A Randomized, Placebo-Controlled Trial of Antimicrobial Treatment for Children With Clinically Diagnosed Acute Sinusitis

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ABSTRACT. Objective. Although antimicrobial treatment for children with acute sinusitis is used commonly, it is unclear whether it offers significant clinical benefit. The purpose of this study was to evaluate the effectiveness of antimicrobial treatments for acute sinusitis as they are used in community pediatric practice.

Methods. We conducted a randomized, placebo-controlled trial in 3 community pediatric practices in St Louis, Missouri. A total of 188 patients who were between the ages of 1 and 18 years and who had had 10 to 28 days of persistent sinus symptoms and a clinical diagnosis of acute sinusitis were randomized to receive 14 days of amoxicillin (40 mg/kg/d in 3 daily doses), amoxicillin-clavulanate (amoxicillin 45 mg/kg/d in 2 daily doses), or placebo. Change in sinus symptoms was assessed both by a quantitative symptom score (the S5 score) and subjectively by the parent. Secondary outcomes included adverse effects of treatment and recurrence or relapse of sinus symptoms. Outcomes were assessed by telephone interviews over a 2-month period.

Results. Of the 161 patients who were included in the analysis, 58 received amoxicillin, 48 received amoxicillin-clavulanate, and 55 received placebo. Day 14 improvement rates were 79%, 81%, and 79%, respectively. There were no differences in the 14-day change in S5 score among treatment groups. The rates of adverse events (amoxicillin, 19%; amoxicillin-clavulanate, 11%; placebo, 10%), relapse (amoxicillin, 12%; amoxicillin-clavulanate, 13%; placebo, 13%), and recurrence (amoxicillin, 9%; amoxicillin-clavulanate, 13%; placebo, 13%) of sinus symptoms were similar among treatment groups.


ABBREVIATIONS. ANOVA, analysis of variance; MANOVA, multivariate analysis of variance.

Acute sinusitis is a common childhood disease1–3 and the fifth most common diagnosis that warrants an antimicrobial prescription for children in the United States.4 However, it is unclear whether antimicrobial treatment offers any significant benefit, as acute sinusitis is usually a self-limited illness,1 and antimicrobial treatment can be expensive and may cause adverse effects. Overuse of antimicrobial agents has been associated with the emergence and spread of antimicrobial-resistant bacteria.5

Guidelines for the judicious use of antimicrobial agents for children who have acute sinusitis recommend initial treatment with a first-line antimicrobial agent, such as amoxicillin, for patients who have “prolonged nonspecific upper respiratory signs and symptoms (ie, rhinosinusitis and cough without improvement for 10–14 days).”2 Use of diagnostic imaging is not recommended. However, evidence to support these treatment recommendations is lacking. One randomized controlled trial found that antimicrobial treatment improved outcomes in children who were attending hospital clinics for prolonged sinus symptoms and radiologically confirmed disease.3 Patient selection criteria and changes in antimicrobial resistance patterns in the past 15 years6 may limit the generalizability of these findings to current community care.

Amoxicillin-clavulanate has an extended spectrum of activity against β-lactamase–producing bacteria7 and has been associated with initial cure rates for acute sinusitis in children from 64%3 to 93%.8 However, the drug has been associated with significant gastrointestinal side effects3 and is approximately 10 times more expensive than amoxicillin.9 Increased use of such broad-spectrum antimicrobial agents has been observed recently.10

The goal of this study was to establish whether there is any clinical benefit to antimicrobial treatment for children who have clinically diagnosed, uncomplicated acute sinusitis. We compared amoxicillin, amoxicillin-clavulanate, and placebo in a randomized, controlled trial that was conducted in community pediatric offices.

