JAMA Insights

Antibiotics for Pediatric Acute Bacterial Sinusitis

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Acute bacterial rhinosinusitis (ABRS), defined as a bacterial infection of the nasal cavity and one or more sinuses persisting for less than 4 weeks, is a common diagnostic consideration in pediatric care. Nearly 5 million US children are prescribed antibiotics for ABRS annually in ambulatory settings. The Infectious Diseases Society of America (IDSA)[1] and American Academy of Pediatrics (AAP)[2] published guidelines for management of ABRS in 2012 and 2013, respectively. However, these guidelines are more than 10 years old and they differ in their recommendations for first-line antibiotic therapy. The IDSA recommends amoxicillin-clavulanate and the AAP recommends amoxicillin or amoxicillin-clavulanate. This article reviews antibiotic selection for ABRS, considering evidence published since 2013.

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Diagnosis

Selecting appropriate therapy for ABRS begins at diagnosis. ABRS must be distinguished from more commonly encountered viral acute respiratory tract infections (ARTIs). Establishing a likely diagnosis of ABRS is important before determining whether any antibiotics should be prescribed. The IDSA and AAP guidelines require at least 1 of the following criteria to diagnose ABRS[1,2]:

- Persistent symptoms: daytime cough and/or nasal discharge for more than 10 days without improvement;
- Worsening symptoms: worsening or new onset of nasal discharge, daytime cough, or fever after initial improvement ("double sickening"); or
- Severe symptoms: temperature ≥39 °C and purulent nasal discharge for at least 3 consecutive days.

Even in children meeting these criteria, substantial overlap exists between ABRS and viral ARTIs, particularly when considering a child with persistent symptoms alone, which accounts for approximately 80% of ABRS in published trials.[3,4] Clinicians must therefore carefully differentiate children who are truly not improving from those who are improving slowly or who have acquired a new viral infection. Incorporating a short (eg, up to 3 days) observation period without antibiotics may help differentiate these common scenarios.[2]

Evolving Microbiology

Before pneumococcal conjugate vaccines became available in 2000, *Streptococcus pneumoniae* was considered the most common cause of ABRS in the US. Currently, *Haemophilus influenzae* accounts for an estimated 30% to 40% of cases, *S pneumoniae* accounts for 20%, and *Moraxella catarrhalis* accounts for approximately 15%, with no bacterial pathogen identified in the remaining cases.[5] Although approximately 90% of *S pneumoniae* isolates are susceptible to high-dose amoxicillin, nearly all *M catarrhalis* and approximately half of *H influenzae* isolates are resistant to amoxicillin due to production of β-lactamase enzymes.[2,5] Based only on these in vitro data, amoxicillin-clavulanate would therefore be required to treat the majority of contemporary ABRS isolates.[1,2] However, amoxicillin without clavulanate[6]—and even no antibiotic treatment at all[7,8]—is associated with high rates of cure, suggesting that guideline recommendations relying primarily on in vitro data warrant reconsideration.

Antibiotic Treatment

Most randomized clinical trials conducted prior to 2013 compared amoxicillin or amoxicillin-clavulanate with placebo and demonstrated the efficacy of antibiotic treatment over placebo, prompting guidelines to recommend antibiotics for treatment of ABRS.[1-3,7,8] However, between 14% and nearly 80% of patients treated with placebo recovered spontaneously, suggesting that antibiotics may only benefit a small subset of patients.[3,7,8]

More recently, Shaikh et al conducted a randomized clinical trial comparing amoxicillin-clavulanate with placebo in 515 children with ABRS diagnosed based on persistent or worsening symptoms.[4] The authors also evaluated the effect of antibiotic treatment in 2 prespecified subgroups: (1) those with nasopharyngeal cultures positive for *S pneumoniae, H influenzae,* or *M catarrhalis*; and (2) those with colored nasal discharge. Consistent with the results of previous smaller trials, treatment with amoxicillin-clavulanate improved sinusitis symptom scores, sinusitis symptom resolution (7 vs 9 days; $P = .01$), and reduced rates of treatment failure that required another antibiotic (14% vs 26%; $P < .001$). The benefit of antibiotic therapy for ABRS was limited to those with positive nasopharyngeal cultures, who experienced a modest reduction in sinusitis symptom scores relative to placebo (between-group difference, −1.95 points [95% CI, −2.40 to −1.51]), whereas no difference was detected in those with negative cultures. The effect of antibiotic treatment was not different in patients with or without colored nasal discharge.[4] Those given antibiotics were less likely to have subsequent otitis media (0% vs 3%) and more often had diarrhea (11% vs 5%). No serious adverse events occurred in either group.

