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Ondansetron Prescription for Home Use in a Pediatric Emergency Department

James M. Gray, MB, BCh[*], **Jaya D. Maewal, MD**[†], **Scott A. Lunos, MS**[‡], **Ronald A. Furnival, MD**[*], **Marissa A. Hendrickson, MD**[*]

[*]Department of Pediatrics, University of Minnesota, Minneapolis, MN

[†]Department of Pediatrics, University of California, Davis, Sacramento, CA

[‡]Clinical and Translational Science Institute/Biostatistical Design and Analysis Center, University of Minnesota, Minneapolis, MN

Abstract

Objectives: Ondansetron has been shown to decrease admission rate and the need for intravenous fluids among pediatric emergency department (ED) patients with acute gastroenteritis, but there is limited evidence regarding its use after ED discharge. This study describes prescribing patterns for ondansetron and assesses the effects of ondansetron home prescription on rate of return.

Methods: Data were gathered from the electronic health record on 2 separate but overlapping groups of patients seen in a pediatric ED from 2012 to 2014. The Gastroenteritis Group included all patients with a discharge diagnosis of gastroenteritis by *International Classification of Diseases, Ninth Revision*, code. The All Ondansetron Group included any child prescribed ondansetron at discharge. Patterns of ondansetron use and 3- and 7-day ED return rate were assessed for both groups. Discharge diagnosis was evaluated for the All Ondansetron Group.

Results: A total of 996 patients with acute gastroenteritis were identified during the study period. Of these, 76% received ondansetron in the ED, and 71% were discharged with prescriptions for ondansetron. Seven-day ED return rates were similar between groups (6% with prescription, 5% without, $P = 0.66$). A total of 2287 patients received home prescriptions for ondansetron. Fifty-four percent of these patients' discharge diagnoses were classed as gastrointestinal complaints, 14% other infectious conditions, 9% respiratory, and 4% injuries. Their return rate was 6%. There was wide variation in the number of doses prescribed.

Conclusions: Home-use ondansetron is widely prescribed in this urban academic pediatric ED for a variety of indications, without effect on 3- or 7-day ED return. Further prospective studies are necessary to determine the efficacy of this practice.

Keywords

ondansetron; gastroenteritis; home prescription; discharge

Reprints: Marissa A. Hendrickson, MD, Division of Pediatric Emergency Medicine, Department of Pediatrics, University of Minnesota Medical School, M654 East Bldg, 2450 Riverside Ave, Minneapolis, MN 55454 (mhendric@umn.edu).

The use of ondansetron in pediatric emergency departments (EDs) is widespread. Its efficacy for the treatment of acute gastroenteritis (AGE) in children is well-established by multiple studies showing reductions in the use of intravenous fluids (IVFs), vomiting, admissions, and return visits to the ED.[1,2]

Although ondansetron has long been used on an ongoing outpatient basis in pediatric oncology, there is a relative paucity of literature on its home use after discharge from the ED in pediatric AGE.[3] Two randomized controlled trials have included a brief course of scheduled ondansetron after discharge, with variable results.[4,5] Despite the lack of clear literature addressing the practice of prescribing ondansetron for as needed use, one large study reported that 34% of children seen for gastroenteritis or vomiting in 1 of 2 EDs were discharged with prescriptions for ondansetron.[6] They found no significant difference in rate of admission or ED return between those with prescriptions and those without but did not provide details of dosing or quantity prescribed.

Although the use of ondansetron in the ED has been increasing dramatically in recent years, both for AGE and a wide variety of other indications, there remains little literature to guide the optimal dosing or duration of therapy for ongoing use after discharge.[7,8] The objective of this study is to describe the pattern of ondansetron prescription for patients discharged from the pediatric ED at a single institution, for AGE and other diagnoses, and to determine the rate of ED return visits among these patients.