METHODS

Study Design and Patient Population

Children who were between the ages of 1 and 18 years and who had persistent upper respiratory symptoms for 10 to 28 days and a clinical diagnosis of acute sinusitis were eligible for study participation. Patients were excluded from the study if they had fulminant sinusitis (more severe upper respiratory tract signs and symptoms, ie, fever ≥39°C, facial swelling, facial pain),1,2 or were allergic to 1 of the antimicrobial treatments, had a concurrent illness that required antimicrobial treatment, had complications of sinus disease or chronic sinus disease (>28 days of symptoms),...
had received antimicrobial treatment in the preceding 2 weeks, or had cystic fibrosis. Severity of symptoms was assessed using the S5 score, a validated pediatric sinus symptom score ranging in value from 0 to 3 (see "Outcome Measures"). Patients who had mild symptoms as assessed by an S5 score of <1 were ineligible for the study. The study was conducted at 3 suburban primary care pediatric practices in St Louis, Missouri. Patients were enrolled between November 21, 1997, and February 5, 1999. The study was approved by the Human Studies Committee of Washington University School of Medicine.

The parent or caregiver of a patient who presented with a suspected upper respiratory illness completed a 16-item self-administered eligibility questionnaire. The primary care provider obtained informed consent and completed the provider form, confirming patient eligibility and selecting the product formulation (suspension or capsules). The provider form was faxed to a central hospital pharmacy for treatment assignment. Patients, parents, medical care providers, and the investigators were blinded to treatment assignment. At study enrollment, the parent or caregiver completed a self-administered questionnaire, providing patient and family demographic information, history of the present illness, presence of prognostic factors, and medical history.

Treatments

Patients were stratified by age (<7 and ≥7 years) and symptom severity (S5 score ≥2) and then randomly assigned to receive 14 days of amoxicillin, amoxicillin-clavulanate, or placebo. Treatment assignment was determined by the investigational pharmacist, using computer-generated random numbers with a block size of 6. Amoxicillin was given at a dosage of 40 mg/kg/d in divided doses up to a maximum of 500 mg three times a day. Amoxicillin-clavulanate was prescribed according to the amoxicillin component at a dosage of 45 mg/kg/d in divided doses up to a maximum of 875 mg twice daily. Patients in the placebo group were randomly assigned to 2 dosing regimens, either 2 or 3 times daily. Placebo was dispensed in a similar manner and quantity to the active products and was comparable in appearance, smell, and taste. Treatment was delivered by courier to the patient’s home, usually within 4 hours of the office visit. Additional prescriptions or over-the-counter symptom treatments were used according to provider and parent preferences.

Outcome Measures

Outcomes were assessed by telephone interview at 3, 7, 10, 14, 21, 28, and 60 days. We attempted to interview the same respondent (the parent, primary caregiver, or patient [if older than 12 years]) on each occasion. The primary outcome was change in sinus symptoms. Secondary outcomes included adverse effects of treatment, recurrence or relapse of sinus symptoms, change in functional status, lost time from school or day care, and satisfaction with treatment.

Sinus Symptoms

At each interview, sinus symptoms were assessed quantitatively and subjectively. The S5 score was used for quantitative assessment. The S5 score was developed to assess sinus symptoms in children and is reliable and responsive to symptom improvement in children who have clinically diagnosed acute sinusitis. To calculate the S5 score, respondents rate the degree to which the patient is bothered by each of 5 sinus symptoms (nasal obstruction, daytime coughing, nighttime coughing, headache or facial pain, and colored nasal mucus) on a scale from 0 (absent) to 3 (large problem). The S5 score is the mean symptom score (range: 0–5). The respondent was also asked to compare the child’s current sinus disease status with that at study enrollment and rate it on a 5-point scale. Response options included a little or a lot better, the same, or a little or a lot worse. Patients who were rated as a little or a lot better were classified as improved, and those who were rated as a little or a lot worse were classified as not improved.

Secondary Outcomes

Relapse of sinus symptoms was defined as a subjective symptom rating of either the same or not improved at day 21 or 28 in a patient who at day 14 was rated as improved. Recurrence of sinus symptoms was defined as sinus symptoms for at least 10 days in the second month of follow-up in a patient who at day 28 was rated as improved.

Adverse effects of antibiotic treatment were assessed at day 14.

Respondents were asked whether the patient had experienced any side effects from study medication, followed by specific questions about known adverse effects.

