# Critical Review Form

## Therapy

Emergency Department Treatment of Viral Gastritis Using Intravenous Ondansetron or Dexamethasone in Children, Acad EM 2006; 13: 1027-1033

**Objectives**: "To determine if administration of dexamethasone or ondansetron in addition to rehydration with IV fluids would result in a decrease in hospitalization rate compared with IV rehydration with or without dexamethasone in children presenting with dehydration secondary to acute viral gastritis who had failed attempts at oral hydration." (p 1028).

**Methods**: Prospective, blinded, placebo-controlled, randomized trial in children aged 6 months to 12 years presenting to the State University of New York Upstate Medical University Pediatric ED in Syracuse with > 3 episodes of vomiting in preceding 24-hours diagnosed by the board-certified Pediatric EM physician as acute gastritis or gastroenteritis and meeting criteria for mild or moderate dehydration (see table at the bottom). Exclusion criteria included current chronic medical illness (except asthma), abdominal surgery history, corticosteroid use, or physical exam findings inconsistent with the diagnosis of viral gastritis. Such inconsistent findings included focal neurologic findings, right lower quadrant tenderness, peritoneal signs, radiographic obstruction, guaiac-positive stools, shock or severe dehydration.Subjects were randomized to dexamethasone, ondansetron or placebo (normal saline).

Randomization into one of three groups occurred in the pharmacy via a table of random numbers. All subjects received IV NS at 10-20ml/kg/hr while the randomization schemes were: dexamethasone 1 mg/kg IV (max 15mg), ondansetron 0.15 mg/kg IV, or a 10 ml bolus of normal saline (placebo). All preparations were uniform in design, color and packaging. Those not tolerating PO fluids at 4 hours were admitted. Those discharged home before 72-hours were followed via phone to ascertain continued vomiting or health care recidivism.

The primary study outcome was hospitalization rates between groups, while secondary outcomes were tolerance of oral hydration and dehydration status at two- and four-hours. The study was powered at 80% to detect a 20% relative reduction in hospitalizations and followed an intention-to-treat model.

| Guide | | Comments |
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| **I.** | **Are the results valid?** | The study was underpowered |
| **A.** | **Did experimental and control groups begin the study with a similar prognosis (answer the questions posed below)?** | |
| 1. | Were patients randomized? | Yes via random numbers table |

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| 2. | Was randomization concealed (blinded)? | Yes, the study was blinded with the nurses, investigators and patients unaware of assignments. The authors do not clearly state whether those accessing outcomes were blinded to group allocation. |
| 3. | Were patients analyzed in the groups to which they were randomized? | Yes |
| 4. | Were patients in the treatment and control groups similar with respect to known prognostic factors? | Yes, but the ondansetron patients had a higher median number of emesis at the start possibly indicating they could have been "sicker" |
| **B.** | **Did experimental and control groups retain a similar prognosis after the study started (answer the questions posed below)?** | |
| 1. | Were patients aware of group allocation? | No |
| 2. | Were clinicians aware of group allocation? | No |
| 3. | Were outcome assessors aware of group allocation? | Uncertain. The authors do not clearly state whether those accessing outcomes were blinded to group allocation. If outcome assessors have knowledge of the treatment arm, *verification bias* may result. In other words, if the knowing researcher has a bias favoring ondansetron (for example) he/she may ask the dexamethasone or placebo group again "Are you SURE you didn't have any more vomiting after you left the hospital?" whereas he/she may ask the ondansetron arm only once "So, you didn't have any more vomiting after you left the hospital, did you?" |
| 4. | Was follow-up complete? | No. After 2 hours a substantial number are lost to follow-up. Starting with 166 initially randomized, 10 never had any data form completed, 10 refused after randomization, and 130 completed two-hours while 58 completed four-hours. To be complete, the authors ought to conduct a sensitivity analysis assuming the best and the worst case scenario for those lost to follow-up at both the two- and four-hour intervals. |

