

Evaluation of Antiemetic Use in Pediatric Gastroenteritis in Damietta Governorate

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Abstract: Background: gastroenteritis is a common pediatric health problem. Antiemetics are frequently prescribed, irrespective of the absence of guideline recommendations to support this practice. **Aim of the work** is to review the use of antiemetics for pediatric AGE and to define prescribing patterns of physicians. **Methodology:** 100 physicians from Damietta were included in the present study. They were 77 pediatricians, 20 general practitioners and 3 emergency physicians. All physicians completed a standardized written questionnaire. The questionnaire included certification, frequency of gastroenteritis diagnosis at the last month and pattern of and response to antiemetics. In addition, any adverse effects or limiting factors for antiemetics use were recorded. **Results:** 90% of physicians prescribed antiemetic in the last month; 93% did not have any concern with prescription; 42% do not prescribe antiemetic below certain age (6 months by 27%); 36% noted adverse effects and 99% prefer parenteral route. Most physicians prefer ondansetron as first choice. Metoclopramide was reported as first choice by emergency (33%) and general practitioners (15%) more than Pediatricians (only 3%), with significant difference. In addition, ondansetron was reported to participate in recovery from vomiting other than other antiemetics. Metoclopramide was reported to share recovery from vomiting by GPs (25%) and emergency physicians (33%) more than Pediatricians (6.5%), with significant difference. **Conclusion:** Antiemetics are frequently used by all physicians of Damietta governorate included in the present work for treatment of vomiting in pediatric gastroenteritis. Ondansetron is the first choice, and metoclopramide is used by general practitioners and emergency doctors more than Pediatricians.

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1. Introduction

The term gastroenteritis describes infections of the gastrointestinal tract (GIT) due to bacterial, viral, or parasitic organisms. These GIT infections are usually food borne. The clinical manifestations described in such infection include diarrhea and/or vomiting. In addition, systemic features such as abdominal pain and fever may be the manifestations of such illnesses (**Zulfiyaq Ahmed Bhutta, 2016**).

Acute gastroenteritis (AGE) is the main etiology of vomiting in children less than 3 years of age and is a leading cause of emergency department attendance of children and adolescents. Globally, AGE is responsible for about one million deaths per year in children less than 5 years of age. Also, AGE is a leading cause for admission due to dehydration (**Herikstad et al., 2002**).

Vomiting from AGE is distressing for patients and their families. It is not only a direct cause of dehydration but can also impede successful oral rehydration therapy and represents a major factor leading to failure of oral rehydration therapy. This subsequently lead to an increased use of intravenous rehydration fluids, need for prolonged stays in emergency departments and hospital admissions

(**Ozuah et al., 2002**). Therefore, effective therapy of vomiting would lead to a significant decrease in the use of intravenous therapy. Various antiemetic drugs have been used to stop or decrease vomiting in children with AGE such as phenothiazines, metoclopramide, domperidone and ondansetron. These antiemetic drugs have different mechanism of action and different unwanted side effects like severe dystonic reactions and Electrocardiograph (ECG) interval alterations. Dexamethasone also has anti-emetic effects and is used to treat vomiting associated with cancer chemotherapy. In such patients, it may be used alone or in combination with other anti-emetics such as metoclopramide or 5-hydroxytryptamine (serotonin)-3 (HT3) antagonist (**British Medical Association and the Royal Pharmaceutical Society, 2014**).

In the daily practice, antiemetic therapeutic agents are habitually used in children with AGE. A survey of retrospective nature retrieved data from four databases revealed that use of antiemetic drugs varied significantly. In particular, between 2% and 23% of infants with AGE received antiemetic medications. Dimenhydrinate and diphenhydramine (antihistamines) were most regularly used in Germany

and Canada, whereas promethazine was preferred in the United States. In France, Spain, and Italy, domperidone (dopamine receptor antagonist) used preferentially as antiemetic therapy. Ondansetron was used in a minor percentage of antiemetic prescriptions. A survey from Italy revealed that 79% of clinicians prescribe antiemetic drugs to treat AGE (domperidone in the first followed by metoclopramide) (Pfeil et al., 2008). The extent of antiemetics use in children, especially for AGE, has not been well studied in Egypt and its use is controversial.

Aim of the work

The aim of the present work is to review the use of antiemetics for pediatric AGE and to define prescribing patterns of physicians.