Current functional status was assessed at baseline and at each follow-up interview using a 5-point scale ranging from excellent to poor. The actual or estimated (if a weekend or holiday) number of illness-related days missed from school or day care were recorded.

Satisfaction with treatment was assessed along with treatment in a patient who at day 28 was rated as improved. Patients who were rated as a little or a lot worse were classified as not improved, and those who were rated as the same, or a little or a lot worse. Patients who were rated as a little or a lot better were classified as improved, and those who were rated as the same, or a little or a lot worse.

Statistical Analysis

Statistical analysis was by intention to treat for all eligible randomized patients. A probability of P ≤ 0.05 (2-tailed) was used to establish statistical significance. We used analysis of variance (ANOVA) to compare the 14-day change in sinus symptom score among treatment groups. The effects of treatment on the S5 score at days 3, 7, 10, and 14 were compared among treatment groups using repeated measures MANOVA. In a similar manner, we compared the differences in the proportion of children who were rated as improved in each treatment arm using repeated measures categorical modeling. Patients with incomplete records were excluded from repeated measures analyses.

The means of all normally distributed continuous variables were compared using ANOVA; markedly non-normally distributed variables were compared using the Kruskal-Wallis test. For categorical data, either a χ² test or Fisher’s exact test was used to compare proportions. Continuous variables are reported as mean (standard deviation). All statistical analyses were done using STATA 5.0 (Stata Corp, College Station, TX) or SAS version 6.12 (SAS Institute, Inc, Cary, NC).

Sample Size Calculation

Using pilot data, we estimated that 60 patients in each group would provide 80% power to detect a difference of 0.42 points in the mean 14-day change in S5 scores, using ANOVA (α = 0.05; mean 14-day change in S5: 1.14 [standard deviation: 0.75] in untreated group). This change represents an improvement of 2 grades (large to small problem) in 1 symptom or 1 grade in 2 symptoms in the S5 score and is how we defined the minimum clinically significant difference for sample size estimation.

RESULTS

Patients

A total of 188 patients were enrolled in the study during a 15-month period. Nineteen patients were excluded from the analysis because they failed to meet eligibility criteria: 16 had an upper respiratory infection, 1 was 20 years old, 1 had symptoms for 3 days only, and 1 had previously been enrolled. Fifty-eight eligible patients were randomized to receive amoxicillin, 48 were randomized to receive amoxicillin-clavulanate, and 55 were randomized to receive placebo. The most frequent reasons for study exclusion in 241 patients who completed the eligibility questionnaire were duration of symptoms <10 days (51%), a concurrent illness that required antimicrobial treatment (most commonly Streptococcal pharyngitis or acute otitis media; 20%), and parental refusal (11%).

Ninety-seven percent of all follow-up interviews
were completed. The mother was interviewed most frequently (91%). The same respondent completed all follow-up interviews for 119 (74%) patients and for at least 7 of 8 interviews for 139 (86%). Most patients (75%) were enrolled during the winter months (October to March).

At baseline, patient sociodemographic characteristics, medical history, and home environments were similar in the 3 treatment groups (Table 1). The only exceptions were gender distribution and number of children living at home. Most children attended school or child care 5 days per week, and few (12%) attended neither. Baseline sinus symptom status was similar among groups, except for symptom duration (Table 1). All patients had nasal discharge (86%), daytime cough (97%), or both (83%). Most patients (93%) who had daytime cough also complained of having a nighttime cough. Headache or facial pain occurred more commonly in children aged 7 or older.

**Treatment Use**

There were no differences among groups for duration of treatment or treatment compliance (Table 2). Three patients did not start the study medication, 1 from each treatment group. Concurrent ancillary drug use was common (Table 3).

