Amoxicillin for acute rhinosinusitis: A randomized controlled trial

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Abstract

Context—Evidence to support antibiotic treatment for acute rhinosinusitis is scant, yet antibiotics are commonly used.

Objective—To determine the incremental effect of amoxicillin treatment over symptomatic treatments for adults with clinically diagnosed acute rhinosinusitis.

Design—Randomized placebo-controlled trial

Participants and Setting—Adults with uncomplicated, acute rhinosinusitis were recruited from 10 community practices in Missouri between November 1st 2006 and May 1st 2009

Interventions—Ten-day course of either amoxicillin (1500mg/day) or placebo administered in three doses/day. All patients received a 5-7-day supply of symptomatic treatments for pain, fever, cough and nasal congestion to use as needed.

Main Outcome Measures—The primary outcome was improvement in the disease-specific quality of life after 3–4 days of treatment assessed with the *SNOT-16* (minimally important difference 0.5 on 0 to 3 scale). Secondary outcomes included the patients' retrospective assessment of change in sinus symptoms and functional status, recurrence or relapse, satisfaction with and adverse effects of treatment. Outcomes were assessed by telephone interview at Days 3, 7, 10 and 28.

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Results—166 adults (36% male, 78% Caucasian) were randomized to amoxicillin (85) or placebo (81); 92% concurrently used 1 symptomatic treatment (amoxicillin, 94%, placebo 90%, p=0.34). The mean change in *SNOT-16* scores was not significantly different between groups on Day 3 (mean difference between groups 0.03, 95% CI –0.12 to 0.19) and Day 10, but differed at Day 7 favoring amoxicillin (mean difference between groups 0.19, 95% CI 0.024 to 0.35). At Day 7 more participants treated with amoxicillin reported symptom improvement (74% vs. 56%, p=0.0205; NNT = 6, 95% CI 3 to 34), with no difference at Day-3 or Day-10. No between group differences were found for any other secondary outcomes. No serious adverse events occurred.

Conclusion—Among patients with acute rhinosinusitis, a 10-day course of amoxicillin compared with placebo did not reduce symptoms at day 3 of treatment.

Acute rhinosinusitis is a common disease associated with significant morbidity, lost time from work, and treatment costs.[1, 2] In the face of the public health threat posed by increasing antibiotic resistance,[3] strong evidence of symptom relief is needed to justify antibiotic prescribing for this usually self-limiting disease. Placebo-controlled clinical trials to evaluate antibiotic treatment have had conflicting results, likely due to differences in diagnostic criteria and outcome assessment. Studies requiring confirmatory tests such as x-ray have tended to show treatment benefit,[4–7] but meta-analyses of these studies have generally concluded that clinical benefit with antibiotic treatment was small due to the high rate of spontaneous improvement (~69%).[8, 9] Studies using clinical diagnostic criteria tend to show no or minimal treatment benefit and higher spontaneous resolution (~80%).[10–13] Despite the controversy regarding their clinical benefit and concerns about resistance, antibiotics for sinusitis account for one in five antibiotic prescriptions for adults In the United States (U.S.).[14, 15]

In 2001, a CDC-sponsored expert panel developed evidence-based guidelines for the evaluation and treatment of adults with acute rhinosinusitis that recommended using clinical criteria for diagnosis, reserving antibiotic treatment for patients with moderately severe or severe symptoms, and treating with the most narrow spectrum antibiotic active against *Streptococcus pneumoniae* and *Haemophilus influenza*.[1] The goal of this study was to evaluate these clinical guidelines in the community setting. Our objective was to determine the incremental effect of amoxicillin treatment over symptomatic treatments on disease-related quality of life in adults with clinically diagnosed acute bacterial rhinosinusitis.

DESIGN AND METHODS

We conducted this randomized, placebo-controlled trial in ten offices of primary care physicians (PCPs) in St Louis, MO. The study protocol was approved by the institutional review board at Washington University: written informed consent was obtained from each participant.

