

# Comparison of Ondansetron versus Metoclopramide for the Management of Females Presenting with Hyperemesis Gravidarum

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## ABSTRACT

**Objective:** To compare the outcome of ondansetron versus metoclopramide for the management of females presenting with hyperemesis gravidarum.

**Methodology:** It was a quasi-experimental study conducted in the Department of Gynaecology & Obstetrics, Services Hospital, Lahore. The study was completed in the period from March to August 2020. Patients diagnosed with diabetes mellitus, hypertension, multiple gestations, and allergic to medication were excluded from the study. The study comprised 60 participants who were divided into two groups. In the ondansetron group, females were given a single dose of 4 mg ondansetron diluted in 100 mL of normal saline. In the metoclopramide group, females were given a single dose of 10 mg metoclopramide diluted in 100 mL of normal saline. After 24 hours, females were asked for any episode of vomiting and nausea score. Data was analyzed using Statistical Package for the Social Sciences (SPSS) version 22.

**Results:** Out of 60 females included in the study, 30 were enrolled in each group. In the ondansetron group, vomiting was found in 13(43.3%) patients in the last 24 hours after administration of the drug. In the metoclopramide group, episodes of vomiting were found in 19(63.3%) patients within 24 hours after administration of metoclopramide. The difference between the two study groups was not statistically significant ( $p$ -value=0.121). The mean nausea score was  $6.70 \pm 1.09$  in subjects who took ondansetron while in patients who were given metoclopramide, the score was  $6.40 \pm 1.33$ . This difference was also not significant ( $p$ -value=0.343) in the metoclopramide group.

**Conclusion:** Both ondansetron and metoclopramide are equally effective for the management of females presenting with hyperemesis gravidarum.

**Keywords:** *Hyperemesis gravidarum. Ondansetron. Metoclopramide.*

## INTRODUCTION

Hyperemesis gravidarum is a condition affecting pregnancy in 0.5-1% although it is less likely associated with mortality but has an impact on maternal morbidity. Severe symptoms of nausea and vomiting in pregnancy are termed hyperemesis gravidarum which complicates less than 1% of pregnant patients.<sup>1</sup> It is associated with weight loss, electrolyte imbalance, and hospital admission. These patients should be given venous thromboprophylaxis as they are potentially at risk of venous thromboembolism. It is considered as one of the major reasons for women presenting in an emergency in the first half of pregnancies. It has multifactorial etiology but the exact cause is unknown.<sup>2</sup> Almost 80% of all pregnant women suffer from nausea and vomiting. Genetic predisposition, hormonal changes, and infections in some cases are considered contributory factors.<sup>3</sup> Women suffering from severe symptoms are associated with poor maternal and fetal outcomes. These outcomes include psychological upset, financial burdens, and underlying nutritional deficiencies leading to early miscarriage and low birth

weight babies.<sup>4</sup> The mainstay of treatment is supportive therapy but the stepwise treatment of antiemetics is considered in patients with intractable symptoms.<sup>5</sup> Ondansetron and metoclopramide are two drugs that have been used in practice to treat hyperemesis and their efficacy and side effect profile vary according to the response of patients.<sup>6</sup> Literature showed that both drugs have equal efficacy in averting nausea and vomiting in pregnant females.<sup>7,8</sup>

Metoclopramide is an antiemetic medication that is used to treat the symptoms. Common side effects associated with metoclopramide are extrapyramidal effects that lead to poor compliance.<sup>9</sup> Ondansetron, a second-line antiemetic, has potent efficacy by inhibiting the action of serotonin as a selective antagonist at the 5-hydroxytryptamine receptor. It is also used in chemotherapy-induced nausea and vomiting. Obstetricians are using ondansetron these days because of a better experience in improving symptoms and safety profile.<sup>10</sup>

In the local context, data pertaining to the comparison between the outcomes of ondansetron versus metoclopramide for the management of females presenting with hyperemesis gravidarum is limited. There is a need to set a protocol to manage females with more effective drugs and fewer side effects. The results might help clinicians to reduce hyperemesis gravidarum and its related complications in pregnancy.

