovery of adult patients undergoing general anesthetic surgery, but it might increase the incidence of bradycardia.

PONV is unsatisfactory experience and painful adverse event for patients, especially in the first day after surgery. Its incidence is approximately 30% and up to 80% without prevention[1; 28]. Moreover, some surgical types were associated with the high occurrence of PONV, especially in gynecological surgery, otolaryngology surgery and neurosurgery[3]. There are many risk factors that can increase the incidence of PONV by 20% respectively in patients, including anesthetic factors, surgical factors, female, non-smokers, and the medical history of motion sickness or/and PONV[29]. These risk factors might also vary with the premedication, anesthetic technique and

postoperative management[30]. Among the factors of anesthesia, general anesthesia is more likely to cause PONV compared with regional anesthesia[31]. The pathophysiology process of PONV is very elusive. A study suggested that injuries from operation, anesthesia, visceral nerve stimulation, hypoxia, hypotension, and pain were the major irritants, which could trigger the vomiting response when they reach the cortical/thalamic, cerebellar and vestibular nuclei, and the chemoreceptor triggering band outside of the blood-brain barrier[32]. Although there are multiple methods and drugs to prevent PONV in clinical practice, the efficacy of PONV prophylaxis remains unsatisfactory especially in high-risk patients[1].

DEX exerts the anxiolytic, sedative and analgesic effects by reducing the release of norepinephrine induced by α2 adrenergic receptors in the spinal cord and locus coeruleus. However, it could not result in excessive sedation or respiratory depression as the results of accumulation[33]. Therefore, DEX was used as an appropriate short-acting sedative for patients under general anesthesia in perioperative period. Previous articles indicated that DEX reduced the occurrence of PONV, which were similar to our result. For instance, a study reported that DEX administered could decrease the occurrence of PONV in patients experiencing intestinal surgery[27], another study discovered that intraoperative use of DEX could be a valid measure to prevent the PONV in patients after laparoscopic radical prostatectomy[16]. But the mechanisms for the effect of DEX on PONV are still obscure. Previous articles reported DEX could decrease the occurrence of PONV by modulating 5-HT and dopamine release, suppressing the histamine-induced expression of IL-6, and reducing sympathetic outflow and total catecholamine release[34; 35]. So, one of the key mechanisms about the effect of DEX on PONV might be attributable to the regulation of neurotransmitters. Moreover, it is well known to us that the amount of intraoperative opioid use

directly influenced the frequency and degree of PONV[31].

DEX also can prevent the perioperative stress response by regulating heart rate and blood pressure, however, DEX might produce some adverse events like bradycardia especially in patient with atrioventricular block or hypovolemia[36]. Similar consequence with our article, a meta-analysis of 3638 patients from 9 high-quality RCTs reported that DEX could increase the incidence of bradycardia[37], which might be due to presynaptic a-2 receptor stimulation by DEX results in decreasing norepinephrine release.

Additionally, it was interesting to found that DEX could short the time to extubation in this meta-analysis, which was similar to the result of one previous meta-analysis[38]. However, because of the limited data and the high heterogeneity among the studies, the pooled result should be interpreted cautiously and further investigations were needed to support the conclusion.

In fact, there were two previous meta-analyses also reported that DEX could low the occurrence of PONV compared to the control group[30; 39]. The included population of these two meta-analyses was the children and adults, and one study didn't limit the methods of anesthesia and the administration of DEX. Notably, we mainly focused on the adult patient population under general anesthesia, and the intervention was perioperative intravenous DEX, which differed from the two previous meta-analyses. Moreover, the RCTs that DEX comparing with opioids agents were excluded in our meta-analysis to eliminate the effect of opioids on PONV. Additionally, our study was involved a number of updated RCTs and added some indicators about the recovery after surgery. Ultimately, our results suggested that DEX did decrease the occurrence of PONV, and accelerated the recovery of adult patients after general anesthesia.

Clinical significance

The results of this meta-analysis might help the doctors and nurses to formulate plans to prevent PONV and offer a new testimony to expand the clinical significance of DEX apart from its conventional usage for sedation and analgesia.

LIMITATIONS

There were several limitations to this meta-analysis. Firstly, the included articles did not give consistent doses of DEX, the influence of diverse doses of DEX on PONV in adult patients after general anesthesia needs to be further explored. Secondly, the severity degree of PONV was not quantified using a formal scale, so further study is required to explore the effect of DEX on different severity degree of PONV.

CONCLUSION

In a word, DEX could decrease the occurrence of PONV in adult patients who experiencing general anesthesia, and accelerate postoperative recovery. Thus, DEX can be used as an adjuvant drug for general anesthesia to prevent the development of PONV in clinical practice. However, it is essential to be vigilant the occurrence of bradycardia during surgery.