Subject eligibility and enrollment

Adult patients (18 to 70 years old) who met the CDC's Expert panel's diagnostic criteria for acute bacterial rhinosinusitis[1] and assessed their symptoms as moderate, severe or very severe were eligible to participate. Diagnosis required history of maxillary pain or tenderness in the face or teeth <u>and</u> purulent nasal secretions, and rhinosinusitis symptoms for 7 days and 28 days that were not improving or worsening, or rhinosinusitis symptoms for < 7 days that had significantly worsened after initial improvement.

Patients were excluded if they had: allergy to penicillin or amoxicillin; prior antibiotic treatment within 4 weeks; complications of sinusitis; a comorbidity that may impair their immune response; cystic fibrosis; required an antibiotic for a concurrent condition; were pregnant; or rated their symptoms as very mild or mild.

Eligible patients attending study sites when a research assistant (RA) was present (office hours Monday to Friday) were invited to participate by their PCP. The RA discussed participation requirements and completed the eligibility assessment and the consent process.

Randomization

Randomization was done in advance by the investigational pharmacist who did not participate in patient enrollment or outcome assessment. Using a blocked randomization scheme, computer generated random-numbers determined how the two study drugs were allocated to the consecutively numbered study treatment packages. Randomization occurred when the RA assigned the treatment package.

Study participants received a 10-day course of either amoxicillin at a daily dose of 1500mg administered in three doses per day (500mg/dose) or placebo similar in appearance and taste and dispensed in the same fashion. Unless their PCP felt it was contraindicated, all patients received a 5-7-day supply of the following symptomatic treatments to be used as needed: acetaminophen for pain or fever at a dose of 500mg every 6 hours, guaifenesin to thin secretions at a dose of 600mg every 12 hours, dextromethorphan hydrobromide (10mg/5ml) with guaifenesin (100mg/5ml) for cough at a dose of 10mls every 4 to 6 hours, pseudoephedrine sustained action for nasal congestion at a dose of 120mg every 12 hours, and 0.65% Saline Spray using 2 puffs per nostril as needed.

Measurement

The primary outcome, the effect of treatment on disease-specific QOL at Day 3 was measured using the modified-*SNOT-16*, a validated and responsive measure.[16–18] Considering both severity and frequency, the participant scored how much each of 16 sinus-related symptoms bothered them in the past few days (0, no problem to 3, severe problem). The *SNOT-16* score, the mean score of all completed items ranged from 0 to 3, with a minimally important difference (MID)[19] of 0.5 units on this scale.[18]

Participants used a 6-point scale (a lot or a little worse or better, the same, no symptoms) to retrospectively assess symptom change since enrollment. Those reporting their symptoms were a lot better or absent were categorized as significantly improved. Change in functional status was assessed as days unable to do usual activities and days missed from work. Recurrent sinus infection was defined as any patient who at Day 7 and Day 10 reported no symptoms, and at Day 28 reported their symptoms were unchanged or worse. Relapse was defined as any patient who at Day 10 was significantly improved, but on Day 28 reported their symptoms were unchanged or worse. Satisfaction with treatment, adverse effects of treatment and treatment compliance and adequacy of blinding were assessed at Day 10. Participants rated their level of agreement with the statement: "The study medication that I received for my sinus problem helped a lot" (strongly agree, agree, neutral, disagree or strongly disagree). Responses of strongly agree and agree were classified as satisfied with treatment. Adverse effects of antibiotic treatment were assessed using an open-ended question (Have you had any side effects from the study medication?) followed by specific questions about potential adverse effects associated with amoxicillin treatment. Treatment compliance was assessed by self-report (missed <3 doses of study drug), and subjects were asked to guess their study group to assess blinding.

Data collection

At study enrollment (Day 0), the participant completed a brief interview with the RA to complete the *SNOT-16*, and provide demographic and disease-related information to describe the study sample. Demographic information including race and ethnicity were provided by selecting from options included in the baseline questionnaire. The PCP completed a 1-page form documenting symptoms and signs. The *SNOT-16* was repeated by telephone interview later that day to standardize the mode of data collection. (The office visit Day 0 *SNOT-16* score was used for 4 participants who missed the phone interview). Outcomes were assessed by telephone interview at 3, 7, 10 and 28 days following treatment initiation. Interviews comprised a structured questionnaire and were conducted by trained RAs blinded to group assignment.

