EFFECT OF PROPHYLACTIC DEXAMETHASONE ON NAUSEA AND VOMITING AFTER LAPAROSCOPIC GYNECOLOGICAL OPERATION: META-ANALYSIS

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Abstract

Keywords: dexamethasone; postoperative nausea and vomiting; laparoscopic gynecological operation; meta-analysis

Background: Sex of female and laraproscopic surgery are both risk factors related to postoperative nausea and vomiting, and dexamethasone is used as anti-emetic in some operations. A meta-analysis of randomized trials was performed to determine the effect of prophylactic dexamethasone administration on postoperative nausea and vomiting, pain and complications in patients undergoing laparoscopic gynecological operation.

Methods: A systematic literature search was conducted to identify all randomized clinical trials. The primary outcome was the incidence and severity of postoperative nausea and vomiting. The secondary outcomes include postoperative pain and complications.

Results: Totally 1801 patients were enrolled in 11 eligible randomized trials comparing effect of prophylactic dexamethasone administration on postoperative nausea and vomiting with placebo. The pooled incidence of nausea, vomiting, nausea and vomiting, and rescue anti-emetic was significantly lower in dexamethasone group than placebo group during post-anesthesia care unit (10.5% vs 18.2%, OR 0.51, 95% CI 0.31-0.84; 6.5% vs 17.1%, OR 0.31, 95% CI 0.17-0.56; 17.0% vs 35.4%, OR 0.33, 95% CI 0.21-0.50; 6.7% vs 23.3%, OR 0.22, 95% CI 0.10-0.49, P<0.00001) and within the first postoperative 24 hours (25.2% vs 40.3%, OR 0.46, 95% CI 0.32-0.66; 14.4% vs 36.6%, OR 0.27, 95% CI 0.19-0.40; 33.0% vs 69.0%, OR 0.18, 95% CI 0.13-0.26; 21.0% vs 51.1%, OR 0.26, 95% CI 0.16-0.41, P<0.00001). No significant difference was found about the incidence of rescue analgesia between dexamethasone group and placebo group (48.5% vs 56.4%, OR 0.68, 95% CI 0.40-1.18, P=0.17).

Conclusion: Prophylactic dexamethasone administration decreases the incidence of nausea and vomiting after laparoscopic gynecological operations during post-anesthesia care unit and within the first postoperative 24 hours. (286 words)

Postoperative nausea and vomiting are the most common complications after anesthesia and surgery, and both sex of female and type of laparoscopic operation are risk factors[1]. It is certain of a remarkably high incidence after laparoscopic gynecological surgery, which is reported as nearly 70% within the first postoperative 24 hours[2]. It is very important to find an effective treatment to alleviate postoperative nausea and vomiting.

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Dexamethasone was first used as an anti-emetic in patients receiving chemotherapy for cancer treatment by a central mechanism involving endogenous prostaglandin and opioid production[3,4]. And then some trials showed that dexamethasone alone or combination with traditional anti-emetics may decrease the incidence and severity of postoperative nausea and vomiting[5,6]. Furthermore, perioperative dexamethasone administration may decrease postoperative pain by modulationg the systemic physiologic response in favor of anti-inflammatory mediators. Researchers have reviewed the pathophysiologic effects and clinical implications of perioperative dexamethasone administration, but the variability in surgical procedures has precluded definitive conclusions regarding the effectiveness of dexamethasone[5].

The present meta-analysis was conducted to determine the effect of prophylactic dexamethasone administration on postoperative nausea and vomiting, pain, and complications after laparoscopic gynecological operation.

Methods

Criteria for study selection

Randomized clinical trials that investigate effect of prophylactic dexamethasone administration on postoperative nausea and vomiting in patients undergoing laparoscopic gynecological operations were included.

Data sources and search strategy

We carried out this meta-analysis in accordance with the standard protocol recommended by the quality of reporting of meta-analyses group and the guidelines of Cochrane handbook of systematic reviews of interventions 4.2. We searched Pubmed, EMBASE, ISI Web of Science and the Cochrane Central Register of Controlled Trials for randomized trials investigate impact of prophylactic dexamethasone administration on postoperative nausea and vomiting in patients undergoing laparoscopic gynecological operations. We included following terms: laparoscopic, gynecological operation, steroid, dexamethasone, nausea, vomiting. Searches were restricted to the period from January 1, 1998 to December 31, 2009 and language of English.

