

Comparing Prophylactic Effect of Dexamethasone Alone Vs Combination of Dexamethasone and Ondansetron on Nausea and Vomiting in Pregnant Women Undergoing Cesarean Section: A Systematic Review and Meta-Analysis of Published Randomized Controlled Trials

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Abstract:

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The efficacy of dexamethasone and ondansetron on intra and post-operative nausea and vomiting is confusing and still debatable. We conducted this systematic review and meta-analysis to synthesize evidence from published studies on the efficacy and the impact of dexamethasone and ondansetron for cutting the risk of nausea and vomiting in pregnant women. We followed the standard methods of the Cochrane Handbook of Systematic Reviews for interventions and the PRISMA statement guidelines 2020 when conducting and reporting this study. A computer literature search- of PubMed, Scopus, Web of Science, and Cochrane Central Register of Controlled Trials- conducted from inception until January 2022. We selected randomized controlled trials (RCTs) assessing the efficacy of dexamethasone alone Vs combination of dexamethasone and ondansetron, on nausea and vomiting in pregnant women undergoing cesarean section. All relevant outcomes were pooled in the meta-analysis using Review Manager Software. Five RCTs were included in our study with only four RCTs included in the meta-analysis. The pooled risk ratio suggested that there is no significant difference between Ondansetron and combination or dexamethasone in reducing pre-operative vomiting as following respectively: [RR=1.9,95%CI (0.164,22.2), P= 0.605], and [RR=0.549, 95%CI (0.160,1.882), P=0.17]. Also, regarding pre-operative nausea there is no significant difference between ondansetron and combination or between dexamethasone and combination as following: [RR =0.7,95%CI (0.3,1.64), P=0.41], and [RR =1.91,95%CI(0.98,3.71),P=0.06]. while combination intervention reduces the incidence of post-operative nausea and vomiting compared to both ondansetron and dexamethasone as following respectively:[RR

=2.44,95% CI (1.28,4.63),P=0.007],and[RR= 7.29,95% CI (2.46,21.54),P= 0.0003]. Combination of dexamethasone and ondansetron reduce intra operative vomiting and post-operative nausea and vomiting.

Keywords: Emesis, dexamethasone, intraoperative, ondansetron, caesarean.

Introduction

Nausea and vomiting are well known distressing complications that commonly occur during spinal anesthesia in women undergoing elective cesarean section. The incidence rate of nausea and vomiting reached 80% (1, 2). Recently, this incidence rate was found to be 66% of total patients(3). Mental status of the patient, stretching over visceral peritoneum, over tightening of the uterus, and the procedure itself- are all directly affecting the occurrence of these complications (4, 5). There is no doubt that nausea and vomiting during operation are distressing. They may disrupt the diaphragmatic contraction and cause abdominal visceral protrusion (6). By the end, the operation will be more difficult.

Usual agents that prevent these nausea and vomiting have many side effects like extrapyramidal manifestation(7). Ondansetron which is antagonist to 5-hydroxytryptamine 3 (5HT3) was found to be capable of minimizing intra or post-operative nausea and vomiting but can't completely prevent it totally(7). On the other hand, Dexamethasone- which is anti-emetic and anti-inflammatory agent- can

totally prevent nausea and vomiting (8). Anti-emetic mechanism of dexamethasone isn't clear, but this may be mediated through prostaglandin inhibition and by its anti-inflammatory effect (9).

We should take into consideration that all antiemetic agents should be given after clamping the cord (10).

In our systematic review and meta-analysis, we aim to synthesize evidence from published studies on the efficacy and the impact of dexamethasone alone Vs combination of dexamethasone and ondansetron on peri-operative nausea and vomiting in pregnant women undergoing cesarean section.

Methods:

We conducted our study according to Systematic Review and Meta-Analysis (PRISMA) criteria in conducting this meta-analysis(11).

Search strategy

We utilized results from PubMed, Cochrane Library, Web of Science, and SCOPUS. We searched by using Mesh terms of Dexamethasone, Ondansetron and cesarean section and included any available randomized control trial (RCT)

which compared Dexamethasone or ondansetron or a combination of both. We conducted our search on 3 February 2020. We excluded irrelevant articles which didn't follow our PICO's criteria. Also, we included only English papers with available full text published in 2012 till now.