Statistical Analysis

Using pilot data, we estimated that a sample of 100 participants/group would provide 83% power to detect a true difference of 0.25 in *SNOT-16* scores at Day-3.

All the analyses adhered to the intention-to-treat principle, and a probability of p 0.05 (2-tailed) was used to establish statistical significance. Improvement in the disease-specific QOL was assessed as the reduction in *SNOT-16* scores from Day 0 to Day 3, 7 and 10. We compared differences across study groups using analysis of variance, controlling for disease severity at baseline (with the Day 0 *SNOT-16* score). Reported p-values are adjusted for this covariate. There were few missing data, but we repeated the primary analyses imputing the missing *SNOT-16* data 20 times. As the statistical significance pattern for these additional analyses remained the same as with the unimputed data, we report the results of the unimputed data.

For the secondary analyses and to compare treatment groups at baseline, the means of continuous variables were compared by analysis of variance. For categorical data, either a chi-square test or Fisher's exact test was used for comparison of proportions. We used logistic regression to identify predictors of benefit with antibiotic treatment, controlling for intervention group. All statistical analyses were done using SAS (SAS Institute.2007. The SAS System version 9.12, Cary, NC).

RESULTS

Patients

Between November 1st 2006 and May 1st 2009, 244 adults were screened, 174 were eligible and 166 were randomized to amoxicillin (85) and placebo (81) (Figure 1). Socio-demographic and disease characteristics were similar in both groups (Table 1). All reported purulent nasal discharge and maxillary pain or tenderness in the face or teeth (94 bilateral, 56 unilateral, 16 laterality unknown); 143 (88%) reported rhinosinusitis symptoms for 7 days and 28 days that were worsening (n=105) or not improving (n=38), and 23 (14%) reported symptoms for < 7 days that significantly worsened after initial improvement. Symptoms most frequently recorded by the provider were: facial congestion/fullness (79%), facial pain or pressure (70%), cough (60%), ear pain (58%), post-nasal discharge (55%), nasal obstruction (54%), and headache (54%). Dental pain (10%), hyposmia/anosmia (7%), and halitosis (3%) were rare. The frequency and scores for items in the *SNOT-16* are provided in Table 2.

Follow-up interviews at Days 3, 7, 10 and 28 were completed by 155 (93%), 155 (93%), 152 (92%) and 159 (96%) participants respectively, with no difference by study group.

Treatment Use

Duration of use or self-reported adherence did not differ between groups (Table 3). In total, 23 (14%) subjects (11 amoxicillin, 12 control, p=0.73) did not complete the 10-day course of treatment: 8 had stopped by day 3, 13 by day 7 and 2 more by day 10. Reasons were: failure to improve (2 amoxicillin, 6 control), worsening symptoms (3 amoxicillin, 4 control), improved symptoms (4 amoxicillin), and adverse effects of treatment (1 amoxicillin). No reason was recorded for 3 participants (1 amoxicillin, 2 control). Sixteen were treated with another antimicrobial (5 amoxicillin, 11 control p=0.093) including amoxicillin-clavulanate (11), amoxicillin (4) and azithromycin (1). The percentage of participants who guessed their treatment assignment correctly did not differ by study group (amoxicillin, 36%, control, 37%, p=0.20).

Concurrent use of symptomatic treatments was common (92%, 95%CI 88% to 96%) and did not vary by study group (Table 4). No new nasal steroid use was reported.

Effectiveness of Treatment

Treatment outcomes are presented in Table 3.

Disease-specific quality of life—The mean change in *SNOT-16* scores was similar in both groups at Day 3 (amoxicillin, 0.59, 95% CI 0.47 to 0.71; control, 0.54, 95% CI 0.41 to 0.67; p=0.69) and Day 10, but differed at Day 7 favoring amoxicillin (mean difference between groups 0.19, 95% CI 0.024 to 0.35).