Author Contributions WZ and JL were involved in the conception and design of this meta-analysis. NW and ZW conducted the data extraction. HZ and ML contributed to statistical analysis. WZ analyzed the data and drafted the manuscript. JH, DY and MZ offered major comments and revised the manuscript. All authors have read and approved the manuscript.

Funding The work was supported by the Key Research and Development Program of Hebei Province (Grant No. 19277714D). The funding bodies had no role in the design of the study, and will have no role in the data collection, analysis, interpretation of data, and writing of the manuscript.

Ethics approval statement This study was a meta-analysis of previously published literatures, ethical approval was not necessary.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information.

ORCID Jianli Li: https://orcid.org/0000-0001-6867-7825

REFERENCES

1. Gan TJ, Belani KG, Bergese S, et al. 2020. Fourth Consensus Guidelines for the Management of Postoperative Nausea and Vomiting. *Anesth Analg* 131:411-48. https://doi.org/10.1213/ane.0000000000004833
2. Ishikawa E, Iwamoto R, Hojo T, et al. 2022. Cross-sectional Study of PONV Risk Factors for Oral Surgery After Intubated General Anesthesia With Total Intravenous Anesthesia. *Anesth Prog* 69:18-23. https://doi.org/10.2344/anpr-68-03-12
3. Elvir-Lazo OL, White PF, Yumul R, et al. 2020. Management strategies for the treatment and prevention of postoperative/postdischarge nausea and vomiting: an updated review. *F1000Res* 9. https://doi.org/10.12688/f1000research.21832.1
4. Li HJ, Liu S, Geng ZY, et al. 2020. Adding dexmedetomidine to morphine-based analgesia reduces early postoperative nausea in patients undergoing gynecological laparoscopic surgery: a randomized controlled trial. *BMC Anesthesiol* 20:11. https://doi.org/10.1186/s12871-019-0928-y
5. Lee J, Hwang HW, Jeong JY, et al. 2022. The Effect of Low-Dose Dexmedetomidine on Pain and Inflammation in Patients Undergoing Laparoscopic Hysterectomy. *J Clin Med* 11. https://doi.org/10.3390/jcm11102802
6. Xie C, Zhang C, Sun H, et al. 2021. Effects of Dexmedetomidine on Postoperative Nausea and Vomiting in Adult Patients Undergoing Ambulatory Thyroidectomy: A Randomized Clinical Trial. *Front Med (Lausanne)* 8:781689. https://doi.org/10.3389/fmed.2021.781689
7. Yan C, Ti-jun D. 2021. Effects of Intraoperative Dexmedetomidine Infusion on

Postoperative Delirium in Elderly Patients Undergoing Total Hip Arthroplasty. *International Surgery* 105:328-35. https://doi.org/10.9738/intsurg-d-17-00029.1

8. Page MJ, McKenzie JE, Bossuyt PM, et al. 2021. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *Syst Rev* 10:89. https://doi.org/10.1186/s13643-021-01626-4

9. van Loveren C, Aartman IH. 2007. [The PICO (Patient-Intervention-Comparison-Outcome) question]. *Ned Tijdschr Tandheelkd* 114:172-8.

10. Higgins JP, Altman DG, Gøtzsche PC, et al. 2011. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *Bmj* 343:d5928. https://doi.org/10.1136/bmj.d5928

11. Bakri MH, Ismail EA, Ibrahim A. 2015. Comparison of dexmedetomidine and dexamethasone for prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy. *Korean J Anesthesiol* 68:254-60. https://doi.org/10.4097/kjae.2015.68.3.254

12. Peng K, Jin XH, Liu SL, et al. 2015. Effect of Intraoperative Dexmedetomidine on Post-Craniotomy Pain. *Clin Ther* 37:1114-21 e1. https://doi.org/10.1016/j.clinthera.2015.02.011

13. Chen C, Huang P, Lai L, et al. 2016. Dexmedetomidine improves gastrointestinal motility after laparoscopic resection of colorectal cancer: A randomized clinical trial. *Medicine (Baltimore)* 95:e4295. https://doi.org/10.1097/MD.0000000000004295

14. Bielka K, Kuchyn I, Babych V, et al. 2018. Dexmedetomidine infusion as an analgesic adjuvant during laparoscopic small es, Cyrillicholecystectomy: a randomized controlled

study. *BMC Anesthesiol* 18:44. https://doi.org/10.1186/s12871-018-0508-6

15. Das R, Das RK, Sahoo S, et al. 2018. Role of dexmedetomidine as an anaesthetic adjuvant in breast cancer surgery as a day-care procedure: A randomised controlled study. *Indian J Anaesth* 62:182-7. https://doi.org/10.4103/ija.IJA_752_17

