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PEDRO A. PIEDRA, MD, EDITOR-IN-CHIEF; ROBERT C. WELLIVER SR, MD, REVIEWER; BARBARA GUIDOS, SENIOR MANAGING EDITOR; MARK PALANGIO, SENIOR MEDICAL WRITER

High Rate of Otitis Media Complications in Young Children With Viral Upper Respiratory Tract Infection

Upper respiratory tract infection (URI) in young children is frequently complicated by otitis media (OM). OM is classified as 2 types: acute OM (AOM), an acute symptomatic disease, and OM with effusion (OME), an asymptomatic disease involving fluid collection in the middle ear. Preventing URI in children has been shown to prevent OM, yet the incidence and characteristics of OM in the setting of viral URI have not been thoroughly evaluated. Consequently, Chonmaitree and colleagues performed a prospective, longitudinal cohort study of young children to obtain epidemiologic information on viral URI and OM.

The most important predictor of acute otitis media that complicated upper respiratory tract infection was young age followed by virus type.

This prospective, longitudinal cohort study observed 294 healthy young children over the course of 1 year to assess the occurrence of viral URI, acute AOM, and OME. Performed at the University of Texas Medical Branch (Galveston, TX), this study enrolled children between the ages of 6 months and 3 years during the period of January 2003 through March 2006. Of the entire group, 46% entered the study in the first year of life, 42% in the second year, and 12% in the third year.

In this study population, there were a total of 1,295 URI episodes (5.06 episodes per child-year) and 440 AOM episodes (1.72 episodes per child-year). The median age at the time of URI onset was 17.7 months and of AOM was 15.9 months. Respiratory viruses were detected in specimens collected during 547 of 864 (63%) URI episodes. The most frequently detected viruses during URI were rhinovirus and adenovirus. In 28 URI episodes, OME was already present before a new URI onset. The overall incidence of URI complicated by OM was 61%, which included a 37% incidence of AOM and a 24% incidence of OME. The most important predictor of AOM that complicated URI was young age followed by virus type. For age, the odds ratio was 0.96 (95% confidence interval, 0.94-0.98). Thus, with each additional month of age in a new URI episode, the chances of the child developing AOM decreased by 4%.

Adenovirus, respiratory syncytial virus (RSV),

Continued

Disclosures:

Dr Piedra is professor of pediatrics and molecular virology and microbiology at Baylor College of Medicine. He has indicated relevant financial relationships as noted: he receives grant/research support from MedImmune, Inc., Novartis, and Sanofi Pasteur; he is a member of the speakers bureau for MedImmune, Inc.; he is an ad hoc consultant for MedImmune, Inc., GlaxoSmithKline, Novartis, Sanofi Pasteur, and Roche; and he is part of a collaborative research agreement with NIH and Baylor.

Dr Welliver indicated that he is a member of the speakers bureau, receives clinical trial support, and received a fellowship award from MedImmune, Inc.; he is an ad hoc consultant for Amylin Pharmaceuticals, Inc. and MedImmune Inc.; and he receives research support from Symphogen, Inc.

PPS Staff: Barbara Guidos, senior managing editor; Mark Palangio, senior medical writer; Terri Setteducato, senior program director; Karla Castro, program director; and Wadee'ah Terry, CME program manager have indicated no relevant financial relationships.

prci Pediatric Respiratory Care Initiative™

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LEARNING OBJECTIVES

After studying the literature presented in this issue, participants will be able to:

- Delineate the incidence and characteristics of otitis media in the setting of viral upper respiratory tract infection among young children.
- Describe the effects of antibiotic therapy on hospitalization duration among infants and young children with mild to moderate respiratory syncytial virus lower respiratory disease.

TARGET AUDIENCE

This educational activity is designed for pediatricians, primary care physicians, pediatric and family nurse practitioners, neonatologists, infectious disease specialists, allergists, pulmonologists, immunologists, and other healthcare professionals involved in the care and management of pediatric respiratory patients.

