Do Antibiotics Improve Outcomes in Patients With Acute Asthma Exacerbations?

TAKE-HOME MESSAGE

Moderate- to low-quality evidence suggests that antibiotics may reduce symptoms and improve pulmonary function but do not improve other outcomes in patients with acute asthma exacerbations.

METHODS

DATA SOURCES

MEDLINE, EMBASE, the Cumulative Index of Nursing and Allied Health, PsycINFO, and EBSCO databases; ClinicalTrials.gov; the World Health Organization International Clinical Trials Registry Platform; and the Cochrane Central Register of Controlled Trials were searched from inception through October 2017.[1] No language restrictions were applied. Manufacturer Web sites were also searched. Hand searches of the proceedings of major respiratory conferences were also undertaken. Bibliographies of identified articles were scanned for further relevant articles. Trial authors, colleagues, and researchers in the field were contacted to identify further unpublished studies and ongoing trials.

STUDY SELECTION

Studies of adults or children presenting to an emergency department (ED), outpatient clinic, or inpatient ward with an asthma exacerbation were included. Exclusion criteria included a diagnosis of pneumonia, chronic obstructive pulmonary disease, or bronchiectasis or already receiving

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Editor's Note: This is a clinical synopsis, a regular feature of the *Annals'* Systematic Review Snapshot (SRS) series. The source for this systematic review snapshot is: **Normansell R, Sayer B, Waterson S, et al. Antibiotics for exacerbations of asthma. *Cochrane Database Syst Rev.* 2018;6:CD002741.**

Results

Table 1. Summary characteristics of included studies.

Study	No. of Adults	No. of Children	Study Location	Study Country	Antibiotic Regimen (vs Placebo)
Fonseca-Atten, 2006	None	43	ED	United States	Clarithromycin
Graham, 1982	60	None	Inpatient	United Kingdom	Amoxicillin
Johnston, 2006	278	None	Urgent care, ED, inpatient	Multicenter, international	Telithromycin
Johnston, 2016	199	None	Inpatient	United Kingdom	Azithromycin
Koutsoubari, 2012	None	40	Outpatient	Greece	Clarithromycin
Shapiro, 1974	None	50	Inpatient	United States	Hetacillin

Table 2. Results of included trials.

Outcome	No. of Studies	No. of Patients	MD/OR/RD (95% CI)	Treatment Favored
Symptom score*	2	416	MD=−0.34 (−0.60 to −0.08)	Favors antibiotics
All adverse events	3	506	OR=0.99 (0.69 to 1.43)	No difference
Serious adverse events	3	502	RD=0.00 (−0.03 to 0.03)	No difference
Peak expiratory flow, L/min	2	416	MD=23.42 (5.23 to 41.60)	Favors antibiotics

MD, Mean difference; *OR*, odds ratio; *RD*, risk difference; *CI*, confidence interval.
*Both studies used a modified diary card to assess symptoms at day 10 on a 7-point scale.

antibiotics for any reason. Other concomitant medications such as steroids or β-agonists were permissible. Randomized trials that compared antibiotic therapy versus control in adults or children with an acute asthma exacerbation were included. There were no limits on route of antibiotic administration (oral or parenteral) or duration.

DATA EXTRACTION AND SYNTHESIS

Two authors independently extracted data, using a standardized data collection form. Discrepancies were resolved by consensus or with the addition of a third author. Outcomes included admission to the ICU, duration of symptoms, mortality, length of hospital admission, relapse, peak flow, and adverse events (nausea, diarrhea, and upper abdominal pain). Bias was assessed with the Cochrane Risk of Bias Tool and data were combined, reporting odds ratios for dichotomous outcomes, risk differences for rare events, and mean differences for continuous variables. Heterogeneity was assessed with the I^2 statistic.

Six studies with a total of 681 adults and children were included (Table 1), mostly recruited from the ED setting; 2 of them were carried out more than 35 years ago. The definition of asthma exacerbation varied across studies. Moderate-quality evidence suggests antibiotics improve peak expiratory flow and improve symptoms, but not other outcomes (Table 2). The evidence for adverse events and serious adverse events was of low quality, with very few events (10 total) reported overall. Mortality was not reported in any of the studies. There was low statistical heterogeneity between the studies for each of the outcomes reported (I^2=0).

Commentary

Asthma is a chronic respiratory condition that results in constriction of the airways because of inflammation and excess mucus production. Asthmatic patients typically have wheezing caused by narrowed airways, and symptoms are usually controlled with inhaled β-agonists and corticosteroids. A minority of asthma exacerbations are due to bacterial infection.

Antibiotics stewardship means being judicious about their use to limit adverse events, resistance, and unnecessary cost. Although the guidance is clear on administering antibiotics for asthma only when physical examination signs or ancillary testing is suggestive of bacterial infection,[2,3] evidence suggests that practicing clinicians still widely prescribe antibiotics even in the absence of these indicators.[4-6] Given the worldwide prevalence of asthma, the authors of this Cochrane review sought to determine the efficacy and safety of antibiotics for acute asthma exacerbation.

This Cochrane review had limitations: it excluded patients for whom the need for antibiotic therapy was already indicated (eg, those with pneumonia) and those to whom prophylactic antibiotics were given for any reason. Despite an extensive search, few studies were identified, with a small number of patients overall and limited data for most outcomes. This review included a total of only 6 studies spanning a wide range of dates (1974 to 2016), and treatment patterns may have changed during this time. There was significant clinical heterogeneity between studies and patient populations (despite low statistical heterogeneity), including different treatment settings and different antibiotic regimens (type of drug and route). Furthermore, one of the aims of the meta-analysis was to assess adverse events, but too few were reported, rendering the studies underpowered. Also, there is no mechanism to identify the effect of antibiotics given in these studies on development of drug-resistant organisms.

This review suggests that antibiotics may improve symptoms and peak expiratory flow but does not alter other identified outcomes. Antibiotics may be considered for select patients, but further work will be needed to best identify those who are most likely to benefit from antibiotics.

1. Normansell R, Sayer B, Waterson S, et al. Antibiotics for exacerbations of asthma. *Cochrane Database Syst Rev*. 2018;6:CD002741.
2. British Thoracic Society; Scottish Intercollegiate Guidelines Network. British guideline on the management of asthma. *Thorax*. 2014;69(Suppl 1):1-192.
3. Longmore M, Li LJ, Huang GZ, et al. *Oxford Handbook of Clinical Medicine*. 9th ed. Oxford, UK: Oxford University Press; 2014.
4. Kozyrskyj AL, Dahl ME, Ungar WJ, et al. Antibiotic treatment of wheezing in children with asthma: what is the practice? *Pediatrics*. 2006;117:e1104-e1110.
5. Paul IM, Maselli JH, Hersh AL, et al. Antibiotic prescribing during pediatric ambulatory care visits for asthma. *Pediatrics*. 2011;127:1014-1021.
6. Vanderweil SG, Tsai CL, Pelletier AJ, et al. Inappropriate use of antibiotics for acute asthma in United States emergency departments. *Acad Emerg Med*. 2008;15:736-743.