16. Wu S, Yao H, Cheng N, et al. 2019. Determining whether dexmedetomidine provides a reno-protective effect in patients receiving laparoscopic radical prostatectomy: a pilot study. *Int Urol Nephrol* 51:1553-61. https://doi.org/10.1007/s11255-019-02171-9

17. Bala R, Chaturvedi A, Pandia MP, et al. 2019. Intraoperative Dexmedetomidine Maintains Hemodynamic Stability and Hastens Postoperative Recovery in Patients Undergoing Transsphenoidal Pituitary Surgery. *J Neurosci Rural Pract* 10:599-605. https://doi.org/10.1055/s-0039-3399402

18. Wu F, Duan H, Xie Y. 2019. Preventive Effects of Dexmedetomidine on Renal Dysfunction and Hemodynamic Stability in Malignant Obstructive Jaundice Patients During Peri-Operative Period. *Med Sci Monit* 25:6782-7. https://doi.org/10.12659/MSM.916329

19. Bakshi SG, Paulin SV, Bhawalkar P. 2020. A randomised controlled trial to evaluate the peri-operative role of intraoperative dexmedetomidine infusion in robotic-assisted laparoscopic oncosurgeries. *Indian J Anaesth* 64:784-9. https://doi.org/10.4103/ija.IJA_664_20

20. Chen. X, Chen X. 2020. Dexmedetomidine contributes to reduced anesthesia dosages and improves anesthetic effectiveness in the radical resection of gastric cancer. *Int J Clin Exp Med* 13:6533-41.

21. Asri S, Hosseinzadeh H, Eydi M, et al. 2020. Effect of Dexmedetomidine Combined with Inhalation of Isoflurane on Oxygenation Following One-Lung Ventilation in Thoracic Surgery. *Anesth Pain Med* 10:e95287. https://doi.org/10.5812/aapm.95287

22. Pi. Y, Yang Y. 2021. Application value of conventional anesthesia combined with dexmedetomidine in thoracoscopic radical resection of lung cancer. *Int J Clin Exp Med* 14:1301-8.

23. Lu Y, Fang PP, Yu YQ, et al. 2021. Effect of Intraoperative Dexmedetomidine on Recovery of Gastrointestinal Function After Abdominal Surgery in Older Adults: A Randomized Clinical Trial. *JAMA Netw Open* 4:e2128886. https://doi.org/10.1001/jamanetworkopen.2021.28886

24. Bafna U, Sharma P, Singhal RK, et al. 2021. Comparison of hypotensive properties of dexmedetomidine versus clonidine for induced hypotension during functional endoscopic sinus surgery: A randomised, double-blind interventional study. *Indian J Anaesth* 65:579-85. https://doi.org/10.4103/ija.IJA_57_21

25. Dr. RadhikaAgarwala DPKH, Dr. UshaSaha,. 2021. Dexmedetomidine Infusion in Patients Undergoing Elective Laparoscopic Cholecystectomy under General Anesthesia: Postoperative Analgesia and Complications. *European Journal of Molecular & Clinical Medicine* 8:1906-11.

26. Chen. J, Chen. B, Chen. A. 2021. Effects of anesthesia induction using dexmedetomidine in thoracoscopic pulmonary segmentectomy on the safety and protection of lung function. *Int J Clin Exp Med* 14:565-72.

27. Chen R, Kang Z, Wang Y, et al. 2021. The Anti-inflammatory Effect of

Dexmedetomidine Administration on Patients Undergoing Intestinal Surgery: A Randomized Study. *Drugs R D* 21:445-53. https://doi.org/10.1007/s40268-021-00368-x

28. Gloor Y, Czarnetzki C, Curtin F, et al. 2021. Genetic Susceptibility Toward Nausea and Vomiting in Surgical Patients. *Front Genet* 12:816908. https://doi.org/10.3389/fgene.2021.816908

29. Lu H, Zheng C, Liang B, et al. 2021. Mechanism and risk factors of nausea and vomiting after TACE: a retrospective analysis. *BMC Cancer* 21:513. https://doi.org/10.1186/s12885-021-08253-1

30. Liang X, Zhou M, Feng JJ, et al. 2015. Efficacy of dexmedetomidine on postoperative nausea and vomiting: a meta-analysis of randomized controlled trials. *Int J Clin Exp Med* 8:8450-71.

