**Effect of dexmedetomidine on postoperative nausea and vomiting in patients under general anaesthesia: an updated meta-analysis of randomised controlled trials**

Weihong Zhao,1 Jianli Li,1 Na Wang,2 Zhibin Wang,3 Meng Zhang,1 Huanhuan Zhang,1 Meinv Liu,1 Jinhua He,1 Dongdong Yu1

ABSTRACT

**Objectives** To explore the effect of dexmedetomidine (DEX) on postoperative nausea and vomiting (PONV) in adult patients after general anaesthesia.

**Design** Systematic review and meta-analysis.

**Eligibility criteria for selecting studies** Randomised controlled trials (RCTs) comparing the efficacy of DEX with placebo or a single drug on PONV in adult patients after general anaesthesia.

**Data sources** We searched the PubMed, the Web of Science, the Cochrane Library and Embase (1 January 2000 to 30 June 2022) to select the relevant RCTs.

**Data analysis** All the relevant data were analyzed by using RevMan V.5.4. Heterogeneity was tested for each outcome, and random-effect or fixed-effect models were selected according to the level of heterogeneity. The primary outcome was the incidence of PONV. The secondary outcomes were the incidence of bradycardia, perioperative opioid consumption, extubation time and the length of hospitalisation.

**Results** A total of 18 trials involving 2081 patients were included in this meta-analysis. Notably, 15 updated studies were not involved in the previous meta-analysis. The incidence of PONV in DEX group was lower than that in the control group (OR=0.49, 95% CI: 0.36 to 0.67) and the perioperative opioid consumption in DEX group was also decreased significantly (standard mean difference [SMD]=−1.04, 95% CI: −1.53 to −0.54). Moreover, the length of hospitalisation (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 DEX group were shorter. Whereas, more number of patients receiving DEX might increase the occurrence of bradycardia (OR=1.60, 95% CI: 1.13 to 2.27).

**Conclusions** DEX could decrease the occurrence of PONV in adult patients under general anaesthesia and promote the recovery after surgery. However, DEX might increase the occurrence of bradycardia.

**PROSPERO registration number** CRD 42022341548.

INTRODUCTION

Postoperative nausea and vomiting (PONV), as a familiar negative event after operation, is known as nausea, vomiting or retching within 1 day after operation, which may be due to the effect of anaesthetics on the emetic control centre in the medulla oblongata.1 The incidence of PONV is about 30% and even rising to 60%–80% in high-risk populations. PONV, an extremely poor medical experience for patients undergoing general anaesthetic surgery, leads to many adverse influences including stomach discomfort, dehydration, water-electrolyte disorders, wound dehiscence, oesophageal injury, reflux and aspiration, which extend the time of hospitalisation 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 adrenergic 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 presentations of numerous negative events during anaesthesia. For the last few years, the effect of DEX on PONV attracted increasing attention from anaesthesiologists. One clinical study reported that postoperative administration of DEX, as patient-controlled analgesia regimen, produced early antiemetic effects. Another research indicated that intravenous DEX could prevent the occurrence of PONV in adult patients after laparoscopic hysterectomy. While different results were observed in the similar articles, it is still disputed whether intraoperative use of DEX can ameliorate the occurrence of PONV in patients after general anaesthesia.

As far as we know, no updated analysis of the data about the effect of DEX on PONV was performed during general anaesthesia. Therefore, in order to obtain the most recent proof, we thoroughly evaluated the effect of intraoperative use of DEX on PONV in adult patients

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**Figure 1** The risk-of-bias of included studies.

**Figure 2** Flow diagram of the inclusion and exclusion process. RCTs, randomised controlled trials.
### Table 1: Characteristics of the included trials