Inclusion criteria (PICO's)

P: females undergoing cesarean delivery.

I: Dexamethasone or ondansetron or combination.

C: compared with each other.

O: nausea and vomiting intraoperative and postoperative.

S: RCTs.

Data extraction

We extracted the following data from each study: (1) the name of the first author and the publishing year of the article, (2) Site, (3) study design, (4) inclusion criteria, (5) primary outcome, (6) results for each study, (7) sample; (8) age at baseline (9), and (10) weight (Kg). Also, we extracted the results of the data related to our outcomes which included nausea and vomiting intra-operative and post-operative.

Risk of bias assessment

We used the Cochrane Handbook for Systematic Reviews of Interventions, Second Edition, to evaluate the quality of

RCTs. Methodological quality was evaluated in light of the selection and performance biases, as well as detection and attrition biases, that were found. An "+" means the study had no bias, while a "?" means the study had one or more unclear criteria, and a "-" means the study had high risk of bias(12).

Statistical analysis

We conducted our meta-analysis using the Review manager V5.4 and Open meta-analyst software. For each outcome, risk ratios (RR) and 95% confidence intervals were calculated. We measured the degree of heterogeneity using Cochrane's Q tests and I² statistics. A P-value of 0.05 or an I² of 50% indicated considerable heterogeneity. To minimize heterogeneity, we used a random-effects model. A p-value higher than 0.1 was considered statistically significant.

Study selection process and characteristics of studies:

By using our search strategy, we found 219 articles in these databases. After reviewing their titles and abstracts, we ruled out 207 articles. Among the remaining 12 articles, seven articles were excluded. Finally, five studies were involved (13-17). Of them, four studies were included in our analysis Fig 1.

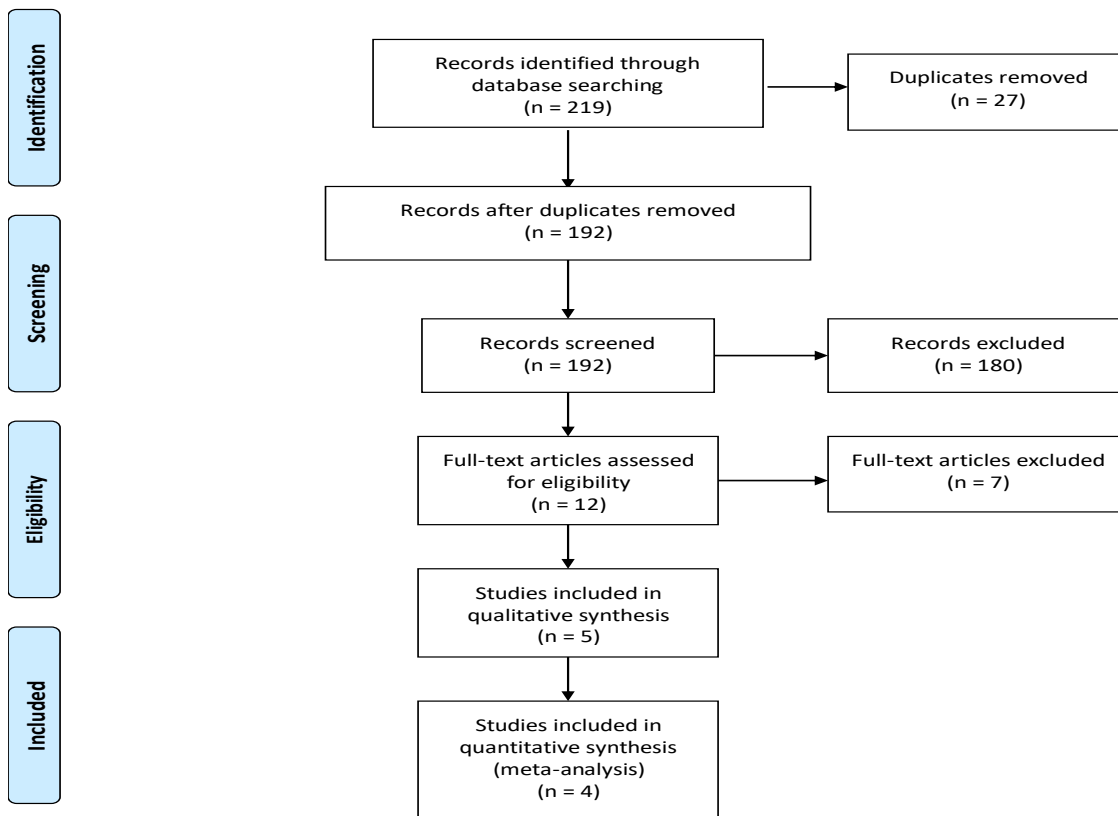


Fig 1: Prisma flow diagram of our search.