31. Poon YY, Ke TY, Hung KC, et al. 2021. Risk Factors of Postoperative Vomiting in the Eye of "Real-World Evidence"-Modifiable and Clinical Setting-Dependent Risk Factors in Surgical Trauma Patients. *J Pers Med* 11. https://doi.org/10.3390/jpm11050386

32. Konno D, Sugino S, Shibata TF, et al. 2022. Antiemetic effects of baclofen in a shrew model of postoperative nausea and vomiting: Whole-transcriptome analysis in the nucleus of the solitary tract. *CNS Neurosci Ther* 28:922-31. https://doi.org/10.1111/cns.13823

33. Zhang J, Yu Y, Miao S, et al. 2019. Effects of peri-operative intravenous administration of dexmedetomidine on emergence agitation after general anesthesia in adults: a meta-analysis of randomized controlled trials. *Drug Des Devel Ther* 13:2853-64.

https://doi.org/10.2147/DDDT.S207016

34. Xu S, Hu S, Ju X, et al. 2021. Effects of intravenous lidocaine, dexmedetomidine, and their combination on IL-1, IL-6 and TNF-α in patients undergoing laparoscopic hysterectomy: a prospective, randomized controlled trial. *BMC Anesthesiol* 21:3. https://doi.org/10.1186/s12871-020-01219-z

35. Zhang W, Wang R, Li B, et al. 2022. The Effect of Dexmedetomidine on Postoperative Nausea and Vomiting in Patients Undergoing Thoracic Surgery-A Meta-Analysis of a Randomized Controlled Trial. *Front Surg* 9:863249. https://doi.org/10.3389/fsurg.2022.863249

36. Misra S, Behera BK, Mitra JK, et al. 2021. Effect of preoperative dexmedetomidine nebulization on the hemodynamic response to laryngoscopy and intubation: a randomized control trial. *Korean J Anesthesiol* 74:150-7. https://doi.org/10.4097/kja.20153

37. Lin C, Tu H, Jie Z, et al. 2021. Effect of Dexmedetomidine on Delirium in Elderly Surgical Patients: A Meta-analysis of Randomized Controlled Trials. *Ann Pharmacother* 55:624-36. https://doi.org/10.1177/1060028020951954

38. Pan H, Liu C, Ma X, et al. 2019. Perioperative dexmedetomidine reduces delirium in elderly patients after non-cardiac surgery: a systematic review and meta-analysis of randomized-controlled trials. *Can J Anaesth* 66:1489-500. https://doi.org/10.1007/s12630-019-01440-6

39. Jin S, Liang DD, Chen C, et al. 2017. Dexmedetomidine prevent postoperative nausea and vomiting on patients during general anesthesia: A PRISMA-compliant meta

analysis of randomized controlled trials. *Medicine (Baltimore)* 96:e5770. https://doi.org/10.1097/md.0000000000005770

Figure legends

Figure 1: The risk of bias of included studies.

Figure 2: Flow diagram of the inclusion and exclusion process.

Figure 3: The total effect of dexmedetomidine on postoperative nausea and vomiting.

Figure 4: Perioperative opioid consumption in dexmedetomidine and control group.

Figure 5: The effect of dexmedetomidine on the length of hospitalization.

Figure 6: The effect of dexmedetomidine on the extubation time.

Figure 7: Incidence of bradycardia in dexmedetomidine and control group.

Figure 8: Test for publication bias of the studies included in the incidence of postoperative nausea and vomiting.

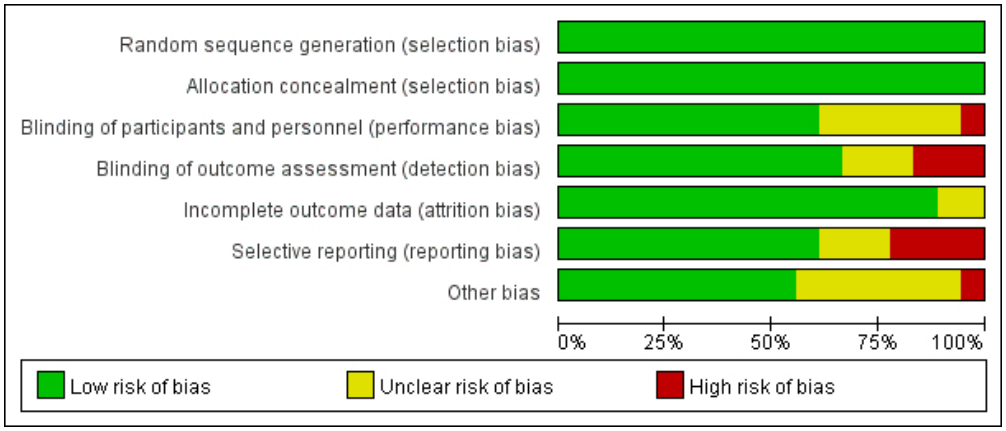

Figure 1: The risk of bias of included studies.

