Original Article

Preoperative dexamethasone administration in reducing the incidence of nausea and vomiting after thyroidectomy: a systematic review and meta-analysis of drug dosage

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Background: Postoperative nausea and vomiting (PONV) are key contributors to the delay of recovery and cause patients' considerable discomfort. This study aimed to evaluate the influence of a specific dexamethasone dosage on PONV incidence, with a secondary objective of assessing its impact on postoperative pain in patients undergoing thyroid surgery.

Methods: A meta-analysis was performed to examine the effects of preoperatively administering various doses of dexamethasone in combination with saline on PONV and pain relief in patients undergoing thyroidectomy. Relevant trials published before December 30, 2022, were searched in the PubMed, Embase, Cochrane Library, and Web of Science databases. The collected data were analyzed using RevMan 5.3 software (Cochrane), and a random-effects model or fixed-effects model was employed to conduct the meta-analysis.

Results: Our meta-analysis included 11 randomized controlled trials (RCTs) with a total of 1,544 participants. The results suggested that administering dexamethasone at a dosage of 8–10 mg can reduce the incidence of PONV in patients after thyroid surgery [odds ratio (OR) 0.27; 95% CI: 0.15–0.50; I^2=82%; P<0.0001]. Additionally, administering dexamethasone at a dosage of 8–10 mg was found to be significantly more effective in reducing the incidence of PONV than was a dosage of 4–5 mg (OR 0.39; 95% CI: 0.19–0.80; I^2=29%; P=0.01). The study also revealed that administering dexamethasone at a dosage of 8–10 mg can significantly reduce pain in patients undergoing thyroidectomy [mean difference (MD): –1.19; 95% CI: –1.97 to –0.41; I^2=96%; P=0.003]. However, administering dexamethasone at a dosage of 4–5 mg did not significantly reduce pain (MD: –0.27; 95% CI: –1.00 to 0.45; I^2=0%; P=0.46) according to the subgroup analysis. Our study found that the intervention of administering dexamethasone did not have a significant impact on the consumption of analgesic drugs (MD: –0.19; 95% CI: –0.45 to 0.08; I^2=62%; P=0.16).

Conclusions: A preoperative single dose of 8–10 mg of dexamethasone can significantly reduce PONV and the requirement for additional antiemetic medications, as well as alleviate postoperative pain after thyroidectomy. However, more RCTs should be conducted to determine the effects of varied dexamethasone dosages, particularly 4–5 mg, on the incidence of PONV and pain.

Keywords: Dexamethasone; thyroid surgery; postoperative nausea and vomiting (PONV); pain; meta-analysis

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Introduction

Thyroid cancer, as one of the most common endocrine diseases affecting the thyroid gland, has been a global healthcare concern over recent years. Although the incidence of thyroid cancer varies according to region and period, interest in this disease has remained relatively high (1-3). In the United States, thyroid cancer has become more prevalent in both men and women, with rates rising from 4.9 cases per 100,000 in 1975 to 14.3 cases per 100,000 in 2014 (4). Surgical resection is the most common treatment for this type of cancer, but patients frequently experience postoperative nausea and vomiting (PONV), which are unavoidable sequelae of the procedure (5,6). Additionally, patients may experience other significant postoperative problems that adversely affect their comfort (7).

Numerous types of medication have been applied to prevent PONV before thyroid cancer surgery, such as 5-HT3 receptor antagonists, droperidol, and metoclopramide (8). However, these all share common side effects, including headaches, constipation, elevated liver enzyme levels, restlessness, anxiety, and irregular heartbeat, among others (9-11). Studies have suggested that dexamethasone, a cost-effective medication with minimal side effects, may be beneficial for reducing PONV (12-14). However, the effectiveness of dexamethasone in alleviating PONV and pain in patients undergoing thyroidectomy remains controversial (15-17). Chen *et al.*'s review indicated that dexamethasone can significantly decrease the incidence of PONV, 24-hour visual analog pain scores (VAS), and analgesic use (18). Additionally, Li *et al.* reviewed seven relevant studies and reported that a single preoperative application of dexamethasone can reduce the incidence and severity of PONV in patients undergoing thyroidectomy, but it may not have an effect on pain or analgesic consumption (19). De Oliveira *et al.* found that using a dose of 8–10 mg of dexamethasone did not have any clinical advantage over a dose of 4–5 mg in reducing the incidence of PONV (20). However, a study conducted by Barros *et al.* found that a single low dose of 4 mg of dexamethasone had limited effects on postoperative pain and tramadol demand after thyroidectomy (21). Another meta-analysis has affirmed the safety and efficacy of intravenously administering prophylactic dexamethasone (8–10 mg) before anesthesia induction (22).

