Does ondansetron work for acute gastroenteritis?

Freedman et al. Oral ondansetron for gastroenteritis in a pediatric emergency department. N Engl J Med 2006; 354: 1698-705.

Take Home Message: A single dose of ondansetron reduces vomiting in children with gastroenteritis and improves the success of oral-rehydration therapy.

Highlights: Oral rehydration therapy for acute gastroenteritis is limited by vomiting and is underused, with many providers choosing intravenous rehydration when vomiting is involved. Published in 2006, Freedman et al.[i] randomized 214 children with gastroenteritis with vomiting in the emergency room at Children's Memorial Hospital in Chicago to a single dose of ondansetron or placebo prior to attempting oral-rehydration therapy. Children in the ondansetron group were significantly less likely to vomit during oral-rehydration therapy. They also had significantly fewer mean episodes of vomiting, were less likely to receive intravenous rehydration, had a greater oral intake of fluids, and a shorter stay in the emergency department. The only side effect was a higher rate of diarrhea in the children receiving ondansetron.

This study established ondansetron as a useful therapy in children with gastroenteritis to decrease vomiting and improve oral rehydration therapy, which is recommended for children with mild-moderate dehydration. In 2014, the same first author, S. Freedman, with a different group, conducted a multicenter retrospective cohort study[ii] to determine whether the increased ondansetron use in the past decade has been associated with a real-world concomitant decline in IV rehydration use. Identifying 804,000 children in 18 emergency departments from 2002-2011, they found that the median rate of oral ondansetron use increased from 0.11% in 2002 to 42.2% 2012, but intravenous rehydration rates were unchanged, being given to 18.7%

of children in 2002 and 17.8% in 2011. More than 85% of patients who received IV rehydration had not been given oral ondansetron.

The Nitty-Gritty:

- **Design:**
    - Prospective, randomized, double-blind, placebo-controlled trial
    - N= 214
        - Ondansetron group (n= 107)
        - Placebo group (n=107)
    - Setting: 1 urban tertiary center emergency department in US
    - Enrollment 2004-2005
    - Primary outcome: proportion of children who vomited while receiving oral-rehydration therapy
    - Analysis: intention-to-treat
- **Population:**
    - **Inclusion Criteria**
        - 6 months-10 years

- § had at least one reported episode of nonbilious, non-bloody vomiting in preceding 4 hours
- § had at least one episode of diarrhea during the illness
- § had mild-moderate dehydration (based on dehydration score)

- o **Exclusion Criteria**
  - § Body weight <8kg
  - § Severe dehydration
  - § Underlying disease that could affect assessment of hydration (e.g. renal failure, hypoalbuminemia)
  - § History of abdominal surgery
  - § Hypersensitivity to ondansetron
  - § Previous enrollment

- o **Baseline Characteristics –** from the ondansetron group, no significant differences between the two groups
  - § Male sex: 56%
  - § Age: 26+-21 months

§ Weight 13.1 +- 5.3 kg

§ Heart rate: 141+- 20 bpm

§ Dehydration score (unvalidated scale, higher scores (range 7-21) indicate more severe dehydration, with 9-16 representing mild-to-moderate dehydration):

- 9-10: 27%
- 11-12: 48%
- 13-14: 19%
- 15-16: 7%

§ Urine specific gravity: 1.026+-0.007

§ Urine ketones 2.6 +-1.6

§ No of episodes of vomiting in preceding 24 hours: 9.0 +- 6.0

§ No of episodes of diarrhea in preceding 24 hours: 5.8+-4.5 Serum values:

- Sodium mmol/liter: 138 +-6.7
- Potassium mmol/liter: 4.2 +-0.5
- Bicarbonate mmol/liter: 17.1 +- 3.4

- Blood urea nitrogen mg/dl: 15.4 +- 10.0
- Creatinine mg/dl: 0.49 +- 0.12
- Glucose mg/dl: 91+-24

- **Intervention**: randomized to receive either orally-disintegrating ondansetron or placebo prior to oral rehydration trials

- **Outcomes:** comparisons are ondansetron group vs. placebo group
  - **Primary outcome:** proportion of children in each group who vomited while receiving oral-rehydration therapy
    - *14% vs. 35% (p<0.001, RR 0.40 95% CI 0.26-0.61)*
  - **Secondary outcomes:**
    - Mean number of episodes of vomiting
      - 0.18 vs. 0.65 (p<0.001, RR 0.30 95% CI 0.18-0.50)
    - Intravenous rehydration
      - 14% vs. 31% (p=0.003, RR 0.46 95% CI 0.26-0.79)
    - Hospitalization
      - 4% vs. 5% (p=1.00)

- § Oral rehydration fluid consumed - ml
  - 239+-112 vs. 196+- 92 (p=0.001)
- § Intravenous fluid administered – ml/kg
  - 38+-8.9 vs. 46+-9.1 (p=0.002)
- § Length of stay in emergency department – min
  - 106+-53 vs. 120 +-63 (p=0.02)

- **Adverse Events**
  - o Children in ondanseton group had more episodes of diarrhea while undergoing oral rehydration than those who received placebo (1.4 vs. 0.5, p<0.001)

[i] Freedman et al. Oral ondansetron for gastroenteritis in a pediatric emergency department. N Engl J Med 2006; 354: 1698-705.

[ii] Freedman et al. Impact of increasing ondansetron use on clinical outcomes in children with gastroenteritis. JAMA Pediatr 2014; 168(4): 321-329.