213x90mm (72 x 72 DPI)

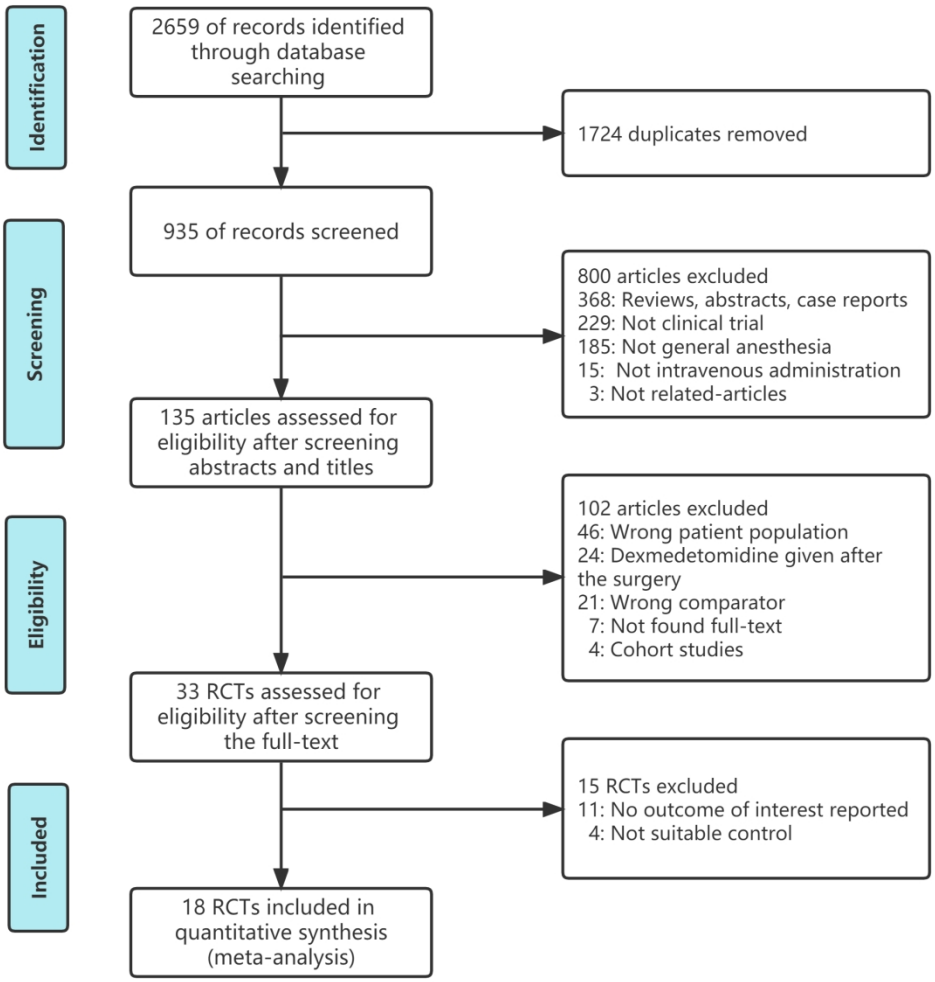

Figure 2: Flow diagram of the inclusion and exclusion process.

720x751mm (72 x 72 DPI)