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OFF-LABEL DISCLOSURE

Some of the drug treatments discussed in this issue may note uses not approved by the Food and Drug Administration. Articles containing such uses will be noted at the end of the article.

High Rate of Otitis Media Complications *(Continued)*

and coronavirus were among the viruses associated with a higher rate of AOM. AOM occurred in approximately one-half of children with URI attributed to adenovirus, RSV, or coronavirus and in approximately one-third of those with URI attributed to influenza virus, parainfluenza virus, enterovirus, or rhinovirus. Molecular diagnostic tests were not conducted for human metapneumovirus and bocavirus.

This study demonstrated a high susceptibility of young children to URI and an exceedingly high rate of OM complications. Approximately 60% of symptomatic URI cases were complicated by AOM and/or OME. Predictors of URI complicated by AOM were young age and specific virus types. The study investigators recommended that strategies to prevent OM among young children should entail prevention of viral URI, particularly URI caused by adenovirus and RSV.

Chonmaitree T, Revai K, Grady JJ, et al. Viral upper respiratory tract infection and otitis media complication in young children. *Clin Infect Dis*. 2008;46(6):815-823.

COMMENTARY

ROBERT C. WELLIVER SR, MD, Professor of Pediatrics, State University of New York at Buffalo, Women and Children's Hospital, Buffalo, New York.

This study of the epidemiology of acute otitis media (AOM) contains a large amount of "fun" data: The attack rate for upper respiratory tract infection (URI) in children is still approximately 5 episodes per year through 36 months of age; perhaps a third of all URI results in AOM; left-sided AOM may be 50% more common than right-sided AOM; all viruses conveyed a relatively similar rate (30%-50%) of AOM as a complication; and attack rates for AOM in the era of pneumococcal vaccine are not much lower than those reported in years preceding the vaccine era. High rates of AOM complicating viral URI may provide incentive to companies developing antiviral compounds, because the prevention of AOM by such therapy presents additional cost-effectiveness leverage. However, the broad range of viruses that are quite capable of inducing AOM suggests that numerous types of antiviral vaccines will need to be administered to produce a significant effect in reducing the incidence of this complication. Additional information regarding which viruses (if any) were associated with more persistent symptoms or effusions would be helpful.

Azithromycin Therapy Is Not Beneficial in Hospitalized Infants With Mild to Moderate Respiratory Syncytial Virus Lower Respiratory Tract Disease: Dutch Antibiotics in RSV Trial

Respiratory syncytial virus (RSV) is the leading cause of viral lower respiratory disease (LRTD) among infants and young children. Based on suspected secondary bacterial infection (SBI), parenteral antimicrobial agents are used in nearly half of all hospitalized infants with RSV LRTD. However, several studies have demonstrated that the incidence of severe SBI in this setting is <1%. Therefore, in many of these cases, use of antimicrobial agents might be unjustified. As such, Kneyber and associates performed a randomized, double-blind, placebo-controlled multicenter equivalence study to examine whether the use of antibiotics would affect hospitalization duration in mild to moderate RSV LRTD.

As part of the Dutch Antibiotics in RSV Trial (DART), patients ≤24 months of age with a virologically confirmed clinical diagnosis of mild to moderate RSV LRTD were recruited during 3 separate RSV seasons (October-March; 2002-2004, and 2005-2006). Patients who were treated with antibiotics within 7 days prior to hospitalization were excluded. A total of 71 patients were randomized to azithromycin 10 mg/kg/day (n=32) or placebo (n=39) administered in a single dose for 3 days. The primary endpoint was duration of hospitalization; secondary endpoints included

Continued

Azithromycin Therapy *(Continued)*

duration of oxygen supplementation and nasogastric tube feeding, course of RSV symptom score, number of pediatric intensive care unit referrals, and number of patients who received additional antibiotic treatment.