We conducted meta-analysis to offer a more precise and comprehensive understanding of the benefits of dexamethasone usage in clinical practice. The findings may be useful for clinicians who are considering the use of dexamethasone for reducing the incidence of PONV and improving pain relief in their patients. We present this article in accordance with the PRISMA reporting checklist (available at https://gs.amegroups.com/article/view/10.21037/gs-23-260/rc).

Highlight box

Key findings

- The study found that a preoperative single dose of 8–10 mg of dexamethasone significantly reduces postoperative nausea and vomiting (PONV) and the need for additional antiemetic medications while additionally alleviating postoperative pain after thyroidectomy.

What is known and what is new?

- Dexamethasone has a positive impact on PONV and pain.
- The meta-analysis confirmed a specific dosage range of 8–10 mg for dexamethasone as an effective preoperative treatment.

What is the implication, and what should change now?

- Healthcare providers should consider using 8–10 mg of dexamethasone preoperatively to reduce PONV and pain in patients undergoing thyroidectomy.
- There is need for further randomized controlled trials to investigate the effects of varied dosages (e.g., 4–5 mg) of dexamethasone on postoperative pain, which could potentially refine treatment protocols.

Methods

Search strategies

The PubMed, Web of Science, EMBASE, and Cochrane Library databased were searched for randomized controlled trials (RCTs) conducted prior to December 30, 2022, in both the English and Chinese languages, and a similar search for unpublished data was also performed. The retrieval strategy was determined based on a combination of subject words and free words, which was adjusted according to the specific database. English database search terms included "dexamethasone", "thyroidectomy", "surgery", "randomized controlled trial", and "random". The optimal combination of the above phrases was applied to search for relevant articles.

Inclusion and exclusion criteria

Inclusion criteria

The inclusion criteria for the trials were as follows: (I)

RCTs, (II) enrollment of patients undergoing thyroidectomy without any other surgical intervention, (III) absence of any prior intake of analgesic or antiemetic medications by patients before the operation, and (IV) administration of intravenous dexamethasone to the experimental group and 0.9% normal saline placebo to the control group.

Exclusion criteria

The following material was excluded from the analysis: (I) duplicate trials; (II) studies with an imprecise definition of the evaluation index for research outcomes that could have led to classification errors; (III) studies that did not include original data in their findings; and (IV) literature such as case studies, case analyses, reviews, and other types of nonoriginal research.

Literature quality evaluation and data

Two independent reviewers conducted literature screening and data extraction for the meta-analysis. This involved collecting information related to the title, author, basic data of the research participants, sample size, outcome indicators, research results, and other relevant data. In cases where there was disagreement about the literature's inclusion, the researchers discussed the study and sought the input of a third reviewer before making a final decision. Additionally, each researcher individually assessed the quality of the included literature using the Jadad Scale, a tool designed to evaluate RCTs.

Statistical analysis

A meta-analysis was conducted using RevMan 5.3 software (Cochrane). The mean difference (MD) was calculated for continuous data, the odds ratio (OR) was calculated for binary data, and the Cochrane Q test was used to assess heterogeneity between studies. The 95% confidence interval (CI) was calculated for all analyses. If studies were statistically heterogeneous (P>0.01 and I^2<50%), a fixed-effects model was used. If studies were heterogeneous (P<0.01 and I^2≥50%), but there was no clinical heterogeneity in the results, a random-effects model was used. If the source of heterogeneity could not be determined, a descriptive analysis was performed. TSA v. 0.9.5.10 Beta software (Copenhagen Clinical Trial Center), was used to perform trial sequential analysis (TSA) on the main outcome indicators to assess the accuracy of the evidence. The TSA-adjusted target sample size is referred to as the "expected sample size", which is determined based on detecting a predetermined clinically meaningful effect. The traditional significance level (α=0.05) was used to construct the TSA monitoring boundary and calculate the *Z* statistic for each trial. A cumulative *Z* curve was then constructed based on the included studies.