## METHODOLOGY

It was a quasi-experimental study conducted in the Department of Gynaecology & Obstetrics, Services

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Hospital, Lahore. The study was completed in the period from March to August 2020. A total of 60 pregnant females were enrolled in the study. They were divided into two groups with 30 in each group who were selected after fulfilling the selection criteria. The study was approved by the hospital ethical board (Letter No: IRB/2020/629/SIMS, 07-02-2020). All patients were included after informed consent by consecutive sampling technique. All pregnant females of age 18-40 years, parity <5, and duration of 6-14 weeks pregnancy based on last menstrual period presenting with hyperemesis gravidarum were included in this study. Patients diagnosed with diabetes mellitus, hypertension, multiple gestations, and allergic to medication were excluded from the study. Detailed biodata of patients including their age, parity, gestational age, and educational status was mentioned on the designed proforma. In the ondansetron group, females were given a single dose of 4 mg ondansetron in 100 mL of normal saline. In the metoclopramide group, a single dose of 10 mg metoclopramide in 100 mL of normal saline was given. Then females were followed-up in the gynecology ward for 24 hours. Patients were assessed for improvement of symptoms after 24 hours. Pregnancy-unique quantification of emesis (PUQE) was used to assess the severity of nausea and vomiting. It is a validated tool and focuses on the number of vomiting episodes daily and the length of nausea in hours per day.<sup>11</sup>

### STATISTICAL ANALYSIS

Data analysis was done through Statistical Package for the Social Sciences (SPSS) version 22. Quantitative variables including the age of the patient, gestational

age, and nausea score were calculated as mean±SD. Qualitative variables such as vomiting episodes were presented as frequency and percentage. Parity was presented as frequency. The comparison between two groups for nausea scores was done using an independent t-test and Chi-square was used for vomiting episodes. A p-value ≤0.05 was considered significant.

### RESULTS

A total of 60 patients were included in this study. The patients in the study had a mean age of 27.52±6.67 years. Out of them, 20(33.33%) patients were nulliparous in the study and 14(23.33%) had parity 1, 7(11.67%) patients had parity 2, 9(15%) had parity 3 and 10(16.67%) patients had parity 4.

Among the ondansetron group, vomiting was found in 13(43.3%) patients whereas in the metoclopramide group vomiting was found in 19(63.3%) patients within 24 hours after the administration of the drugs. The difference between the two study groups was not statistically significant (p-value=0.121).

The mean nausea score was 6.70±1.09 in subjects who took ondansetron while in patients who were given metoclopramide, the score was 6.40±1.33. This difference was also not significant (p-value=0.343).

Data was stratified and compared based on age, gestational age, body mass index (BMI) & parity of the study participants for vomiting episodes (Table 1).

Nausea score was also compared in both study groups, based on data stratification of age, gestational age, BMI & parity (Table 2). It was found that vomiting and nausea scores in both study groups and sub-groups did not differ significantly.

**Table 1: Comparison of Vomiting during Last 24 Hours between Study Groups Stratified by Age, Gestational Age, BMI & Parity**

Study Variables		Vomiting during the Last 24 Hours	Groups		Total	p-value
			Ondansetron	Metoclopramide		
Age (Years)	≤30	Yes	9(40.9%)	11(55%)	20(47.6%)	0.361
		No	13(59.1%)	9(45%)	22(52.4%)	
	>30	Yes	4(50%)	8(80%)	12(66.7%)	0.180
		No	4(50%)	2(20%)	6(33.3%)	
Gestational Age (Weeks)	12-14	Yes	6(42.9%)	14(73.7%)	20(60.6%)	0.073
		No	8(57.1%)	5(26.3%)	13(39.4%)	
	>14	Yes	7(43.8%)	5(45.5%)	12(44.4%)	0.930
		No	9(56.2%)	6(54.5%)	15(55.6%)	
BMI	≤25	Yes	9(47.4%)	10(52.6%)	19(50%)	0.746
		No	10(52.6%)	9(47.4%)	19(50%)	
	>25	Yes	4(36.4%)	9(81.8%)	13(59.1%)	0.030
		No	7(63.6%)	2(18.2%)	9(40.9%)	
Parity	Null & Primary	Yes	3(18.8%)	12(66.7%)	15(44.1%)	0.005
		No	13(81.2%)	6(33.3%)	19(55.9%)	
	Multiple	Yes	10(71.4%)	7(58.3%)	17(65.4%)	0.484
		No	4(28.6%)	5(41.7%)	9(34.6%)	