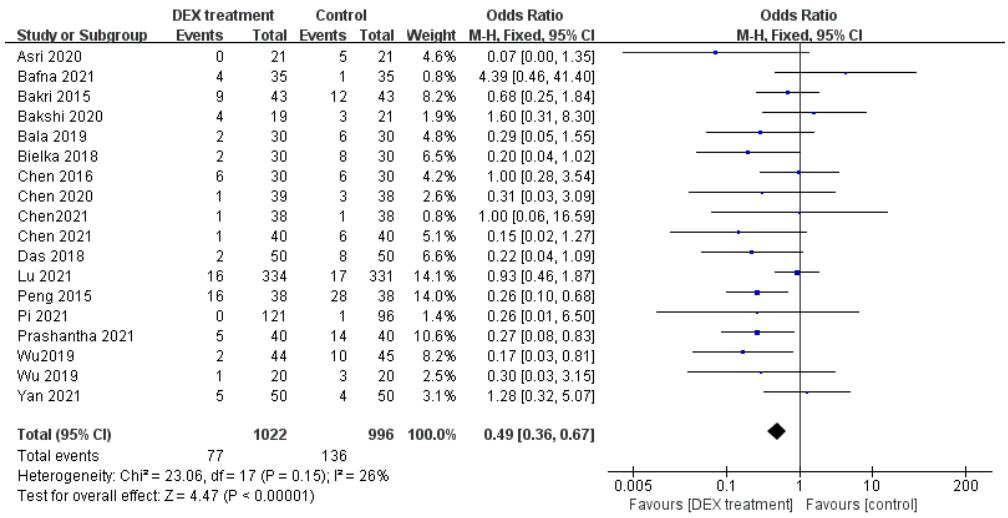

Figure 3: The total effect of dexmedetomidine on postoperative nausea and vomiting.

283x146mm (72 x 72 DPI)

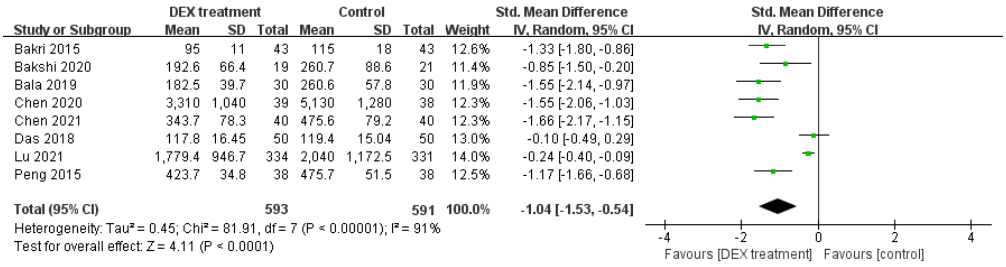

Figure 4: Perioperative opioid consumption in dexmedetomidine and control group.

314x84mm (72 x 72 DPI)

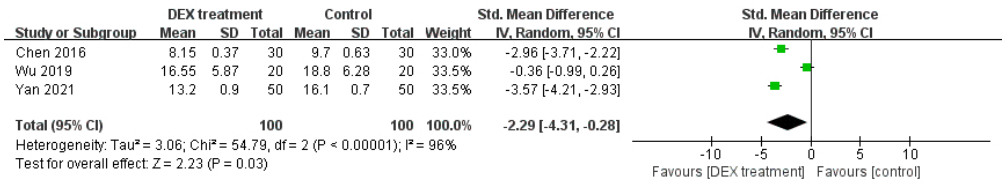

Figure 5: The effect of dexmedetomidine on the length of hospitalization.

303x56mm (72 x 72 DPI)

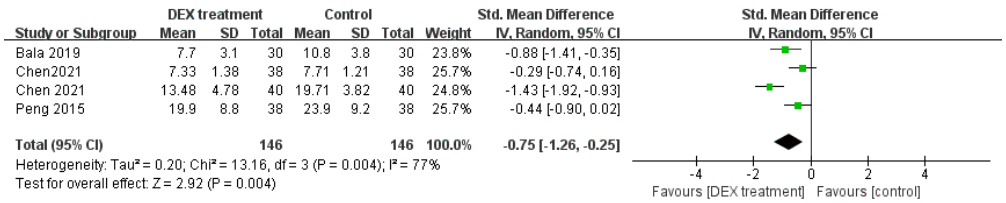

Figure 6: The effect of dexmedetomidine on the extubation time.

303x62mm (72 x 72 DPI)

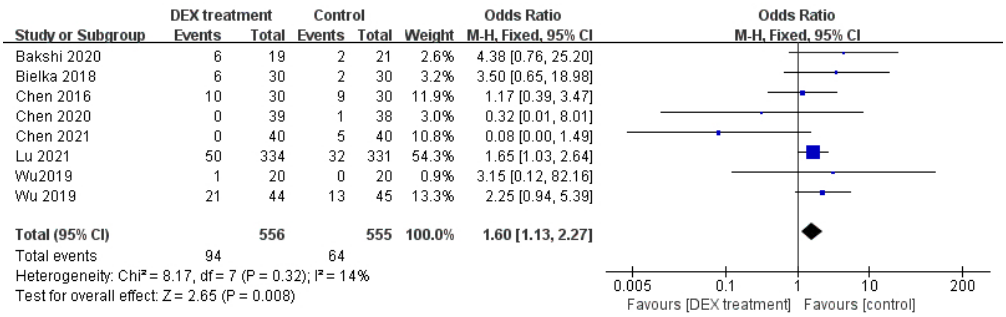

Figure 7: Incidence of bradycardia in dexmedetomidine and control group.