Eighteen patients discontinued the study drug (4 amoxicillin, 8 amoxicillin-clavulanate, 6 placebo). The main reasons for stopping were development of an intercurrent illness that required antimicrobial treatment (n = 6 [2 amoxicillin-clavulanate, 4 placebo] 2 pneumonia, 3 acute otitis media, 1 chlamydial cervicitis), adverse effects (n = 6 [2 amoxicillin, 3 amoxicillin-clavulanate, 1 placebo] 2 allergic, 4 gastrointestinal), and treatment failure assessed by the

**TABLE 1. Baseline Patient Sociodemographic Characteristics, Medical History, Home Environment, and Sinus Symptoms by Treatment Group**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Amoxicillin (n = 58)</th>
<th>Amoxicillin-Clavulanate (n = 48)</th>
<th>Placebo (n = 55)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sociodemographic characteristics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age† (7.50 (4.12) 8.13 (5.51))</td>
<td>7.68 (4.93)</td>
<td>.79</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;7 y</td>
<td>50% 50%</td>
<td>51%</td>
<td></td>
<td>.99</td>
</tr>
<tr>
<td>&lt;3 y</td>
<td>12% 25%</td>
<td>20%</td>
<td></td>
<td>.22</td>
</tr>
<tr>
<td>Male gender</td>
<td>48% 33%</td>
<td>62%</td>
<td></td>
<td>.02</td>
</tr>
<tr>
<td>White race</td>
<td>93% 83%</td>
<td>87%</td>
<td>.27</td>
<td></td>
</tr>
<tr>
<td>Patient at school or day care 5 d per wk</td>
<td>74% 75%</td>
<td>64%</td>
<td></td>
<td>.67</td>
</tr>
<tr>
<td>Parental education post high school</td>
<td>86% 69%</td>
<td>84%</td>
<td></td>
<td>.21</td>
</tr>
<tr>
<td>Annual family income &gt;$50 000</td>
<td>60% 44%</td>
<td>56%</td>
<td></td>
<td>.21</td>
</tr>
<tr>
<td><strong>Medical history</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Usual health excellent or very good</td>
<td>83% 71%</td>
<td>85%</td>
<td></td>
<td>.27</td>
</tr>
<tr>
<td>Usual function excellent or very good</td>
<td>93% 92%</td>
<td>91%</td>
<td></td>
<td>.63</td>
</tr>
<tr>
<td>History of sinus disease</td>
<td>57% 52%</td>
<td>55%</td>
<td></td>
<td>.88</td>
</tr>
<tr>
<td>History of allergy</td>
<td>31% 15%</td>
<td>20%</td>
<td></td>
<td>.11</td>
</tr>
<tr>
<td>Asthma</td>
<td>12% 6%</td>
<td>16%</td>
<td></td>
<td>.28</td>
</tr>
<tr>
<td>Ear infection within 3 mo</td>
<td>10% 17%</td>
<td>13%</td>
<td></td>
<td>.63</td>
</tr>
<tr>
<td><strong>Home environment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Two-parent home</td>
<td>90% 90%</td>
<td>93%</td>
<td></td>
<td>.81</td>
</tr>
<tr>
<td>More than 1 child at home</td>
<td>57% 75%</td>
<td>89%</td>
<td></td>
<td>.001</td>
</tr>
<tr>
<td>Two adults working outside the home</td>
<td>60% 48%</td>
<td>51%</td>
<td></td>
<td>.34</td>
</tr>
<tr>
<td>Tobacco used at home</td>
<td>21% 15%</td>
<td>22%</td>
<td></td>
<td>.61</td>
</tr>
<tr>
<td>Woodstove at home</td>
<td>17% 21%</td>
<td>20%</td>
<td></td>
<td>.88</td>
</tr>
<tr>
<td><strong>Initial sinus disease status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nasal obstruction</td>
<td>97% 100%</td>
<td>94%</td>
<td></td>
<td>.32</td>
</tr>
<tr>
<td>Day cough</td>
<td>100% 96%</td>
<td>96%</td>
<td></td>
<td>.37</td>
</tr>
<tr>
<td>Night cough</td>
<td>98% 90%</td>
<td>93%</td>
<td></td>
<td>.14</td>
</tr>
<tr>
<td>Any nasal mucus</td>
<td>90% 83%</td>
<td>84%</td>
<td></td>
<td>.72</td>
</tr>
<tr>
<td>Colored</td>
<td>39 28</td>
<td>31</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clear</td>
<td>13 12</td>
<td>15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache/face pain</td>
<td>66% (33/50) 74% (28/38)</td>
<td>69% (33/48)</td>
<td>.73</td>
<td></td>
</tr>
<tr>
<td>Initial S5 score†‡</td>
<td>1.98 (0.51)</td>
<td>2.02 (0.52)</td>
<td>1.89 (0.57)</td>
<td>.42</td>
</tr>
<tr>
<td>Days of symptoms†</td>
<td>15.76 (5.60)</td>
<td>18.50 (5.83)</td>
<td>15.36 (5.30)</td>
<td>.01</td>
</tr>
<tr>
<td>Recent functional status excellent or very good</td>
<td>62% 56%</td>
<td>65%</td>
<td></td>
<td>.85</td>
</tr>
<tr>
<td>Days missed from school or daycare before visit†</td>
<td>1.17 (1.64)</td>
<td>0.88 (1.19)</td>
<td>1.25 (1.18)</td>
<td>.45</td>
</tr>
<tr>
<td>Parental diagnosis of a cold or sinus infection</td>
<td>85%</td>
<td>83%</td>
<td>80%</td>
<td>.97</td>
</tr>
<tr>
<td>Used symptom treatment before visit</td>
<td>71%</td>
<td>67%</td>
<td>67%</td>
<td>.71</td>
</tr>
</tbody>
</table>

