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The Effect of Intramuscular Ondansetron Treatment on Prognosis in Patients Diagnosed with Acute Gastroenteritis

Akut Gastroenterit Tanılı Hastalarda İntramusküler Ondansetron Tedavisinin Prognoza Etkisi

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Abstract

Introduction: Vomiting is an important symptom that limits oral intake and may result in hospitalizations and prolonged hospital stays for intravenous fluid therapy. In our study, we aimed to compare the rates of hospital revisit and hospitalization due to vomiting within seven days of admission in children with acute gastroenteritis in two groups who received and did not receive intramuscular ondansetron.

Methods: Files of patients aged 6 months-15 years (without dehydration) diagnosed with acute gastroenteritis (ICD A09) in our pediatric emergency clinic between December 2015-February 2016 (non-ondansetron period) and December 2019-February 2020 (intramuscular ondansetron period) were analyzed retrospectively. The patients included in the study were evaluated in two groups, the first group receiving a single dose of intramuscular ondansetron and the second group not receiving ondansetron treatment. Our primary aim was to determine the rates of readmission and hospitalization in the first 7 days of both groups

Results: It was determined that 21% of the patients who received ondansetron and 28% of the group who did not receive ondansetron were admitted to the emergency department due to vomiting in the first 7 days. In comparison of both groups, 5% of group I patients and 13% of group II patients needed intravenous fluids (odds ratio =0.3; 95% confidence interval =0.19-0.59) at repeated admission and required hospitalization in the emergency department.

Conclusion: Intramuscular ondansetron treatment reduces the rate of hospital readmission, hospitalization and intravenous fluid requirement during re-admission in children with acute gastroenteritis with vomiting.

Keywords: Child, gastroenteritis, ondansetron

Öz

Giriş: Kusma oral alımı sınırlayan önemli bir semptomdur, hastaların damar içi sıvı tedavisi için hastane yatışına ve uzamış hastanede kalış süresine neden olabilir. Çalışmamızda akut gastroenteritli çocuklarda intramusküler ondansetron alan ve almayan iki grupta başvurudan sonraki yedi gün içinde kusma nedeniyle hastaneye yatış ve hastaneye tekrar başvuru oranlarını karşılaştırmayı amaçladık.

Yöntemler: Aralık 2015-Şubat 2016 (ondansetron olmayan dönem) ve Aralık 2019-Şubat 2020 (kas içi ondansetron dönemi) arasında çocuk acil kliniğimizde akut gastroenterit (ICD A09) tanısı alan 6 ay-15 yaş arası (dehidratasyonsuz) hastaların dosyaları) geriye dönük olarak analiz edildi. Çalışmaya dahil edilen hastalar, tek doz intramusküler ondansetron alanlar birinci grup, ondansetron tedavisi almayanlar ikinci grup olmak üzere iki grupta incelendi. Birincil amacımız her iki grubun ilk 7 gün içinde tekrar başvuru ve yatış oranlarının belirlenmesiydi.

Bulgular: Ondansetron tedavisi alan hastaların %21'inin, ondansetron almayan grubun %28'inin ilk 7 gün içinde acil servise kusma nedeniyle tekrar başvurduğu saptandı. Her iki grubun karşılaştırılmasında, tekrarlayan başvuruda grup I hastalarının %5'i ve grup II hastalarının %13'ü damar içi sıvı ihtiyacı (olasılık oranı= 0,3; %95 güven aralığı =0,19-0,59) oldu ve acil serviste yatış gerekti.

Sonuç: İntramusküler ondansetron tedavisi kusması olan akut gastroenteritli çocuklarda hastaneye tekrar başvuru oranını, tekrar başvuru esnasındaki yatış ve damar içi sıvı ihtiyacını azaltır.

Anahtar Kelimeler: Çocuk, gastroenterit, ondansetron

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Introduction

Acute gastroenteritis is a clinical picture defined by ≥3 watery stools within 24 hours with or without vomiting, fever or abdominal pain.[1] Viral gastroenteritis is one of the common causes of morbidity and mortality in developing countries, especially in young children. It is responsible for approximately 200,000 deaths annually and the frequency of epidemics increases in winter.[2] In the European guidelines published in 2014, oral and intravenous ondansetron was reported to be both effective and safe treatment in children with vomiting due to acute gastroenteritis.[1] It has been emphasized that ondansetron treatment is the only antiemetic that provides a significant reduction in the prevention of vomiting episodes, intravenous fluid requirement, and hospitalization.[3]

There are not enough studies yet on the use of intramuscular ondansetron to support oral intake in children diagnosed with acute gastroenteritis. The primary aim of this study is to examine the effects of intramuscular administration of ondansetron for the treatment of vomiting episodes in patients with acute gastroenteritis without dehydration on the rates of readmission and hospitalization. The secondary aim is to investigate whether there is a difference between the degrees of dehydration and the days of hospitalization in patients requiring hospitalization at the time of readmission.