283x90mm (72 x 72 DPI)

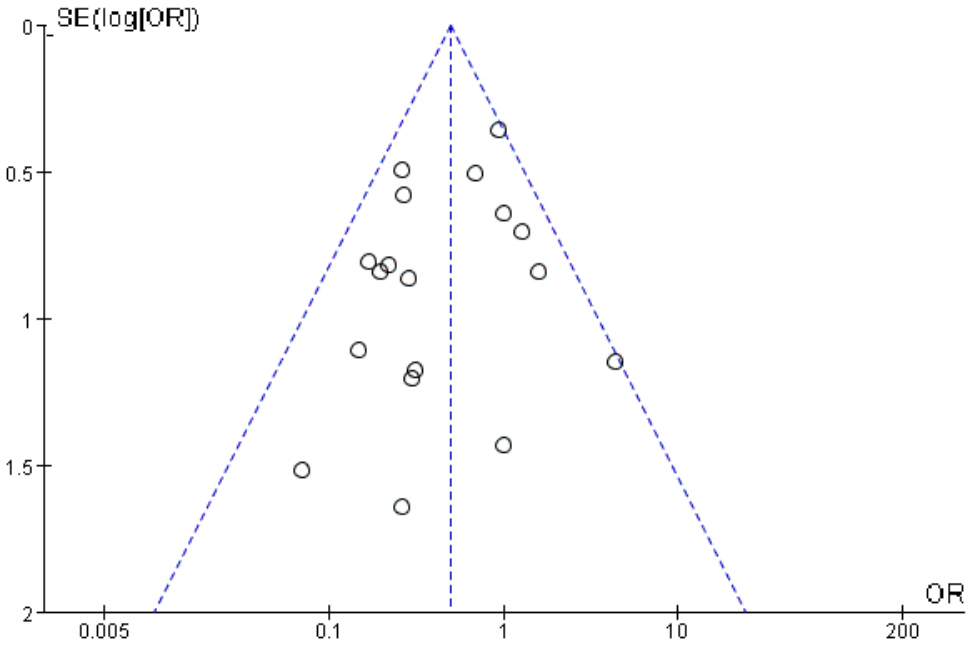

Figure 8: Test for publication bias of the studies included in the incidence of postoperative nausea and vomiting.

544x362mm (28 x 28 DPI)

Supplementary document 1

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Page 2-3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page 3-4
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 4
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page 5
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 5 Supplementary document 2
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Supplementary document 2
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page 6
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 6
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (eg. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page 6
	10b	List and define all other variables for which data were sought (e .g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Page 6
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 6
Effect measures	12	Specify for each outcome the effect measure(s) (e .g. risk ratio, mean difference) used in the synthesis or presentation of results.	Page 6
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Table 1
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data	Page 6

Section and Topic	Item #	Checklist item	Location where item is reported
		conversions.	
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Page 6
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Page 6
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Page 6
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Page 6
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Page 6
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	NA
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Figure 2
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Figure 2
Study characteristics	17	Cite each included study and present its characteristics.	Page 7
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Page 11 Figure 8
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Page 10-11
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Page 10-11
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Page 10-11
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	NA
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Supplementary document 3
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Page 11
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	NA
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Page 11-13
	23b	Discuss any limitations of the evidence included in the review.	Page 14

Section and Topic	Item #	Checklist item	Location where item is reported
	23c	Discuss any limitations of the review processes used.	Page 14
	23d	Discuss implications of the results for practice, policy, and future research.	Page 13-14
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Page 5
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Page 5
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	NA
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page 14
Competing interests	26	Declare any competing interests of review authors.	Page 15
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Page 15

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10. 1136/bmj.n71

For more information, visit:http://www.prisma-statement.org/

Supplementary document 2: The search strategy

Pubmed (https://pubmed.ncbi.nlm.nih.gov/)

Search: (((((((Dexmedetomidine[MeSH Terms]) OR (Dexmedetomidine[Title/Abstract])) OR (MPV-1440[Title/Abstract])) OR (MPV 1440[Title/Abstract])) OR (MPV1440[Title/Abstract])) OR (Precedex[Title/Abstract])) OR (Dexmedetomidine Hydrochloride[Title/Abstract])) OR (Hydrochloride, Dexmedetomidine[Title/Abstract]) AND (("Postoperative Nausea and Vomiting"[Mesh]) OR ((((((((((PONV[Title/Abstract]) OR (Nausea[Title/Abstract] AND Vomiting, Postoperative[Title/Abstract])) OR (Vomiting, Postoperative[Title/Abstract])) OR (Postoperative Emesis[Title/Abstract])) OR (Postoperative Vomiting[Title/Abstract])) OR (Emesis, Postoperative[Title/Abstract])) OR (Emeses, Postoperative[Title/Abstract])) OR (Postoperative Emeses[Title/Abstract])) OR (Postoperative Nausea[Title/Abstract])) OR (Nausea, Postoperative[Title/Abstract]))) AND (2000:2022[pdat])

