

# It Doesn't Have to be EviDense

## AN INFLUENZA CURE: THE WHITE WHALE

Although we all use oseltamivir with regularity in the winter, there remains controversy surrounding outcomes after treatment. For this one, we look to the adult literature.

### The study.

This meta-analysis was conducted to assess the effect of oseltamivir on duration of symptoms, complications, and hospitalizations in adults and included all published and unpublished randomized, double-blinded, placebo-controlled trials that compared oseltamivir with placebo in patients with suspected or confirmed influenza.

### The key findings.

Eleven studies (4769 patients) met the meta-analysis criteria. Five studies reported duration of symptoms in the intention-to-treat (ITT) population with a mean reduction of 21 hours (confidence interval 13.3–28.0;  $I^2 = 0\%$ ). Risk difference between oseltamivir and placebo was not statistically significant for patients requiring additional hospitalization or developing pneumonia.

### Why do we care?

The drug costs roughly \$100 per course, for what amounts to less than a day of symptom relief without a corresponding decrease in hospitalization due to respiratory complications, sepsis, or dehydration. Furthermore, adverse effects of oseltamivir, such as nausea and vomiting, occur in at least 10% of patients. The authors also found that high-quality, unpublished randomized controlled trial performed by the manufacturer demonstrated a less favorable treatment effect than did the published literature.

### Straight from the author's mouth...

"Much of the literature was never published...shameful frankly. All studies were limited to patients presenting within 36 hours—makes you wonder where the FDA got their 48-hour cutoff. There was no difference in rates of complications requiring an antibiotic... and/or hospitalization. [We found] symptom reduction of 21 hours in the ITT population, not 30 hours as they report in published per protocol analyses."

– Dr. Mark H. Ebell, lead author

Citation: Ebell MH, Call M, Shinholser J. Effectiveness of oseltamivir in adults: a meta-analysis of published and unpublished clinical trials. *Fam Pract*. 2013; 30(2):125–133

### AUTHOR

Eric Biondi, MD

Department of Pediatrics, University of Rochester, Rochester, New York

### KEY WORDS

evidence-based medicine; pediatric hospital medicine

### ABBREVIATIONS

FDA: Federal Drug Administration

FLACC: Face, Legs, Activity, Cry, Consolability scale

ICT: integrative care therapy

INR: international normalized ratio

ITT: intention-to-treat

NRS-11: 11-item Numerical Rating Scale

[www.hospitalpediatrics.org](http://www.hospitalpediatrics.org)

doi:10.1542/hpeds.2014-0013

Address correspondence to Eric Biondi, MD, University of Rochester, 601 Elmwood Ave, Box 667, Rochester, NY 14642. E-mail: [eric\\_biondi@urmc.rochester.edu](mailto:eric_biondi@urmc.rochester.edu)

HOSPITAL PEDIATRICS (ISSN Numbers: Print, 2154 - 1663; Online, 2154 - 1671).

Copyright © 2014 by the American Academy of Pediatrics

**FINANCIAL DISCLOSURE:** The author has indicated he has no financial relationships relevant to this article to disclose.

**FUNDING:** No external funding.

### POTENTIAL CONFLICT OF INTEREST:

The author has indicated he has no potential conflicts of interest to disclose.

**SIMPLE IS BETTER ( $P = .037$ )\***

*Sometimes it's nice to be reminded that reading primary literature doesn't have to be tedious or involve terms such as "Gaussian distribution." In the following case, researchers simply asked: does obesity change the time to therapeutic international normalized ratio (INR) in children started on warfarin?*

\* $P$  value is unlikely to be correct, given that it is completely fabricated.

**The study.**

Children aged 2 to 18 years who were obese (BMI  $\geq$ 95th percentile) and initiated on warfarin therapy as inpatients were retrospectively matched with non-obese patients who were initiated on warfarin therapy. Measurements of INR were followed in both cohorts, and time to therapeutic INR was used as the primary endpoint to determine whether obesity, as has been shown in adults, should influence our warfarin dosing.

**The key findings.**

Ten obese cases and 20 control cases were included in the study. The 2 groups had similar baseline INR, maximum INR, and discharge INR values. The median time to therapeutic INR in obese patients was twice as long as nonobese patients (median: 6 vs 3 days;  $P < .01$ ).