Classification of outcome and definitions

The outcome of interest included the incidence and severity of postoperative nausea and vomiting, and one or more of pain, postoperative complications. The incidence and severity of postoperative nausea and vomiting were evaluated using these four variables: the incidence of (1) nausea, (2) vomiting, (3) PONV (nausea + vomiting), and (4) rescue anti-emetic used. And retching was considered as vomiting. Furthermore, the incidence and severity of postoperative nausea and vomiting included two time interval: during post-anesthesia care unit (PACU) and within the first postoperative 24 hours. Postoperative pain was assessed as the incidence of rescue analgesia.

Data abstraction and assessment of quality

Studies were selected and data were extracted independently by two reviewers. Disagreements were resolved by consensus. We referred to the guidelines of the Cochrane handbook for systematic reviews of interventions 4.2 for our meta-analysis.

Statistical methods

Binary outcomes from individual studies were analyzed according to the Mantel–Haenszel model to compute individual odds ratios (*ORs*) with pertinent 95% confidence intervals (*CIs*), and a pooled summary effect estimate was calculated by means of fixed effect. Statistical heterogeneity and inconsistency was measured using, respectively, Cochran Q tests and I^2 values. Computations were performed with SPSS 11.0 (SPSS, Chicago, IL) and RevMan 4.2 (a freeware available from The Cochrane Collaboration). All P values were two-sided, and $P<0.05$ was considered as statistically significant.

Results

Description of included studies

Overall 11 randomized double-blind clinical trials[7-17] investigate effect of prophylactic dexamethasone administration on postoperative nausea and vomiting in patients undergoing laparoscopic gynecological operations were identified, in which 1801 patients were involved, and all belonged to

Table 1
Prophylactic dexamethasone administration

Trial	Dexamethasone administration	Rescue-antimetic	Rescue analgesia
Chu	dexamethasone 5 mg, iv 15 min after induction	Ondansetron 4 mg iv	Ketorolac 30 mg iv
Fujii	Dexamethasone 4 mg/8 mg, iv At end of the sugery	Not mentioned	50 mg indomethacin rectally
Michael	Dexamethasone 4 mg/2mg, iv At end of the sugery	Prochlorperazine 12.5 mg iv, followed by droperidol 1 mg iv as necessary	Not mentioned
Yuksek	Dexamethasone 8 mg, iv 2 min before induction	Metroclopramide 10 mg, iv	3 mg morphine first, and 50 μg fentanyl repeated if necessary
Maddali	Dexamethasone 8 mg, iv 2 min before induction	Not mentioned	Not mentioned
Lee	Dexamethasone 8 mg, iv 2 min before induction	Metoclopramide 10 mg, iv	Ketorolac 15 mg iv
Eliana	Dexamethasone 8 mg, iv 2 min before induction	Ondansteron 4 mg iv	Tramadol 50 mg iv
Huang	Dexamethasone 5 mg, iv After tracheal intubation	Ondansteron 4 mg iv	Not mentioned
wang	Dexamethasone 10 mg, iv at induction	Ondansteron 4 mg iv	Not mentioned
Rajeeva	Dexamethasone 8 mg, iv after induction	Metoclopramide 0.15 mg/kg, iv	75mg diclofenac im
Rothenberg	Dexamethasone 0.017 mg/kg, iv, just prior to abdominal incision	Not mentioned	Ketorolac 30-60 mg iv, then morphine 1-2 mg iv if necessary

ASA(America Society of Anethesiologists) grade I or II. Laparoscopic operations included tubal ligation, myonectomy, hysterectomy, salpingo-oophorectomy, oophorocysterctomy and diagnostic laparoscopy.

All of the studies administered a single dose of dexamethasone intravenously, with the timing of administration ranging from immediately before anesthesia induction to the end of the surgery (Table

Fig. 1
Forest plot for the comparison of incidence of nausea, vomiting, PONV, and need for rescue anti-emetic during PACU between dexamethasone group and placebo group.