**Table 2: Comparison of Nausea Score between Study Groups Stratified by Age, Gestational Age, BMI & Parity**

Study Variables		Study Groups	Nausea Score	p-value
			Mean±SD	
Age (Years)	≤30	Ondansetron	6.77±1.11	0.402
		Metoclopramide	6.45±1.36	
	>30	Ondansetron	6.5±1.07	0.894
		Metoclopramide	6.3±1.34	
Gestational Age (Weeks)	12-14	Ondansetron	6.43±0.94	0.298
		Metoclopramide	6.37±1.46	
	>14	Ondansetron	6.94±1.18	0.944
		Metoclopramide	6.45±1.13	
BMI	≤25	Ondansetron	6.94±1.26	0.07
		Metoclopramide	6.33±1.38	
	>25	Ondansetron	6.82±0.75	0.818
		Metoclopramide	6.1±1.18	
Parity	Null & Primary	Ondansetron	6.75±1.00	0.451
		Metoclopramide	6.44±1.29	
	Multiple	Ondansetron	6.64±1.22	0.557
		Metoclopramide	6.33±1.43	

## DISCUSSION

Nausea and vomiting are the most common presentations of patients in early pregnancy.<sup>12</sup> Majority of the cases (almost 80%) are managed conservatively but the symptoms affect the quality of life.<sup>13</sup> Severity of the symptoms in these patients is assessed by the PUQE score.<sup>14</sup> Hyperemesis gravidarum is a severe form affecting 0.3-1.0% of pregnancies.<sup>15</sup>

In our study, vomiting was found in 32(53.3%) patients within 24 hours of administration of drugs. In the ondansetron group, it was found in 13(43.3%) patients whereas in the metoclopramide group it was in 19(63.3%) patients. The difference between the two study groups was not statistically significant (p-value=0.121). In the ondansetron group, the mean nausea score was 6.70±1.09 while it was 6.40±1.33 in the metoclopramide group. This difference is not statistically significant (p-value=0.343). Similar results were found in a randomized control trial conducted by Boelig et al. They evaluated the efficacy of various antiemetics like metoclopramide, ondansetron, and promethazine. The results indicated that the efficacy and safety of all the drugs are comparable.<sup>15</sup> Another study conducted by Shapira et al. suggested that ondansetron is a safe treatment option for nausea and vomiting in pregnancy.<sup>16</sup>

A meta-analysis was conducted to investigate the efficacy of metoclopramide versus ondansetron in the treatment of hyperemesis gravidarum. Both groups were compared regarding the pregnancy-unique

quantification of emesis & nausea score and a statistically significant difference was found. Both drugs have comparable efficacy.<sup>17</sup>

A large multi-centered cohort study concluded that there is no association between ondansetron and the risk of spontaneous abortion, fetal death, stillbirth, and congenital malformations. So, ondansetron can be used frequently to treat nausea and vomiting in pregnancy.<sup>18</sup>

Another study was conducted in Holy Family Hospital, Rawalpindi to compare the outcomes of ondansetron and metoclopramide. They included 230 pregnant females who presented with hyperemesis gravidarum. They were randomly divided into groups by lottery method. Group A included patients treated with ondansetron and group B with metoclopramide. The efficacy and safety of both drugs were observed and they concluded that the efficacy and safety of ondansetron are better than metoclopramide.<sup>19</sup>

A double-blind randomized clinical trial was conducted by Moradiha et al. They included 153 pregnant females who presented with nausea and vomiting. These patients were divided into metoclopramide and ondansetron groups. The severity of nausea and vomiting was assessed by the PUQE questionnaire. They concluded that ondansetron is an effective and safe alternative for metoclopramide in the treatment of hyperemesis gravidarum.<sup>20</sup> A study was conducted by Lonah et al. to assess the efficacy and cost of ondansetron and metoclopramide in the treatment of hyperemesis gravidarum. They found no significant

difference in the cost and effectiveness of ondansetron versus metoclopramide.<sup>21</sup>

## CONCLUSION

Both ondansetron and metoclopramide are equally effective for the management of females presenting with hyperemesis gravidarum.

## LIMITATIONS & RECOMMENDATIONS

Study needs to be seen in context of its limitations. Small sample size and data from single center remains the major limiting factor. However, similarities of the findings with international research suggest generalizability of these results. Further studies are recommended to see the efficacy of these drugs for longer duration, and evaluate the safety in terms of side effects.

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