Results

Basic information of the included literature

After searches were conducted up to December 30, 2022, a total of 337 articles were identified. After the titles and abstracts were screened, 163 articles were identified as potentially eligible for inclusion. We retrieved the full-text articles and analyzed them, with 11 RCTs ultimately being deemed eligible (11,21,23-31) (*Figure 1*).

Basic features of the included literature

A total of 1,544 participants who had undergone thyroid surgery were finally included among the 11 eligible RCTs conducted in the following countries: Italy, Japan, Switzerland, China, Korea, and Portugal. Among these studies, ten reported on the effectiveness of dexamethasone in preventing PONV in patients undergoing thyroidectomy while nine reported on its pain-relief effects. Ten trials scored 5 or higher on the Jadad scale. More basic characteristics of the included literature are presented in *Table 1*.

Meta-analysis results on the efficacy of dexamethasone in preventing PONV

A total of 1,475 patients were included in the meta-analysis, and 772 cases were placed in a dexamethasone treatment group and 703 cases in a placebo group. The analysis showed significant heterogeneity among studies. Specifically, ten studies indicated that dexamethasone at a dose of 8–10 mg significantly reduced the 24-hour incidence of PONV (OR: 0.27; 95% CI: 0.15–0.50; I^2=82%; P<0.0001), as depicted in *Figure 2*. However, in a subgroup analysis of two studies, dexamethasone at a dose of 4–5 mg did not significantly reduce PONV incidence (OR 0.22; 95% CI: 0.03–1.33; I^2=80%; P=0.1).

Further analyses revealed that dexamethasone at a dose of 8–10 mg had a significantly greater effect in reducing the incidence of PONV than did dexamethasone at a