Materials and Methods

Our study was conducted in a tertiary pediatric hospital with an annual average of 200,000 emergency department admissions. The files of the patients aged 6 months -15 years, who were admitted to our pediatric emergency clinic between December 2015 and February 2016 (non-ondansetron period) and between December 2019 and February 2020 [intramuscular (IM) ondansetron period] with vomiting and diagnosed with acute gastroenteritis (ICD A09), and who had no signs of dehydration at the time of admission according to the clinical dehydration scale of the World Health Organization (WHO), were examined retrospectively. Those with concomitant infections (meningitis, sepsis, urinary tract infection, upper respiratory tract infection, etc.), those with underlying chronic diseases, parasitic and bacterial gastroenteritis, those having food poisoning, those receiving antibiotic treatment, those using antiemetics other than ondansetron within 24 hours before the first admission to the emergency department or within 7 days after the admission, those who were operated at the time of admission, those who had signs of dehydration and need for intravenous fluids at the first admission, and/or those who were hospitalized were excluded from the study.

For group I (treatment group) and group II (control group), patients' gender, age, duration of symptoms, number of vomiting and diarrhea in the last 24 hours before admission, and presence of additional symptoms (fever, abdominal pain) were recorded from electronic medical records. Following examination or IM drug administration, both groups of patients were followed up in the emergency department for approximately 2 hours with appropriate fluid and food intake. Patients who did not vomit after oral intake were sent home.

After 7 days after the first admission, readmission to the emergency department due to vomiting, presence and degree of dehydration, hospitalization requirement, duration of hospitalization, and side effects related to ondansetron were recorded. In our study, IM ondansetron treatment was used as 0.15 mg/kg/dose (maximum dose 8 mg). The ethical approval of our study was provided from University of Health Sciences Turkey, Dr. Sami Ulus Maternity and Child Health and Diseases Training and Research Hospital on 15.09.2021 with the number E-21/09-209.

Statistical Analysis

The obtained data were evaluated using SPSS version 20 program and descriptive statistics were used. The Kolmogorov-Smirnov test was used to evaluate whether the data showed normal distribution. The categorical variables were expressed as number and percentage (%), the normally distributed numerical data as mean and standard deviation, and the non-normally distributed numerical data as median, and interquartile range. In the categorical comparisons between the groups, cross-table statistics were given and the significance levels were checked with the chi-square test. The Student's t-test was used in comparison of two independent groups for normally distributed data, and the Mann-Whitney U test was used for data not normally distributed. Odds ratio (OR) and 95% confidence interval (CI) were given to determine the risk factor between the groups. Statistical significance level was accepted as $p<0.05$.

Results

A total of 722 patients were included in the study. The cases were divided as group I, including 401 (56%) patients receiving IM ondansetron, and group II, including 321 (44%) patients not receiving the treatment. There was no significant difference between the two groups in terms of gender and age. Demographic data and clinical symptoms of the patients are given in Table 1.

Among the patients, the number of patients with recurrent admissions due to the continuation of vomiting in 7 days after admission was 84 (21%) in group I and 90 (28%) in

Table 1. Comparison of demographic and clinical characteristics of patients

	Group I	Group II	p-values
Patient n (%)	401 (55)	321 (45)	
Sex n (%)			
Male	226 (56)	201 (62)	**0.150**
Female	175 (44)	120 (38)	
Age, month, median (IQR)*	22 (14-38)	17 (10-39)	**0.058**
Complaints at admission			
Number of vomiting, mean ± SD**	4.08±2.3	4.4±1.9	**0.031**
Number of diarrhea	4.6±2.0	5.5±2.1	**<0.001**
Fever ≥38 °C	91	47	0.008
Duration of symptoms, day, mean ± SD	1.5±0.9	2.1±1.4	**<0.001**
Re-visit rate on the first 7 days n (%)	85 (21)	90 (28)	**0.036**
Hospitalization, n (%)	20 (5)	41 (13)	**<0.001**
1. degree dehydration n (%)	8 (2)	19 (6)	**0.018**
2. degree dehydration n (%)	12 (3)	22 (7)	**0.035**
IV* fluid administration in the emergency department during re-admission n (%)**	20 (5)	41(13)	**<0.001**

p<0.05 significant, statistical analysis: Student's t-test, Mann-Whitney U test, *IQR: Interquartile range, **SD: Standard deviation, ***Intravenous

group II, and there was a significant difference between the two groups (p=0.036). In recurrent emergency department admissions, 20 (5%) of group I patients and 41 (13%) of group II patients were hospitalized, and there was a significant difference between the two groups in terms of dehydration and hospitalization (Table 1). IM ondansetron use was found to be associated with a reduced probability of intravenous fluid administration and a reduced rate of hospitalization (OR=0.3; 95% CI=0.19-0.59, p<0.001). While the hospitalization period was 1.6±1.0 days in group I patients, it was 1.6±1.1 days in group II patients, and there was no significant difference between the groups (p=0.918). Urticaria developed in only one patient after ondansetron use.

