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Original Article

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Effectiveness of Ondansetron in comparison to Domperidone for treating vomiting in acute gastroenteritis among children in a tertiary care hospital setting: A quasi-experimental study

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ABSTRACT

BACKGROUND & OBJECTIVE: There is inconsistent evidence on using antiemetic drugs (ondansetron and domperidone) in children with vomiting associated with gastroenteritis having dehydration. The study's objective was to compare the effectiveness of oral domperidone with ondansetron for treating vomiting during acute gastroenteritis in children with either mild or moderate dehydration.

METHODOLOGY: This non-controlled quasi-experimental study was conducted at Allama Iqbal Teaching Hospital, Sialkot, in the department of Pediatrics from 1st October 2019 to 31st December 2019. Sixty children aged 1-12 years having acute gastroenteritis, with mild or moderate dehydration after the failure of initial oral rehydration therapy, were included. Children in-group A (n=30) received a single dose of an orally disintegrating tablet of ondansetron, and children in-group B (n=30) were treated with domperidone. The absence of vomiting for 6 hours and subsequent successful rehydration in these two groups was the primary outcome. The Chi-square test was applied to compare the frequency of primary outcome between the ondansetron and domperidone groups, considering p-value ≤0.05 was considered statistically significant.

RESULTS: The mean age of patients was 4.4±1.8 years in group A compared to 5.1±2.7 years in group B. Oral Ondansetron was successful in controlling vomiting in 19(63.4%) patients compared to 11(36.6%) in domperidone group (p=0.39).

CONCLUSION: The single dose of oral ondansetron compared to domperidone was significantly effective in controlling the vomiting in-patient with acute gastroenteritis presented with either mild or moderate dehydration, resulting in effective oral rehydration subsequently.

KEYWORDS: Acute gastroenteritis, Children, Ondansetron, Domperidone, Effectiveness, Dehydration, Vomiting.

INTRODUCTION

Acute gastroenteritis (AGE) is a major cause of morbidity and mortality among children, leading to repeated visits to pediatric emergency department and hospitalizations. It usually lasts 3-7 days and is self-limited [1]. Worldwide, there are almost 4 billion cases of diarrhea and 3 million pediatric deaths every year and almost 2 million of these deaths occur in developing countries [2].

Vomiting is commonly observed in AGE and associated with discomfort and, if left untreated, leads to dehydration [1,2]. Oral rehydration therapy (ORT) is the most effective treatment for AGE but is usually difficult in case of persistent and refractory vomiting [2]. Pediatric guidelines support the use of intravenous (IV) rehydration after the failure of initial ORT due to persistent vomiting [3,4]. Symptomatic treatment with antiemetics for vomiting in pediatric AGE is still not included systematically in current practice [5]. Clinical observations suggest that effective antiemetic treatment may result in successful oral rehydration therapy, avoidance of intravenous rehydration and hospitalizations. Different antiemetic drugs are available for off-label use in children to control vomiting associated with AGE [6].

Domperidone, a dopamine receptor antagonist, is one of the commonly recommended antiemetic treatments in many countries for the last few decades [7, 8]. Ondansetron,

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a serotonin antagonist, has been used previously to control vomiting resulted due to radiotherapy, chemotherapy and surgical interventions. Recently it has been increasingly prescribed in pediatric patients to settle vomiting in case of AGE [9,10]. A meta-analysis showed ondansetron to be effective compared to placebo in vomiting cessation up to 1 hour after administration, but there was no significant difference among the two groups after 4, 24, and 48 hours. Treatment with ondansetron compared with placebo decreased the risk of ORT failure and thus lowered the risk of hospitalization [4].

A similar study has shown that among children having vomiting associated with AGE, ondansetron was effective in 62.2% compared to 44.4% treated with domperidone [11]. Another study reported that ondansetron was successful in controlling vomiting in 83% of cases compared to 56% treated with domperidone [12]. Although these reports provided considerable evidence that ondansetron compared to other antiemetic medicine in controlling vomiting, however, these reports used heterogeneous populations, having a variable degree of risks, costs and benefits, and the success of ORT after this antiemetic medicine was not sufficiently assessed. Considering these issues, the current study was planned to compare the effectiveness of ondansetron and domperidone in treating vomiting associated with acute gastroenteritis among children with mild or moderate dehydration and subsequent successful ORT. The results of this comparative study would provide essential evidence for using ondansetron in pediatric clinical practice.