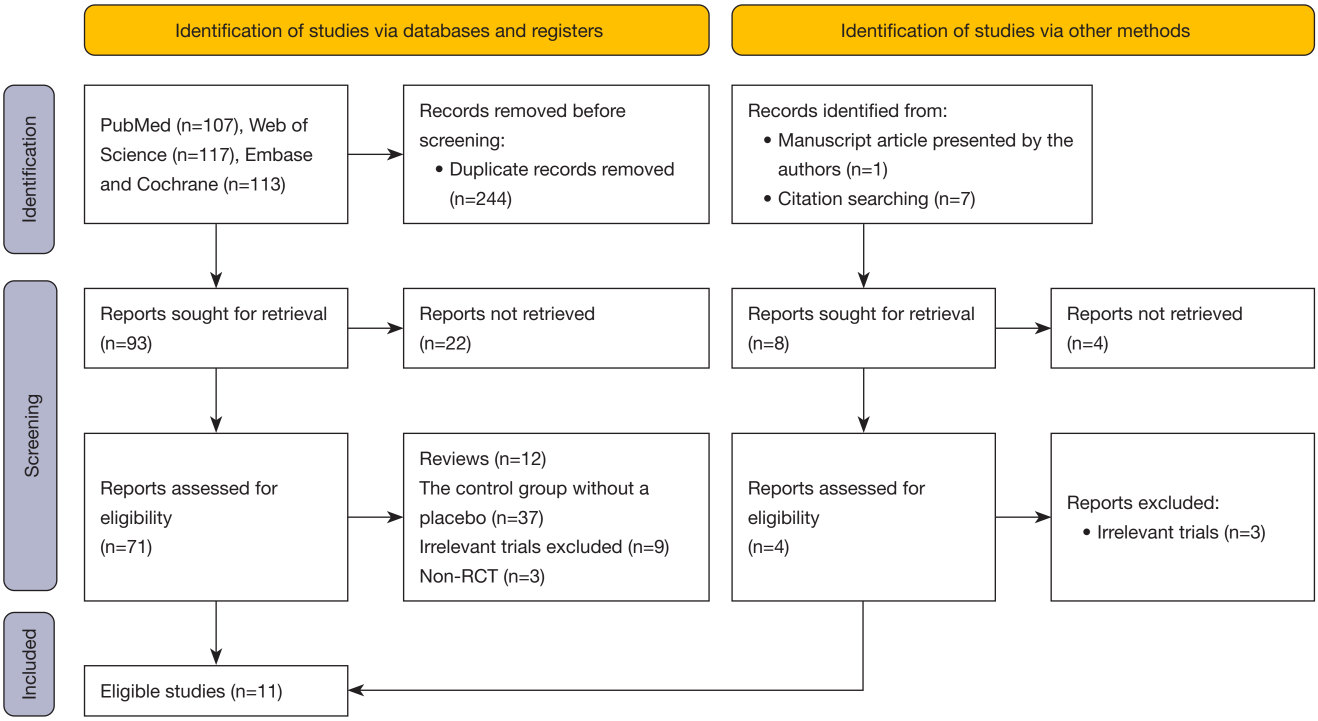

Figure 1 Flowchart of the study selection process. RCT, randomized controlled trial.

Table 1 Clinical data included in this study

First author	Journal	Country/region	Experimental	Control	Result (effective)	Jadad score
Ahmad, R (23)	*Cureus*	Pakistan	Dexamethasone 8 mg/2 mL	Saline (0.9%)	PONV and pain	4
Lee, Y (24)	*Acta anaesthesiologica Sinica*	Taipei	Dexamethasone 5 mg/8 mg	Saline (0.9%)	PONV and pain	5
Worni, M (25)	*Annals of Surgery*	Switzerland	Dexamethasone 8 mg/2 mL	Saline (0.9%)	PONV and pain	7
Doksrod, S (26)	*Acta Anaesthesiologica Scandinavica*	Norway	Dexamethasone 0.15 mg/kg	Saline (0.9%) 2 mL	PONV and pain	6
Feroci, F (27)	*Head & Neck*	Italy	Dexamethasone 8 mg/2 mL	Saline (0.9%) 10 mL	PONV and pain	7
Fujii, Y (28)	*Otolaryngology–Head and Neck Surgery*	Japan	Dexamethasone 4 mg/8 mg	Placebo	PONV	5
Tarantino, I (29)	*Annals of Surgery*	Switzerland	Dexamethasone 8 mg/2 mL	Placebo	PONV	5
Wang, JJ (11)	*Anesthesia & Analgesia*	Taipei	Dexamethasone 10 mg/2 mL	Saline (0.9%) 2 mL	PONV and pain	5
Chen, W (30)	*Journal of the American College of Surgeons*	China	Dexamethasone 10 mg/2 mL	Saline (0.9%) 2 mL	PONV and pain	7
Barros, A (21)	*Pharmacology*	Portugal	Dexamethasone 4 mg/2 mL	Saline (0.9%) 2 mL	PONV and pain	5
Song, YK (31)	*Journal of Anesthesia*	Korea	Dexamethasone 4 mg/2 mL	Saline (0.9%) 2 mL	PONV and pain	6

PONV, postoperative nausea and vomiting.