Symptom change—No statistically significant difference in reported symptom improvement were found at Day-3 or Day-10. At Day 7 more participants treated with amoxicillin reported symptom improvement (74% vs. 56%, p=0.02; NNT = 6, 95% CI 3 to 34).

We repeated the analyses comparing change in *SNOT-16* and symptom improvement across study groups for those who completed 10-days of treatment with the study drug (per protocol analysis: n=143, amoxicillin, 74, control, 69), and those with symptoms for 7 and 28 days (n= 143, amoxicillin, 73 control, 70). Findings were consistent with the primary analysis.

Other secondary outcomes—Days missed from work or unable to do usual activities, rates of relapse and recurrence by 28-days, additional healthcare use and satisfaction with treatment did not differ by study group. The most common additional services were calls to the physician (amoxicillin 5%, control 10%, p=0.35) and additional office visits (amoxicillin 2%, control 4%, p=0.66). Only one patient had a sinus X-ray and another saw a specialist (both in the amoxicillin group).

Adverse events—No serious adverse events occurred. Study groups did not differ in reporting side effects from the study medication. The most common side effects identified with specific questioning were headache (amoxicillin 22%, control 23%, p=0.96) and excessive tiredness (amoxicillin 11%, control 21%, p=0.12). Few subjects indicated they had nausea (7%), diarrhea (9%), abdominal pain (5%), or vaginitis (6% of women), with no differences by study group.

Prognostic factors—The only symptom that predicted benefit with antibiotic treatment at Day 7 (self reported improvement) was nasal obstruction recorded by the physician. Among those with nasal obstruction (n=83), the odds of improvement by day 7 with antibiotic treatment vs. no treatment was 4.59 (95% CI 1.16 to 18.12), with no benefit in the group

without obstruction. Smoking, duration of symptoms, prior sinus infection, asthma, allergic rhinitis, severity of symptoms (by report and baseline *SNOT-16* score), and laterality of disease did not predict benefit with antibiotic treatment.

COMMENT

Our findings support recommendations to avoid routine antibiotic treatment for patients with uncomplicated acute rhinosinusitis.[15, 20] All study participants met the recommended clinical criteria for acute rhinosinusitis[1] and are representative of patients for whom antibiotics might be prescribed. To our knowledge, this is the first trial of antibiotic treatment for acute rhinosinusitis to assess improvement in disease-specific QOL as the primary outcome, an outcome that is important to patients. The *SNOT-16* was developed using established psychometric methods including patient input and assesses functional limitations, physical problems and emotional consequences of rhinosinusitis and is valid and responsive to change in patients with acute and chronic sinusitis.[16, 18] In both study groups, disease-specific QOL and sinus symptoms improved over time, with no significant difference at 10 days for these outcomes or functional status, disease relapse or recurrence, satisfaction with care, or treatment side-effects. Symptoms more frequently identified as bothersome by study subjects including nasal symptoms and cough were likely to persist for at least 10 days.

Some studies have reported more rapid resolution of rhinosinusitis symptoms for adults treated with antibiotics[5, 11, 21] while others found no difference.[6, 12] In this study, retrospective assessment of change in sinus symptoms suggested that antibiotic treatment may provide more rapid resolution of symptoms for some patients by Day 7. However, when improvement was assessed as the difference in *SNOT-16* scores, the statistically significant benefit at Day 7 was too small to represent any clinically important change. Inaccurate recollection of the baseline condition may explain the larger effect size observed with retrospective rather than serial measures.[11, 22, 23]

Clinical criteria used to diagnose acute rhinosinusitis in this community-based clinical trial are likely more rigorous than those routinely used in practice,[1] yet they failed to identify those for whom 10 days of treatment with amoxicillin provided any significant clinical benefit. It is unlikely that this finding was due to an inadequate dose of amoxicillin as the prevalence of amoxicillin-resistant *S. pneumoniae* in our community at the time of the study was very low,[24] and there is no evidence that any other antibiotic is superior to amoxicillin.[9, 13] It is also unlikely that our findings are due to inadequate power. Our post hoc power calculation showed 89% power to detect a between group difference of at least 0.3 in the 3, 7 and 10-day change in *SNOT-16* scores, much smaller than the 0.5 MID representing a clinically significant effect.[18, 19, 25, 26] The triple-blind design, high treatment adherence and the high level of patient retention across both treatment groups strengthen the validity of study findings.