Risk of bias assessment:

In general, all studies have a good quality with some exceptions. The protocol registration was not reported at their study (12, 1⁴) and we considered it a reason for high risk. Also, in their study (12) the method of randomization and allocation concealment was not clarified, Fig.2 and Fig.3.

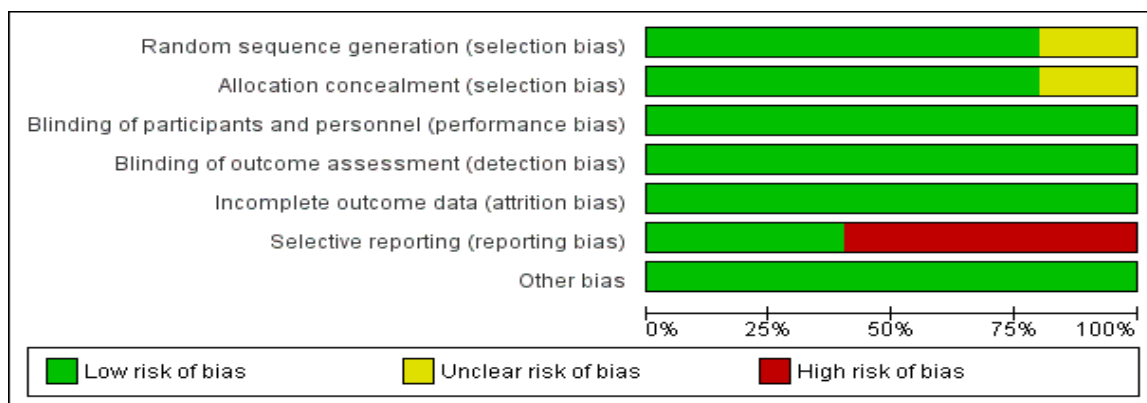


Fig 2: Risk of bias graph.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Ankouni et al 2021	+	+	+	+	+	+	+
Demirhan et al. 2013	+	+	+	+	+	+	+
Imeh et al. 2014	+	+	+	+	+	+	+
Sane et al. 2015	?	?	+	+	+	+	+
Shokrpour et al. 2018	+	+	+	+	+	+	+

Fig3: Risk of bias summery.

Results:

Intra-operative vomiting:

There was no significant difference between Ondansetron and combination or dexamethasone as following respectively: [RR=1.9, 95% CI (0.164,22.2), P= 0.605], and [RR=0.549, 95% CI (0.160,1.882), P=

0.17]. The data were homogenous in both as following: [I2=0%, (P=0.658)], and: [I2=0%, (P=0.737)]. Combination reduces the incidence of intraoperative vomiting compared to dexamethasone as following: [RR=9.9, 95% CI (1.2,79.9), P= 0.03], and the data was homogenous, [I2=0 %, (P=0.324)] Fig.4.

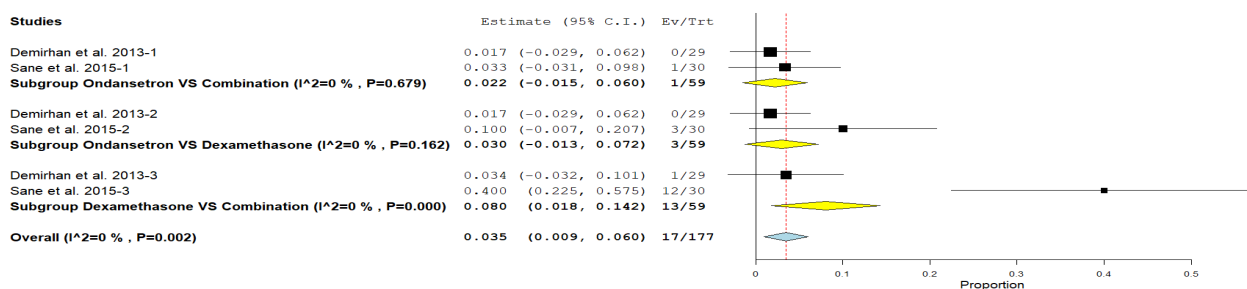


Fig.4: Forest plot of comparison; Intra-operative vomiting.

