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A supplementary home dose of oral ondansetron given in anticipation of recurrent emesis in paediatric acute gastroenteritis

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A supplementary home dose of oral ondansetron given in anticipation of recurrent emesis in paediatric acute gastroenteritis

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You are a physician working in a paediatric emergency department (ED) in a large urban hospital. A two-year-old boy presents with a recent history of fever, emesis and abdominal pain. After examining him, you diagnose him with acute gastroenteritis and give him a 2 mg oral dose of ondansetron. Thirty minutes later, his symptoms have subsided and he is tolerating oral fluids. His parents ask you if they can go home with a 'back-up' dose of ondansetron in case his symptoms recur. What do you do?

INTERVENTIONS

Acute gastroenteritis affects approximately 16 million children <5 years of age annually in the United States and accounts for roughly three million physician visits (1). The typical presentation includes acute onset of fever, abdominal cramps, emesis and diarrhea (2). Viruses are the most common cause, although bacteria and parasites are also implicated (3). In most cases, acute gastroenteritis is self-limited and does not require pharmacotherapy (4). Increased morbidity typically results from dehydration and electrolyte imbalances (5). Oral rehydration therapy and correction of electrolyte imbalances are the most important steps in management (5). In the United States, approximately 220,000 children <5 years of age are hospitalized annually for treatment of dehydration (1), with comparable rates in Canada (6). Rotavirus, the most common cause of severe gastroenteritis, is estimated to have a societal cost of $1 billion annually (7). The development and implementation of a rotavirus vaccine has reduced ED visit rates and hospitalization significantly (8); however, acute gastroenteritis remains a commonly encountered presentation in paediatric emergency departments, and carries a societal cost of up to $18.4 million annually in Canada (9).

Ondansetron is an antiemetic medication indicated for the prevention of nausea and vomiting in patients undergoing chemotherapy, radiation therapy and surgery (10). When taken orally, it is absorbed into the gastrointestinal tract and reaches maximum plasma concentration after 1.5 h (11). Ondansetron is a serotonin 5-HT_3 receptor antagonist and is believed to function by suppressing the vomiting centres in the brain and blocking afferent depolarization of vagal nerves peripherally in the intestines (11). While the exact mechanism of emesis is not known, it has been proposed that the cause of emesis in acute gastroenteritis occurs due to viral- or bacterial-induced damage to the intestinal mucosa (12). This leads to the release of serotonin by gut enterochromaffin cells, which bind to the 5-HT_3 receptors in the bowel to provoke an emetic response (12).

Ondansetron has gained popularity among paediatric ED physicians for the treatment of acute gastroenteritis (13). It is known to be an effective antiemetic and is relatively safe, with the most common side effect being diarrhea, which is usually mild and self-limited to 48 h (14,15). Two systematic reviews have concluded that ondansetron is effective in reducing persistent vomiting, the need for intravenous fluids and the rate of hospitalization (15,16). Additionally, the use of ondansetron appears to decrease ED length of stay and ED revisit rate (17). In countries that use intravenous fluids, the use of ondansetron leads to significant cost savings (18). Alternative antiemetics including metoclopramide, trimethobenzamide and pyrilamine-pentobarbital have also been studied; however, these studies were of lower quality and reported inconsistent results (15). The Canadian Paediatric Society currently recommends a single dose of oral ondansetron for the management of patients six months to 12 years of age who present to the ED with vomiting and dehydration due to suspected gastroenteritis, and those failing oral rehydration therapy (ORT) (19). The use of ondansetron in patients with predominantly diarrhea is not recommended (19). Ondansetron should also be avoided in patients with congenital long QT syndrome due to the risk for Torsade de Pointes. The Food and Drug Administration has recommended electrocardiographic monitoring in patients with electrolyte abnormalities (ie, hypokalemia), congestive heart failure, bradyarrhythmias or patients on other QT-prolonging medications (20).