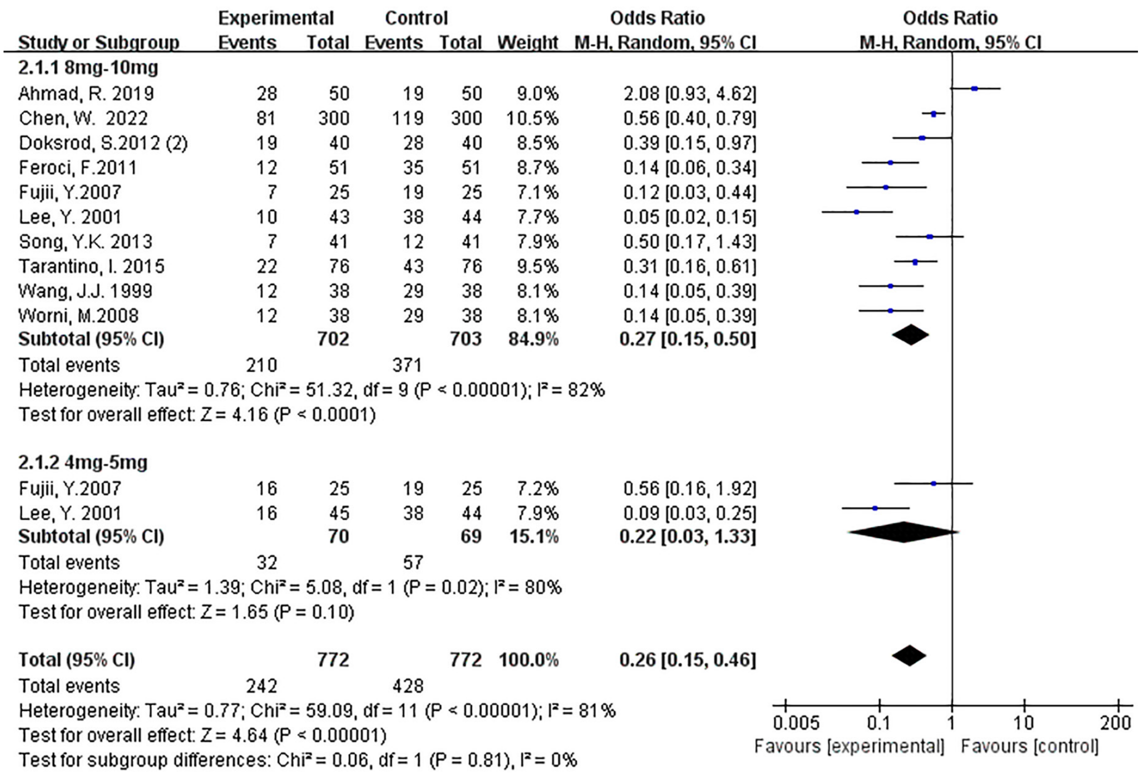

Figure 2 Forest plot comparing the incidence of postoperative nausea and vomiting. CI, confidence interval.

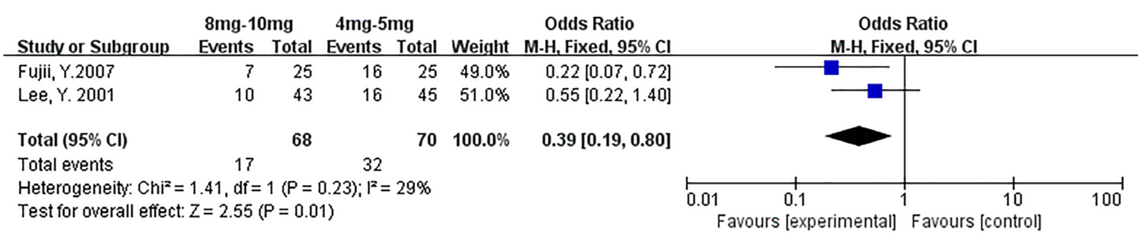

Figure 3 Forest plot comparing the incidence of postoperative nausea and vomiting according to dosage. CI, confidence interval.

dose of 4–5 mg (OR 0.39; 95% CI: 0.19–0.80; I^2=29%; P=0.01), as illustrated in *Figure 3*. Additionally, three studies reported antiemetic usage, and dexamethasone was found to be significantly effective in reducing the use of rescue antiemetics compared to placebo (OR 0.59; 95% CI: 0.38–0.92; I^2=25%; P=0.02), as shown in *Figure 4*.

Efficacy of dexamethasone's in postoperative pain management

The meta-analysis included a total of 722 patients with postoperative pain, with 362 being placed in the dexamethasone treatment group and 360 in a placebo group. The results indicated that administering dexamethasone at a dosage of 8–10 mg can significantly reduce pain VAS score in patients undergoing thyroidectomy (MD: –1.19; 95% CI: –1.97 to –0.41; I^2=96%; P=0.003). However, subgroup analysis for a dosage of 4–5 mg did not demonstrate a significant reduction in pain score (MD: –0.27; 95% CI: –1.00 to 0.45; I^2=0%; P=0.46) (*Figure 5*).

The consumption of analgesics was reported in five studies, but it did not show a significant effect on postoperative pain in the dexamethasone group (MD: –0.19, 95% CI: –0.45 to 0.08; I^2=62%; P=0.16) (*Figure 6*).

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Chen, W. 2022	21	300	26	300	47.6%	0.79 [0.44, 1.44]
Doksrod, S. 2012	8	40	13	40	20.5%	0.52 [0.19, 1.44]
Song, Y.K. 2013	12	41	23	41	32.0%	0.32 [0.13, 0.81]
Total (95% CI)		**381**		**381**	**100.0%**	**0.59 [0.38, 0.92]**
Total events	41		62			

Heterogeneity: Chi² = 2.66, df = 2 (P = 0.26); I² = 25%
Test for overall effect: Z = 2.34 (P = 0.02)

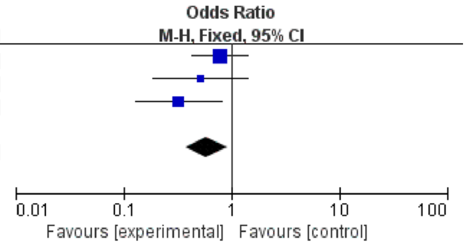

Figure 4 Forest plot comparing the use of rescue antiemetics. CI, confidence interval.

