Oral Ondansetron for Gastroenteritis in a Pediatric Emergency Department

Background

Vomiting limits the success of oral rehydration in children with gastroenteritis. We conducted a double-blind trial to determine whether a single oral dose of ondansetron,an antiemetic, would improve outcomes in children with gastroenteritis

Methods

We enrolled 215 children 6 months through 10 years of age who were treated in a pediatric emergency department for gastroenteritis and dehydration. After being randomly assigned to treatment with orally disintegrating ondansetron tablets or placebo, the children received oral-rehydration therapy according to a standardized protocol.

The primary outcome was the proportion who vomited while receiving oral rehydration. The secondary outcomes were the number of episodes of vomiting and the proportions who were treated with intravenous rehydration or hospitalized.

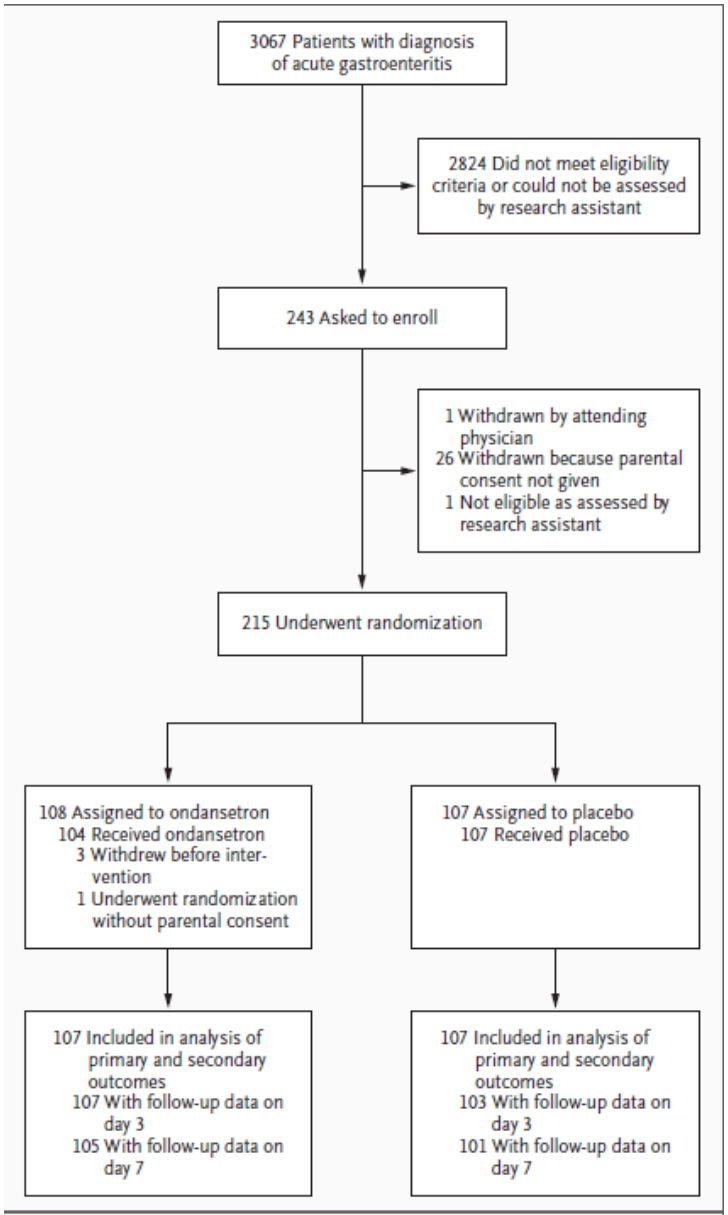

Figure 1. Enrollment and Outcomes.

The primary outcome was vomiting during oral rehydration in the emergency department after the receipt of ondansetron or placebo. The secondary outcomes were the mean number of episodes of vomiting, the rate of treatment with intravenous rehydration, and the rate of hospitalization.

Table 2. Baseline Characteristics of the Patients.*

Characteristic	Ondansetron Group (N=107)	Placebo Group (N=107)
Male sex — no. (%)	60 (56)	62 (58)
Age — mo	26±21	30±20
Weight — kg	13.1±5.3	13.7±5.5
Heart rate — beats/min	141±20	140±17
Dehydration score — no. (%)†		
9–10	29 (27)	24 (22)
11–12	51 (48)	58 (54)
13–14	20 (19)	20 (19)
15–16	7 (7)	5 (5)
Urinary measurements‡		
Specific gravity	1.026±0.007	1.025±0.006
Ketones	2.6±1.6	2.6±1.5
Vomiting — no. of episodes in preceding 24 hr	9.0±6.0	9.3±6.8
Diarrhea — no. of episodes in preceding 24 hr	5.8±4.5	6.2±5.2
Serum values at catheterization§		
Sodium — mmol/liter	138.8±6.7	136.8±2.9
Potassium — mmol/liter	4.2±0.5	4.1±0.5
Bicarbonate — mmol/liter	17.1±3.4	17.5±3.2
Blood urea nitrogen — mg/dl	16.4±10.0	18.3±6.4
Creatinine — mg/dl	0.49±0.12	0.54±0.14
Glucose — mg/dl	91±24	92±24