Limitations of this study should be noted. It is possible that not all patients included in the study sample had acute rhonosinusitis as, absent any accurate, acceptable objective tests to guide management, current guidelines recommend clinical criteria for diagnosis of bacterial infection.[1, 2, 15] Nevertheless, the study population is representative of patients for whom antibiotics are prescribed. The wording of the *SNOT-16* instrument may make it difficult to ascertain the exact timing of significant differences between the study groups since participants are asked to evaluate their symptoms over the past few day. However, as the time period of reference is the same for every interview, between group comparisons at the timepoint when the instrument was administered is valid. Concurrent use of symptomatic treatments although common, was similar in both groups and unlikely to bias study findings.

There is a now a considerable body of evidence from clinical trails conducted in the primary care setting that antibiotics provide little if any benefit for patients with clinically diagnosed acute rhinosinusitis.[11, 12, 21] Yet, antibiotic treatment for upper respiratory infections is often both expected by patients and prescribed by doctors.[14, 27] Indeed, patient's expectation that antibiotic treatment is needed to resolve sinus symptoms may explain their reluctance to participate in this randomized trial where antibiotic treatment was not assured, but we do not have data to confirm this. The NICE guidelines in the UK, and more recent guidelines in the U.S. suggest an alternative approach to management for patients for whom reassessment is possible that delays and may preclude antibiotic treatment: watchful waiting with symptomatic treatments and an explanation of the natural history of the disease.[15, 20] Delayed antibiotic prescriptions, a strategy more commonly used in Europe than the U.S.,[27] was effective in a study from the Netherlands.[28] Analgesics are recommended, but additional therapies to provide symptom relief and a feasible alternative to antibiotic treatment are needed. Intranasal steroids have not proved to be as widely effective as first hoped, but may reduce symptoms for some patients with mild disease.[12, 29, 30] Promising alternative treatments such nasal irrigation with the "neti-pot"[31] need further investigation.

In conclusion, evidence from this study suggests that treatment with amoxicillin for 10 days offers little clinical benefit for most patients with clinically diagnosed uncomplicated acute rhinosinusitis. It is important to note that patients with symptoms indicative of serious complications were excluded from this trial and likely need a different management strategy.

Acknowledgments

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Enrollment

Assessed for eligibility (n=244)

Excluded (n=78)
Not meeting inclusion criteria
(n=70: May have >1 exclusion
criteria)
- 6 allergic to amoxicillin
- 13 prior antibiotic treatment
- 4 prior sinus surgery
- 15 concurrent chronic illness
- 1 pregnant
- 13 symptoms mild or improving
- 20 symptom duration >28 days
- 5 symptom duration <7 days
- 25 no nasal discharge
- 16 no facial pain
Declined to participate (n=8)

Randomized (n=166)

Allocation

Allocated to and received
amoxicillin (n=85)

Allocated to and received placebo
(n=81)

Follow-up

81 were assessed at Day 3
80 were assessed at Day 7
81 were assessed at Day 10
82 were assessed at Day 28

11 Discontinued intervention
2 failed to improve
3 had worsening symptoms
4 discontinued as they were
improved
1 discontinued due to side-
effects
1 reason unknown

74 were assessed at Day 3
75 were assessed at Day 7
71 were assessed at Day 10
77 were assessed at Day 28

12 Discontinued intervention
6 failed to improve
4 had worsening symptoms
2 reason unknown

Analysis

81 were analyzed at Day 3 (4
excluded, missing data)
80 were analyzed at Day 7
81 were analyzed at Day 10
82 were analyzed at Day 28