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Age (years)</th>
<th>Gender</th>
<th>Sample size</th>
<th>Type of surgery</th>
<th>Administration mode</th>
<th>Comparisons</th>
<th>Numbers of nausea and/or vomiting DEX/control</th>
<th>Scale used for assessing PONV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bakri et al(8)</td>
<td>2015</td>
<td>31.1±2.4</td>
<td>15/71</td>
<td>43/43</td>
<td>Laparoscopic cholecystectomy</td>
<td>1 µg/kg DEX intravenous</td>
<td>8 mg DEX intravenous</td>
<td>9/12</td>
<td>A VAS of 0–100 mm, 0 score meant no nausea, while 100 score meant the worst imaginable nausea</td>
</tr>
<tr>
<td>Peng et al(7)</td>
<td>2015</td>
<td>42.3±10.8</td>
<td>33/43</td>
<td>38/38</td>
<td>Craniotomy</td>
<td>Continuous infusion of DEX 0.5 µg/kg/hour intravenous</td>
<td>Equal volume of saline</td>
<td>16/28</td>
<td>0, absent; 1, nausea not requiring treatment; 2, nausea requiring treatment; and 3, vomiting.</td>
</tr>
<tr>
<td>Chen et al(9)</td>
<td>2016</td>
<td>56.67±7.05</td>
<td>29/31</td>
<td>30/30</td>
<td>Laparoscopic resection of colorectal cancer</td>
<td>Loading dose 1 µg/kg DEX, continuous infusion of 0.3 µg/kg/hour intravenous</td>
<td>Equal volume of saline</td>
<td>6/6</td>
<td>0, absent; 1, nausea not requiring treatment; 2, nausea requiring treatment; and 3, vomiting.</td>
</tr>
<tr>
<td>Bielka et al(20)</td>
<td>2018</td>
<td>55 (49–61)</td>
<td>July 53</td>
<td>30/30</td>
<td>Laparoscopic cholecystectomy</td>
<td>Continuous infusion of DEX 0.5 µg/kg/hour intravenous</td>
<td>Equal volume of saline</td>
<td>2/8</td>
<td>NR</td>
</tr>
<tr>
<td>Das et al(27)</td>
<td>2018</td>
<td>50.74±9.05</td>
<td>47.92±8.08</td>
<td>50/50</td>
<td>Breast cancer surgery</td>
<td>Continuous infusion of DEX 0.5 µg/kg/hour intravenous</td>
<td>Equal volume of saline</td>
<td>2/8</td>
<td>NR</td>
</tr>
<tr>
<td>Wu et al(17)</td>
<td>2019</td>
<td>67</td>
<td>69</td>
<td>NR</td>
<td>Laparoscopic radical prostatectomy</td>
<td>Loading dose 1 µg/kg DEX, continuous infusion of 0.5 µg/kg/hour intravenous</td>
<td>Equal volume of saline</td>
<td>2/10</td>
<td>NR</td>
</tr>
<tr>
<td>Bala et al(29)</td>
<td>2019</td>
<td>37.2±11.0</td>
<td>41±13.4</td>
<td>33/27</td>
<td>Transsphenoidal pituitary surgery</td>
<td>Loading dose 1 µg/kg DEX, continuous infusion of 0.5 µg/kg/hour intravenous</td>
<td>Equal volume of saline</td>
<td>2/6</td>
<td>NR</td>
</tr>
<tr>
<td>Wu et al(10)</td>
<td>2019</td>
<td>55.00±5.07</td>
<td>54.85±4.96</td>
<td>25/15</td>
<td>Cholangiojejunostomy or resection of tumour</td>
<td>Loading dose 0.5 µg/kg DEX, continuous infusion of 0.5 µg/kg/hour intravenous</td>
<td>Equal volume of saline</td>
<td>1/3</td>
<td>NR</td>
</tr>
<tr>
<td>Bakshi et al(33)</td>
<td>2020</td>
<td>51.8±12</td>
<td>47.2±13</td>
<td>14/26</td>
<td>Robotic-assisted laparoscopic oncoursgeries</td>
<td>Loading dose 1 µg/kg DEX, continuous infusion of 0.2 µg/kg/hour intravenous</td>
<td>Equal volume of saline</td>
<td>4/3</td>
<td>NR</td>
</tr>
<tr>
<td>Chen and Chen(2)</td>
<td>2020</td>
<td>42.68±7.59</td>
<td>43.35±6.82</td>
<td>41/36</td>
<td>Radical resection of gastric cancer</td>
<td>Loading dose 0.6 µg/kg DEX, continuous infusion of 0.4 µg/kg/hour intravenous</td>
<td>Equal volume of saline</td>
<td>1/3</td>
<td>NR</td>
</tr>
<tr>
<td>Asri et al(23)</td>
<td>2020</td>
<td>51±12</td>
<td>46±16</td>
<td>32/10</td>
<td>Thoracic surgery</td>
<td>Continuous infusion of DEX 0.3 µg/kg/hour intravenous</td>
<td>Equal volume of saline</td>
<td>0/5</td>
<td>NR</td>
</tr>
<tr>
<td>Pi and Yang(34)</td>
<td>2021</td>
<td>42.15±1.34</td>
<td>41.88±1.56</td>
<td>162/55</td>
<td>Thoracoscopic radial resection of lung cancer</td>
<td>Loading dose 0.4 µg/kg DEX, continuous infusion of 0.2 µg/kg/hour intravenous</td>
<td>Equal volume of saline</td>
<td>0/1</td>
<td>NR</td>
</tr>
<tr>
<td>Lu et al(35)</td>
<td>2021</td>
<td>70.1±5.8</td>
<td>70.4±6.5</td>
<td>445/230</td>
<td>Abdominal Surgery</td>
<td>Loading dose 0.5 µg/kg DEX, continuous infusion of 0.2 µg/kg/hour intravenous</td>
<td>Equal volume of saline</td>
<td>16/17</td>
<td>10-point rating scale: 0: no PONV and 10: maximal PONV</td>
</tr>
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Continued
experiencing general anaesthesia according to the results from the 18 randomised 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 Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines8 (online supplemental 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 is shown in online supplemental document 2. In order to ensure the contemporary practice, the literature was searched from 1 January 2000 to 30 June 2022.

