ORIGINAL ARTICLE

Comparison of Efficacy and Tolerability of Ondansetron Versus Metoclopramide in the Treatment of Hyperemesis Gravidarum

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ABSTRACT

Objectives: To compare efficacy and tolerability of Ondansetron versus Metoclopramide in the treatment of Hyperemesis Gravidarum.

Study Design: Randomized controlled trial

Place and Duration: Department of Obstetrics &Gynaecology Unit- II, Holy Family Hospital, Rawalpindi for duration of six months from August 2015 to January 2016.

Methodology: A total of 230 pregnant ladies (<16 weeks of gestational age) with hyperemesis gravidarum, 18 to 40 years of age were included. Patients with pre-existing medical condition e.g. Urinary tract infection, gastritis, Gastroesophagel reflux disease and acid peptic disease were excluded. Then selected patients were placed randomly into two groups i.e. Group A (ondansetron) & Group B (metoclopramide), by using lottery method. Outcome variables like efficacy and tolerability were noted.

Results: Mean age was 29.26±6.26 years. Mean gestational age was 7.92±3.16 weeks. Mean nausea intensity score was 9.03±0.39. Mean number of emesis episodes were 4.53±2.69 / week. Efficacy of Group A (ondansetrone group) was 103 (89.57%) while in Group B (metoclopramide group) efficacy was found in 89 (77.39%) patients with p-value = 0.013.

Conclusion: This study concluded that efficacy and tolerability of ondansetron is better as compared to metoclopramide in hyperemesis gravidarum.

Keywords: Hyperemesis Gravidarum, Antiemetics, Xerostomia.

INTRODUCTION

The medical disorder of very persistent nausea and vomiting during pregnancy is Hyperemesis gravidarum[1]. It is a severe pregnancy complication, marked by unwieldy nausea, vomiting and dehydration. It is estimated that 0.5–2.0 per cent of pregnant women are affected. [2-4] This problem can also lead to malnutrition and other severe problems, such as fluid or electrolyte imbalances. This serious condition can lead to dehydration, loss of weight and electrolyte imbalances if left unchecked. Gravidarum hyperemesis varies from morning disease. [5] Morning sickness is characterized by vomiting or no nausea. Morning illness is most common in the first trimester, often starting two weeks after pregnancy and affecting up to 90% of women. [6] Sickness in the morning is also the first sign of a woman becoming pregnant. The cause of this nausea and vomiting, which normally decreases after the first trimester, is thought to be associated with the rapidly increasing blood level of a human chorionic gonadotropin (HCG). The placenta releases HCG. An approximate 70-85% of pregnant women experience nausea and vomiting[7], typically starting at fourth week and ending up in the fourth month of their pregnancy. [8] Around 0.5-2 percent of pregnant women are suffering from hyperemesis gravidarum (HG), which has been characterized as recurrent nausea and insecurity sufficient vomiting to trigger dehydration and metabolic intensity disruption to involve hospitalisation. 7 HG appears to increase during the last half of pregnancy, but it may remain until delivery[8] and may be sufficiently serious to lead to the need to quit or even to maternal death. [9] HG in combination with a weight increase of less than 7 kg in pregnancies is associated with an increased risk of premature and low birth weight. [8] Multiple factors including the severity of symptoms, metabolism and mother's and fetal well-being are affected in treating HG. [10] Many antiemetics, including pyridoxine/doxylamine, antihistamines (such as diphenhydramine and phenothiazines, are efficient and safe in your pregnancy (such as promethazine). Regarding efficacy, it is unclear whether one is superior to the other and also small proof of major impact in hyperemesis gravidarum in all pharmacological therapy. [11]

Dimenhydrinate, metoclopramide or promethzine was recommended as first line alternatives by America College of Obstetricians and GYnecologists in 2004, with ondansetron as a second line parenteral antiemetic in the case of hospital-based gravidarum hyperemesis.[8]

These metoclopramids have a better safety profile than promethzine[13] and are currently the most effective antiemetic used in gravidarum hyperemesis. [14] Metoclopramide has good protection with regard to fetal consequences. [15] Ondansetron's superiority is still not proven in hyperemesis gravidarum[7], but its use is recommended and is used increasingly as first-line antiemetic during pregnancy. In a 2014 review, comparing efficacy of the tolerability of ondansetron to metoclopramide, the efficacy of vomiting control but better ondansetron tolerability with 10% xerostomia compared with 23% for metoclopramide was observed in 12.5% versus 30% for drowsiness and 12.5 versus 30% for ketone urea. [7] Pasternak et al. proved, in 2013, that their use is not teratogenic during pregnancy. [16] In a number of situations,

including chemotherapy and post-operatively, ondansetron is superior to metoclopramid as an antiemetic. Seven,[17]

The lack of local ondansetron research evidence in hyperemesis gravidarum requires an assessment of their effectiveness and tolerance in our environments. In order to treat patients with improved results and decrease morbidity.