74 were analyzed at Day 3 (7
excluded, missing data)
75 were analyzed at Day 7
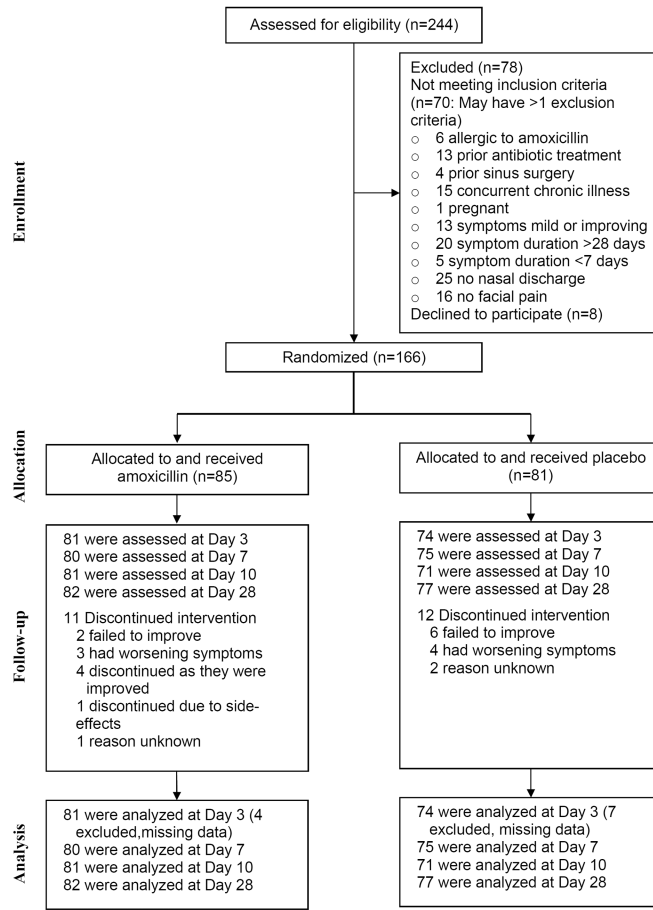71 were analyzed at Day 10
77 were analyzed at Day 28

Figure 1.
Recruitment of study participants

Table 1

Baseline Characteristics Of 166 Study Participants With Clinically Diagnosed Acute Sinusitis, By Treatment Group

Variable	Intervention Group (n=85)	Control Group (n=81)	*p*-Value
Sociodemographic characteristics			
Age in years, median (range)	32 (18–69)	31 (18–66)	0.22
Male gender, n (%)	31 (36%)	29 (36%)	0.93
Racial group, n (%)			
White	61 (72%)	69 (85%)	0.11
Black	17 (20%)	9 (11%)	
Other	7 (8%)	3 (4%)	
Hispanic, n (%)	4 (5%)	1 (1%)	0.37
Educational level, n (%)			
High school or less	50 (59%)	63 (78%)	0.0158
Bachelors degree	19 (22%)	13 (16%)	
Post graduate/professional degree	16 (19%)	5 (6%)	
Health insurance, n (%)			
Employment-based/Private	56 (66%)	56 (69%)	0.59
Government	9 (11%)	6 (7%)	
No insurance	5 (6%)	2 (2%)	
Private	15 (18%)	17 (21%)	
Lives alone, n (%)	15 (18%)	14 (17%)	0.95
Family income/year			
< $10,000	5 (6%)	4 (5%)	0.65
$10,000 – $24,999	11 (13%)	5 (6%)	
$25,000 – $49,999	13 (15%)	15 (19%)	
$50,000 – $99,999	23 (27%)	28 (35%)	
$100,000	20 (24%)	16 (20%)	
Declined to answer	13 (15%)	13 (16%)	
Number (%) of participants with children at home who are:			
< 18 years old	33 (39%)	24 (30%)	0.21
< 2 years old	3 (4%)	5 (6%)	0.49
In daycare	4 (5%)	6 (7%)	0.34
Medical History n (%)			
Usual health excellent or very good	41 (48%)	50 (62%)	0.08
History of sinus disease	62 (77%)	60 (82%)	0.39
Allergic rhinitis	27 (32%)	27 (33%)	0.83
Nasal polyps	3 (4%)	0	0.25
History of allergy	14 (16%)	14 (17%)	0.89
Positive test to mold, dust, pollen, or animal dander.	34 (49%)	35 (52%)	0.67
Asthma	9 (11%)	9 (11%)	0.91
COPD	0	0	

