



## Combination of dexamethasone and ondansetron in prophylaxis nausea and vomiting in gynecological operation

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### ABSTRACT

**Background:** Postoperative nausea and vomiting occur in about 20–30% of women; however, some reports have estimated the rate at 70% in at-risk individuals. Gynecological and obstetrical operations are among the most frequent types of surgeries to be associated with nausea and vomiting postoperatively. Ondansetron and dexamethasone have been compared in a variety of studies for postoperative prophylaxis.

**Aim of the Study:** This study was conducted in order to compare the efficacy and safety of dexamethasone and ondansetron, alone or in combination, for prevention of postoperative nausea and vomiting in a sample of Iraqi women undergoing gynecological surgeries.

**Patients and Methods:** The study was conducted in Al-Diwaniyah Province, a region belonging to the Mid-Euphrates sector of Iraq, at the Child and Maternity Teaching Hospital. The study started in June 2021 and the work with the research was accomplished in September 2022. The study included a total of 100 women undergoing different gynecological surgeries such as ovarian cystectomy, oophorectomy, ectopic pregnancy, total abdominal hysterectomy, and myomectomy. All participants involved in the study were categorized randomly into four groups, namely, dexamethasone, ondansetron, combined, and placebo groups.

**Results:** The rates of nausea in the different groups were analyzed. The rates of nausea in dexamethasone, ondansetron, and combined groups revealed a significant decrease compared with that of placebo group ( $P < 0.05$ ), and the rate was significantly lower in combined group when compared with dexamethasone and

ondansetron groups ( $P < 0.05$ ). The rate of nausea in combined group was significantly lower than that of dexamethasone and ondansetron groups. The rate of vomiting in combined group was significantly lower than that of placebo group and less than that of the dexamethasone group ( $P < 0.05$ ).

**Conclusion:** Based on our study and previous reports, both dexamethasone and ondansetron are efficient and safe in preventing nausea and vomiting in gynecological operations; however, combination of both provides the best results.

**Keywords:** *dexamethasone; gynecological operation; nausea; ondansetron; vomiting.*

## INTRODUCTION

One of the major complications experienced by patients undergoing major surgeries under general anesthesia is the development of nausea and vomiting.<sup>1–3</sup> Indeed, this complication can be viewed as the most frequent cause of morbidity following general anesthesia,<sup>4,5</sup> and both these symptoms reduced patients' satisfaction to a great extent.<sup>6</sup> The postoperative nausea and vomiting occur in about 20–30% of women; however, some reports have estimated the rate at 70% in at-risk individuals.<sup>4,7</sup> Gynecological and obstetrical operations are among the most frequent types of surgeries associated with nausea and vomiting postoperatively.<sup>8</sup> Nausea and vomiting occur in about 80–95% of women who are administered low dose of prophylactic antiemetic medication within the first 24 h following surgery.<sup>8,9</sup> It has been shown that female gender and gynecological operations are among the strong predictors of postoperative vomiting.<sup>10–12</sup> Due to the misery caused by the vomiting, including electrolyte imbalance, wound dehiscence, and the additional costs required due to delayed discharge, this has significant psychological, physical, emotional, and financial repercussions. As a result, considerable effort has been made to develop a strong antiemetic that would significantly lower the incidence of postoperative nausea in patients.<sup>4</sup> The current published articles dealing with the issue of postoperative vomiting and nausea in women undergoing gynecological operations are extremely inconsistent concerning management, prediction, incidence, and risk factors.<sup>8</sup>

The multifactorial nature of the etiology of this postoperative health issue has been widely evaluated with the eventual recognition of a number of independent risk factors (e.g., female gender and smoking) and emetogenic factors (including length of anesthesia, inhaled or balanced anesthesia, and perioperative use of opioids).<sup>13</sup> Female gender is at the top of the list of risk factors, followed by history of postoperative nausea and vomiting and history of motion sickness.<sup>13–15</sup> Premenstrual syndromes, history of vomiting and nausea at time of pregnancy, and pregnancy with a female baby are among the other possible risk factors.<sup>13,15</sup> Ethnicity, pharmacogenomic pleomorphism, psychosocial factors, and sex hormone levels may be associated with increased risk of postoperative incidence of nausea and vomiting according to some authors.<sup>8</sup>