While ondansetron is widely used as an adjunct in the treatment of acute gastroenteritis by paediatric ED physicians (13), sparse literature exists on the utility of discharging patients with an at-home oral dose of ondansetron to be used as prophylaxis for recurrent emesis. The symptomatic period of acute gastroenteritis can exceed seven days (2). The terminal elimination half-life of ondansetron is only approximately 2 h to 4 h (11). Presumably, a proportion of patients who had taken ondansetron in the ED and were asymptomatic at the time of discharge may develop recurrent emesis at home. As a result, they may ultimately return to the ED, leading to increased use of hospital resources. In Canada, the point-of-care administration of ondansetron is estimated to cost $12.86 while an ED visit costs $229.93, not including intravenous catheter insertion ($84), possible hospitalization ($955) or travel expenses for patients ($21.59) (18). A recent small study found that 24% of paediatric patients who were treated with a single dose of ondansetron for acute gastroenteritis in the ED reported experiencing recurrent emesis within 24 h of discharge (21). Perhaps the use of a physician-dispensed, as-needed home dose of ondansetron given to patients in anticipation of recurrent emesis and risk of dehydration may prevent a return to the ED. While a 2010 study found no change improvement in ED revisit rates after discharging patients home with a written prescription for ondansetron, the authors caution that they did not track the number of patients who actually filled their prescriptions (22). A home dose of ondansetron given to patients by the ED physician as part of discharge planning may

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promote compliance of using ondansetron on an outpatient basis (21). Moreover, it may serve to reassure some parents who may be otherwise uncomfortable in taking their children home. It needs to be emphasized that ORT remains the cornerstone of therapy for acute gastroenteritis, and parents need to be educated to recognize the signs and symptoms of dehydration and to only administer ondansetron if ORT fails due to recurrent emesis. This may be accomplished through teaching by the discharging physician (or an ED nurse) and an information sheet for parents.

A commonly cited reason against prescribing ondansetron for home use is fear of masking other diseases not identified at the initial visit (21). Due to this caution, many physicians use ondansetron in the ED but hesitate to prescribe it for home use (21). A recent small study involving paediatric patients with acute gastroenteritis found that a single dose of ondansetron given at home does not appear to increase the rate of alternative diagnoses (21). Additional studies are needed to more clearly delineate the relationship between the home use of ondansetron and the potential masking of other conditions with a similar presentation. Until then, we caution against dispensing more than one additional dose of ondansetron.

SUMMARY

Ondansetron is a useful adjunct for the treatment of acute gastroenteritis in the paediatric ED. The use of ondansetron is associated with many benefits including decreased emesis, decreased need for intravenous fluids, decreased rate of admission, decreased length of stay, decreased revisit rates and increased cost savings (15-18). There may be value in giving patients a second as-needed home dose of ondansetron as part of ED discharge planning, with the appropriate patient education, in anticipation of recurrent emesis. This practice may further reduce ED revisit rates and also prevent morbidity and hospitalization associated with severe dehydration for patients who do eventually return to the ED, especially those in rural communities where timely treatment and access to an ED is difficult. The decision to dispense ondansetron should be made clinically by the ED physician for patients who have failed ORT whose symptoms are predominantly emesis as opposed to diarrhea, and when the discharging physician is reasonably certain of a diagnosis of acute gastroenteritis and not something more sinister.

There is currently no consensus on the role of ED-provided ondansetron for out-of-hospital use for paediatric patients with acute gastroenteritis. Future studies are needed to determine the potential impact on morbidity and the health care economy.