**Why do we care?**

This is a relatively small study, but it suggests that warfarin dosing algorithms for pediatric patients may need to consider correcting for obesity, potentially by excluding a maximum initial dose when dosed by weight. As hospitalists, many of us participate in the development of these sorts of protocols.

**In the words of the expert...**

Given the growing prevalence of obesity among children and adolescents, the authors focus attention to the tip of the iceberg of the huge problem of appropriate dosing and medication management in our patients with obesity. For pediatric hospitalists, this paper identifies warfarin dosing in obese patients as an important factor to consider in management of anticoagulation in addition to the well-known confounders of age, diet, medication interactions, and compliance.

– Dr. Barbara Asselin, pediatric heme-oncologist and pediatric hospitalist

Citation: Moffett BS, Bomgaars LR. Response to warfarin therapy in obese pediatric patients dosed according to institutional guidelines [published online ahead of print January 22, 2014]. *J Pediatr Oncol*. PMID: 24458250

**YOU DOWN WITH ICT?**

*One of the goals of our journal club is to provide you with some exposure to journals or topics that may have some relevance to your practice but may not always be on your radar. The following study about complementary adjunctive approaches to pain management, I think, fulfills these 2 criteria.*

**The study.**

Pediatric inpatients referred, secondary to pain, to the integrative care therapy (ICT) service by a member of the patient care team at a large academic medical center were included in the study. Pain ratings were provided immediately before and after ICT using either the FLACC (Face, Legs, Activity, Cry, Consolability scale; generally children aged  $<8$  years) or the 11-item Numerical Rating Scale (NRS-11). ICT was provided by trained therapists and included body-based therapy (eg, massage, 77%), energy

therapies (eg, healing touch, 21%), and, to a lesser extent, music therapy and breathing techniques as adjunctive treatments. For nonverbal patients, the ICT provider filled out the pre- and posttreatment scores using the FLACC pain score.

**The key findings.**

In total, 519 children (mean age: 10.2 years) received ICT. Mean pain scores decreased after therapy from 4.4 to 2.9 (NRS-11;  $P \leq .001$ ) and 2.6 to 0.8 (FLACC;  $P \leq .001$ ). Pain reduction was  $>50\%$  for 77% of subjects in the FLACC subgroup and 39% of subjects in the NRS-11 subgroup.

**Why do we care?**

Well, pain is always, always, always a big deal in the inpatient pediatric setting. I plan to bring this study to the next pain committee meeting. Although I doubt this will spark our hospital to develop an ICT service, I do think we should consider incorporating some of these therapeutic concepts into our current pain management strategies.

**Straight from the author's mouth...**

Integrative care therapies (e.g., massage therapy, acupuncture, relaxation techniques) are often not considered when treating pediatric pain. However, when used in combination with conventional pharmacologic approaches, these techniques have the potential to reduce pain, increase relaxation, and improve overall patient experience and outcomes.

– Dr. Sain Cotton, lead author

Citation: Cotton S, Luberto CM, Bogenschutz LH, Pelley TJ, Dusek J. Integrative care therapies and pain in hospitalized children and adolescents: a retrospective database review. *J Altern Complement Med*. 2014;20(2):98–102

## **It Doesn't Have to be EviDense**

Eric Biondi

*Hospital Pediatrics* 2014;4;188

DOI: 10.1542/hpeds.2014-0013

### **Updated Information & Services**

including high resolution figures, can be found at:  
<http://hosppeds.aappublications.org/content/4/3/188>

### **Permissions & Licensing**

Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:  
<https://shop.aap.org/licensing-permissions/>

### **Reprints**

Information about ordering reprints can be found online:  
<http://classic.hosppeds.aappublications.org/content/reprints>



**It Doesn't Have to be EviDense**

Eric Biondi

*Hospital Pediatrics* 2014;4;188

DOI: 10.1542/hpeds.2014-0013

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://hosppeds.aappublications.org/content/4/3/188>

Hospital Pediatrics is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 2012. Hospital Pediatrics is owned, published, and trademarked by the American Academy of Pediatrics, 345 Park Avenue, Itasca, Illinois, 60143. Copyright © 2014 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 2154-1663.

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