The use of dexamethasone as a pharmacological agent with documented role in prevention and reduction of impact of postoperative nausea and vomiting has been discussed by several authors previously,<sup>16–18</sup> however, its use has also been discouraged by some authors because of the possible side effects.<sup>19</sup> Among the list of other pharmacological agents that has been used as a prophylactic measure for postoperative nausea is the 5HT<sub>3</sub> antagonist (ondansetron). No medication, however, has been discovered to offer total prevention. Ondansetron and dexamethasone have been compared in a variety of studies for postoperative prophylaxis. There is, however, a disagreement on how these trials

should present their findings and which medication is superior for prophylaxis.<sup>20</sup>

Therefore, this study was planned and conducted to compare the efficacy and safety of dexamethasone and ondansetron, alone or in combination, for prevention of postoperative nausea and vomiting in a sample of Iraqi women undergoing gynecological surgeries.

## PATIENTS AND METHODS

This study was conducted in Adiwaniyah Province, a region belonging to the Mid-Euphrates sector of Iraq, at the Child and Maternity Teaching Hospital. The study began in June 2021, and the work with the research was accomplished in September 2022. The study included a total of 100 women who were undergoing different gynecological surgeries such as ovarian cystectomy, oophorectomy, ectopic pregnancy, total abdominal hysterectomy, and myomectomy. All participants involved in the study were categorized randomly into four groups. The first group received dexamethasone, the second group received ondansetron, and the third group received a combination of dexamethasone and ondansetron as a prophylactic measure against postoperative nausea and vomiting. The fourth group received placebo ( $n = 25$ ). All groups had 25 women participants each. The outcome variables to be compared were nausea and vomiting 2, 12, 24, and 48 h following surgery.

The data were evaluated statistically using the Statistical Package for Social Sciences (SPSS) Version 16 and Microsoft Office Excel 2007. The variables were expressed as numbers and percentage, and chi-square test was used to compare proportions among various enrolled groups. The level of significance was regarded at  $P < 0.05$ .

## RESULTS

The demographic characteristics of patients included in this study are shown in Table 1.

Regarding age, most of the women were between 20 and 40 years of age, with 60, 72, 68, and 64% in dexamethasone, ondansetron, combined, and placebo groups, respectively. Women within 40–60 years of age accounted for 28, 20, 20, and 32% in the dexamethasone, ondansetron, combined, and placebo groups, respectively. Women older than 60 years accounted for 12, 8, 12, and 4% in the dexamethasone, ondansetron, combined, and placebo groups, respectively.

With respect to body mass index (BMI), women less than 25 kg/m<sup>2</sup> accounted for 12, 16, 16, and 12% in the dexamethasone, ondansetron, combined, and placebo groups, respectively; overweight women between 25 and 30 kg/m<sup>2</sup> accounted for 52, 56, 64, and 56% in the dexamethasone, ondansetron, combined, and placebo groups, respectively; obese women who were above 30 kg/m<sup>2</sup> accounted for 12, 8, 8, and 4% in the dexamethasone, ondansetron, combined, and placebo groups, respectively.

Types of surgeries included in the study are shown in Table 2. Dexamethasone group reported ovarian cystectomy, oophorectomy, ectopic pregnancy removal, total abdominal hysterectomy, and myomectomy in 16, 20, 24, 20, and 20%, respectively, while it was 36, 16, 8, 28, and 12%, respectively, in ondansetron group, 16, 20, 20, 24, and 32%, respectively, in combined group, and 36, 28, 20, 12, and 4%, respectively, in the placebo group.