METHODOLOGY

This quasi-experimental study was conducted in the pediatric unit of Allama Iqbal Teaching Hospital, Sialkot from 1st October 2019 to 31st December 2019 for 3 months, after approval from the Ethical Review Committee of Khawaja Muhammad Safdar Medical College, Sialkot (letter number:70/REC/KMSMC). This study aim is to compare the effectiveness of domperidone suspension with oral disintegrated ondansetron tablets to prevent AGE-associated vomiting in patients aged 1-12. Written informed consent was taken from the parents or caregivers of 60 participants. Participants could withdraw anytime from the study and were ensured of their data privacy. Patients who reported having two or more episodes of non-bilious vomiting within the last 24 hours, along with other signs and symptoms consistent with AGE (loose motions, pain or discomfort in the abdomen, bloating, low-grade fever) were included. Whereas patients who took antiemetic medication within 4 hours prior to a hospital visit and had underlying chronic disease involving kidneys, liver, heart or central nervous system, immune deficiency, malignancy, diabetes mellitus or previous abdominal surgery, and had severe dehydration or, having symptoms of involvement of any other system (sepsis), had a history of allergy to domperidone or ondansetron were excluded. A sample of 60 (30 in each group) was calculated at 5% (two-sided) confidence interval with a power of 80%; the expected prevalence used was 83.2% [12], expected prevalence of (effectiveness) p2 was 44.4 % [11]. Consecutive recruitment of patients attending the emergency department was used.

After randomization using the envelope method, thirty patients each were included in ondansetron group (Group A) and domperidone group (Group B) (Figure-I). The Group A participants received orally disintegrated ondansetron tablets, and Group B received domperidone suspension according to their body weight. The prescribed dose was 2 mg for patients having weight <15kg, 4 mg for those weighing 15-30kg, and 8 mg for patients weighing >30kg. The prescribed dose of domperidone was 2.5mg for patients weighing < 15kg, 5 mg for those weighing 15-30kg and 10 mg for patients weighing >30kg. If any child had an episode of vomiting soon after the administration of the antiemetic, another dose of the same antiemetic was given. Patients were observed for 6 hours, and those who tolerated ORT and had no vomiting were sent home after guiding on a plan of ORT, danger signs and when to visit back to the hospital immediately. In the case of persistent vomiting, despite antiemetic administration, the case was labelled as “treatment failure”, and a child was admitted for intravenous rehydration. Patients were followed for 6 hours post-administration for the primary outcome.

Data analysis was performed adopting “Statistical Package for Social Sciences (SPSS)”, version 26.0. For continuous variables, mean and standard deviation (SD) were calculated. Frequencies and percentages were calculated for categorical variables, including gender and primary outcome (control of vomiting and successful ORT). A chi-square test was applied to compare the demographic and clinical features. Logistic regression model was used to compare the effectiveness of ondansetron against domperidone (reference) for controlling vomiting in participants, considering p-value≤0.05 as statistically significant.

RESULTS

The mean age of children was 4.4± 1.8 years of children in the Ondansetron group (Group A), while 5.1±2.7 years in the domperidone group (Group B). The mean duration of illness was 55 ±22 hours in the Ondansetron Group and 52±25 hours in the domperidone group, respectively. The mean weight of the children was 16.3±3.6Kg in Group A, and 18.2±6.4 Kg in Group B. Age was further divided into two groups, 1 to 6 years and 7 to 12 years; duration of symptoms was divided into <48 hours and >48 hours, whereas weight was also categorized in two groups (<20kg and >20kg). The ratio of males to females was 1.5:1 in Group A and 2:1 in Group B. There was no significant difference between the two groups regarding age, gender, weight, duration of symptoms and degree of dehydration (Table-I). Ondansetron was effective in treating vomiting in 19(63.4%) patients, whereas in 11(36.6%) patients domperidone was effective (p=0.039), hence suggesting that ondansetron had significantly effective for controlling vomiting and leading to successful ORT in patients of acute gastroenteritis. No

side effects of these medications were observed. A flow diagram showing recruitment, assignment and follow-up of participants in this study (Figure-I).