| II. | What are the results (answer the questions posed below)? | |
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| 1. | How large was the treatment effect? | • The study was terminated prematurely "in response to a large increase in the use by out-of-hospital and ED personnel of antiemetics." (p 1029).<br><br>• Admission rates for the three groups were normal saline 20.5%, dexamethasone 14.9%, and ondansetron 4.4% ($p = 0.07$ – perhaps would have reached significance had the study not been terminated).<br><br>• To prevent one hospitalization the NNT for ondansetron was 6 (95% CI 3-31) compared with dexamethasone with NNT 18.<br><br>• To help one child tolerate oral rehydration at two-hours, the ondansetron NNT was 5 (95% CI 3-20), although at four-hours the difference between ondansetron and placebo was not significant. Keep in mind that four-hour data was only available for 42% of the cohort, however.<br><br>• No differences between the groups were noted at 24- and 72-hour follow-up when the median number of episodes of vomiting was zero. |
| 2. | How precise was the estimate of the treatment effect? | Fairly narrow as demonstrated by the Confidence Intervals above. When analyzing the degree of precision, ask yourself whether either end of the 95% CI spectrum would change your decision about this intervention. For instance, if the true-value for increasing oral tolerance was 20 rather than 5 for IV ondansetron would that dissuade you from using it? If not, the CI is sufficiently narrow. |

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| **III.** | **How can I apply the results to patient care (answer the questions posed below)?** | |
| 1. | Were the study patients similar to my patient? | Yes, but their oral hydration method not defined. |
| 2. | Were all clinically important outcomes considered? | No. The authors neglected parent/patient satisfaction scores reported nor other patient-important outcomes liked missed work or school-days or time to cessation of vomiting. No side-effect profiles were analyzed or reported. |
| 3. | Are the likely treatment benefits worth the potential harm and costs? | No cost-effectiveness data were presented. IV Ondansetron appears to reduce admission rates and enhance two-hour oral fluid tolerance rates. |

## Limitations

1) **Industry sponsored research.**
2) **Unspecified oral hydration protocol.**
3) **Lack of patient-important outcomes like satisfaction scores, missed work/school, time to vomiting cessation, or side-effect profiles.**
4) **Premature cessation limiting power of the study or reader's ability to reach definitive conclusions.**
5) **Large number of subjects lost to follow-up or with incomplete data collection and no sensitivity analysis performed to assess the potential impact of these missing subjects.**
6) **Single-center study limits external validity, although no reason to suspect Syracuse Pediatric ED any different than St. Louis Children's Hospital.**

## Bottom Line

**A single-center study with premature termination and excessive loss to follow-up demonstrates that compared with placebo, intravenous ondansetron in vomiting children with suspected viral gastroenteritis reduces hospitalization rates (NNT 6) and two-hour oral rehydration tolerance (NNT 5). These benefits were not demonstrated at four-hours, one- or three-days.**

# Syracuse Dehydration Scale (non-validated)

| Variable | Normal Hydration | Mild (3-5%) Dehydration | Moderate (6-9%) Dehydration | Severe (>10%) Dehydration |
|---|---|---|---|---|
| **BP** | Normal | Normal | **Normal** | Normal to reduced |
| **Pulse Quality** | Normal | Normal | **Slightly decreased** | Moderately decreased |
| **Heart Rate** | Normal | Normal | **Increased** | Increased/Decreased (severe cases) |
| **Skin Turgor** | Normal | Normal | **Decreased** | Decreased |
| **Fontanelle** | Normal | Normal | **Sunken** | Sunken |
| **Mucous Membranes** | Moist | Slightly Dry | **Dry** | Dry |
| **Eyes** | Normal | Normal | **Sunken orbits** | Deeply sunken orbits |
| **Extremities** | Normal cap refill | Normal cap refill | **Delayed cap refill** | Cool, mottled |
| **Mental Status** | Normal | Normal | **Listless** | Lethargic to comatose |
| **Urine Output** | Normal | Slightly decreased | **<1 mL/kg/hr** | << 1 mg/kg/hr |
| **Thirst** | Normal | Slightly *decreased* | **Moderately increased** | Very thirsty or too lethargic to indicate |