The rates of nausea and vomiting in patients' groups after surgery are shown in Table 3. Following 2 h after surgery, the rates of nausea in combined group revealed significant decrease compared with that of placebo group, the vomiting rates in combined group and ondansetron group were significantly lower when compared with placebo group ( $P < 0.05$ ), whereas the rates of nausea and vomiting among intervention groups (dexamethasone, ondansetron, and combined groups) exhibited an insignificant difference ( $P > 0.05$ ).

Following 12 h after surgery, the rates of nausea and vomiting in dexamethasone, combined groups, and ondansetron were less considerable when

**TABLE 1.** Demographic characteristics of patients included in the study.

Characteristic	Dexamethasone n = 25	Ondansetron n = 25	Combined n = 25	Placebo n = 25	P
Age (years)					
20–40, n (%)	15 (60)	18 (72)	17 (68)	16 (64)	0.857 C <sup>†</sup> NS
40–60, n (%)	7 (28)	5 (20)	5 (20)	8 (32)	
>60, n (%)	3 (12)	2 (8)	3 (12)	1 (4)	
BMI (kg/m <sup>2</sup> )					
19–25, n (%)	3 (12)	4 (16)	4 (16)	3 (12)	0.952 C <sup>†</sup> NS
25–30, n (%)	13 (52)	14 (56)	16 (64)	14 (56)	
>30, n (%)	6 (24)	5 (20)	3 (12)	7 (28)	
>35, n (%)	3 (12)	2 (8)	2 (8)	1 (4)	

BMI, body mass index; C, chi-square test; n, number of cases; NS, not significant.

**TABLE 2.** Types of surgeries included in the study.

Type of surgery	Dexamethasone n = 25	Ondansetron n = 25	Combined n = 25	Placebo n = 25	P
Ovarian cystectomy, n (%)	4 (16)	9 (36)	4 (16)	9 (36)	0.186 C <sup>†</sup> NS
Oophorectomy, n (%)	5 (20)	4 (16)	5 (20)	7 (28)	
Ectopic pregnancy, n (%)	6 (24)	2 (8)	2 (20)	5 (20)	
Total abdominal hysterectomy, n (%)	5 (20)	7 (28)	6 (24)	3 (12)	
Myomectomy, n (%)	5 (20)	3 (12)	8 (32)	1 (4)	

C, chi-square test; n, number of cases; NS, not significant.

<sup>†</sup>indicates that more than 20% of the cells have an expected count of less than 5.

**TABLE 3.** The rates of nausea and vomiting in patients' groups after surgery.

Time	Characteristic	Dexamethasone n = 25	Ondansetron n = 25	Combined n = 25	Placebo n = 25
2 h	Nausea, n (%)	4 (16)	5 (20)	3 (12)*	10 (40)
	Vomiting, n (%)	3 (12)	1 (4)*	1 (4)*	6 (24)
12 h	Nausea, n (%)	8 (32)*	8 (16)*	3 (12)*	20 (80)
	Vomiting, n (%)	5 (20)*	3 (12)*	1 (4)*	17 (68)
24 h	Nausea, n (%)	10 (40)*	15 (60)**	4 (16)*	20 (80)
	Vomiting, n (%)	7 (28)*	4 (16)*	2 (8)*	15 (60)
48 h	Nausea, n (%)	10 (40)***	10 (40)**	2 (8)*	19 (76)
	Vomiting, n (%)	7 (28)**	3 (12)	1 (4)*	7 (28)

n, number of cases.

\*Significant difference between placebo group and any one of the other groups; \*\*Significant difference between combined group in comparison to dexamethasone or ondansetron group.

compared with placebo group ( $P < 0.05$ ), whereas the rates among intervention groups (dexamethasone, ondansetron, and combined groups) exhibited an insignificant difference ( $P > 0.05$ ).

Following 24 h, the rates of nausea in combined and dexamethasone groups were considerably less in comparison with placebo group ( $P < 0.05$ ), and the rates of vomiting in combined, dexamethasone, and ondansetron groups were considerably less in comparison with the placebo group ( $P < 0.05$ ). The rate of nausea in combined group was significantly lower than that of the ondansetron group ( $P < 0.05$ ).