Table-I: Demographics and clinical features of participants.

Characteristics		Group A (n=30)	Group B(n=30)	p-value
Age	1-6 years	27 (90.0 %)	21 (70.0 %)	0.053
	7-12 years	03 (10.0 %)	09 (30.0 %)	
Gender	Male	18 (60.0 %)	20 (66.7 %)	0.059
	Female	12 (40.0 %)	10 (33.3 %)	
Weight	<20 Kg	26 (86.6 %)	21 (70.0 %)	0.051
	≥ 20 Kg	04 (13.3 %)	09 (30.0 %)	
Duration of symptoms	<48 hours	20 (66.7 %)	22 (73.3 %)	0.573
	≥ 48 hours	10 (33.3 %)	08 (26.7 %)	
Dehydration status	Mild	22 (73.3%)	24 (80%)	0.541
	Moderate	08 (26.7%)	06 (20%)	
Effectiveness of medication	Yes	19 (63.3%)	11 (36.6%)	0.0391
	No	11(36.6%)	19(63.3%)	

- The p-value was calculated by applying the Chi-square test, and a value <0.05 was considered statistically significant
- Results are presented as n(%) in all rows and columns until mentioned elsewhere.

Table-II: Unadjusted and Adjusted odds ratio comparing the effectiveness of ondansetron against domperidone (reference) for controlling vomiting in participants

Medication	Unadjusted estimates			Adjusted estimates		
	OR	95% CI	p	OR	95% CI	p
Domperidone	Reference	Reference	-	Reference	Reference	-
Ondansetron	2.98	1.04-8.52	0.04	2.95	0.97-8.94	0.05

Abbreviations: OR odds ratio; CI, confidence interval,
*Domperidone=reference
Logistic regression modelling was used, and the model was adjusted with age, gender, weight and clinical condition.

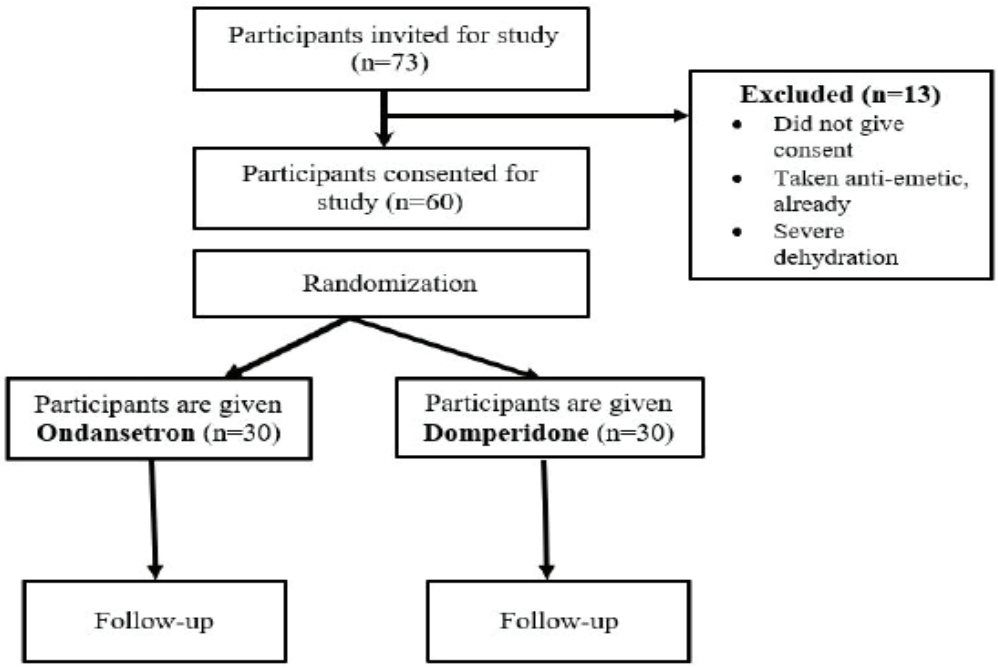

Figure-I: Flow diagram showing recruitment, assignment and follow-up of participants in the study.

