

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

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### FROM 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 (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.

#### Conclusion.

Neither amoxicillin nor amoxicillin-clavulanate offered any clinical benefit compared with placebo for children with clinically diagnosed acute sinusitis.

## THESE AUTHORS ALSO NOTE:

"Acute sinusitis is a common childhood disease and the fifth most common diagnosis that warrants an antimicrobial prescription for children in the United States."

"It is unclear whether antimicrobial treatment offers any significant benefit, as acute sinusitis is usually a self-limited illness, 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."

"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).'" **[IMPORTANT]**

Amoxicillin-clavulanate is often used and has been associated with significant gastrointestinal side effects and is approximately 10 times more expensive than amoxicillin.

## METHODS

The patient population was children between the ages of 1 - 18 years who had persistent upper respiratory symptoms for 10 to 28 days and a clinical diagnosis of acute sinusitis.

Patients were randomly assigned to receive 14 days of amoxicillin, amoxicillin-clavulanate, or placebo.

Outcomes were assessed by telephone interview at 3, 7, 10, 14, 21, 28, and 60 days. 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.

Also, response included "a little or a lot better, the same, or a little or a lot worse."

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."

Satisfaction with treatment was assessed by asking whether the parent/caregiver strongly agreed, agreed, were neutral, disagreed, or strongly disagreed with the following statements:

"The medication that my child has received for sinus infection helped to cure his/her infection, and, if my child gets another sinus infection, I would be satisfied if the same medicine was prescribed."

## RESULTS

"Patient outcomes did not differ by treatment group."

"Change in sinus symptoms was the same in all groups, regardless of the outcome assessment method used."

There was "no difference in resolution of sinus symptoms among treatment groups at days 3, 7, 10, and 14."

"In all groups, symptoms improved over time, with no significant difference among groups."

"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."

## 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."

"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."

#### CONCLUSIONS:

- (1) Recommended clinical diagnostic criteria fail to identify children who will benefit from antimicrobial treatment.
- (2) Delaying 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.
- (3) 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."

This study's 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 also found no benefit to antimicrobial treatment.

(Stalman W, van Essen GA, van Der Graaf Y, de Melker RA; The end of antibiotic treatment in adults with acute sinusitis-like complaints in general practice? A placebo-controlled double blind randomized doxycycline trial. *Br J Gen Pract* 1997; 47:794-799.)

The authors "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.)"

"Clinically diagnosed, uncomplicated, acute sinusitis in children is usually a self-limited illness of short duration."