Embase (http://www.embase.com/)

- #1 Dexmedetomidine
- #2 'mpv- 1440':ab,ti OR 'mpv 1440':ab,ti OR 'mpv1440':ab,ti OR 'precedex':ab,ti OR 'dexmedetomidine hydrochloride':ab,ti OR 'hydrochloride, dexmedetomidine':ab,ti
- #3 #1 OR #2
- #4 postoperative nausea and vomiting
- #5 'ponv':ab,ti OR 'nausea and vomiting, postoperative':ab,ti OR 'vomiting, postoperative':ab,ti OR 'postoperative emesis':ab,ti OR 'postoperative vomiting':ab,ti OR 'emesis, postoperative':ab,ti OR 'emeses, postoperative':ab,ti OR 'postoperative emeses':ab,ti OR 'postoperative nausea':ab,ti OR 'nausea, postoperative':ab,ti
- #6 #4 OR #5
- #7 [2000-2022]/py
- #8 #3 AND #6 AND #7

Cochrane (https://www.cochranelibrary.com/)

- #1 Dexmedetomidine
- #2 (MPV- 1440):ti,ab,kw OR (MPV 1440):ti,ab,kw OR (MPV1440):ti,ab,kw OR (Precedex):ti,ab,kw OR (Dexmedetomidine Hydrochloride):ti,ab,kw OR (Hydrochloride, Dexmedetomidine):ti,ab,kw
- #3 #1 OR #2
- #4 Postoperative nausea and vomiting
- #5 (PONV):ti,ab,kw OR (Nausea and Vomiting, Postoperative):ti,ab,kw OR (Vomiting, Postoperative):ti,ab,kw OR (Postoperative Emesis):ti,ab,kw OR (Postoperative

Vomiting):ti,ab,kw OR (Emesis, Postoperative):ti,ab,kw OR (Emeses, Postoperative):ti,ab,kw OR (Postoperative Emeses):ti,ab,kw OR (Postoperative Nausea):ti,ab,kw OR (Nausea, Postoperative):ti,ab,kw

- #6 #4 OR #5
- #7 #3 AND #6 (with Publication Year from 2000 to 2022)

Web of Science (http://apps.webofknowledge.com/)

- #1 TS= (Postoperative nausea and vomiting OR PONV OR Nausea and Vomiting, Postoperative OR Vomiting, Postoperative OR Postoperative Emesis OR Postoperative Vomiting OR Emesis, Postoperative OR Emeses, Postoperative OR Postoperative Emeses OR Postoperative Nausea OR Nausea, Postoperative)
- #2 TS= (Dexmedetomidine OR MPV-1440 OR MPV 1440 OR MPV1440 OR Precedex OR Dexmedetomidine Hydrochloride OR Hydrochloride, Dexmedetomidine)
- #3 PY= (2000-2022)
- #4 #1 and #2 and #3

Supplementary document 3: The sensitivity analysis of effect of dexmedetomidine on PONV

Study	Odds Ratio	95% CI
Omitting Asri 2020	0.51	[0.37, 0.70]
Omitting Bafna 2021	0.46	[0.33, 0.63]
Omitting Bakri 2015	0.47	[0.34, 0.66]
Omitting Bakshi 2020	0.47	[0.34, 0.64]
Omitting Bala 2019	0.50	[0.36, 0.69]
Omitting Bielka 2018	0.51	[0.37, 0.70]
Omitting Chen 2016	0.47	[0.34, 0.65]
Omitting Chen 2020	0.49	[0.36, 0.68]
Omitting Chen2021	0.49	[0.35, 0.67]
Omitting Chen 2021	0.51	[0.37, 0.70]
Omitting Das 2018	0.51	[0.37, 0.70]
Omitting Lu 2021	0.42	[0.29, 0.60]
Omitting Peng 2015	0.53	[0.38, 0.73]
Omitting Pi 2021	0.49	[0.36, 0.68]
Omitting Prashantha 2021	0.52	[0.37, 0.72]
Omitting Wu2019	0.52	[0.38, 0.71]
Omitting Wu 2019	0.49	[0.36, 0.68]
Omitting Yan 2021	0.46	[0.34, 0.64]
Random effects model	**0.48**	**[0.32, 0.73]**