*The reported P value refers to the comparison among the 3 treatment groups. The denominator is given if it is other than the total number of patients in the treatment group.
†Continuous data are expressed as mean (standard deviation).
‡The S5 score is the mean of the symptom scores for nasal obstruction, headache/facial pain, day cough, night cough, and colored nasal discharge (0 = no symptoms, 3 = symptoms are a large problem).
primary care provider (n = 3: on days 3 [placebo], 12 [amoxicillin], and 13 [amoxicillin-clavulanate]). All patients who were considered to be treatment failures and those who had intercurrent illnesses were treated with another antimicrobial agent.

### Treatment Outcomes

Patient outcomes did not differ by treatment group (Table 2). Change in sinus symptoms was the same in all groups, regardless of the outcome assessment method used (Table 2). In addition, using repeated measures MANOVA, we found no difference in resolution of sinus symptoms among treatment groups at days 3, 7, 10, and 14 using the S5 score (n = 145; P = .61, Wilk’s λ) or improvement rate (n = 147; P = .23). Repeated measures analyses and the 14-day change in S5 score are adjusted for gender variance at baseline and age. (Inclusion of history of allergy and 1 child at home as additional covariates did not significantly alter our results.) In all groups, symptoms improved over time, with no significant difference among groups (P = .80; Fig 1). The most persistent symptoms at day 14 were nasal obstruction and daytime cough, reported as a medium or large problem for 20% and 15% of patients, respectively.

There were no differences among groups in functional status, rates of relapse and recurrence, or parental satisfaction scores. Twenty-one respondents (13%) reported having a treatment side effect, most commonly gastrointestinal. Patients who were treated with amoxicillin were more likely to report abdominal pain (P = .017). Twenty-one patients (13%; 8 amoxicillin, 6 amoxicillin-clavulanate, 7 placebo) reported seeking additional health care for sinus symptoms after completing study treatment (11, ≥28 days; 10, >28 days). Of these, 18 were treated with an additional antimicrobial agent. No serious disease complications occurred in any treatment group.

The results are similar if patients who were treated with amoxicillin and amoxicillin-clavulanate are considered together. Antimicrobial treatment resulted in a 14-day change in the S5 score of 1.48 (0.77) and a
day 14 improvement rate of 80%. The difference in the 14-day change in symptoms comparing antimicrobial treatment with placebo was 0.16 (95% confidence interval: 0.10–0.41; P = .22) points in the S5 score and 1% (95% confidence interval: 12.3%–14.6%; P = .87) in the improvement rate.

