The Journal of Emergency Medicine, Vol. 51, No. 5, pp. 491–497, 2016

0736-4679/$ - see front matter

http://dx.doi.org/10.1016/j.jemermed.2016.06.051

Original Contributions

ONDANSETRON ORAL DISSOLVE TAB VS. ORAL SOLUTION IN CHILDREN PRESENTING TO THE EMERGENCY DEPARTMENT WITH GASTROENTERITIS

Graham C. Thompson, MD,* Ellen L. Morrison, MD,† David Chaulk, MD,‡ Holly Wobma, BSC,§ Simon Kwong, MSC,‖ and David W. Johnson, MD*

*Department of Pediatrics, Alberta Children's Hospital, University of Calgary, Calgary, Alberta, Canada, †Department of Pediatrics, Stollery Children's Hospital, University of Alberta, Edmonton, Alberta, Canada, ‡Department of Pediatrics, Primary Children's Hospital, University of Utah, Salt Lake City, Utah, §Faculty of Medicine, Columbia University, New York, New York, and ‖Faculty of Medicine, University of British Columbia, Vancouver, British Columbia, Canada

Reprint Address: Graham C. Thompson, MD, Alberta Children's Hospital, 2888 Shaganappi Trail NW, Calgary, AB T3B 6A8, Canada

☐ **Abstract—Background: Ondansetron is often used in the emergency department (ED) to promote oral rehydration in children with acute gastroenteritis (AGE), yet medication solutions administered orally may be poorly tolerated in this population. Objectives: We compared the tolerability of ondansetron oral dissolve tab (ODT) to oral solution (OS) in children presenting to the ED with AGE. Methods: Using alternate-day controlled clinical trial design, children aged 3 months to 10 years received either ondansetron ODT or OS. Our primary outcome was early vomiting (within 15 min of drug administration). The secondary outcome was intravenous (i.v.) fluid administration. Results: There were 462/534 eligible children who met study criteria. Demographics, severity, and duration of illness were similar between groups. Using *intention-to-treat* analysis, early vomiting occurred in 8/209 ODT vs. 19/253 OS children (3.8% vs. 7.5%; odds ratio [OR] 0.49; 95% confidence interval [CI] 0.18–1.21). Using *as-treated* analysis, 6/222 (2.7%) children receiving ODT experienced early vomiting, compared with 21/221 (9.5%) of the OS group (OR 0.26; 95% CI 0.09–0.70). The proportion of children discharged without i.v. fluids was not different (*intention-to-treat*: ODT = 91.4% (191/209), OS = 94.1% (238/253), OR 1.49, 95% CI 0.69–3.28; *as-treated:* ODT = 92.3% (205/222), OS = 93.2% (206/221), OR 0.88, 95% CI 0.40–1.93). Conclusions: Using a conservative *intention-to-treat* analysis, we found that children presenting to an ED with AGE did not have statistically less early vomiting with ondansetron ODT as compared with OS. However, our *as-treated* analysis demonstrates that children receiving ondansetron ODT experienced early vomiting approximately one-third as often as those receiving OS. The rate of i.v. fluid administration was no different between groups regardless of the type of analysis used.** © 2016 Elsevier Inc. All rights reserved.

☐ **Keywords—ondansetron; gastroenteritis; child; emergency department**

INTRODUCTION

Acute gastroenteritis is a common childhood illness, resulting in an estimated 239,000 emergency department (ED) visits annually in Canada, and 1.5 million outpatient visits in the United States (1,2). It is also a significant cause of inpatient pediatric stays, with approximately 200,000 hospital admissions annually in the United States alone (2,3). Oral rehydration therapy is the mainstay of treatment for children with acute gastroenteritis and mild-to-moderate dehydration, though previous studies have noted that significant or persistent vomiting is perceived as a barrier to oral rehydration (4,5). Ondansetron has been shown to support oral rehydration through the reduction of vomiting and

RECEIVED: 18 February 2016; FINAL SUBMISSION RECEIVED: 7 June 2016;
ACCEPTED: 29 June 2016

intravenous (i.v.) fluid use in children with vomiting secondary to acute gastroenteritis (1,6–10).