Intraoperative nausea:

There was no significant difference between ondansetron and combination or between dexamethasone and combination as following: [RR=0.7, 95% CI (0.3,1.64),

P= 0.41], and [RR=1.91, 95% CI (0.98,3.71), P= 0.06]. The data were not homogenous in both as following: [I2=73%, (P=0.06)], and: [I2=88%, (P=0.6)], This heterogeneity wasn't

resolved after using Random-effect model and the results remain insignificant as following: [RR=1.21, 95% CI (0.07,21.68), P= 0.9], and [RR=3.69, 95% CI (0.06,247), P= 0.54], and the heterogeneity was as following: [I2=73%, (P=0.06)], and: [I2=88%, (P=0.003)].

Ondansetron is better than dexamethasone in decreasing intraoperative nausea as following: [RR=0.35, 95% CI (0.16,0.77), P= 0.009], and the data was homogenous [I2=0%, (P=0.39)], Fig.5.

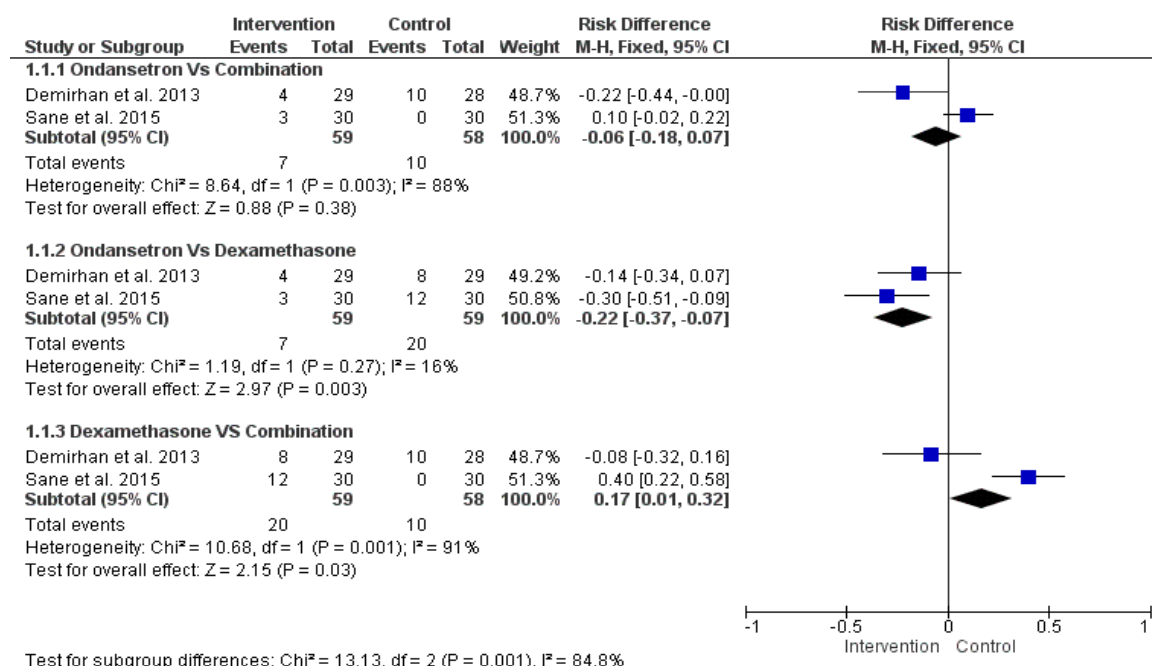


Fig.5: Forest plot of comparison; Intraoperative nausea.