METHODS

Study Design and Setting

This study was a retrospective analysis of ondansetron prescribing in the ED of an urban, tertiary-care, and quaternarycare pediatric university teaching hospital with an annual ED census of approximately 14,000 visits. This ED is primarily staffed by attending physicians board-certified in pediatric emergency medicine, supervising residents for approximately 19 hours per day and working independently during the other 5 hours. Additional coverage is provided by general pediatricians functioning as independent second attending physicians approximately 8 hours per day.

The institution's human subjects institutional review board reviewed and approved this study.

Patient Selection

Two separate but overlapping groups of patients were extracted from the electronic health record. Both groups included children between 0 and 18 years of age at the time of the encounter who were discharged from the ED between January 1, 2012 and December 31, 2014. Patients who were admitted to the hospital were not included.

The Gastroenteritis Group included all children who received a discharge diagnosis of AGE, defined as *International Classification of Diseases*, *Ninth Revision*, codes 009.0, 009.1, 008.8, and 558.9. The All Ondansetron Group included all children who were prescribed ondansetron at discharge, regardless of diagnosis.

Data Collection

For each group, we electronically extracted from the medical record the patient's age, sex, race, ethnicity, discharge diagnoses, ED administration and discharge prescription of ondansetron, and any revisit to the ED within 3 or 7 days, time periods that have been studied and reported previously.[1,6]

Data Analysis and Outcomes

The primary outcome assessed for the Gastroenteritis Group was rate of prescription of ondansetron at discharge for home use. For the All Ondansetron Group, the primary data point assessed was the visit discharge diagnosis. Secondary outcomes for both groups included return to the ED within 7 days and the use of oral or intravenous ondansetron during the ED stay. Oral liquid, orally dissolving tablet, and standard tablet formations were considered to be equivalent.

Statistical analysis was performed using SAS version 9.3, from the SAS Institute, Cary, NC. Fisher exact tests were used to compare return rates. A Wilcoxon rank sum test was used to compare length of stays. Diagnoses for the All Ondansetron Group were categorized and simplified using Clinical Classifications Software for *International Classification of Diseases*, *Ninth Revision*, *Clinical Modification* from the Healthcare Cost and Utilization Project, with further simplification by direct review by a physician investigator.

RESULTS

During the 3-year study period, we identified 996 patients with a diagnosis of AGE and 2287 patients who were prescribed homegoing ondansetron for any indication; 97% of prescriptions were advised as needed dosing. Demographic and length of stay characteristics of the groups are described in Table 1. Within the gastroenteritis group, length of stay was found to be slightly higher in patients who did receive versus those who did not receive prescriptions for ondansetron at discharge ($P = 0.03$).

Table 2 lists the ondansetron usage characteristics for the Gastroenteritis Group. Of these 996 patients, 65% received oral ondansetron in the ED and 16% received intravenous ondansetron. Approximately 71% of this group was discharged with a prescription for home ondansetron.

Seven-day rates of ED return for Gastroenteritis Group patients are outlined in Table 3. There was no significant difference in this rate between those who received a home prescription for ondansetron and those who did not (6% and 5%, respectively, $P = 0.66$). Likewise, no significant difference was found between patients who did and did not receive ondansetron in the ED.

Table 4 shows the characteristics and return rate of the 2287 patients in the All Ondansetron Group. By definition, all of these patients were provided prescriptions for ondansetron at ED discharge. Seventy-four percent of them also received ondansetron in the ED. Their ED return rate was similar to that of the gastroenteritis patients, at 6%. These patients were assigned a total of 4071 diagnoses. Fifty-four percent were primary abdominal or

gastrointestinal complaints, 14% other infectious conditions, 9% respiratory diagnoses, and 4% injuries, with wide variation in the remaining diagnoses.

Table 5 describes the doses and quantities of ondansetron prescribed at discharge for patients in the All Ondansetron Group. The median dose given was 0.127 mg/kg, with an interquartile range of 0.10 to 0.16 mg/kg. The median number of doses prescribed was 10, and the interquartile range was 6 to 12.