REFERENCES

1. Glass RI, Lew JF, Gangarosa RE, et al. Estimates of morbidity and mortality rates for diarrheal diseases in American children. J Pediatr 1991;118(4 Pt 2):S27-33.
2. Elliot EJ. Acute gastroenteritis in children. BMJ 2007;334:35-40.
3. National Collaborating Centre for Women's and Children's Health (UK). Diarrhoea and vomiting caused by gastroenteritis: Diagnosis, assessment and management in children younger than 5 years. London: RCOG Press; 2009 April. (NICE Clinical Guidelines, No. 84.) <www.ncbi.nlm.nih.gov/books/NBK63844/> (Accessed June 14, 2013)
4. Guarino A, Albano F, Ashkenazi S, et al. European Society for Paediatric Gastroenterology, Hepatology, and Nutrition/European Society for Paediatric Infectious Diseases evidence-based guidelines for the management of acute gastroenteritis in children in Europe. J Pediatr Gastroenterol Nutr 2008;46(Suppl 2):S81-122.
5. King CK, Glass R, Bresee JS, et al. Managing acute gastroenteritis among children: Oral rehydration, maintenance and nutritional therapy. MMWR Recomm Rep 2003;52(RR-16):1-16.
6. Leung A, Prince T; Canadian Paediatric Society, Nutrition and Gastroenterology Committee. Oral rehydration therapy and early refeeding in the management of childhood gastroenteritis. Paediatr Child Health 2006;11:527-31.
7. Tucker AW, Haddix AC, Bresee JS, et al. Cost-effectiveness analysis of a rotavirus immunization program for the United States. JAMA 1998;279:1371-6.
8. Goldman RD. Effectiveness of rotavirus vaccine in preventing severe acute gastroenteritis in children. Can Fam Physician 2012;58:270-71.
9. Le Saux N, Bettinger J, Dery P, et al. The hidden costs and characteristics of childhood rotavirus emergency visits in Canada. Pediatr Infect Dis J 2012;31:159-63.
10. US Food and Drug Administration. Silver Spring: US Food and Drug Administration; Ondansetron (marketed as Zofran) Information. December 4, 2012. <www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm271924.htm> (Accessed October 10, 2013).
11. Ye JH, Ponnudurai R, Schaefer R. Ondansetron: A selective 5-HT(3) receptor antagonist and its applications in CNS related disorders. CNS Drug Rev 2001;7:199-213.
12. Cubeddu LX, Trujillo LM, Talmaciu I, et al. Antiemetic activity of ondansetron in acute gastroenteritis. Aliment Pharmacol Ther 1997;11:185-91.
13. Kwon KT, Rudkin SE, Langdorf MI. Antiemetic use in pediatric gastroenteritis: A national survey of emergency physicians, pediatricians, and pediatric emergency physicians. Clin Pediatr 2002;41:641-52.
14. Manteuffel J. Use of antiemetics in children with acute gastroenteritis: Are they safe and effective? J Emerg Trauma Shock 2009;2:3-5.
15. DeCamp LR, Byerley JS, Doshi N, et al. Use of antiemetic agents in acute gastroenteritis: A systematic review and meta-analysis. Arch Pediatr Adolesc Med 2008;162:858-65.
16. Carter B, Fedorowicz Z. Antiemetic treatment for acute gastroenteritis in children: An updated Cochrane systematic review with meta-analysis and mixed treatment comparison in a Bayesian framework. BMJ Open 2012;2:pii:e000622.
17. Freedman SB, Tung C, Cho D, et al. Time-series analysis of ondansetron use in pediatric gastroenteritis. J Pediatr Gastroenterol Nutr 2012;54:381-6.
18. Freedman SB, Steiner MJ, Chan KJ. Oral ondansetron administration in emergency departments to children with gastroenteritis: An economic analysis. PLoS Med 2010;7:pii:e1000350.
19. Cheng A; Canadian Paediatric Society, Acute Care Committee. Emergency department use of oral ondansetron for acute gastroenteritis-related vomiting in infants and children. Paediatr Child Health 2011;16:117-79.
20. FDA. FDA Drug Safety Communication: Abnormal heart rhythms may be associated with use of Zofran (ondansetron). 2011. <www.fda.gov/Drugs/DrugSafety/ucm271913.htm> (Accessed September 15, 2013)
21. Haines E, Amerongen RV, Birkhahn R, et al. Evaluating outcomes associated with a discharge action plan employing single-dose home use of ondansetron in patients with acute gastroenteritis. Open Access Emerg Med 2012;4:1-4.
22. Sturm JJ, Hirsh DA, Schweickert A, et al. Ondansetron use in the pediatric emergency department and effects on hospitalization and return rates: Are we masking alternative diagnoses? Ann Emerg Med 2010;55:415-22.