2. Patients and Methods

This study is designed as a cross sectional study which carried out to review the usage of antiemetics for pediatric EG and to determine prescribing patterns of physicians. The study was conducted during the academic year 2016-2017. It included 100 physicians from Damietta governorate, who were chosen randomly by simple random sample. They are working in different health institutes including 77 pediatricians, 20 general practitioners and 3 emergency doctors. All physicians were asked to complete a standardized written questionnaire. Some copies of the questionnaire were translated into Arabic. The questionnaire was adapted from a national survey, which was carried out in the United State of America by Kenneth (2002). The questionnaire included the following items: 1) Medical certification, 2) Frequency of diagnosis of AGE in pediatrics at the last month, 3) Any concerns with prescription of antiemetics for AGE in pediatrics, 4) Frequency of antiemetics prescription for AGE in pediatric patients at the last month, 5) Minimum age at which the antiemetics were prescribed, 6) Order according to frequency of a group of antiemetics (domperidone, metoclopramide, pyridoxine and ondansetron), 6) problems at availability of antiemetics at the market or hospitals, 7) The preferable route for administration of antiemetics, 8) adverse reaction after administering antiemetics, 9) Antiemetic with higher rate of recovery.

Statistical analysis of data:

The collected data were statically analyzed using statistical package for social science (SPSS Inc., Chicago, Illinois, USA). Categorical data were presented as frequency and percent distribution and for comparison between groups; the Chi square was used. Quantitative data were presented as mean \pm standard deviation (SD) for comparison between two means,

the independent Student test (t) was used. For interpretation of results, the p value <0.05 was considered significant.

3. Results

In the present work, Pediatricians constituted most of the participant physicians (77%); while general practitioners represented 20% and emergency doctors only 3%.

Descriptive statistics of the study demonstrated that all physicians had diagnosed at least a case of GE in the last month with a mean of 8.53 cases. The mean number of antiemetic prescription was 3.21 times. Frequency statistics of the study revealed that 90% of physicians prescribed antiemetic for Pediatric GE in the last month; and 93% did not have any concern with such prescription; however, 42% of physicians do not prescribe antiemetic below certain age, which was considered as 6 months by 27 physicians. However, 36% of physicians noted adverse effects from antiemetics, 34% of physicians reported adverse effect in the form of extrapyramidal manifestations from metoclopramide and two physicians noted sedation and increase frequency of diarrhea after ondansetron administration, however 25% of physicians noted paucity of cortigen B6 in pharmacies and hospitals at the time of survey. Finally, 99% of physicians prefer parenteral route and none prefer rectal route (Table 1).

Regarding the use of antiemetic in Pediatric GE, most physicians prefer ondansetron as first choice followed by domperidone; there is equality of the other three drugs as a second choice (Table 2).

In the present work, emergency doctors had significantly diagnosed more cases of GE than GPs and Pediatricians (13, 9.05 and 8.22 respectively); however, there was no significant difference as regard the use of antiemetics. The majority of physicians had used antiemetic drug in the last month, with no statistically significant difference between specialties. The majority of physicians do not have concern with antiemetic use in Pediatric GE, with no statistically significant difference between specialties. In addition, 58% physicians do not have limited age for antiemetic use in Pediatric GE, with no statistically significant difference between specialties. Most of physicians 58% have no concerns about age for antiemetics prescription, and most of physicians who reported age of limitation for antiemetic use have considered the age of 6 months as the minimum age below which they do not prescribe antiemetics. Pediatricians and emergency doctors reported higher rate of encountered side effects than general practitioners with statistically significant difference. There was no significant difference between specialties regarding their first choice of all antiemetic drugs, except for metoclopramide, which was reported as first choice by

emergency doctors (33%) and general practitioners (15%) more than Pediatricians (only 3%), with statistically significant difference. Also, ondansetron was reported by most of the physicians to participate in recovery from vomiting other than other

antiemetics. Metoclopramide was reported to share recovery from vomiting by GPs (25%) and emergency doctors (33%) more than Pediatricians (6.5%), with statistically significant difference.

Table (1): Data about antiemetic use in the last month among studied physicians

Question	Statistics	
How many times you diagnosed Pediatric GE at the last month?	8.35±---; 1-36	
How many times you prescribed antiemetics for GE at last month?	3.21±---; 0-30	
Had you prescribed antiemetics for Pediatrics GE in the last month?	Yes	90(90.0%)
	No	10(10.0%)
Do you have any concerns with prescribing antiemetics for Pediatric GE?	Yes	7(7.0%)
	No	93(3.0%)
Is there a minimum age below which you wouldn't prescribe antiemetic?	Yes	42(42.0%)
	No	58(58.0%)
What is the minimum age below which you wouldn't prescribe antiemetic?	6 months	28 (28.0%)
	12 months	10 (10.0%)
	24 months	4 (4.0%)
Do you face problems at availability of antiemetic?	Yes (cortigen B6)	25(25.0%)
	No	75(75.0%)
What route of administration of antiemetic drugs do you prefer for pediatric gastroenteritis?	Oral	1(1.0%)
	Parenteral	99(99.0%)
	Rectal	0(0.0%)
Have you ever observed an adverse reaction after administrating a single dose of antiemetic drug?	Yes	36(36.0%)
	No	64(64.0%)
The form of adverse reaction	Extrapyramidal	34 (34.0%)
	Sedation and diarrhea	2(2.0%)
Have you ever discharged a Pediatric GE patient after recovery from vomiting with antiemetic prescription?	Ondansetron	77(77.0%)
	Metoclopramide	11(11.0%)
	Pyridoxine	5(5.0%)
	Domperidone	2(2.0%)