Variable	Intervention Group (n=85)	Control Group (n=81)	*p*-Value
Using nasal steroids daily	7 (8%)	4 (5%)	0.39
Smoker	11 (13%)	21 (26%)	0.0340
Sinus Symptoms			
SNOT-16 score [†]			
Mean, sd	1.71 (0.53)	1.70 (0.51)	0.88
Median, IQ range	1.75 (1.31 to 2.12)	1.62 (1.38 to 2.06)	
Symptom severity			
Moderate	41 (48%)	39 (48%)	0.93
Severe	37 (44%)	34 (42%)	
Very severe	7 (8%)	8 (10%)	
Days of symptoms			
Mean, sd	11.2 (5.7)	11.1 (5.8)	0.87
Median, IQ range	10.0 (7.0 to 14.0)	10.0 (7.0 to 14.0)	
Days missed from work before visit			
Mean, sd	1.1 (2.0)	1.7 (4.1)	0.23
Median, IQ range	0 (0 to 2.0)	0 (0 to 2.0)	
Days unable to do usual non-work activities before visit			
Mean, sd	3.2 (3.6)	3.3 (3.8)	0.88
Median, IQ range	2.0 (0 to 5.0)	2.0 (0 to 5.0)	
Used symptomatic treatment before visit, n (%)	82 (96%)	74(91%)	0.17
Flu shot this winter, n (%)	23 (27%)	26 (32%)	0.48

Abbreviations: IQ range, Interquartile (25% to 75%) range; sd, standard deviation

[†] The SNOT-16 score is the mean of the 16 sinusitis symptom (0=no symptoms, 3=symptoms are a large problem).

Table 2

Item scores for the *SNOT-16* over time by study group.

| | Symptom present (%) | | Mean SNOT-16 Score | | | | | | | |
| | Day 0 | Day 10 | Day 0 | | Day 3 | | Day 7 | | Day 10 | |
	N=166	N=152	Intv	Control	Intv	Control	Intv	Control	Intv	Control
Need to blow nose	93%	63%	1.89	2.12	1.52	1.62	1.03	1.39	0.74	0.86
Sneezing	77%	41%	1.20	1.10	0.79	0.74	0.51	0.47	0.46	0.48
Runny nose	87%	49%	1.64	1.86	1.15	1.22	0.80	1.17	0.60	0.65
Cough	89%	55%	1.87	1.73	1.52	1.45	0.90	1.21	0.70	0.70
Post-nasal discharge	92%	55%	2.05	1.85	1.49	1.49	1.15	1.16	0.70	0.75
Thick nasal discharge	93%	47%	1.91	1.95	1.31	1.32	0.88	1.05	0.57	0.66
Ear fullness	74%	31%	1.55	1.51	0.84	1.03	0.58	0.77	0.46	0.48
Headache	83%	39%	1.75	1.74	1.05	1.09	0.66	0.73	0.51	0.55
Facial pain/pressure	90%	31%	1.79	1.85	1.10	1.08	0.54	0.71	0.41	0.37
Wake up at night	82%	26%	1.73	1.63	0.94	0.92	0.54	0.63	0.41	0.24
Lack of a good night's sleep	84%	29%	1.89	1.69	1.00	1.01	0.56	0.73	0.42	0.30
Wake up tired	87%	39%	1.93	1.84	1.12	1.27	0.63	0.83	0.49	0.52
Fatigue	93%	37%	1.93	1.90	1.25	1.24	0.59	0.89	0.49	0.51
Reduced productivity	86%	23%	1.59	1.68	1.02	1.03	0.35	0.60	0.27	0.28
Reduced concentration	80%	24%	1.45	1.47	0.93	0.78	0.34	0.51	0.30	0.28
Frustrated/restless/irritable	72%	23%	1.27	1.31	0.86	0.89	0.40	0.55	0.22	0.30
SNOT-16 score			1.71	1.70	1.12	1.14	0.65	0.84	0.48	0.49

