

Prescription and cost-analysis of antiemetic medication use in pediatric wards: a prospective observational study

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ABSTRACT

Background: Use of anti-emetic drugs in pediatric population is often warranted, but choice of drug remains questionable within pediatricians. Objective of current study is: to study prescribing pattern and to calculate cost of antiemetic drug therapy in pediatric wards.

Methods: A prospective, observational study was conducted in pediatric wards of a tertiary care hospital of over 14 month's duration. Institutional ethics committee approval was obtained and written informed consent of parents/guardians was taken. Data of any pediatric patient receiving anti-emetic agent were included in the study.

Results: A total of 218 prescriptions were collected. Mean age of patients was 4.39±3.16 (range 4 months to 12 years). Gastroenteritis was the most frequently diagnosed disease in 137(63%) patients. Domperidone was prescribed in 52.4% and ondansetron in 47.6% children. Oral liquid dosage formulation was prescribed in 109 (48.4%) followed by solid dosage form 47 (20.9%). Mean cost of domperidone therapy was 25.34±6.55 INR and for ondansetron it was 36.62±17.94 INR.

Conclusions: Gastroenteritis was most frequent indication for use of anti-emetics. Domperidone pharmacotherapy was cheaper and most frequently prescribed than ondansetron.

Keywords: Anti-emetic, Children, Drug utilization, Gastroenteritis

INTRODUCTION

Vomiting is an organized, autonomic response that ultimately results in the forceful expulsion of gastric contents through the mouth.¹ Gastroenteritis is the most common cause of vomiting in children. Worldwide, gastroenteritis affects 3 to 5 billion cases and lead to around 13% of hospitalizations for children younger than 5 years.^{2,3} In the initial phase of viral acute gastroenteritis, vomiting is a typical symptom⁴ and during the first 1 to 3 days, repeated vomiting is present in 75% of children.⁵ In particular, between 2% and 23% of children with gastroenteritis received prescriptions for antiemetic medications.⁶ At least half of all physicians

caring for children with gastroenteritis report prescribing antiemetic agents and 10% of children with gastroenteritis who undergo outpatient care fill a prescription for an antiemetic drug.^{7,8}

Antiemetic drugs are often used because vomiting is an unpleasant and a distressing symptom which can increase the likelihood of dehydration, electrolyte imbalance, pulmonary aspiration, and most importantly the need for intravenous hydration or hospitalization.^{8,9}

The American Academy of Pediatrics (AAP), Centers for Disease Control and Prevention (CDC), European Society for Pediatric Gastroenterology and Nutrition, and the World Health Organization (WHO) all strongly support the use of oral rehydration therapy as the first-line therapy for the treatment of acute gastroenteritis, except in cases of severe dehydration.^{3,10-12} Although treatment guidelines do not recommend antiemetic medications in children with Gastroenteritis related vomiting, their use seems to be rather common in clinical practice.^{13,14}

The reasons why antiemetics are not commonly recommended for gastroenteritis related vomiting are because vomiting is self-limiting, vomiting is a normal physiological reaction for ridding the body of toxic substances, and antiemetics can have adverse sideeffects.¹⁵⁻¹⁷ Multiple medications have been used in an attempt to limit vomiting and facilitate oral rehydration but have not gained acceptance because of their limited success and high rates of complicating adverse effects.^{8,18} Traditional antiemetics such as promethazine, prochlorperazine and metoclopramide have not gained acceptance, because of their limited success and high rates of complicating adverse effects that like extrapyramidal reactions, lethargy, respiratory depression and cardiac dysrhythmias.^{7,8,18} Domperidone remains first line drug in children due to its good side effect profile.¹⁴ Domperidone is extremely well tolerated. There are adverse effects only if domperidone is used parenterally. Because it does not cross the blood-brain barrier to a significant degree, neuropsychiatric and extrapyramidal effects are rare as compared to metoclopramide.¹⁹

Ondansetron have been safely used in children as young as 1 month old for the treatment of postoperative or chemotherapy-associated nausea and vomiting. Several recent studies have also evaluated the use of ondansetron in children with vomiting from gastroenteritis.^{4,20-22}

Drug utilization studies of anti-emetic drugs were carried out in Sri Lanka, Italy and multi country trial^{6,14,23} similar

studies particularly in children is lacking in India so we decided to conduct this study in our hospital setting.

This study was undertaken to study the utilization pattern of antiemetic drugs prescribed in hospitalized children with gastroenteritis and cost analysis of different antiemetic medication.

METHODS

The observational prospective study was carried out from June 2010 to July 2011 in pediatric ward of a tertiary care teaching hospital. The protocol was approved by Institutional Ethics Committee. Data of all patients up to 12 years of age of either gender admitted in pediatric wards receiving antiemetic agents was collected in a pre-designed proforma after taking written informed consent from parents or legal guardian. Patients less than one month of age, with history of malignancy of any type or pre-operative patients were excluded from the study.