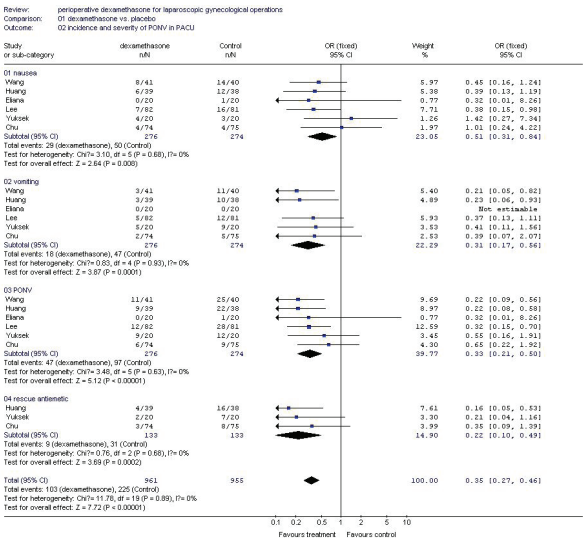


Fig 2
Forest plot for the comparison of incidence of nausea, vomiting, PONV, and need for rescue anti-emetic within 24 h between dexamethasone group and placebo group.

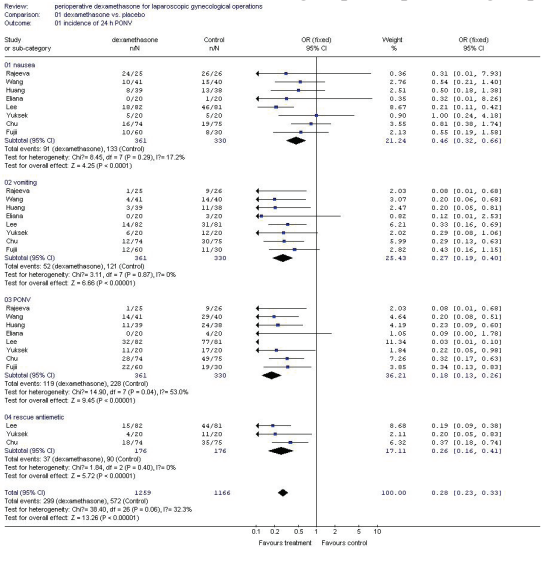


Table 2
Baseline characteristics of patients

Trial	n	Age (y) *	Weight (kg)*	MS (%)	Previous PONV (%)	Smoker (%)	To (min)*	Ta (min)*
Chu	372	43.1(4.7)	57.2(9.2)	17	7	----	91.9(24.8)	114.5(29.0)
Fujii	90	35.6(6.4)	53.0(7.0)	0	0	27	85.3(33.1)	123.0(34.6)
Michael	614	32.5(6.3)	64.0(6.8)	----	16	38	---	40.0(18,1)
Yuksek	60	31.1(5.2)	61.9(7.3)	0	----	----	57.3(10.6)	71.7(16.4)
Maddali	120	29.1(7.2)	62.8(12.6)	----	-----	----	62.9(24.6)	----
Lee	164	39.3(8.0)	56.9(6.8)	0	0	0	113.8(23.0)	137.9(21.9)
Eliana	40	30.5(6.5)	60.5(10.1)	0	0	----	62.0(37.7)	88.5(37.6)
Huang	115	34.0(6.4)	55.0(7.7)	0	0	----	42.0(12.2)	65.0(17.3)
wang	81	33.0(6.2)	55.0(8.1)	---	----	----	44.0(11.8)	66.5(17.3)
Rajeeva	51	28.7(4.8)	49.8(6.7)	0	0	----	28.7(4.0)	----
Rothenberg	94	32.0(5.5)	66.1(7.8)	12	8	----	41.8(12.7)	----

* mean(sd); MS: motion sickness; To: time of operation; Ta: time of anesthesia

1). All the studies measured incidence of postoperative nausea and vomiting, and a substantial proportion measured pain. Not enough reported complications, health-related quality of life or hospital length of stay to allow us to pool the results. The baseline characteristics revealed a relatively young and healthy population, and a relatively short time of anesthesia and operation (Table 2).