MATERIALS AND METHODS

This randomized control trial was conducted at Department ofObstetrics &Gynaecology Unit- II, Holy Family Hospital, Rawalpindi for duration of six months from August 2015 to January 2016. A total of 230 pregnant ladies (<16 weeks of gestational age) with hyperemesis gravidarum, 18 to 40 years of age were included. Detailed demographics were recorded after taking written informed consent. Patients with pre-existing medical condition e.g. Urinary tract infection, gastritis, Gastroesophagel reflux disease and acid peptic disease were excluded.

Patients fulfilling the criteria were divided randomly into two groups A and B by lottery method. Baseline assessments was made and recorded in Performa. Group A was given injection ondansetron 4 mg every 8 hourly for 24 hours. Group B was given injection metoclopramide 10 mg every 8 hourly for 24 hours. Nausea intensity was recorded using a 10 point visual numeric scale at enrollment and at 24 hours. Number of emesis episodes was recorded for 24 hours of treatment as well as the presence of xerostomia and drowsiness.

Data was analyzed by SPSS (Version 17). Mean and Standard deviation were calculated for quantitative variables i.e. age, gestational age, nausea intensity score and number of emesis episodes. Frequencies and percentages were calculated for qualitative variables i.e. efficacy. Chi square test was used to compare the proportions of efficacy in both study groups at 5% level of significance. P value <0.05 was considered statistically significant.

RESULTS

The mean age of women in group A was 29.43±6.48 years and in group B was 29.12±6.07 years. Majority of the patients 126 (54.78%) were between 20 to 30 years of age. Mean gestational age in group A was 7.93±3.11 weeks and in group B it was 7.88±3.21 weeks. Majority of the patients 135 (58.70%) had 1-8 weeks gestational age. The mean nausea intensity score in group A was 9.05±0.37 and in group B was 9.08±0.32. The mean number of emesis episodes in group A was 4.48±2.75 / week and in group B was 4.56±2.68 / week. (Table 1)

Table No 1: Baseline details of all the patients

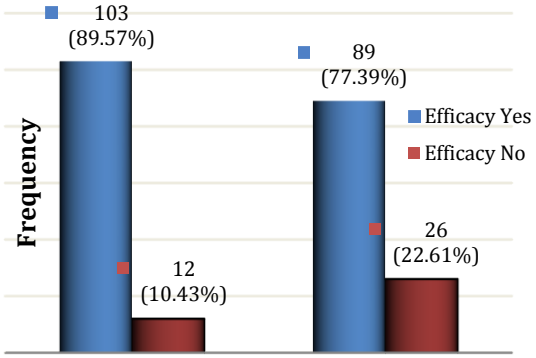
Variables	Group A	Group B
Mean age (yrs)	29.43±6.48	29.12±6.07
Mean Gestational Age (weeks)	7.93±3.11	7.88±3.21
Nausea Intensity Score	9.05±0.37	9.08±0.32
Emesis episodes (weeks)	4.48±2.75	4.56±2.68

Efficacy of Group A (ondansetrone group) was 103 (89.57%) while in Group B (metoclopramide group) was 89 (77.39%) as shown in Table II (p-value = 0.013).