Following 48 h, the rates of nausea in combined, dexamethasone, and ondansetron groups were considerably less in comparison with the placebo group ( $P < 0.05$ ) and was less significant in combined group when compared with dexamethasone and ondansetron groups ( $P < 0.05$ ). The rate of nausea in combined group was significantly lower than that of dexamethasone and ondansetron groups. The rate of vomiting in combined group was significantly lower than that of placebo and dexamethasone groups ( $P < 0.05$ ).

## DISCUSSION

The occurrence of nausea and vomiting in women undergoing gynecological surgeries has a great negative impact on patient satisfaction; therefore, efforts should be afforded by the team of doctors dealing with such operations to prevent or at least reduce the rate of such complications. Several previous authors raised the issue and suggested the use of a number of pharmacological agents to reduce such events; however, the big picture is that, there is no single agent that can be regarded as the optimum drug in dealing with postoperative health issues.

Coadministration of dexamethasone and ondansetron to avoid postoperative nausea and vomiting provided best results as evidenced by the lower rates of nausea and vomiting in comparison with either drug alone during the 48 h of follow-up.

It is worth mentioning that we reported no significant side effects when combined dexamethasone and ondansetron approach was used.

The efficacy and safety of dexamethasone and ondansetron is still controversial in gynecological as well as in nongynecological studies.<sup>21–24</sup> In all these studies, patients experienced negligible side effects. The rate of postoperative nausea and vomiting that happened within 24 h was evaluated in several previous reports.<sup>21–27</sup> Overall, 33.3 and 36.7% of the patients in the dexamethasone and ondansetron groups experienced postoperative nausea and vomiting. Although there was no evidence of heterogeneity among the other studies, dexamethasone was not related with a substantial decrease in the incidence of postsurgical nausea and vomiting rates.

Wang et al.<sup>28</sup> compared the efficacy of ondansetron and dexamethasone for the prevention of nausea and vomiting in the postoperative stage via a meta-analysis of the subgroups. In the first 6 h following surgery, dexamethasone did not perform better than ondansetron in preventing nausea and vomiting, and there were significant differences in the results of the study. Dexamethasone exhibited significant effectiveness in preventing nausea and vomiting compared with ondansetron in the same meta-analysis for the late postoperative period (24 h), whereas the diversity among the studies was less significant for these results than the early postoperative period.

Glucocorticoids activate gene transcription by attaching to intracellular glucocorticoid receptors.<sup>29</sup> Majority of the effects of corticosteroids take several hours to manifest because the gene expression and protein synthesis take several hours. Thus, depending on the route of administration, glucocorticoids often take 1–2 h to produce physiologic effects.<sup>30</sup> This helps explain the reason for the dramatic reduction in nausea and vomiting rates in the late postoperative stage after dexamethasone administration than the early postoperative stage, as reported in some earlier researches. It is interesting to note that the prolonged biological half-life



of dexamethasone (between 36 and 72 h) may be responsible for its delayed start and protracted anti-emetic effects.<sup>31</sup> As a result, the dexamethasone dosing time is crucial. Dexamethasone must be administered 1-2 h prior to surgery, especially for quick surgical procedures.<sup>32</sup>

In the study by D'souza et al.<sup>21</sup>, 93 women were separated into three groups and given either 4 or 8 mg of dexamethasone or 4 mg of ondansetron, with the purpose of comparing intravenous dexamethasone and ondansetron for the prophylaxis of postoperative nausea and vomiting. Dexamethasone was proven to be an effective and affordable medication for the prevention of nausea and vomiting, according to the study findings.

## CONCLUSION

Based on our study and previous reports, both dexamethasone and ondansetron are efficient and safe in preventing nausea and vomiting in gynecological operations; however, a combination of both provides the best results.

## ETHICAL APPROVAL

This study was approved by the Ethical Committee of College of Medicine, University of Al-Qadisiyah.

## FUNDING

This study did not receive any grants from any sources.

## CONFLICT OF INTEREST

No conflict of interest was declared by the author.

## INFORMED CONSENT

Verbal consent was gained from all participants.

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