Statistical analysis

Data were analyzed for demographic characteristics, morbidity pattern, WHO core drug prescribing indicators, antiemetic prescription and cost of antiemetic therapy. Microsoft Excel 2010® was used to analyze.

RESULTS

A total of 218 prescriptions were collected. Overall mean age was 4.39 ± 3.16 years. Number of males enrolled in the study was 115 (51.1%) and rests were female. Under 5 year's age group constitute a majority 144 (66%) of the patients. Mean duration of antiemetic treatment was 2.08 ± 0.93 days. Most of the patients presented with gastroenteritis 137 (62.84%). Analysis of prescribing indicators reveals that the mean number of drugs per prescription was 6.16 ± 1.71 . Provisional diagnoses of pediatric patients receiving antiemetic drugs are shown in Table 1. Frequency of prescribed antiemetic drugs is shown in Table 2. Age wise distribution of patients is shown in Figure 1.

Table 1: Frequency of disease conditions of children receiving antiemetics (n=218).

Disease condition	[ICD-10 code*]	No. of patients	Percentage
Gastroenteritis		137	62.85
Acute gastroenteritis	[A08,A09]	97	44.5
Gastroenteritis by <i>S. typhi</i> (Enteric fever)	[A01]	19	8.72
Gastroenteritis by <i>V. cholerae</i> (Cholera)	[A00]	13	5.96
Gastroenteritis (Alleged h/o food poisoning)	[A04,A05]	8	3.67
Malaria	[B50,B54]	24	11
Hepatitis	[B15-19]	15	6.90
Meningitis	[A39,A87]	13	5.96
Miscellaneous		13	5.93
Urinary tract infection	[A41]	10	4.58
Convulsion under investigation	[R56]	6	2.75

*The international statistical classification of diseases and related health problems, 10th revision.

Table 2: Frequency of prescribed antiemetic drugs (n=218).

Generic Name	Brand Names (company name)	No. of prescriptions	Percentage
Domperidone (52.4%)	Domstal (Torrent)	108	48
	Dombaby (Torrent)	10	4.4
Ondansetron (47.6%)	Emeset (Cipla)	34	15.1
	Ondem (Alkem)	38	16.9
	Vomikind (Mankind)	23	10.2
	Periset (IPCA)	12	5.3
7 prescriptions contained two antiemetic agents.			

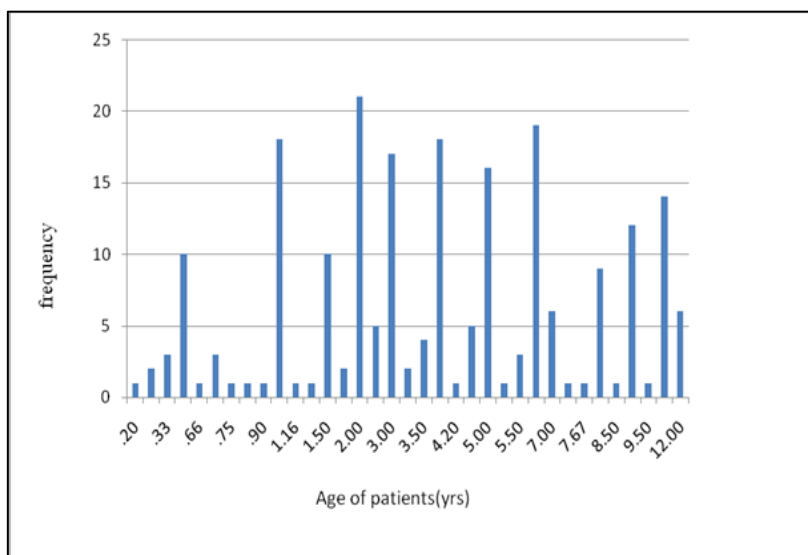


Figure 1: Age wise distribution of patients (n=218).

Most antiemetic drugs were prescribed by oral route 156 (69.33%) and rest were intravenous injection and intramuscular injection. Most common dosage formulation was suspension/syrup 99 (44%) followed by oral tablet and oral drops. Mean cost of antiemetic

medication per patient was 30.70 ± 14.40 INR ranging from 12 to 113 INR. WHO drug utilization indicators²⁴ were shown in Table 3. Table 4 shows percentage cost variation within two drugs for various brands used in our study.

Table 3: WHO core prescribing indicators (n=218).

Indicators	Value
Average no. of drugs per prescription	6.16 ± 1.71
Percentage of encounters with an injection prescribed	100
Percentage of encounters with antimicrobials prescribed	82.2
Percentage of drugs prescribed by generic name	30.11
Percentage of drugs prescribed from the hospital formulary	24.08

Table 4: Percentage cost variation within various brands.