DISCUSSION

This single-center retrospective study reports a large case series documenting the evolving usage of as needed homegoing doses of ondansetron in children cared for in an academic pediatric ED for gastroenteritis and other diagnoses. To our knowledge, it is the first report specifically addressing this type of as-needed dosing in gastroenteritis and assessing the mix of diagnoses for which homegoing ondansetron is being used overall.

The safety and efficacy of single-dose ondansetron for children with AGE treated in the ED setting are well established in the literature.[1,2,9,10] In particular, multiple systematic reviews have indicated a reduction in the use of IVF, protracted vomiting, hospital admissions, and return visits to the ED within 3 days with the use of single-dose ondansetron in AGE.[2,11] However, one recent large database study failed to find a decrease in IVF at the system level, despite increasing use of ondansetron, with wide variability by institution.[8] The study noted that only 13% of patients who received IVF were given oral ondansetron, perhaps indicating inadequate trial of oral therapy prior to initiating IVF.

Ondansetron has been used on an ongoing outpatient basis in adults and children for pregnancy and chemotherapy-related nausea with minimal adverse events.[3,12] However, there is a relative paucity of literature on its ongoing use after discharge from the ED in pediatric gastroenteritis. Although avoiding the need to return to the ED by effectively controlling vomiting at home is a plausible goal of ondansetron use after discharge, to date, no studies have identified a decrease in ED readmissions or hospitalizations among patients given prescriptions.[4,5,7,11] However, the question of whether this practice has potential to decrease vomiting, no doubt an outcome valued by patients and their parents, has not been clearly answered. On this issue, the 2 randomized controlled trials that included the use of ondansetron prescriptions for home have reported mixed results. Ramsook et al[4] assigned 145 patients to receive placebo or 5 additional doses of ondansetron to be given on a scheduled basis after ED discharge. They showed a decreased need for IVF and hospital admission during the ED visit but found no difference in rate of return to the ED nor in reported vomiting in the first 48 hours after ED discharge. The study was limited by significant loss to follow-up, inclusion of patients without diarrhea, and the inclusion of relatively well children. Yilmaz et al[5] performed a similar trial of 109 children, providing a total of 24 hours of placebo or ondansetron orally, with the first 8 hours of observation conducted in an ED observation unit. In contrast to the findings of Ramsook et al,[4] they identified a substantial decrease in vomiting, with 72% of placebo patients having vomiting in the first 24 hours compared with 11% of the ondansetron patients ($P < 0.001$). The only other description of the use of ondansetron after ED discharge for pediatric gastroenteritis

patients that we are aware of is in the retrospective analysis by Sturm et al.[6] They reported 34,117 patients with diagnoses of vomiting or gastroenteritis and found that in their setting 34% were prescribed ondansetron for home use. However, their focus was on the question of masking alternative diagnoses, so they did not report other outcomes such as vomiting or diarrhea, nor did they address the questions of as-needed versus scheduled use or the number of doses prescribed.

Regarding side effects, both the Yilmaz et al[5] and Ramsook et al[4] studies showed small increases in the mean number of episodes of diarrhea during multiple dose ondansetron administration when compared with placebo; however, in neither study were any serious adverse events reported.[4,5] Of note, both of these studies reported scheduled rather than as-needed administration; to our knowledge, outcomes of as-needed home administration have not been studied. Some studies of single-dose ondansetron use in the ED have also shown an increase in diarrhea prevalence, although others have not found a difference.[1,13,14] It seems plausible that clinicians who are aware of these findings would consider that an increase in diarrhea would be preferable to patients and families when compared with ongoing vomiting, but to our knowledge, family preference in this matter has not been studied.

