Translating Best Evidence into Best Care

EDITOR'S NOTE: Studies for this issue were identified using the Clinical Queries feature of PubMed, "hand" searching *JAMA Pediatrics*, *Pediatrics*, and *The Journal of Pediatrics*, and from customized EvidenceUpdates alerts.

EBM PEARL: THE 95% CONFIDENCE INTERVAL (CI), PART 2 – CLINICAL USE: The 95% CI has clinical use. As an example, consider the number needed to treat (NNT) and its 95% CI (see piece by Freedman below regarding article by Danewa et al; *J Pediatr* 2016;169:105-9). You are not particularly impressed with the use of ondansetron in dehydration with vomiting, and have decided that your personal NNT cutoff is 5. You need to be 95% confident that you would not have to treat more than 5 patients to see benefit in one. The results of the study found the ondansetron NNT 4 (95% CI, 3 to 7). As the upper end of the 95% CI crosses your treatment threshold of 5, you cannot be 95% confident that you may have to treat as many of 7 patients to a benefit one patient. The study demonstrated statistical significance, but it did not meet your personal criteria for clinical significance.

LITERATURE SEARCH PEARL: THE H-INDEX: The h-index, first described by Jorge Hirsch (*Proc Natl Acad Sci USA* 2005;102:16569-72), is a researcher-level productivity measure. The h-index combines, in a specific way, the total number of papers published and the number of citations for each paper. If the researcher has published "h" number of papers, the h-index is the number of papers cited at least "h" number of times. The h-index is not significantly increased by a single highly-cited paper or many sparsely-cited papers. The h-index may be used to compare individual researchers and groups of researchers (eg, research departments) (*J Pediatr* 2016;169:272-6). For further information and to calculate your h-index, go to researchguides.uic.edu/if/hindex.

Jordan Hupert, MD

Ondansetron enhances efficacy of oral rehydration

Danewa AS, Shah D, Batra P, Bhattacharya SK, Gupta P. Oral Ondansetron in Management of Dehydrating Diarrhea with Vomiting in Children Aged 3 Months to 5 Years: A Randomized Controlled Trial. *J Pediatr* 2016;169:105-9.

Question Among children with diarrhea, vomiting, and dehydration, what is the therapeutic efficacy of ondansetron, compared with placebo, as measured by successful oral rehydration?

Design Block-randomized, controlled trial.

Setting Emergency department, Delhi, India.

Participants Children, aged 3 months to 5 years, with gastroenteritis, dehydration (as defined by the World Health Organization), and vomiting (2 episodes in the last 6 hours).

Intervention One dose of ondansetron versus placebo.

Outcomes Failure of oral rehydration therapy (ORT).

Main Results Failure of ORT was significantly less in children receiving ondansetron compared with those receiving placebo, number needed to treat 4 (95% CI, 3 to 7).

Conclusions A single ondansetron dose enhanced the efficacy of ORT.

Commentary In this pragmatic study of children with acute gastroenteritis presenting for emergency department care in India, Danewa et al suggest that the administration of a single dose of oral ondansetron results in improved oral rehydration. What is most impressive is the difference in treatment groups as it relates to the primary outcome of ORT failure: World Health Organization-defined "some dehydration" (persisting after 4 hours of ORT) or "severe dehydration" (at any time during assessment). However, excitement over the benefit documented is tempered by the presence of 3 unique primary outcomes without evidence of adjustment for multiple analyses. Unlike prior clinical trial[1] and cohort studies[2] that have demonstrated a reduction in intravenous rehydration associated with ondansetron administration, the lack of benefit in this study likely relates to lower rates of intravenous rehydration use in the placebo group due to ORT attempts lasting up to 8 hours. Prior studies, which have had total lengths of stay below 2 hours, provided significantly smaller volumes of oral rehydration fluids. A final concern relates to the lack of follow-up data to confirm safety and success following discharge. Nonetheless, this study, whose findings parallel an Iranian clinical trial,[3] provides promising evidence that ondansetron can improve ORT success in a developing country. It will be important to ensure appropriate knowledge-translation approaches are in place in low and middle-income countries to promote clinical implementation.

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References

1. Freedman SB, Pasichnyk D, Black KJ, Fitzpatrick E, Gouin S, Milne A, et al. Gastroenteritis Therapies in Developed Countries: Systematic Review and Meta-Analysis. PLoS One 2015;10:e0128754.

2. Freedman SB, Tung C, Cho D, Rumantir M, Chan KJ. Time-series analysis of ondansetron use in pediatric gastroenteritis. J Pediatr Gastroenterol Nutr 2012;54:381-6.
3. Golshekan K, Badeli H, Rezaieian S, Mohammadpour H, Hassanzadehrad A. Effect of oral ondansetron on decreasing the vomiting associated with acute gastroenteritis in Iranian children. Iran J Pediatr 2013;23:557-63.