**DISCUSSION**

We found no clinical benefit to antimicrobial treatment with either amoxicillin or amoxicillin-clavulanate compared with placebo for pediatric patients who had a clinical diagnosis of acute sinusitis. Antimicrobial treatment offered no benefit in overall symptom resolution, duration of symptoms, recovery to usual functional status, days missed from school or child care, or relapse and recurrence of sinus symptoms. No serious disease complications occurred during the 2-month follow-up period. Clinical outcomes for patients who were treated with amoxicillin and amoxicillin-clavulanate were the same and equivalent to placebo. Eighty-one percent of patients were improved 7 days after the study entry regardless of treatment, and 87% were improved by 10 days.

The overall rate of reported side effects did not differ among treatment groups, although abdominal pain occurred more frequently in patients who were treated with amoxicillin. The incidence of diarrhea was the same in all treatment groups (20%). The high frequency of symptoms elicited in response to specific questions in all treatment groups is surprising. We suspect that this reflects the systemic effects of viral illness in children.

The effectiveness of recommended primary care antimicrobial treatment strategies for acute sinusitis have not been evaluated previously. In the absence of an acceptable, reliable diagnostic test, use of clinical criteria for the diagnosis of acute sinusitis is suggested. We evaluated this approach to patient management. Diagnostic certainty is not possible without sinus aspiration, but this is an invasive test that is not used in routine clinical practice. Imaging techniques, including radiograph and computed tomographic scans, have high false-positive rates, and their false-negative rates are unknown. These tests are expensive, are time-consuming, may require patient sedation, and are not recommended for use in primary care. Although variation in clinical findings that are used to diagnose sinusitis has been reported, the study patients are representative of patients in whom antimicrobial treatment is currently recommended. All had persistent nonspecific upper respiratory symptoms (including rhinorrhea, daytime cough, or both) for at least 10 days that failed to improve. Our findings suggest 3 important conclusions. First, recommended clinical diagnostic criteria fail to identify children who will benefit from antimicrobial treatment. Second, delaying initiation of treatment for 3 weeks after initiation of symptoms may decrease unnecessary antimicrobial use and will result in spontaneous symptom resolution in at least 80% of untreated patients. Third, if antimicrobial treatment is initiated after 10 days of symptoms, amoxicillin rather than amoxicillin-clavulanate should be used. We believe that these findings are directly generalizable to most primary care pediatric patients who have at least 10 days of persistent sinus symptoms and a clinical diagnosis of acute sinusitis.

We assessed sinus symptoms quantitatively with the S5 score. The score was used not to replace the clinical diagnosis but rather to assess symptom severity at study entry and for outcome assessment. The S5 score was developed in the primary care setting for use in sinusitis treatment studies. It was administered easily and allowed assessment of treatment effects without a physician’s evaluation, which facilitated completion of the study in the primary care setting. Colored nasal discharge is included in the S5 score as it was frequently reported by primary care patients who had a clinical diagnosis of acute sinusitis, although others have found nasal discharge regardless of color to be associated with sinus disease.
Our findings differ from the only other published randomized controlled treatment trial of children with acute sinusitis. In the early 1980s, Wald et al compared the effectiveness of amoxicillin and amoxicillin-clavulanate in a placebo-controlled trial. That study found that antimicrobial treatment was more likely to result in cure at 3 and 10 days, with no difference in effectiveness between the 2 antimicrobial agents. Patient selection criteria and methodologic differences likely explain the inconsistencies in study findings. In both studies, all patients had a clinical diagnosis of acute sinusitis defined as persistent sinus symptoms (10–30 days of nasal discharge or daytime cough or both) that were not improving. Wald’s study patients differed in that they were drawn from hospital clinics and all had radiologically-confirmed maxillary sinus disease. This requirement for radiograph evidence of sinus disease resulted in exclusion of 20% (35 of 171) of patients who had clinically diagnosed acute sinusitis. No symptomatic treatments were prescribed, and use of over-the-counter products for symptom relief was not reported. Other important differences include a high dropout rate and lack of intention-to-treat analysis (of the 136 patients randomized to 10 days of treatment, 43 [32%] were excluded from the final analysis), and the symptom score that was used to define cure in some patients was not validated. We believe that patient selection criteria and methodologic issues limit generalizability of that study’s findings to current primary care treatment of children with acute sinusitis and likely explain the difference between study findings. Our findings are comparable to those of the only published placebo-controlled randomized trial of antimicrobial treatment in adult patients with clinically diagnosed acute sinus disease, which found no benefit to antimicrobial treatment.