In addition to the possibility of increasing diarrhea, critics have raised questions about more serious adverse effects from ondansetron. One such concern is the possibility of masking alternative diagnoses. In 2010, Sturm et al[6] specifically examined the question of masking more serious diagnoses, with a database of over 34,000 patients. They found no increase in subsequent serious diagnoses among patients who received single doses of ondansetron, nor among the 34% of patients studied who received ondansetron prescriptions. More concerning is the question of life-threatening cardiac arrhythmias associated with prolonged QTc, which may be not have been diagnosed at the time ondansetron is given. A 2014 systematic review and postmarketing analysis identified 23 individual reports of arrhythmia as a complication of ondansetron use; 6 of these were children.[15] None of the reported cases involved single oral doses of ondansetron. The 2 cases identified (1 adult and 1 child) where there was significant arrhythmia associated with oral ondansetron involved ongoing dosing as well as electrolyte abnormalities and significant polypharmacy.[16,17] Likewise, the pediatric cases in which intravenous ondansetron use was associated with significant arrhythmia generally involved polypharmacy with chemotherapy or anesthetic drugs, although 1 report of bradycardia (which resolved with intervention) seems to have occurred in an otherwise healthy 8-year-old child.[18] However, combining concerns about the rare possibility of arrhythmia as well as the potential increase in diarrhea, some authors have specifically recommended against the use of multiple dose regimens for gastroenteritis, despite the mixed evidence.[11,19]

Although a handful of controlled studies have included the recommendation of scheduled doses at home in children discharged from the ED with gastroenteritis, our current retrospective study is the first specific description of which we are aware of the use of ondansetron on an as-needed basis in these patients. We demonstrate that the prescription of ondansetron at discharge has become quite routine in this urban, academic ED, with a rate of home prescription well above that reported by Sturm et al[6] (71% vs 34%). This may reflect a changing practice as physicians become more comfortable with ondansetron. In these

findings, we identified wide variability in prescribing habits, even within a single academic institution. Although the interquartile range of doses we report approximates the 0.15 mg/kg dose which has been included in product labeling and generally matches the simplified dosing reported in the gastroenteritis literature,[1] the range includes doses as high as 0.58 mg/kg, likely representing a frank prescribing error. Likewise, although most of the attending physicians in the group report that they prescribe “a few” doses of ondansetron at discharge (personal communication), the median number of doses prescribed was 10, with a range including an outlier value as high as 112.5. As a retrospective study, this investigation did not exert any control over the dosing prescribed, but it did uncover a potential weakness in our system. This variability is likely due in part to the presence of rotating residents, who do the majority of prescription writing in our setting. It also demonstrates a potential issue with electronic ordering defaults, because there exists a discharge order default of 10 orally dissolving ondansetron tablets, which could be 20 doses for a smaller child. Correcting such defaults to better match intended practice is a potentially important area for quality improvement.

The similar return rate we found between the ondansetron prescription and no prescription groups indicates that there are no major adverse outcomes that resulted in an increased rate of rehospitalization at the same institution. However, it may also suggest that prescribing it for home use is unnecessary. This may be because many patients present toward the end of their AGE infection and require only the 8 hours of antiemetic coverage that is provided by a single dose of ondansetron. Although our study adds to the already strong literature showing no impact of ondansetron on ED return rates, given that symptom control is an important goal irrespective of ED return rates, further prospective studies will be helpful to assess the symptom-control impact of the provision of additional as-needed doses after discharge.

Limitations

This investigation is limited by its conduction at a single institution. As a result, we are unable to comment on how this practice compares to that in other institutions and regions. In addition, our single-site design raises the possibility that return to the ED rates may have been artificially lowered by patients seeking follow-up care at different institutions. However, we would not expect this to apply differentially to the prescription and no prescription groups, so we expect that the comparison between the rates is reliable. Likewise, although the fact that we did not specifically assess presenting symptoms, patient acuity, or ED course could conceal potential confounders, the fact that the ED lengths of stay were low (median, 1.9–2.0 hours) and similar for all groups makes it unlikely that significant differences in intensity of ED therapy were missed. In particular, although the statistically significant ($P = 0.03$) difference in length of stay between the no prescription group and the prescription group could theoretically indicate that the prescription group was more ill and required more therapy in the ED, the absolute difference in the median length of stay was 0.1 hours or 6 minutes. This is unlikely to have represented a clinically significant difference.