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
3.1.1 8mg-10mg								
Ahmad, R. 2019	1.6	1.26	50	3.6	1.94	50	11.3%	-2.00 [-2.64, -1.36]
Doksrod, S. 2012	3.8	0.7	40	3.5	0.67	40	12.2%	0.30 [-0.00, 0.60]
Feroci, F.2011	1.71	1.976	51	3.27	2.016	51	10.8%	-1.56 [-2.33, -0.79]
Lee, Y. 2001	1.9	0.45	43	2.8	0.5	44	12.4%	-0.90 [-1.10, -0.70]
Song, Y.K. 2013	3.2	0.87	41	3.95	0.95	41	12.0%	-0.75 [-1.14, -0.36]
Wang, J.J. 1999	3.1	0.525	38	5.7	0.95	38	12.1%	-2.60 [-2.95, -2.25]
Worni, M.2008	1.54	1.59	37	2.42	2.06	35	10.5%	-0.88 [-1.73, -0.03]
Subtotal (95% CI)			**300**			**299**	**81.4%**	**-1.19 [-1.97, -0.41]**
Heterogeneity: Tau² = 1.03; Chi² = 168.26, df = 6 (P < 0.00001); I² = 96%								
Test for overall effect: Z = 2.99 (P = 0.003)								
3.1.2 4mg-5mg								
Barros, A.2013	2.2	1.5	17	2.4	0.9	17	10.6%	-0.20 [-1.03, 0.63]
Lee, Y. 2001	2.3	3.6	45	2.8	3.4	44	8.0%	-0.50 [-1.95, 0.95]
Subtotal (95% CI)			**62**			**61**	**18.6%**	**-0.27 [-1.00, 0.45]**
Heterogeneity: Tau² = 0.00; Chi² = 0.12, df = 1 (P = 0.73); I² = 0%								
Test for overall effect: Z = 0.74 (P = 0.46)								
Total (95% CI)			**362**			**360**	**100.0%**	**-1.03 [-1.72, -0.34]**

Heterogeneity: Tau² = 0.98; Chi² = 171.80, df = 8 (P < 0.00001); I² = 95%
Test for overall effect: Z = 2.93 (P = 0.003)
Test for subgroup differences: Chi² = 2.85, df = 1 (P = 0.09), I² = 64.9%

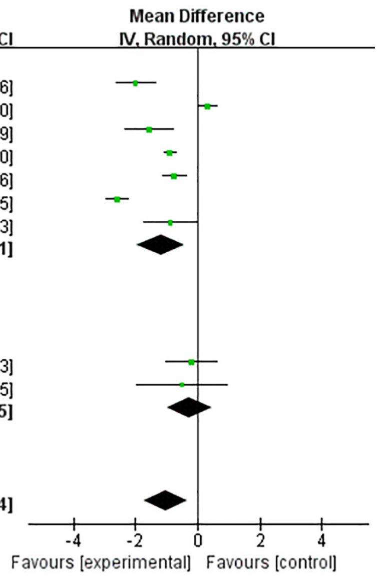

Figure 5 Forest plot comparing the pain score according to different dexamethasone dosages. SD, standard deviation; CI, confidence interval.

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Barros, A.2013	0.3	0.057	17	0.4	0.036	17	52.0%	-0.10 [-0.13, -0.07]
Chen, W. 2022	13	91.5	300	21.67	116.87	300	0.0%	-8.67 [-25.47, 8.13]
Doksrod, S. 2012	1.7	2	40	1.4	1.9	40	8.0%	0.30 [-0.55, 1.15]
Feroci, F.2011	8.57	13.75	51	12.85	15.06	51	0.2%	-4.28 [-9.88, 1.32]
Worni, M.2008	0.91	0.4	37	1.28	0.48	35	39.8%	-0.37 [-0.57, -0.17]
Total (95% CI)			**445**			**443**	**100.0%**	**-0.19 [-0.45, 0.08]**