Discussion

Vomiting is a disturbing condition for children and their families, but can also result in repeated emergency room visits, hospitalizations, and increased costs. A 5-hydroxytryptamine3 receptor antagonist is used safely and effectively in the treatment of nausea and vomiting outpatients and inpatients in emergency departments.[4-6] Peak plasma concentrations are reached in 20-30 minutes after intravenous administration of ondansetron and approximately in 60-90 minutes after oral administration.[7] It has been shown that ondansetron is rapidly absorbed after IM use and its bioavailability is similar to that of intravenous administration.[7] In this study, we evaluated the effect of IM ondansetron treatment on recurrent hospital admissions and hospitalization rates in children admitted to the pediatric emergency department for acute gastroenteritis. The rates of hospital readmission and hospitalization were 21% and 5%, respectively, in patients receiving IM ondansetron therapy, and these rates were significantly lower than those in the untreated group.

In the literature regarding intravenous or oral ondansetron treatment in children with acute gastroenteritis accompanied by vomiting, there are many studies showing different efficiency levels.[8-10] Moreover, some studies show that less intravenous fluid is needed with drug administration by these routes.[10,11] Besides that, in a study comparing single-dose oral ondansetron and placebo groups in children with acute gastroenteritis with mild and moderate dehydration, it was reported that oral medication had effect on vomiting, but not on readmissions to the emergency department and hospitalizations.[5] In a meta-analysis study in which intravenous or oral therapy and placebo were compared in 2313 children with acute gastroenteritis, it was revealed that drug therapy reduced the need for intravenous fluids in children with dehydration but had no significant effect on children without dehydration.[12] In a recently published study on children with acute gastroenteritis but without dehydration, no difference was found in terms of intravenous fluid requirement between the groups that received and did not receive oral ondansetron treatment.[8] The administration routes of ondansetron therapy may affect prognosis. In the ondansetron therapy, catheter placement in intravenous administration has potentially harmful effects, and patients are at risk for the development of phlebitis, longer hospital stays, and nosocomial infections. Taking oral forms of the drug requires cooperation with the patient and it is difficult to achieve this in the pediatric

population. In addition, the dose needs to be repeated in case of vomiting in the first fifteen minutes after oral administration.[5] It has been reported that IM treatment in children with acute gastroenteritis with moderate dehydration reduces hospitalizations and intravenous fluid requirement, similar to the oral route.[13] Since we do not have an oral form of ondansetron in our hospital, the IM route is used.

To our knowledge, our study is the study having the largest sample, evaluating the usefulness of IM ondansetron use in children with acute gastroenteritis. In our study, it was found that readmissions were significantly reduced with the IM ondansetron treatment in children with acute gastroenteritis but without dehydration, compared to the control group. The decrease in the rate of recurrent admissions to the hospital may be associated with the efficacy of IM ondansetron treatment. High severity of dehydration, intravenous fluid requirement and hospitalization rates were found to be significantly higher in the control group.

No serious side effects were encountered with IM administration of ondansetron. In the literature, it has been reported that the use of ondansetron causes an increase in the number of diarrhea, QT prolongation and serious cardiac arrhythmias.[14-16] Transient urticaria was observed in only one of our cases. This result supports that the use of ondansetron is safe and has minimal side effects.[10,17] Ondansetron is extensively metabolized by the liver, especially newborns and patients with reduced hepatic blood flow may be exposed to the circulating drug for a long time.[18] Because newborns, infants younger than 6 months and children with underlying chronic diseases were excluded from our study, no serious side effects were likely encountered. Since the patients included in our study had no cardiac symptoms and signs in the clinical side-effect follow-up, routine ECG recording was not performed.

Study Limitations

Our study has several limitations. Firstly, this study was conducted in a retrospective design. For this reason, information on the number of diarrhea and vomiting in the last 24 hours could not be reached during readmissions. Although the hydration assessment of the patients was made according to the WHO clinical dehydration scale included in the protocols of our clinic, the determination and management of the dehydration severity was made by the clinicians who examined the patients. Since our study was single-center, we may not have been able to identify patients admitted to different centers due to ongoing vomiting attacks.

Conclusion

It was thought that IM administration of ondansetron in outpatient patients with acute gastroenteritis accompanied by vomiting and intolerance of oral intake might reduce readmissions to emergency department, hospitalization, and intravenous fluid requirement. The IM route can be an effective and safe alternative to oral and intravenous administration. However, there is a need for randomized controlled large series studies on IM administration of ondansetron in acute gastroenteritis cases.

Ethics

Ethics Committee Approval: The ethical approval of our study was provided from University of Health Sciences Turkey, Dr. Sami Ulus Maternity and Child Health and Diseases Training and Research Hospital on 15.09.2021 with the number E-21/09-209.

Informed Consent: Retrospective study.

Peer-review: Internally and externally peer-reviwed.

Authorship Contributions

Surgical and Medical Practices: İ.B., M.M.G., B.Ö., Concept: İ.B., A.Gü., R.M.Y., Design: İ.B., C.D.K., Data Collection or Processing: İ.B., A.G., Analysis or Interpretation: İ.B., C.D.K., Literature Search: İ.B., R.M.Y., Writing: İ.B., N.T.

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