In addition, the retrospective and electronic nature of our data collection process did not allow for assessment of the efficacy of ondansetron prescription for symptom control, nor

for how many doses were actually filled by pharmacies and used. In a future study, it would be helpful to contact families shortly after discharge to determine if additional doses were given and the extent to which the patient had ongoing vomiting or diarrhea. However, despite these limitations, this study demonstrates an evolving pattern in the provision of ondansetron for as-needed home use and indicates an avenue for further research.

CONCLUSIONS

Despite the increasing use of ondansetron in AGE, questions remain regarding the safety and efficacy of prescriptions provided for home use after ED discharge. We have demonstrated that, despite a small and mixed literature on its efficacy, pediatric ED physicians in a single academic center have widely adopted the practice of prescribing ondansetron at discharge, for gastroenteritis and a variety of other indications, with significant variation in dose and quantity prescribed. Further research is required to assess the efficacy of this practice in controlling ongoing symptoms of gastroenteritis.

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TABLE 1.

Demographic Characteristics of the Study Populations

	Gastroenteritis Group (Discharge Diagnosis of AGE) (N = 996)	All Ondansetron Group (Received Ondansetron Prescription for Home Use) (N = 2287)
Age, mean (SD), y	4.3 (4.1)	5.0 (4.4)
Sex		
Female	455 (46%)	1140 (50%)
Male	541 (54%)	1147 (50%)
Race		
Black or African American	488 (49%)	1135 (50%)
White	294 (30%)	693 (30%)
Asian	29 (3%)	57 (3%)
American Indian or Alaska Native	27 (3%)	57 (3%)
Unknown, declined or other	161 (16%)	345 (15%)
Ethnicity		
Not Hispanic/Latino	865 (87%)	2036 (89%)
Hispanic/Latino	107 (11%)	206 (9%)
Declined or unknown	24 (2%)	45 (2%)
ED length of stay (LOS)		
Median (IQR), h	2.0 (1.3–2.7)	2.0 (1.5–2.9)
Patients given home ondansetron prescription	2.0 (1.4–2.7) $P = 0.03$	NA
Patients not given home ondansetron prescription	1.9 (1.9–2.6)	NA

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TABLE 2.

Ondansetron Use Characteristics of Children With a Diagnosis of AGE

Gastroenteritis Group	N = 996
Received any ondansetron in the ED *	756 (76%)
Received oral ondansetron	650 (65%)
Received intravenous ondansetron	160 (16%)
Received discharge prescription for ondansetron	705 (71%)

* Some patients received both oral and intravenous ondansetron.

TABLE 3.

ED Return Rates by Ondansetron Use Among Gastroenteritis Patients

Gastroenteritis Group (N = 996)	N for Subgroup	Return to ED Within 3 d	*P*	Return to ED Within 7 d	*P*
Patients given a home ondansetron prescription	705	36 (5%)	0.75	43 (6%)	0.66
Patients NOT given a home ondansetron prescription	291	13 (5%)		15 (5%)	
Patients given ondansetron in the ED	756	36 (5%)	0.73	43 (6%)	0.75
Patients NOT given ondansetron in the ED	240	13 (5%)		15 (6%)	

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TABLE 4.

Characteristics and ED Return Rate of Children Who Received an Ondansetron Prescription for Home Use (All Ondansetron Group)

Patients (N = 2287)	
Received ondansetron in the ED	1698 (74%)
Return to ED within 3 d	105 (5%)
Return to ED within 7 d	136 (6%)
Diagnoses (N = 4071) *	
Abdominal/gastrointestinal diagnoses	2190 (54%)
Other nonabdominal infections	585 (14%)
Respiratory diagnoses	366 (9%)
Injuries	179 (4%)

* Some patients had multiple diagnoses.

TABLE 5.

Dosage and Quantity of Ondansetron Prescribed at Discharge

All Ondansetron Group (N = 2287)	Mean (SD) [Median]	Range	Interquartile Range
Dose, mg/kg	0.135 (0.049) [0.127]	0.034–0.580	0.100–0.164
No. doses prescribed	12.7 (13.2) [10]	1–112.5	6–12

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