Heterogeneity: Tau² = 0.03; Chi² = 10.53, df = 4 (P = 0.03); I² = 62%
Test for overall effect: Z = 1.39 (P = 0.16)

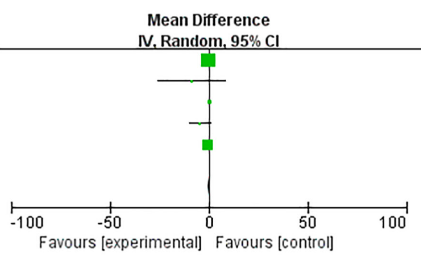

Figure 6 Forest plot comparing analgesic consumption. SD, standard deviation; CI, confidence interval.

Sensitivity analysis and publication bias

Regarding the analysis on sensitivity and publication bias, we observed asymmetry in the funnel plot (*Figure 7*), indicating potential publication bias in assessing the treatment effectiveness for PONV. To further evaluate this, we conducted TSA with α and β error thresholds set at 0.05 and 0.2, respectively, to assess the adequacy of the sample size for evaluating the effect of the intervention. Our TSA analysis showed that the cumulative Z curve crossed both the traditional and the monitoring boundaries at each time point, indicating that the available evidence was sufficient to establish the intervention effect of dexamethasone in preventing PONV. Additionally, TSA analysis indicated that the required sample size was 544 cases, and the cumulative Z curve did exceed the expected sample size (*Figure 8*).

The points indicating the effectiveness of treatments for pain in the funnel plot suggested the presence of publication bias (Figure S1). In our TSA analysis, the cumulative Z curve crossed the traditional boundary, but did not cross the monitoring boundary and thus did not exceed the expected sample size (Figure S2).

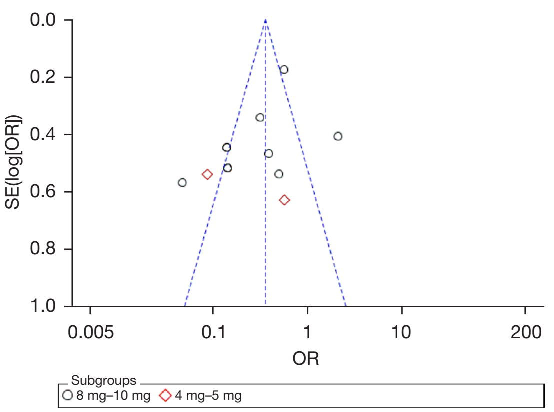

Figure 7 Funnel plot of publication bias for literature on dexamethasone in preventing postoperative nausea and vomiting. SE (log [OR]), the standard error of the logarithm of the effect size. SE, standard error; OR, odds ratio.

Discussion

PONV are the most common postoperative complications, and early prevention and treatment are crucial for avoiding complications, improving patient satisfaction, and accelerating recovery (32,33). Studies have shown that PONV rates in patients undergoing thyroidectomy exceed 80% (34). Lee *et al.* conducted a RCT and found that administering 8 mg of dexamethasone was more effective than was 5 mg for relieving PONV in female patients after surgery for thyroid cancer (24). In a recent systematic review, Li *et al.* concluded that while dexamethasone can reduce the severity of PONV in patients undergoing thyroidectomy, it does not improve patients' postoperative pain (19). However, research by Ahmad *et al.* showed that prophylactic use of dexamethasone can significantly reduce pain in patients undergoing thyroidectomy but did not find a statistically significant correlation with PONV (23). Inconsistency in drug dosage and inconsistent effects on pain make it challenging to provide consistent clinical and nursing care guidance. To address this confusion, the meta-analysis was conducted in which 8 to 10-mg and 4 to 5-mg doses of dexamethasone were used as grouping criteria. The aim of this study was to standardize the preoperative dexamethasone dosage for improved prevention of PONV and pain in patients undergoing surgery for thyroid cancer. A random-effects model was employed to assess the effectiveness of dexamethasone in reducing the incidence of PONV with preoperative doses. The results indicated