Intv=Intervention

Table 3

Treatment Use, Outcomes, and Adverse Effects by Treatment Group[*]

	Intervention Group (n=85)	Control Group (n=81)	*P*-Value
Treatment Use			
Treatment duration (days)			
Mean (sd)	6.89 (4.55)	6.47 (4.75)	0.56
Median (IQ range)	10 (0 to 10)	10 (0 to 10)	
Compliant with 10-day treatment dosing regimen (self-report) (n, %)	55/81 (68%)	51/71 (72%)	0.58
Treatment Outcomes			
Change in *SNOT-16*[‡] scores from Day-0 (mean, 95% CI)			
Day-3	0.59 (0.47 to 0.71)	0.54 (0.41 to 0.67)	0.69
Day-7	1.06 (0.93 to 1.20)	0.86 (0.71 to 1.02)	0.0247
Day-10	1.23 (1.08 to 1.37)	1.20 (1.07 to 1.32)	0.85
Self-reported significant improvement in symptoms since Day 0 (n, %)			
Day-3	37% (27% to 48%)	34% (23% to 45%)	0.67
Day-7	74% (64% to 83%)	56% (45% to 67%)	0.0205
Self-reported significant improvement in symptoms since Day 0 (n, %) (cont)			
Day-10	78% (69% to 87%)	80% (71% to 90%)	0.71
Days missed from work (mean, 95% CI)	0.55 (0.28 to 0.82)	0.55 (0.22 to 0.87)	0.99
Days unable to do usual non-work activities (mean, 95%CI)	1.15 (0.76 to 1.54)	1.67 (1.08 to 2.26)	0.14
Relapse rate (%, 95%CI)	9% (3% to 16%)	6% (1% to 11%)	0.57
Recurrence rate (%, 95%CI)	6% (1% to 11%)	2% (0 to 6%)	0.44
Satisfaction with treatment (%, 95%CI)	53% (42% to 64%)	41% (29% to 52%)	0.13
Treatment Adverse Effects			
Reported any side effects (%, 95%CI)	16% (8% to 24%)	14% (6% to 22%)	0.74
Responded "yes" to 1 specific symptom question (%, 95%CI)	48% (37% to 59%)	52% (39% to 62%)	0.75

Abbreviations: IQ range, Interquartile (25% to 75%) range; sd, standard deviation

[*] The reported P-value refers to the comparison among the 2 treatment groups. The denominator is given if it is other than the total number of patients in the treatment group.

[‡] The SNOT-16 score is the mean of the 16 sinusitis symptom (0=no symptoms, 3=symptoms are a large problem).

Table 4

Reported Concurrent Use of Symptomatic Treatment Medications by Treatment Group[*]

Symptomatic treatment	Intervention Group (n=85) (%, 95%CI)	Control Group (n=81) (%, 95%CI)	*p*-value	Days of use[†] (Median, IQ range)
Any concurrent ancillary drug use	94% (89% to 99%)	90% (84% to 97%)	0.34	
Types				
Pseudoephedrine Sustained Action	72% (62% to 81%)	73% (63% to 83%)	0.88	4 (2 to 6)
Mucinex OTC (guaifenesin).	69% (60% to 81%)	68% (58% to 78%)	0.83	4 (2 to 7)
Acetaminophen	60% (50% to 70%)	60% (50% to 71%)	0.95	4 (2 to 6)
Nasal saline spray	49% (39% to 60%)	53% (42% to 64%)	0.64	3 (2 to 6)
Dextromethorphan hydrobromide (10mg/5ml) with Guaifenesin	51% (40% to 61%)	49% (38% to 60%)	0.88	3 (2 to 5)

[*] The reported P-value refers to the comparison among the 2 treatment groups.

- Acetaminophen. 500mg every 6 hours for pain and/or fever

- Mucinex OTC (guaifenesin). 600mg po every 12 hours to thin secretions

- Dextromethorphan hydrobromide (10mg/5ml) with Guaifenesin (100mg/5ml). 10mls every 4 to 6 hours for cough.

- Pseudoephedrine Sustained Action.

[†] No differences were found for duration of use for each symptomatic treatment by study group.