Protocol-based, septic-shock care may reduce acute kidney injury

Akcan Arikan A, Williams EA, Graf JM, Kennedy CE, Patel B, Cruz AT. Resuscitation Bundle in Pediatric Shock Decreases Acute Kidney Injury and Improves Outcomes. *J Pediatr* 2015;167:1301-5.

Question Among children presenting with septic shock, what is the efficacy of protocol-driven resuscitation, compared with routine resuscitation, in reducing acute kidney injury (AKI)?

Design Retrospective cohort with historical controls.

Setting Emergency department, Texas Children's Hospital.

Participants Children with clinical septic shock.

Intervention Septic shock protocol.

Outcomes Primary: AKI. Secondary: mortality (among other secondary outcomes).

Main Results AKI and mortality were reduced in the protocol group: number needed to treat (NNT) 4 (95% CI, 3 to 9) and NNT 15 (95% CI, 8 to 464), respectively.

Conclusions Protocol-based septic-shock treatment reduced AKI and mortality.

Commentary This study evaluated the prevalence of AKI in children admitted to the intensive care unit with concern for septic shock. The implementation of sepsis care bundles in pediatric emergency departments previously has been demonstrated to improve timeliness of therapy[1,2] and hospital length of stay.[3] However, assessments of improvement in patient-level morbidity and mortality were limited in these studies. The study by Arikan et al demonstrated reduced AKI associated with implementation of a sepsis-care bundle in children. Efforts and research as presented in this article are critical as we attempt to further understand the effect on clinical outcomes from the protocolization of sepsis care. As mortality in this population is rare, we are unlikely to see changes at a single institution level. However, morbidity from sepsis is, unfortunately, both common and significant and we are only beginning to understand its long-term consequences. The impact of sepsis quality-improvement efforts on organ-dysfunction-related morbidity outcomes as presented in this article represent an important first step towards this goal. As research continues, we should learn from some of the limitations of this report. Items that would strengthen this study include: rigorous pre- and post-cohort definitions, a priori defined timing of organ failure determination, and assessment of the persistence of quality improvement interventions over time. Future multicenter prospective studies are needed to determine the true impact of protocolized care on morbidity and mortality outcomes in children with septic shock.

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References

1. Cruz AT, Perry AM, Williams EA, Graf JM, Wuestner ER, Patel B. Implementation of goal-directed therapy for children with suspected sepsis in the emergency department. Pediatrics 2011;127:e758-66.
2. Larsen GY, Mecham N, Greenberg R. An emergency department septic shock protocol and care guideline for children initiated at triage. Pediatrics 2011;127:e1585-92.
3. Paul R, Melendez E, Stack A, Capraro A, Monuteaux M, Neuman MI. Improving Adherence to PALS Septic Shock Guidelines. Pediatrics 2014;133:e1358-66.

Omalizumab pre-season treatment reduces Fall asthma exacerbations

Teach SJ, Gill MA, Togias A, Sorkness CA, Arbes SJ Jr, Calatroni A, et al. Preseasonal treatment with either omalizumab or an inhaled corticosteroid boost to prevent fall asthma exacerbations. *J Allergy Clin Immunol* 2015;136:1476-85.

Question Among children with asthma, what is the therapeutic benefit of pre-seasonal treatment (omalizumab or inhaled corticosteroids [ICS]), in preventing fall exacerbations?

Design Randomized, controlled trial.

Setting 8 urban clinical sites across the US.

Participants 6- to 17-year-olds with asthma, 1 or more asthma exacerbations or hospitalization within the prior 19 months, a positive skin test response to 1 or more perennial allergens, body weight, and total serum IgE levels suitable for omalizumab dosing.

Intervention Omalizumab or ICS or placebo.

Outcomes Fall exacerbation rates.

Main Results The fall exacerbation rate was lower in the omalizumab versus placebo arms, absolute risk reduction (ARR) 9.7% (95% CI, 0.4% to 19.0%), but no difference compared with ICS, ARR 2.7% (95% CI, −4.6% to 10.0%). Among those with an exacerbation during the run-in phase, the fall exacerbation rate was lower in the omalizumab versus the ICS arms, ARR 25.8% (95% CI, 8.1% to 43.5%).

Conclusions Starting omalizumab prior to the fall season prevents asthma exacerbations, particularly among those with a recent exacerbation.

Author review and application Prior studies from the Inner City Asthma Consortium have demonstrated that exacerbations of asthma persist among inner-city youth despite