Effect of prophylactic dexamethasone administration on postoperative nausea and vomiting

The incidence of nausea, vomiting, PONV, and need for rescue anti-emetic was significantly lower in dexamethasone group than in placebo group during PACU (10.5% vs 18.2%, *OR* 0.51, 95% *CI* 0.31-0.84; 6.5% vs 17.1%, *OR* 0.31, 95% *CI* 0.17-0.56; 17.0% vs 35.4%, *OR* 0.33, 95% *CI* 0.21-0.50; 6.7% vs 23.3%, *OR* 0.22, 95% *CI* 0.10-0.49, $P<0.00001$) (Fig. 1) and within the first postoperative 24 hours (25.2% vs 40.3%, *OR* 0.46, 95% *CI* 0.32-0.66; 14.4% vs 36.6%, *OR* 0.27, 95% *CI* 0.19-0.40; 33.0% vs 69.0%, *OR* 0.18, 95% *CI* 0.13-0.26; 21.0% vs 51.1%, *OR* 0.26, 95% *CI* 0.16-0.41, $P<0.00001$) (Fig. 2).

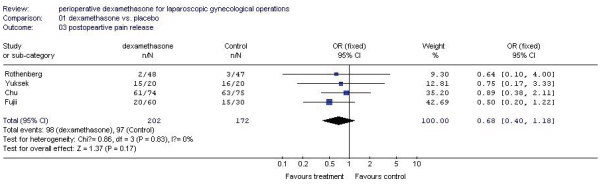
Effect of prophylactic dexamethasone administration on postoperative pain

The incidence of rescue analgesia in dexamethasone group was lower than in placebo group (48.5% vs 56.4%, $P=0.17$), which suggest a trend toward less need for rescue analgesia in dexamethasone group although the CI was wide (*OR* 0.68, 95% *CI,* 0.40-1.18) (Fig. 3).

Discussion

This meta analysis identified 11 randomized and double-blind trials, which investigate the effect of prophylactic dexamethasone administration on postoperative nausea and vomiting in patients undergoing laparoscopic gynecological operations. Although the trials varied with different other anti-emetics, every trial compared dexamethasone with placebo, and presented data for us to pool the results. The pooled results showed that prophylactic dexamethasone administration decreased incidence and severity of postoperative nausea and vomiting during PACU and within the first postoperative 24 hours.

Fig. 3
Forest plot for the comparison of rescue analgesics between dexamethasone group and placebo group.



Prophylactic dexamethasone was administered at different time, varied from 2 minutes before induction to at the end of the operation. Most trials administered dexamethasone soon before or after induction, while just one trial prior to the abdominal incision, and two at the end of the surgery. The optimal timing of dexamethasone administration is still unclear because there was no significant difference between trials with different time of administration.

8 mg or more dexamethasone was administered in 8 trials, and 5 mg or less dexamethasone was administerd in 3 trials. Any dose can decrease incidence and severity of postoperative nausea and vomiting compared with placebo. 8 mg or more dexamethasone was more effective than 5 mg or less on prevention PONV (32% vs 38%). And so 8 mg or more dexamethasone was suggested.

This meta-analysis showed lower incidence of rescue analgesia in dexamethasone group than in placebo group, but the difference was not significantly, which was not consistent with other studies[18]. With repeated reading the trials, all the trials paid more attention to postoperative nausea and vomiting, while only a few trials investigated pain simultaneously, and so a relatively less data about pain could be collected. Another aspect should be taken account that 354 patients underwent diagnostic laparoscopic operation, which was minimal invasive and hardly induced pain. And so it was sure that there was a trend a less need for rescue analgesia in dexamethasone group.

All the trials did not report serious adverse events after prophylactic dexamethasone administration, which suggested its safety. Furthermore, dexamethasone was very cheap compared with other types of anti-emetics. That is to say, dexamethasone is both safe and economic drug to prevent postoperative nausea and vomiting.

Certainly, there are several limitations in this meta-analysis. First, it suffers from inherent limitations of any analysis of aggregate data from published reports to lump study ourcomes rather than data from individual patients. Second, the conclusion of our meta-analysis can not be confined to all patients undergoing laparoscopic gynecological operations, since all the trials excluded obese patients. In fact, there are more and more obese patients. At the same time, our meta-analysis just included trials reported in English.

In conclusion, prophylactic dexamethasone decreases the incidence of nausea and vomiting after laparoscopic gynecological operations during PACU and within the first postoperative 24 hours.

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