Table No 2: Comparison of efficacy between both groups

Variables	Group A	Group B	P-value
Efficacy			0.013
Yes	103 (89.57%)	89 (77.39%)	
No	12 (10.43%)	26 (22.61%)	

Figure No 1: Efficacy between both groups



DISCUSSION

Pregnancy nausea and vomiting is the most common disease in pregnancy and affects 50%–90% of pregnant women. Its severe type, gravidarum (HG) hyperemesis, occurs in 0.5–3% of pregnancies that lead to dehydration, electrolyte imbalance, and hospitalization. The extreme types of NVP are common in up to 80% of the same women, which leads to fears about beginning another pregnancy. [18] Severe NVP was correlated with the demand from women to stop otherwise — desired pregnancies because of the seriousness of symptoms.[19, 20]

The age range was between 18 and 40 years for this analysis with a mean age of 29.26±6.26 years. The mean age was 29.43±6.48 years in group A and 29.12±6.07 in group B. 126 (54.78 %) of patients were aged 18 to 30 years. Group A (ondansetrone group) efficiency stood at 103 (89.57%), while Group B (metoclopramide group) had 89 (77.39%) with p-value = 0.013. Group A (ondansetrone group) tolerability of 106 (92.17%) while Group B (metoclopramide group) tolerability of 86 (74.78%) p-value = 0.000. In a number of situations, including chemotherapy and post-operatively, ondansetron is superior to metoclopramid as an antiemetic.[7, 17] In a study[7], 80 women were randomized to ondansetron or metoclopramide each. Median scores of visual wellbeing numeric rating were 9 (range, 5-10) versus 9 (range, 4-10) (P=.33) In the first 24 hours of vomiting episodes there were 1 (range, 0-9) compared to 2 (range, 0-23) (P=.38) ondansetron compared with metoclopramide. A repeat-measure analysis of the nausea variance showed no difference between drug studies (P=.22). Visual numerical rating scale Rates of drowsiness were recorded (12.5% vs 30%; P =.01%; Number required to gain treatment), xerostomia (10.0% vs 23.8%; P < 01%; Number required to benefit treatment, 8%) and recurrent cetonuria at 24 hours (12.5% vs. 30%; P=.01; Number necessary for benefit treatment, 6%) less frequent with Ondansetron. The hospital stay duration was close. [7]

In this study we found that Group A efficacy (ondansetrone group) was 103 (89.57 percent), while

Group B efficacy was 89 (metoclopramide group) (77.39 %). The disparity was important statistically. Ondansetron, a 5-HT3-receptor antagonist with selective serotonin, appears to have a contradictory safety profile. A case-control study found that the chance of cleft palate was doubled when ondansetron for NVP was taken during the first trimester of pregnancy. [21] There were mixed results from two studies using data from the Danish birth registry. Data on 1,233 births were collected between 2004-2011 by Pasternak and colleagues in 2013, and there was no increased risk of birth defects if mothers had taken ondansetron. [22] However, between 1997 and 2010 Andersen and colleagues gathered data from the same registry for 1,248 births and results showed that heart defects were more at risk. [23] In addition, the United States Food and Drug Administration warned citizens of ondansetron about the potential serious QT prolongation and the Torsade de Pointes. Strict ECG monitoring and follow-up is recommended for patients at risk such as in electrolyte imbalance (hypokalemia/hypomagnesemia) that may occur in women with extreme NVP or HG, or in patient patients with severe heart failure or other drugs that may extend the QT period. [24, 25]

The intravenous metoclopramide (1.2 to 1.8 mg/hour) plus diphenhydramine (50 mg per 6 hours) study indicated that 36 % of the patients received an improvement in vomiting and were more successful than the droperidol (0.5 to 1 mg/hour) plus diphenhydramine combination used in previous patient cohorts. In another series, the number of vomiting episodes was superior to monotherapy with either prochlorperazine or promethazine in combination therapy with metoclopramide and pyridoxin. [26]

Analysis of the national birth defects prevention study (NBDPS) data in the US showed the potential correlation between Ondansetron and isolated palate cleft, but only 55 first-quarter exposures (adjusted OR 2.37, CI 1.18–4.76 95%).[27]

A Swedish study with data from an interview with a midwife or the Swedish prescription registry identified ondansetron associated with an increase in the risk of cardiovascular deficiency (OR 1.62.95% CI 1.04-2.14), especially with a cardiac septum deficiency (OR 2.05, 95% CI 1.19-3.28). [28] In this analysis, 1349 first trimester exposures were assumed. In general, it is concluded that ondansetron is more efficient and tolerable than metoclopramide.

CONCLUSION

This studyconcluded that efficacy and tolerability of ondansetron is better as compared to metoclopramide in hyperemesis gravidarum. So, we recommend that ondansetron should be used as a first line therapy in hyperemesis gravidarum in order to reduce the morbidity of pregnant women, thus improve their social life.

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