Whereas oral administration of ondansetron can be achieved with traditional oral formats such as an oral tablet (OT) or an oral solution (OS), the ondansetron oral dissolve tab (ODT) offers an alternative method of administration. Intuitively, ondansetron ODT may be better tolerated than OT or OS, as the ODT formulation does not require swallowing of either pills or liquid, an action that is difficult for children presenting with acute gastroenteritis who are already predisposed to vomiting. However, there is a paucity of literature comparing the tolerability of oral ondansetron formulations. We therefore designed a study to compare the tolerability of ondansetron ODT to ondansetron OS in children presenting to the ED with acute gastroenteritis.

MATERIALS AND METHODS

Study Design

This study was a controlled clinical trial design comparing ondansetron ODT to ondansetron OS.

Study Setting

The ED at the Alberta Children's Hospital is the free-standing pediatric tertiary care center for southern Alberta, western Saskatchewan and eastern British Columbia. At the time of the study, the ED served a catchment area of approximately 1.8 million and had an annual census of approximately 65,000 patient visits.

Study Population

Children aged 3 months to 10 years who received oral ondansetron as part of their ED care for suspected acute gastroenteritis were potential study candidates. Those who 1) weighed at least 8 kilograms, 2) presented with recent (within the past hour) and significant (more than 6 episodes in 6 h) vomiting, and 3) were observed for at least 30 min after administration of the medication were eligible for enrollment. Children were included regardless of time of day or day of week of the ED presentation. Children were excluded if they had vomiting or diarrhea for > 7 days, localized abdominal pain, chronic medical conditions affecting major organ systems, clinical suspicion of a gastrointestinal obstruction, weighed < 8 kg, or did not have documentation of the dosage format administered.

Study Protocol

Clinical management. All children were managed according to our preexisting standard departmental clinical pathway, which includes criteria/guidelines for 1) pathway inclusion, 2) assessment of dehydration, 3) administration of ondansetron for children with recent and significant vomiting, 4) oral and i.v. fluid administration, 5) escalation of care, and 6) disposition planning and education.

As part of routine acute gastroenteritis care in our ED, parents document timing and volume of intake (oral) and output (vomiting, diarrhea, urine output) on a standardized form. Registered nurses also record the volume of oral or i.v. fluids received and output as per departmental documentation standards.

Ondansetron administration. Using alternate-day controlled clinical trial design, ondansetron was available in the ED in either exclusively ODT or exclusively OS format. Each day within the study period was "assigned" in the study log as either ODT or OS. ED stock of ODT and OS ondansetron was maintained by pharmacy services; stock and daily "assignment" was changed daily at 8:00 a.m. Patients meeting pathway criteria for ondansetron administration received a weight-appropriate dose of the format available in the ED for that day. The actual format (ODT vs. OS) of the medication given to the patient was recorded in the clinical electronic medical record by the nurse administering the medication. Ondansetron dosing was provided according to our local clinical pathway as follows: ODT – 2 mg for children weighing 8–15 kg, 4 mg for those 16–30 kg, and 8 mg for those > 30 kg; OS – 0.2 mg/kg. The remainder of clinical care was left to the discretion of the managing physician.

Study Data Management

Trained research assistants retrospectively entered data from the ED health record (physician and nursing record, parent input/output record, electronic medication record) into a custom study database using detailed standardized operating procedures. Data entry was reviewed for accuracy by a senior member of the research team. Demographics, elements of the history (presence and duration of vomiting, diarrhea, and fever) and ED physical assessment (Canadian Triage and Acuity Score, triage vital signs, Gorelick score) were recorded (11,12). ED interventions (dose and route of administration of ondansetron, other medications, oral or i.v. fluids), output (vomiting, diarrhea, urine output), and disposition were tracked.

Study Outcomes

The primary outcome of interest was the proportion of children receiving ondansetron who experienced early vomiting, defined as vomiting within the first 15 min of receiving the dose of medication. This outcome was