Inclusion and exclusion criteria
The inclusion criteria were in accordance with patient–intervention–comparison–outcome:
1. Patients: adult participants undergoing general anaesthetic surgery.
2. Intervention: received a single or continuously administered intravenous dose of intraoperative DEX.
3. Comparison: received a single or continuously administered intravenous injection of placebo or comparator.
4. Outcomes: the incidence of PONV and bradycardia, the perioperative opioid consumption, the extubation time and the length of hospitalisation.

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 anaesthesia; and (4) full text not available.

Data extraction and analysis
All information of the articles was collected independently by two researchers using standardised 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 hospitalisation. A standardised 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, 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 V.5.4 software to perform statistical analysis. For dichotomous data, we calculated ORs with 95% CIs. And when the outcome was expressed using varied approaches, we used standard mean difference (SMD) and 95% CIs to analyse the continuous data. We used the $I^2$ 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 are 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 are summed up in table 1. Sixteen articles in the included studies investigated the efficacy of DEX compared with saline, two trials examined the efficacy of DEX compared with 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.

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, $I^2=26\%$, figure 3), so a fixed-effects model was chosen. The consequences revealed that the occurrence of PONV in DEX group was lower than that in the control group (OR=0.49, 95% CI: 0.36 to 0.67, figure 3), which indicated that DEX notably prevented the happening of PONV in adult patients after general anaesthetic surgery.

The association between DEX and perioperative opioid consumption
Eight studies assessed the effect of DEX on perioperative opioid consumption. Because of a high heterogeneity (p=0.00001, $I^2=91\%$, figure 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, figure 4). Our results suggested that DEX decreased the perioperative opioid consumption significantly.

Other recovery outcomes
Four literatures including 200 patients involved the length of hospitalisation. The study heterogeneity was high (p=0.00001, $I^2=96\%$, figure 5), so a random-effect model was selected. The consequence found that the length of hospitalisation in DEX group was shorter (SMD= −2.29, 95% CI: −4.31 to −0.28, figure 5). Four trials including 292 subjects referred to the extubation time. A random-effect model was chosen due to high heterogeneity (p=0.004, $I^2=77\%$, figure 6). There was a shorter time to extubation in DEX group (SMD= −0.75, 95% CI: −1.26 to −0.25, figure 6). Therefore, meta-analysis of the eight literatures indicated that DEX could accelerate the recovery of patients after anaesthesia.

Side effects
Eight trials described the incidence of bradycardia. A fixed-effect model was selected considering the little heterogeneity (p=0.32, $I^2=14\%$, figure 7). Compared with the control group, the number of participants who developed bradycardia in the DEX group was higher (OR=1.60, 95% CI: 1.13 to 2.27, figure 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 (figure 8). We removed each study one by one for sensitivity analysis and found that the results did not change (online supplemental 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 anaesthetic surgery, but it might increase the incidence of bradycardia.

PONV is an 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.6,10 Moreover, some surgical types were associated with the high occurrence of PONV, especially in gynaecological surgery, otolaryngology surgery and neurosurgery.3 There are many risk factors that can increase the incidence of PONV by 20%, respectively, in patients, including anaesthetic factors, surgical factors, female, non-smokers and the medical history of motion sickness and/or PONV.11 These risk factors might also vary with the premedication, anaesthetic technique and postoperative management.12 Among the factors of anaesthesia, general anaesthesia is more likely to cause PONV
compared with regional anaesthesia. The pathophysiology process of PONV is very elusive. A study suggested that injuries from operation, anaesthesia, 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. 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.

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. Therefore, DEX was used as an appropriate short-acting sedative for patients under general anaesthesia 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, another study discovered that intraoperative use of DEX could be a valid measure to prevent the PONV in patients after laparoscopic radical prostatectomy. 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-hydroxytryptamine (5-HT) and dopamine release, suppressing the histamine-induced expression of interleukin-6 and reducing sympathetic outflow and total catecholamine release. 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.

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 patients with atrioventricular block or hypovolaemia. Similar consequence with our article, a meta-analysis of 3638 patients from nine high-quality RCTs reported that DEX could increase the incidence of bradycardia, which might be due to presynaptic α2 receptor stimulation by DEX results in decreasing norepinephrine release.

Additionally, it was interesting to find that DEX could shorten the time to extubation in this meta-analysis, which was similar to the result of one previous meta-analysis. 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 with the control group. The included population of these two meta-analyses was the children and adults, and one study did not limit the methods of anaesthesia and the administration of DEX. Notably, we mainly focused on the adult patient population under general anaesthesia, 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 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 anaesthesia.

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 and nurses to formulate plans to prevent PONV.

Limitations

There were several limitations to this meta-analysis. First, the included articles did not give consistent doses of DEX, the influence of diverse doses of DEX on PONV in adult patients after general anaesthesia needs to be further explored. Second, 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 degrees of PONV.

CONCLUSION

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

Contributors

The author acting as guarantor was JL. WZ and JL were involved in the conception and design of this meta-analysis. NW and ZW conducted the data analysis. HZ and ML contributed to statistical analysis. WZ analysed 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.

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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.

Ethics approval

Not applicable.

Provenance and peer review

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Data availability statement

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

Supplemental material

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