DISCUSSION

In acute gastroenteritis among children having mild to moderate dehydration, ORT is preferred, but many times, due to persistent vomiting, the child is unable to tolerate ORT and it adds up to not only anxiety of parents and distress to patient but also leads to hospitalization and increased risk of death, in addition to high financial cost [1-4]. Provided vomiting be effectively controlled by using safe antiemetic, it would result in successful ORT; child can be managed on out-patient basis. In this randomized, non-controlled quasi-experiment, ondansetron showed better effectiveness compared to domperidone, in terms of controlling vomiting at 6 hours and successful ORT subsequently.

A similar study have shown the efficacy of ondansetron to be 62.2% and 44.4% with domperidone for cessation of vomiting during AGE in children [11]. Marchetti F, et al. reported efficacy of ondansetron was 83.2% and 55.5% with domperidone for symptomatic relief of vomiting associated with AGE in children [12]. Another study showed that ondansetron had no such superiority over domperidone at 6 hours [13]. Although the efficacy of domperidone is still not fully established, we choose domperidone for our study because it is commonly prescribed among children in Pakistan. We considered domperidone as the standard of care and hence compared it to ondansetron. Variation in our results compared to other studies might be due to the selection of participants since we included only mild to moderate disease and excluded those having severe dehydration. Mild to moderate disease is often self-limited and generally follows a benign course. This might potentially diminish the positive effect of antiemetics and make the choice of antiemetic difficult. The cessation rate of emesis in our study appears to be somewhat less than most studies in children using ondansetron [14-17].

Factors associated with this difference may be explained based on variations in using a different route of administration or dosage of the drug in previous studies, recruiting different populations, and evaluating cessation of vomiting post-administration at different time points. In terms of safety, our study findings are similar to previous studies [18]. Both drugs were reported to have no adverse effects and were well tolerated. A recent local study performed by Ahmad T et al[19] analyzing 300 children reported that 89.4% of children in Ondansetron group revealed cessation of vomiting at 24 hours in comparison to 80.6% in Domperidone group, while the difference turned out to be statistically significant favoring Domperidone (p=0.0390). Our findings are in agreement with what was found by Ahmad T et al. [19].

The use of different routes of ondansetron administration in children having nausea and vomiting has been studied previously, and it was found that orally disintegrated ondansetron tablet provides an easy and acceptable route of administration. It is non-invasive compared to intravenous ondansetron and hence preferred, especially in children who are eligible to be managed as an out-patient [20]. Our study also shows that orally disintegrated ondansetron is accepted well by children having symptoms of acute gastroenteritis. We retained the patient in the pediatric department for 6 hours and noted the control of vomiting and tolerance of oral rehydration therapy [21]. In logistic regression analysis, through odds ratio indicates the superiority of ondansetron over domperidone, yet a wide confidence interval shows the imprecision of the estimate, which may be due to the small sample size.

The results of our study should be read with a few limitations. Lack of comparison with placebo and with different medication doses and forms may be a source of bias. Placebo was not used due to financial constraints and considering ethical issues. The medications were different in texture; hence patients, as well as doctors, were aware of the medication that patients received (lack of blinding). The small sample size is another limitation. Future studies can use a larger sample size and appropriate control group to compare these two antiemetic medicines.

CONCLUSION

A single dose of oral ondansetron, compared to domperidone, is significantly effective in controlling vomiting in pediatric patients of acute gastroenteritis, with mild to moderate dehydration, and subsequent successful oral rehydration among children.

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Muddassir Zafar: Substantial contributions to the conception or design of the work.
Wajiha Rizwan: Manuscripit writing.
Muhammad Rafique: Acquisition, analysis, or interpretation of data for the work.
Shahid Mahmood: Drafting the work or revising it critically for important intellectual content.
Yasir Javed: Interpretation of the data.

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