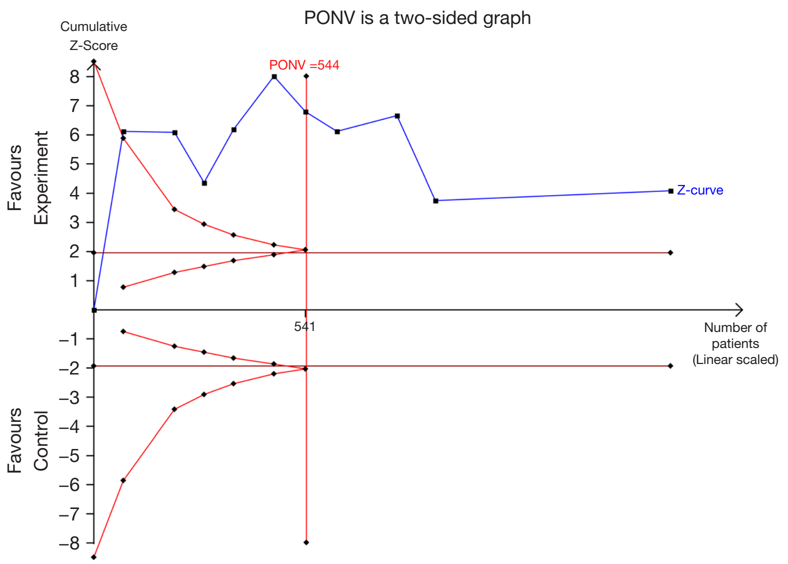

Figure 8 Trial sequential analysis of postoperative nausea and vomiting prevention. PONV, postoperative nausea and vomiting.

that dexamethasone at 8–10 mg was effective in reducing PONV, which is consistent with Li *et al.*'s study (19).

The American Society of Anesthesiologists recommends the use of multimodal methods to manage acute pain after surgery, including drugs with various mechanisms of action such as α2 agonists, N-methyl-D-aspartate (NMDA) receptor antagonists, nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, and duloxetine (35). Dexamethasone, a corticosteroid, has not been extensively discussed in the scientific literature in relation to its potential to introduce complications in microvascular reconstruction surgeries for patients with head and neck cancer (36). Nevertheless, it is worth highlighting that numerous studies offer substantial evidence supporting its effectiveness in effectively alleviating postoperative pain and reducing overall opioid consumption. For example, it has played a pivotal role in expediting the recovery process following total knee arthroplasty (37). Postthyroidectomy pain may result from several factors, including pain at the surgical site incisions, extensive neck manipulation, general anesthesia during intubation, and throat discomfort (38). Studies conducted by Worni *et al.* and Feroci *et al.* indicated that the preoperative use of dexamethasone may effectively reduce postoperative vomiting and pain in patients undergoing thyroid surgery (25,27). However, a systematic review found that it may not affect the pain level or analgesic consumption, while a single preoperative application of dexamethasone can reduce the incidence and severity of PONV after thyroidectomy (19). Our meta-analysis showed that administering dexamethasone at a dosage of 8–10 mg can significantly reduce pain in patients undergoing thyroidectomy. It is worth noting that of the 11 studies, only Tarantino *et al.*'s study reported that anesthesia combined with a cervical plexus block resulted in a decrease in pain scores, with no differences in postoperative pain observed between the dexamethasone treatment group and the control group (29). Furthermore, this study was not included in our pain analysis, so the analysis results of dexamethasone for pain relief were not affected.

After conducting sequential TSA tests, we believe that there is no need to conduct further trials to clarify the effect of dexamethasone in relieving PONV. However, based on the above analysis, the funnel plot on the effectiveness of treatments for pain suggested the presence of publication bias. Therefore, we can also conclude that the available evidence on the preoperative administration of dexamethasone for pain relief in patients undergoing thyroidectomy is not sufficient.

Conclusions

Based on the available evidence, it appears that a single preoperative dose of 8–10 mg of dexamethasone can be effective in reducing the incidence of PONV and pain in patients undergoing thyroidectomy. However, further research is needed to fully understand the effects of dexamethasone on pain relief after thyroidectomy. Large-scale RCTs would be particularly valuable in investigating the potential benefits and drawbacks of this treatment approach.

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Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at https://gs.amegroups.com/article/view/10.21037/gs-23-260/rc

Peer Review File: Available at https://gs.amegroups.com/article/view/10.21037/gs-23-260/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://gs.amegroups.com/article/view/10.21037/gs-23-260/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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