GE: gastroenteritis

Table (2): What antiemetic drug (s) do you use for Pediatric GE, and with what average order of frequency?

	First	Second	Third	Fourth
Ondansetron	75 (75.0%)	14 (14.0%)	6 (6.0%)	3 (3.0%)
Domperidone	12 (12.0%)	27 (27.0%)	29 (29.0%)	30 (30.0%)
Metoclopramide	7 (7.0%)	30 (30.0%)	10 (10.0%)	51 (51.0%)
Pyridoxine	4 (4.0%)	27 (27.0%)	53 (53.0%)	14 (14.0%)
Total	98 (98.0%)			
Unable to rank	2 (2.0%)			

Table (3): Relation between physician specialty and other studied variables

Question	General practitioners	Pediatricians	Emergency doctor	P	
How many times you diagnosed Pediatric GE at the last month?	9.05±2.63	8.22±5.37	13±6.08	0.021*	
How many times you prescribe antiemetics for GE at last month?	2.55±1.57	3.25±4.05	6.67±5.68	0.34 (ns)	
Antiemetic use in last months	Yes	17(85.0%)	70(90.0%)	3(100.0%)	0.55 (ns)
	No	3 (15.0%)	7(10.0%)	0(0.0%)	
Concerns for antiemetic use	Yes	3(15.0%)	4(5.0%)	0(0.0%)	0.3 (ns)
	No	17(85.0%)	73(95.0%)	3(100.0%)	
Presence of limited age	Yes	10(50.0%)	31(40.0%)	1 (33.0%)	0.40(ns)
	No	10(50.0%)	46(60.0%)	2(67.0%)	
Age of limitation	None	10 (50%)	46 (60%)	2 (67%)	0.46 (ns)
	6 m	8 (40%)	20 (26%)	0 (0%)	
	12 m	0 (0%)	9 (11%)	1 (33%)	
	24 m	2 (10%)	2 (3%)	0 (0%)	
Side effect	Yes	3 (15%)	31 (40%)	2 (67%)	0.046*
	No	17 (85%)	46 (60%)	1 (33%)	
First choice for antiemetic drugs	Ondansetron	17 (85%)	56 (72.7%)	2 (67%)	0.57(ns)
	Domperidone	0 (0%)	12 (15.6%)	0 (0%)	0.12(ns)
	Metoclopramide	3 (15%)	3 (3.9%)	1 (33%)	0.047*
	Pyridoxine	0 (0%)	4 (5.2%)	0 (0%)	0.52(ns)
Cases discharged after recovery from vomiting with an antiemetic in last month	Ondansetron	13 (65%)	62 (80.5%)	2 (67%)	0.32
	Domperidone	0 (0%)	2 (2.6%)	0 (0%)	0.59
	Metoclopramide	5 (25%)	5 (6.5%)	1 (33%)	0.023*
	Pyridoxine	1 (5%)	4 (5.2%)	0 (0%)	0.85

4. Discussion

The guidelines for treatment do not recommend antiemetic drugs for treatment of vomiting-related to AGE in pediatrics. However, their use is common in clinical practice. The reasons why antiemetics not recommended for GE-related vomiting are: self-limitation of vomiting, vomiting is a normal physiological reaction to get rid of toxic substances, and antiemetics have adverse effects. Furthermore, multiple medications have been used in an attempt to limit vomiting and facilitate oral rehydration but have not attained acceptance because of limited success and high rates of complications (Patel et al., 2017). Thus, the present study was designed to review the usage of antiemetics for gastroenteritis in pediatrics and to describe the prescribing configuration of physicians in Damietta governorate.

In the present study the overall incidence of pediatric gastroenteritis based on number of cases diagnosed by physicians was relatively high with a mean of 8.53 cases per physician per week. This may be related to the climatic conditions of Damietta governorate at the time of our survey including spring and summer, that's correlate with a study by (Onozuka and Hagihara 2015) who observed that the

overall national maximum-morbidity temperature of gastroenteritis corresponded to approximately the 60th percentile of annual temperature, denoting that infectious GE risk may be higher at this percentile.