Table 3. Outcome Measures.*

Outcome	Ondansetron Group (N=107)	Placebo Group (N=107)	Relative Risk (95% CI)†	P Value‡
Vomited during oral rehydration — no. (%)	15 (14)	37 (35)	0.40 (0.26–0.61)	<0.001
Mean no. of vomiting episodes	0.18	0.65	0.30 (0.18–0.50)	<0.001
Vomiting episodes per patient — no. (%)				
0	92 (86)	70 (65)		<0.001
1	12 (11)	21 (20)		0.13
2	2 (2)	7 (7)		0.17
≥3	1 (1)	9 (8)		0.02
Intravenous rehydration — no. (%)	15 (14)	33 (31)	0.46 (0.26–0.79)	0.003
Hospitalization — no. (%)	4 (4)	5 (5)	0.80 (0.22–2.90)	1.00
Oral-rehydration fluid consumed — ml	239±112	196±92		0.001
Intravenous fluid administered — ml/kg	38±8.9	46±9.1		0.002
Length of stay in emergency department — min	106±53	120±63		0.02

* Plus–minus values are means ±SD.
† The adjusted relative risk is reported for dichotomous outcomes. CI denotes confidence interval.
‡ All reported P values were adjusted as described in the text.

METHODS

PATIENTS

The study was a prospective, double-blind, randomized comparison of ondansetron and placebo to control vomiting among children 6 months through 10 years of age. The trial was conducted in the emergency department of Children's Memorial Hospital in Chicago from January 1, 2004, through April 11, 2005. The study was approved by the hospital's institutional review board.

RANDOMIZATION

The patients were randomly assigned in blocks of six to receive ondansetron or placebo and were stratified according to the dose of medication. An independent statistician provided the code to the pharmacy, which dispensed in an opaque bag a weight-appropriate dose of active drug or a placebo of similar taste and appearance. The weight-based dose was 2 mg for children weighing 8 to 15 kg, 4 mg for children weighing more than 15 kg and up to 30 kg, and 8 mg for children weighing more than 30 kg. GlaxoSmithKline supplied the tablets but had no role in the conception, design, or conduct of the study or in the analysis or interpretation of the data.

RESULTS

As compared with children who received placebo, children who received ondansetron were less likely to vomit (14 percent vs. 35 percent; relative risk, 0.40; 95 percent confidence interval, 0.26 to 0.61), vomited less often (mean number of episodes per child, 0.18 vs. 0.65; $P<0.001$), had greater oral intake (239 ml vs. 196 ml, $P=0.001$), and were less likely to be treated by intravenous rehydration (14 percent vs. 31 percent; relative risk, 0.46; 95 percent confidence interval, 0.26 to 0.79). Although the mean length of stay in the emergency department was reduced by 12 percent in the ondansetron group, as compared with the placebo group ($P=0.02$), the rates of hospitalization (4 percent and 5 percent, respectively; $P=1.00$) and of return visits to the emergency department (19 percent and 22 percent, $P=0.73$) did not differ significantly between groups.

CONCLUSIONS

In children with gastroenteritis and dehydration, a single dose of oral ondansetron reduces vomiting and facilitates oral rehydration and may thus be well suited for use in the emergency department.

The authors of a meta-analysis (163) of 6 RCTs found that ondansetron therapy decreased the risk of persistent vomiting, reduced the need for IV fluids, and decreased the risk of immediate hospital admission in children with vomiting as a result of gastroenteritis; however, compared with placebo, ondansetron significantly increased stool outputs in treated patients, and it did not affect return to care.

A more recent Cochrane review (164) included 7 RCTs that compared ondansetron therapy with placebo and 4 of these investigated oral route of administration. Children age <18 years who presented with vomiting and had a clinical diagnosis of gastroenteritis were enrolled. Compared with placebo, ondansetron significantly increased the proportion of children with cessation of vomiting, and reduced the need for IV therapy and the immediate hospital admission rate. In 3 RCTs, there was a significantly increased rate of stool outputs in the ondansetron group ($P<0.05$). A critical overview of data available in the Cochrane database of systematic reviews showed that children who received oral ondansetron had lower hospital admission rates to ED compared with placebo and lower risk of receiving IV rehydration (140).

Only the Canadian Pediatric Society (165) has recommended that oral ondansetron therapy, as a single dose, be considered forchildren from 6 months to 12 years of age with vomiting related to suspected AGE, and who have mild-to-moderate dehydration or who have failed oral rehydration therapy. The use of ondansetron was not recommended in children with AGE predominantly presenting as moderate-to-severe diarrhea because one of the most common adverse effects of ondansetron is increased frequency of diarrhea.

Ondansetron, at the dosages used in the available studies and administered orally or intravenously, may be effective in young children with vomiting related to AGE. Before a final recommendation is made, a clearance on safety in children is, however, needed (II, B) (strong recommendation, low-quality evidence).