Post-operative nausea and vomiting

The combination intervention reduces the incidence of post-operative nausea and vomiting compared to both ondansetron and dexamethasone as following respectively: [RR=2.44, 95% CI (1.28,4.63), P= 0.007], and [RR=7.29, 95% CI (2.46,21.54), P= 0.0003]. The data were homogenous in both as following:

[I2=25 %, (P=0.25)], and: [I2=14 %, (P=0.54)], Fig.6.

This study was not included in our meta-analysis. The study results showed that ondansetron and dexamethasone were considerably effective in controlling headache, but dexamethasone was much more effective. Dexamethasone-treated mothers scored lower on the pain scale than ondansetron-treated mothers.

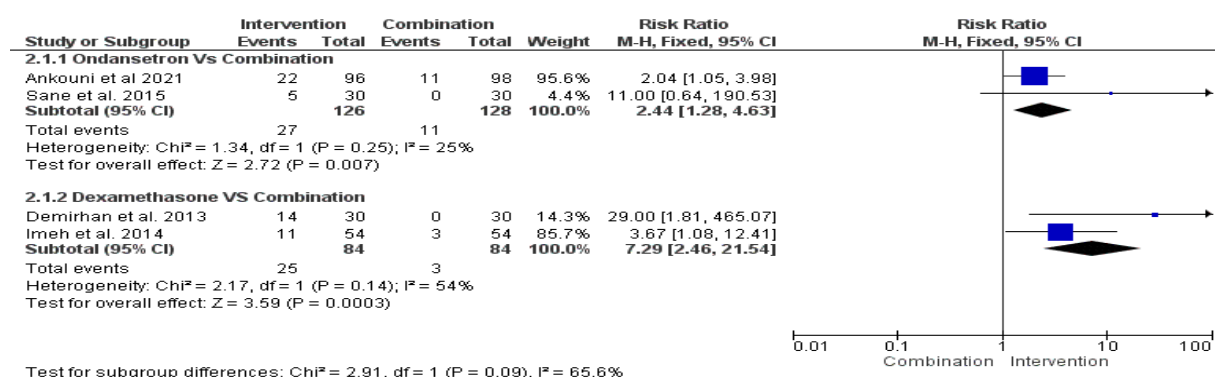


Fig.6: forest plot of comparison; post-operative nausea and vomiting

Discussion:

Summary of the findings

Our systematic review includes five RCTs. Of them, four RCTs were included in our meta-analysis. The results showed that there is no significant difference between ondansetron group or dexamethasone group when compared with combination group in terms of intraoperative vomiting, but the results were significant in this term when combination of dexamethasone and ondansetron were used. Also, there is no significant difference between ondansetron group and combination group or between dexamethasone group and combination group in terms of intraoperative nausea, but the data was significant in this term when ondansetron was used alone. Also, the results were significant between combination group and control group in terms of post-operative nausea and vomiting.

Agreements and disagreements with previous studies

Recently, the influence of antiemetics on cesarean outcomes has been widely debated. The results of our meta-analysis reported that, only the combination of ondansetron and dexamethasone that relieve post operative nausea and vomiting while, other authors (18) and (19) showed that ondansetron alone could prevent nausea and vomiting following epidural morphine for postoperative pain control.

Strength points and limitations

Our study has several strength points (1) we conducted all steps in strict accordance with the Cochrane Handbook of Systematic Reviews for interventions, (2) we followed the standard reporting guidelines of PRISMA statement to report this work, (3) we ran a comprehensive search of multiple electronic databases to identify all relevant studies, and finally (4) Our study reported class 1 evidence that there is association between the combination of ondansetron and dexamethasone group and post operative

nausea and vomiting. Nonetheless, our study has a few limitations. We noticed a lack of studies investigating the effect of dexamethasone alone or ondansetron alone on labor and delivery outcomes in women with associated risk factors like GERD. Also, there are very limited RCTs with controversial conclusions examining the impact of our combination on different maternal and neonatal outcomes. We recommend future well-designed RCTs to investigate this impact, address an unmet clinical need, and fill this evidence gap in the literature.

Conclusion

In conclusion, our meta-analysis showed that combination of dexamethasone and ondansetron reduce intra operative vomiting and post-operative nausea and vomiting. This finding should reassure pregnant women and healthcare providers that this combination reduces some anesthesia side effects.

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