Variation in the effect of temperature on morbidity may also be altered many factors such as social, environmental, and behavioral factors. For example, hot climate may lead to specific behavioral patterns, such as higher water consumption and less reliable hygiene, thereby promoting transmission of diarrhea. Studies also proposed that, food poisoning and electrolyte imbalance are more likely to occur during periods of persistent hot temperatures.

In the present study, the percentage of prescriptions for GE that's contain antiemetic medication is 38%, this percentage is higher than the reported by (Pfeil et al., 2008) from other parts of the world. The reported percentages ranged between 2% and 23% of all prescriptions to children with infectious GE involve antiemetic drugs. About 2.2 million children received antiemetic drugs during illness attributed to confirmed or suspected infectious diarrhea. They analyzed the use of antiemetic drugs in pediatrics with GE and found a strong variation between countries. There is not only a marked

difference in the frequency of antiemetic drug use, but types of antiemetic agents also vary strongly in different countries.

In this regard, the socioeconomic condition in Damietta governorate and the medical context of its physicians may explain the increased ratio of antiemetic drugs prescription in pediatric GE.

In developing world, severe malnutrition, underlying clinical conditions, and concomitant diseases may markedly affect disease severity and clinical outcomes in children with age (**Guarino et al., 2014**). Significant differences have been reported in the treatment of AGE in developed countries at different levels. This is in part explained by heterogeneity—population, setting, causative agents, and nutritional status. Trials from low and middle income countries comprise more severe cases, organisms rarely seen in developed nations, and malnourished infants (**Freedman, Pasichnyk et al., 2015**).

In the present work, most of physicians (58%) have no concerns about age for antiemetics prescription, on the other side most of physicians who reported age of limitation for antiemetic use have considered the age of 6 months as the minimum age below which they do not prescribe antiemetic drugs. This appears doesn't coordinate with the trend among physicians from United States of America, as most physicians (64.8%) reported a minimum age under which they wouldn't administer or prescribe antiemetics, with the most common ages being 1 year and 2 years (**Kwon et al., 2002**).

At the time of our survey, 25% of the included physicians noted paucity of cortigen B6 ampoules in pharmacies and hospitals. In Egypt, drug shortage problem received much of the media attention when Egypt faced political instabilities since 25th January 2011. In more than one condition, this was referred to as the drug shortage crisis. **Abdelrahman et al. (2016)** survey noted that more than half the respondents (54%) of physicians reported facing troubles finding medications to treat patients in their last shift.

In the present work, ondansetron was reported by most of the physicians to participate in recovery from vomiting other than other antiemetics, that's in coordination with a study by (**Freedman et al., 2012**) which analyzed ondansetron usage in pediatric GE and reported an increase in the use of ondansetron in infants with AGE, from 1% to 18%, during a 5-year period. This corresponded with a 46% relative reduction in the use of intravenous rehydration therapy, from 26% to 14%, with evidence of a downward-level break following the introduction of ondansetron. This decrease occurred in conjunction with a decrease in length of stay, emergency

department revisits, and revisits requiring intravenous rehydration.

In 2003, the Centers for Disease Control (CDC) and Prevention distributed a report which proposed that ondansetron could be effective in reducing vomiting and limiting hospital admission. This was recommended by the American Academy for Pediatrics in 2004 and although recommendations do not advocate the routine use of medications, the policy proposed that, ondansetron may be valuable in limiting vomiting and hospital admissions. Similarly, European guideline reported that ondansetron might be of benefit in pediatrics with vomiting associated with GE (**Das et al., 2013**).

In the present work, metoclopramide was reported to share recovery from vomiting by general practitioners (GPs) (25%) and emergency doctors (33%) more than Pediatricians (6.5%), with statistically significant difference. That's may be due to the cheaper price of metoclopramide in comparison to ondansetron at the Egyptian pharmaceutical market. **Cubeddu et al. (1997)** noted that metoclopramide also decreased the number of emetic episodes compared with the placebo, however the results didn't reach statistical significance. The systematic review carried by **Lin et al. (2016)** noted that the available evidence specifies that the most commonly reported adverse effects of metoclopramide in children are extrapyramidal manifestations, diarrhea, and sedation. Also 34% of the physicians included in our survey noted extrapyramidal side effect as result of metoclopramide administration while 2% reported sedation and increase diarrhea frequency due to ondansetron administration.

In summary, results of the present work revealed frequent use of antiemetics by all physicians of Damietta governorate for treatment of vomiting in pediatric GE. Ondansetron is the first choice, and metoclopramide is used by general practitioners and emergency doctors more than Pediatricians.

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