With 161 patients in the analysis, we had adequate power to detect a clinically significant change in symptoms using the 14-day change in S5 score (our primary outcome). Our best estimate of the difference between treatment groups is 0.16 points ($P = .22$), equivalent to an improvement of $<$1 grade (eg, large to medium) in 1 of 5 symptoms included in the S5 score. We believe that this difference is neither clinically nor statistically significant. We are confident that we excluded a benefit in symptom improvement favoring antimicrobial treatment of up to 0.41 points (just less than the 0.42 minimum change used for the sample size calculation and equivalent to less than an improvement of 2 grades in 1 symptom). In addition, we found an absolute difference in day 14 improvement rates between active treatment and placebo of only 1% using the respondent’s subjective assessment of symptom change. (In other words, for every patient who improved on antibiotics, 99 did not.) Not only is this apparent effect not clinically significant, but it almost certainly is attributable to random variation as indicated by the large $P$ value. Our study was not powered to detect a difference in improvement rates, but we are confident that we excluded a difference favoring antimicrobial agents of up to 14%. We do not believe that lack of power to detect this secondary outcome is a threat to our conclusions. We measured many patient outcomes during a 2-month period and failed to find a significant trend toward effectiveness of either antimicrobial agent.

There are several limitations to our study. First, generalizability of our findings is somewhat limited. Most patients were white and from 2-parent, middle-income homes, although patients from all sociodemographic groups were included. We do not have the data to estimate the percentage of eligible patients who were excluded from the study, as not all eligible patients completed the initial questionnaire. Second, use of additional symptom treatments may have confounded the effect of antimicrobial treatment. We do not think that this was the case as the proportion of children who used these products was the same in each group (Table 3). Also, evidence for effectiveness of most symptom therapies is lacking, making it unlikely that usage would affect patient outcomes. Third, we found a trend toward decreased satisfaction with placebo, raising the possibility of inadequate blinding and biased outcome assessment. We do not believe that this was the case as the likely effect of such a bias would be to overestimate antimicrobial benefit, and we found none. Fourth, inclusion of many patients with viral upper respiratory illness could affect the validity of our findings. We used 2 mechanisms to minimize inclusion of such patients in the study. First, prolonged symptoms (at least 10 days) and an S5 score of at least 1.0 were required for study eligibility. Viral upper respiratory illness and acute sinus disease are part of a continuum of diseases with an overlapping clinical picture and S5 score distributions. Prolonged symptoms for at least 10 days is commonly used as a distinguishing clinical criterion. Our previous work suggests that use of an S5 threshold of 1.0 excludes most patients with nonspecific upper respiratory illness and few patients with clinically diagnosed acute sinusitis. Second, patients were excluded from the analysis if they had a diagnosis of upper respiratory infection, despite 10 days of symptoms.

**CONCLUSION**

Clinically diagnosed, uncomplicated, acute sinusitis in children is usually a self-limited illness of short duration. Neither antimicrobial agent offered substantial clinical benefit for primary care management of clinically diagnosed acute sinusitis in children.

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**LAND MINES—THE NOBEL PEACE PRIZE AND THE INTERNET**

... Jody Williams won the Nobel Peace Prize in 1997 for her contribution to the international ban on land mines. She achieved that ban not only without much government help, but in the face of opposition from all the major powers. And what did she say was her secret weapon for organizing 1000 different human rights and arms control groups on 6 continents? “E-mail.”


Noted by JFL, MD