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**Early Administration of Azithromycin for Children with Recurrent, Severe Lower Respiratory Tract Illness May Reduce Severity of Illness**

Among young children with histories of recurrent severe lower respiratory tract illness (LRTI), the use of azithromycin early during an apparent RTI compared with placebo significantly reduced the risk of experiencing progression to severe LRTI, according to a study in the November 17 issue of *JAMA*.

Acute episodes of severe LRTI are common among preschoolers, and up to 14 percent to 26 percent of preschoolers present with recurrent wheezing during the first 6 years of life. These severe episodes are often associated with substantial illness, and may result in visits to urgent care and emergency departments. Although viral infections are often present, bacteria may also contribute to illness development. Identification of treatment approaches that lessen the severity of these recurrent episodes would provide substantial benefit to preschool children with recurrent severe LRTI, according to background information in the article.

Leonard B. Bacharier, M.D., of the Washington University in St. Louis School of Medicine, and colleagues randomly assigned 607 children (age 12 months through 71 months) with histories of recurrent, severe LRTIs to receive the antibiotic azithromycin (for 5 days; n = 307) or matching placebo (n = 300), started early during each predefined RTI (child's signs or symptoms prior to development of LRTI), based on individualized action plans. The trial was conducted across 9 academic U.S. medical centers in the National Heart, Lung, and Blood Institute's AsthmaNet network.

A total of 937 treated RTIs (azithromycin group, 473; placebo group, 464) were experienced by 443 children (azithromycin group, 223; placebo group, 220), including 92 severe LRTIs (azithromycin group, 35; placebo group, 57). The azithromycin group experienced a significantly lower risk of progressing to severe LRTI than the placebo group. Adverse events were infrequently observed.

Although limited to 86 participants at a single study site, the researchers found numerically higher rates of acquisition of azithromycin-resistant organisms in oropharyngeal samples in participants receiving azithromycin and those who did not, along with evidence of acquisition of azithromycin-resistant organisms even in participants not treated with azithromycin. “Real-world rates of development of azithromycin-resistant organisms may be greater, potentially due to failure to complete the full duration of therapy often seen in clinical practice. Given the small sample size, further studies are needed to assess the potential increased risk of antibiotic resistance vs the comparative effectiveness of azithromycin with respect to other asthma medications to prevent severe LRTI,” the authors write.

“In children with the phenotype of wheezing studied herein, clinicians may consider a therapeutic trial of azithromycin early in the course of RTIs based on a parent-initiated individualized plan. Children who demonstrate an azithromycin response, as reflected by less-severe episodes of RTI, may benefit from repeating such therapy with subsequent illnesses.”

“Studies replicating the findings reported herein would provide further support to this conclusion, and future studies comparing the relative benefits of early azithromycin therapy with either daily or intermittent high-dose inhaled corticosteroids may help determine the relative efficacies of these treatment strategies.”

(doi:10.1001/jama.2015.13896; Available pre-embargo to the media at [http:/media.jamanetwork.com](http://media.jamanetwork.com))

**Editor’s Note**: Please see the article for additional information, including other authors, author contributions and affiliations, financial disclosures, funding and support, etc.

**Editorial: Individual Benefit vs Societal Effect of Antibiotic Prescribing for Preschool Children With Recurrent Wheeze**

“Limiting children's loss of days from school (or parents' days from work) and relieving the anxiety that an RTI that may progress to a hospitalization is almost certainly to be of benefit to children and families,” write Robyn T. Cohen, M.D., M.P.H., and Stephen I. Pelton, M.D., of the Boston University School of Medicine, in an accompanying editorial

“The question is how to determine (through studies incorporating biomarkers, airway endotyping, or genetics) which children are most likely to obtain the largest benefit from early initiation of azithromycin. Until a higher-risk population can be prospectively identified (rather than all children with intermittent wheezing associated with viral RTI) for progression to severe LRTI, the consequences of widespread use of azithromycin, both known and hypothesized, outweigh the benefit for most children.”

(doi:10.1001/jama.2015.14953; Available pre-embargo to the media at [http:/media.jamanetwork.com](http://media.jamanetwork.com))

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