Drugs	Lowest priced brand	Highest priced brand	Percentage cost variation
Domperidone-syrup	16.90	35.07	107.51
Domperidone-tablet	15.90	31.40	97.48
Ondansetron-tablet	19	98.44	418.10
Ondansetron-injection	7.99	28.89	261.5

$$\text{Percentage cost variation} = \frac{\text{Cost of highest priced brand} - \text{Cost of lowest priced}}{\text{Cost of lowest priced brand}} \times 100$$

DISCUSSION

This study was undertaken to study the utilization pattern of antiemetic drugs prescribed in hospitalized children and cost analysis of different antiemetic medication. Drug utilization studies are as pointer to the prescribing behavior. Compared to adults, drug used in pediatrics has not been extensively researched.

Gastroenteritis was found frequent in less than 5 years of age. Acute gastroenteritis is the main cause of acute vomiting in children under 3 years of age. Majority of the patients were diagnosed as gastroenteritis which includes acute gastroenteritis, enteric fever, cholera, food poisoning.

Mean duration of antiemetic treatment was 1.82 days (SD = 0.85). Higher use 3.9 days (SD=3.8) was noted in Study of Sri Lanka.²³

In this study, domperidone (52.4%) was frequently prescribed than ondansetron (47.6%). Frequency of domperidone use in our study was much less compared to the study done in Italy (96%) and Sri Lanka (89%).^{14,23} It is because domperidone remains first line drug in children due to its good side effect profile.¹⁴ Domperidone is extremely well tolerated. There are adverse effects only if domperidone is used parenterally. Because it does not cross the blood-brain barrier to a significant degree, neuropsychiatric and extrapyramidal effects are rare as compared to metoclopramide.¹⁹

According to The Indian Academy of Paediatrics (IAP) Recommendations, antiemetics should be reserved for children in whom the vomiting is severe, recurrent and interferes with ORS intake. Among the available antiemetics in use for children, domperidone is the safest with no central nervous system side effects. Therefore, the group recommended a single dose of domperidone in children with severe vomiting. Continued use is not recommended. Domperidone should be used at a dose of 0.1-0.3 mg/kg/dose.²⁵ In our study it has been prescribed in all children with vomiting irrespective of severity. Also, the prescribed dose in children above one year was 5 mg two to three times daily either in solid or liquid form. Moreover multiple doses were given to some of children. Considering these findings, the use of domperidone indiscriminately cannot be considered as rational and needs attention of the prescribers.

Oral liquid dosage form (48%) followed by tablet (20%) was commonly prescribed oral formulations in our study as suspension/syrup is convenient to administer in children. Somewhat higher use 54% (oral liquid dosage form) and 32.5% (tablets) was noted in Sri Lankan study.²³ The cost of an equivalent dose of drug in syrup form is almost twice as that in tablet form. Also syrup/suspension is difficult to transport and has shorter shelf life than tablet form. Hence excess use of syrup/suspension should be checked and

recommendations may be made for use of kid tablets wherever possible.

The cost for domperidone therapy in our study was cheaper by 11.28 INR than ondansetron therapy. Among ondansetron brands, the costliest brand Emeset (Cipla) was used in 18% (highest use). On the other hand, the cheapest brand Vomikind was the most frequently used injection but was not prescribed in oral form to a single patient. This would obviously increase the cost of antiemetic therapy. We calculated percentage cost variation within two drugs for various brands used in our study; the highest percentage cost variation was seen for ondansetron tablet i.e. 418.10 and lowest variation was seen with domperidone tablet i.e. 97.48. This finding suggests that variety of costlier brands were used for ondansetron as compared to domperidone brands. We did not find any other study which has calculated the percentage cost variation.

Currently ondansetron is approved for treatment of chemotherapy-induced vomiting, nausea and vomiting secondary to upper abdominal irradiation, hyperemesis of pregnancy and postoperative nausea.²⁶ Several studies report ondansetron use in vomiting of gastroenteritis in children. Three studies examined the use of oral ondansetron^{21,22,27} and one study examined the use of IV ondansetron²⁰ for vomiting due to acute gastroenteritis were identified.

The Cochrane review found “some albeit, weak and unreliable evidence” in favor of ondansetron to reduce vomiting from gastroenteritis.²⁸

Little information is available about dosage in pediatric patients 4 years of age or younger (Prescribing Information, FDA). Use of ondansetron in children with diarrhea is off-label as it is not approved for vomiting due to diarrheal diseases.²⁹

Polypharmacy remains the main form of irrational prescribing. 70% of drugs were prescribed by brand names. Hospital authorities need to take stringent measures to minimize the influence of pharmaceutical companies and their representatives on the drug prescription.

CONCLUSION

Gastroenteritis was most frequent indication for antiemetics. Domperidone pharmacotherapy was cheaper and most frequently prescribed than ondansetron. Inappropriate and excessive use of domperidone was noted in some of the prescriptions. Off-label use of ondansetron in pediatric age group is highly prevalent in wards as antiemetic. This needs attention of the prescribers. To provide optimal, low-cost, and effective medicines to the patients, it should be made mandatory for the prescribers to attend regular continuing medical

education programmes to update their knowledge on for rational use of this group of drugs in gastroenteritis.

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