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Review

Dexamethasone combined with other antiemetics versus single antiemetics for prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy: An updated systematic review and meta-analysis

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HIGHLIGHTS

- Our meta-analysis shows that adding dexamethasone to antiemetic drugs increases their prophylactic effect against PONV after LC.
- The need for a rescue antiemetic was significantly lower in the combination group, compared to single antiemetic group.
- Future trials should define the optimal prophylactic dose and the underlying mechanism of dexamethasone antiemetic effect.

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ABSTRACT

Objective: A systematic review and meta-analysis of published randomized controlled trials was performed to update the present evidence about the safety and efficacy of dexamethasone combined with other antiemetics versus single antiemetics for the prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy.

Methods: A computer literature search of PubMed, Scopus, Web of Science and Embase was conducted to identify the relevant randomized controlled trials. In addition, a manual search of reference lists of the retrieved articles was conducted. Relevant outcomes were pooled as odds ratio (OR) by RevMan version 5.3 for windows.

Results: Pooled data from 14 RCTs (1542 patients) favored dexamethasone combined with other antiemetics over single antiemetics as a prophylaxis against postoperative nausea and vomiting after laparoscopic cholecystectomy in the early postoperative period (OR = 0.39, 95% CI [0.27 to 0.54], $p < 0.00001$), late postoperative period (OR = 0.36, 95% CI [0.23 to 0.56], $p < 0.00001$), and overall postoperative period (OR = 0.34, 95% CI [0.23 to 0.51], $p < 0.00001$). Subsequently, rescue antiemetic usage was significantly lower in the combination group (OR = 0.25, 95% CI [0.16 to 0.41], $p < 0.00001$). Subgroup analysis showed that all combinations of dexamethasone and other antiemetics were superior to corresponding singel antiemetics except for the combination of dexamethasone and ramosetron which was not superior to ramosetron alone in all postoperative periods and the combination of dexamethasone and granisetron which was not superior to granisetron alone in the early postoperative period (OR = 0.26, 95% CI [0.07 to 1.01], $p = 0.05$). For all adverse events, there was no significant difference between the two groups.

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Conclusion: Dexamethasone combined with other antiemetics provided better prophylaxis than single antiemetics against postoperative nausea and vomiting after laparoscopic cholecystectomy. The underlying mechanism of dexamethasone action and its optimal dose should be further investigated.

1. Introduction

Since its first introduction in 1985, laparoscopic cholecystectomy (LC) has become the standard of care in patients with symptomatic cholelithiasis and has replaced open cholecystectomy for the management of uncomplicated gallbladder disease [1,2]. This technique is widely used around the world because it allows a shorter hospital stay, an earlier return to work and normal activities with less pain associated with the smaller incision and less postoperative ileus, compared to open cholecystectomy [1,3]. However, postoperative nausea and vomiting (PONV) are among the most common distressing side effects associated with LC [1,4–8]. The incidence of PONV after LC ranges from 53% to 72% according to operative, anesthetic and patient-related risk factors [5,8,9]. Untreated PONV increase the risk of post-operative bleeding, wound dehiscence, gastric aspiration and electrolyte imbalance [10]. Moreover, they can prolong post-anesthesia care unit (PACU) stay and cause unexpected hospital admissions that significantly increase the overall health care costs [2,6,11]. Prophylaxis against PONV is essential, especially in high risk patients including females, patients on post-operative opioids and those with a history of motion sickness or PONV [12].

Dexamethasone is a steroid, showed to have a potent antiemetic activity [13]. However, PONV are multifactorial in origin and none of the available antiemetics, including dexamethasone, is solely effective to prevent them [2,11,14,15]. Therefore, several studies added other antiemetics to dexamethasone to improve the antiemetic effect by acting on different receptors [16].

Si et al. [12] conducted a meta-analysis of RCTs comparing dexamethasone combined with other antiemetics versus single antiemetics for prophylaxis against PONV after laparoscopic cholecystectomy. Following the search date of this meta-analysis, several other much larger studies were published. Moreover, it included trials of questioned validity, performed by the author Yoshitaka Fujii. Establishing the precise safety and efficacy of dexamethasone combined with other antiemetics is essential to manage PONV after LC. Therefore, we conducted a meta-analysis to update and broaden the present evidence from published randomized controlled trials (RCTs) about the safety and efficacy of dexamethasone combined with other antiemetics versus single antiemetics for the prevention of PONV after LC.

2. Methods

We followed the preferred reporting items for systematic reviews and meta-analysis (PRISMA) statement guidelines during the preparation of this review and meta-analysis [17]. However, this study was not prospectively registered.

2.1. Inclusion and exclusion criteria

Original studies were included if they met the following inclusion criteria: (I) studies that were randomized controlled trials (RCTs), comparing dexamethasone plus another antiemetic with single antiemetics; (II) studies that enrolled patients undergoing laparoscopic cholecystectomy; and (III) studies that reported the incidence of PONV in each group as dichotomous data.

Exclusion criteria were: (I) non-randomized trials, observational studies, experimental studies, reviews, book chapters, and theses; (II) studies whose full-texts were not available; (III) studies that contained false statements or retracted by the journal; (IV) studies that were not available in the English language; and (V) studies whose data were not reliable for extraction or analysis.

2.2. Literature search strategy

A computer literature search of PubMed, Scopus, Web of Science and Embase was conducted through August 2016 using the following query: “dexamethasone AND cholecystectomy”. We also checked the reference lists of the retrieved articles to make sure that no relevant studies were missed. After removal of duplicates by Endnote X7 (Thompson Reuter, CA, USA), four independent authors screened the retrieved citations in two steps; the first step was to screen the titles and abstracts for eligibility and the second step was to screen the full-text articles of the eligible abstracts according to the aforementioned criteria. Disagreements were resolved upon the opinion of another reviewer.

2.3. Data extraction

Two authors extracted the data independently using an online data extraction form. The extracted data included the following: (1)

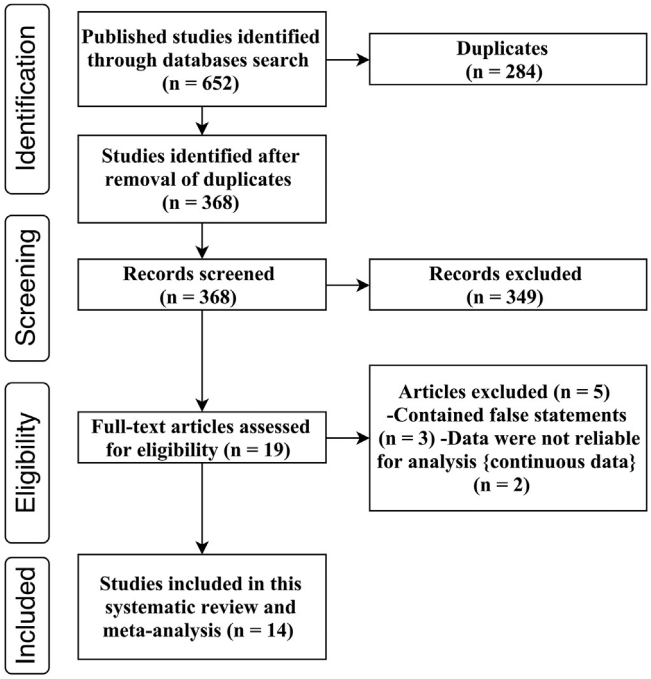

Fig. 1. Shows the PRISMA flow diagram of studies' screening and selection.