HHS Public Access

Author manuscript

JAMA. Author manuscript; available in PMC 2019 April 10.

Published in final edited form as:

JAMA. 2016 May 17; 315(19): 2121–2122. doi:10.1001/jama.2016.0918.

Early Azithromycin Treatment to Prevent Severe Lower Respiratory Tract Illnesses in Children

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To the Editor

The study by Dr Bacharier and colleagues[1] found that using azithromycin in preschool children with a history of wheezing and respiratory tract infection (RTI) prevented progression to “severe” lower respiratory tract illness (LRTI). The authors defined severe LRTI as needing intensive rescue albuterol treatments; it was not defined as pneumonia, the classic definition of severe LRTI. While azithromycin limited the need for intensive rescue albuterol, it did not prevent urgent care or emergency visits, hospitalizations, or future RTI episodes, arguably the most important prevention outcomes.

Furthermore, randomized children who had severe LRTI, needed emergent care, had uncontrolled asthma or had respiratory-related problems at or prior to presentation with RTI were deemed “early termination”, meaning that they were not given the study medication or included in the analyses. More children (109) experienced early termination than children who received study medication and experienced LRTI (92). A more rigorous intention-to-treat (ITT) analysis may not have shown any significant difference in progression to severe LRTI between azithromycin and placebo.

The authors concluded that more information is needed on the development of antimicrobial resistant pathogens using azithromycin to prevent LRTI. A global crisis exists due to emerging antimicrobial resistance among a wide variety of pathogens; thus judicious use of antibiotics is of paramount importance.[2] Azithromycin resistance is increasing among common pediatric pathogens, including *Streptococcus pneumoniae*, group A *Streptococcus*, and *Shigella*.[2] Overprescribing of antibiotics for viral respiratory infections is already a common problem. Without stringent diagnostic criteria, clinicians may be even more likely to prescribe antibiotics for children with common colds, exacerbating the antibiotic resistance problem. Much effort has been undertaken to work with clinicians, patients, parents, veterinarians and the animal agriculture industry to improve antibiotic use.[3]

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Conflict of Interest Disclosures: The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

Furthermore, other potential harms to the individual from azithromycin use are known, including increasing risks of adverse effects, allergies, and *Clostridium difficile* infections. Antibiotic treatment disrupts the microbiome; emerging evidence suggests antibiotic use in childhood can lead to obesity, infectious diseases, and autoimmune diseases.[4] This study raises excellent questions about how best to prevent severe illnesses in preschool children with history of wheezing, but we agree with Drs. Cohen and Pelton[5] that at this time, the risks of azithromycin outweigh the benefit of preventing these children from needing additional rescue albuterol treatments without preventing urgent care or emergency visits, hospitalizations, or future episodes.

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