These data further support the limited utility of antibiotic treatment in many children treated for ABRS, with just 26% of patients treated with placebo requiring subsequent antibiotic treatment. Although there was a modest reduction in symptom burden and duration with antibiotic treatment, particularly in patients with positive nasopharyngeal cultures, these improvements were marginal and may have been outweighed by the 2- to 3-fold higher rate of adverse events in antibiotic-treated patients.[3,4] Antibiotic-associated adverse events have been observed in 25% (narrow-spectrum exposure) to 35% (broad-spectrum exposure) of children receiving antibiotics for ARTIs.[9] Clinicians should therefore consider a "watchful waiting" approach in patients with nonsevere symptoms of ABRS and consider prescribing antibiotics only for those meeting criteria for severe ABRS symptoms or symptoms of sinusitis complications (eg, temperature ≥39 °C, facial swelling, photophobia, or focal neurologic symptoms). Based on the small effect of antibiotic treatment on ABRS symptoms even in patients with positive nasopharyngeal cultures, it is unclear whether such testing would add value beyond more judicious antibiotic prescribing practices. Furthermore, nasopharyngeal cultures would add complexity, including the need for follow-up, patient discomfort during testing, and cost. Additionally, if nasopharyngeal cultures were widely used in patients without criteria for ABRS, indiscriminate testing may contribute to antibiotic overprescribing if positive cultures are misinterpreted because many healthy children are colonized with potential sinus pathogens.[5]

Amoxicillin vs Amoxicillin-Clavulanate

Before 2013, data comparing amoxicillin with amoxicillin-clavulanate were limited to small clinical trials conducted prior to the introduction of the pneumococcal conjugate vaccine, with similar cure rates between groups.[7,8] Subsequently, Savage et al used an administrative dataset and propensity score matching to compare clinical outcomes in children treated with amoxicillin vs amoxicillin-clavulanate between 2017 and 2021.[6] Treatment failure within 14 days of an index ABRS encounter occurred in 3.2% of patients dispensed amoxicillin-clavulanate and 2.9% of patients dispensed amoxicillin (relative risk [RR], 1.10 [95% CI, 1.05-1.16]), whereas there was no difference detected at 30 days (RR, 1.03 [95% CI, 0.99-1.08]). Serious sinusitis complications requiring inpatient care occurred in <0.01% of patients. Adverse events occurred slightly more often in patients receiving amoxicillin-clavulanate than amoxicillin (2.3% vs 2%; RR, 1.15 [95% CI, 1.08-1.22]).[6]

Overall, the extremely low rate of treatment failure with either amoxicillin or amoxicillin-clavulanate suggests that if antibiotics are prescribed for ABRS, amoxicillin is an appropriate first-line treatment for most patients given its narrower spectrum of activity and more favorable adverse effect profile. In rare situations, amoxicillin-clavulanate may be preferred based on the increased prevalence of β-lactamase–producing organisms in the postpneumococcal vaccine era. However, given the absence of clinical data demonstrating the superiority of amoxicillin-clavulanate over amoxicillin and overall marginal benefit of any antibiotic treatment for ABRS, amoxicillin-clavulanate should be reserved for the infrequent occurrence of amoxicillin treatment failure and for severe ABRS (eg, temperature ≥39° C and purulent nasal discharge for >3 days).[2,10]

Conclusions

National guidelines regarding optimal antibiotic treatment of pediatric ABRS have not been updated in more than 10 years and are based on limited evidence. Most children will improve without antibiotics, and if antibiotics are prescribed, amoxicillin is recommended for most children with nonsevere ABRS.

ARTICLE INFORMATION

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Published Online: October 16, 2024. doi:10.1001/jama.2024.2018

Conflict of Interest Disclosures: None reported.

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