The 2 study groups were comparable with respect to baseline demographics, clinical characteristics, laboratory tests, and chest X-rays. The mean hospitalization duration was similar among patients treated with azithromycin (132.0 ± 10.8 hours) and among those receiving placebo (139.6 ± 7.7 hours) (*P*=0.328). Compared with placebo, azithromycin was not associated with a stronger resolution of clinical symptoms based on RSV symptom score or with a shorter duration of supportive therapy. Four patients were treated with antibiotics 72 hours after randomization, 3 of whom were assigned to placebo (*P*=0.406).

These results suggest that routine antibiotic use does not have a beneficial effect on the course of mild to moderate RSV LRTD in hospitalized, previously healthy, non-mechanically ventilated infants and young children. Based on these findings, the investigators concluded that SBI is unlikely in this population, that avoiding antibiotic therapy on admission does not increase susceptibility to SBI complications, and that mild to moderate RSV LRTD is overtreated.

Kneyber MC, van Woensel JB, Uijtendaal E, et al. Azithromycin does not improve disease course in hospitalized infants with respiratory syncytial virus (RSV) lower respiratory tract disease: a randomized equivalence trial. *Pediatr Pulmonol*. 2008;43(2):142-149.

Post-Test

1. In the study by Chonmaitree et al, what percentage of symptomatic URI cases were complicated by OM?
   a. Approximately 20%
   b. Approximately 40%
   c. Approximately 60%
   d. Approximately 80%

2. In the Dutch Antibiotics in RSV Trial, azithromycin therapy, versus placebo, had which of the following effects in infants hospitalized with RSV LRTD?
   a. Stronger resolution of clinical symptons
   b. Decreased hospitalization duration
   c. Increased hospitalization duration
   d. No change in hospitalization duration or resolution of clinical symptoms

ANSWERS

Answer: c. The overall incidence of URI complicated by OM was 61%.
Answer: d. Compared with placebo, azithromycin therapy did not shorten hospitalization duration or improve resolution of clinical symptoms in infants hospitalized with RSV LRTD.

In addition to regular issues of *Clinical Insights® in Pediatric Respiratory Care*, visit **www.PediatricRespiratory.org** for information about upcoming CME activities.

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CME Activity Evaluation/Registration Form

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I have participated in this activity as designed and am claiming _____ *AMA PRA Category 1 Credit*™ (maximum .50)

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Overall Program

	Strongly Disagree		Disagree	Agree		Strongly Agree
1. This activity met the stated objectives in such a way that I am better able to:						
a. Delineate the incidence and characteristics of OM in the setting of viral URI among young children	1	2	3	4	5	6
b. Describe the effects of antibiotic therapy on hospitalization duration among infants with mild to moderate RSV LTD	1	2	3	4	5	6
2. Please rate the following statements:						
a. Activity provided clear evidence to support the content	1	2	3	4	5	6
b. Activity was presented in a way that facilitated learning	1	2	3	4	5	6

3. Did the activity present a balanced view of therapeutic options available for the disease state(s)? ☐ Yes ☐ No*
   * If you checked "No," please explain. _____

4. Did the activity present content that fairly represented, and was based on a reasonable and valid interpretation of the information available on the subject? ☐ Yes ☐ No*
   * If you checked "No," please explain. _____

5. Did the activity appear to place an unreasonable emphasis on one particular product/service? ☐ Yes* ☐ No
   * If you checked "Yes," please explain. _____

6. In reflecting on your practice, what type of impact will this educational activity have? *(Select all that apply.)* I will:
   - ☐ Recognize that strategies to prevent OM among young children should entail prevention of viral URI, particularly URI caused by adenovirus and RSV.
   - ☐ Consider the low risk for serious bacterial infection and drawbacks of antibiotic use in treating infants hospitalized with mild to moderate RSV LRTD.
   - ☐ Other *(please specify)* _____

7. What topics should be dealt with in more detail? *(List topics.)* _____

8. What is the most important thing you learned from this activity? _____

Thank you for your participation.