

Impact of clinical practice guidelines: trends in antibiotic prescriptions for acute rhinosinusitis

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Introduction

As defined by the American Academy of Otolaryngology–Head and Neck Surgery (AAO-HNS), acute rhinosinusitis (ARS) is a clinical diagnosis defined by up to 4 weeks of purulent nasal drainage, nasal obstruction, and/or facial pain-pressure-fullness.¹ Sinusitis is the single diagnosis associated with the most antibiotic prescriptions in the United States.² The overprescription occurs despite recommendations to distinguish acute bacterial rhinosinusitis (ABRS) from viral or noninfectious ARS.^{1,3} Nevertheless, antibiotics are prescribed in 83% of ambulatory ARS visits.⁴

Clinical practice guidelines (CPGs) are statements informed by a systematic review of the evidence.⁵ Multiple organizations have published guidelines detailing ABRS management.^{1,3,6} In 2015, the AAO-HNS CPG recommended amoxicillin-clavulanate for ABRS in the presence of certain risk factors, a shift from a 2007 guideline recommending amoxicillin alone.¹

Assessing guideline adherence provides an opportunity for antibiotic stewardship. The study objective was to evaluate the impact of CPGs on antibiotic therapy in ARS in adult outpatients.

Methods

After institutional review board exemption, EPIC SLICER DICER software (Epic, Verona, WI) was used to query patients age ≥ 18 years presenting with an ambulatory encounter diagnosis of acute sinusitis (15805002, SNOMED-

CT) between January 1, 2014 and December 31, 2019. The setting was a single tertiary-care academic medical center. Demographics, medical history, encounter location, and new encounter-associated antibiotics were retrospectively reviewed. If no antibiotics were ordered, patients were placed in the no-antibiotics group.

The encounters were stratified into 6 cohorts for the years 2014 to 2019. For categorical variables, univariate analysis was performed using Pearson's chi-square tests, whereas linear regression compared age. Simple logistic regression compared antibiotic selection by year. Statistical significance was set at $p \leq 0.05$. Multivariate logistic regression was then performed on all ARS cases, with amoxicillin-clavulanate encounter association the binary outcome of interest. Variables selected included those significant on univariate analysis and patient risk factors that determine treatment with amoxicillin-clavulanate.¹ Age and year were set as numeric variables, whereas other variables were categorical.

To evaluate the overall trend in amoxicillin-clavulanate usage, the electronic medical record was queried for adults with an ambulatory encounter diagnosis of chronic rhinosinusitis (CRS) (40055000, SNOMED-CT) and acute pharyngitis (363746003, SNOMED-CT). A simple logistic regression with year as the predictor was performed between ARS, CRS, and acute pharyngitis, with amoxicillin-clavulanate the outcome of interest. Statistical analysis was performed using R Statistical Software (2017 Foundation for Statistical Computing, Vienna, Austria).

Results

A total of 5544 encounters representing 3841 patients were retrieved. Antibiotics were associated with 82.8% ($n = 4589$) of encounters. ARS encounters associated with amoxicillin-clavulanate increased from 19.7% in 2014 to 33.7% in 2019 ($p < 0.001$). Amoxicillin decreased from 19.7% to 11.0%. Doxycycline increased from 7.1% to 12.5%, azithromycin decreased from 23.4% to 16.8%, and no antibiotic treatment increased from 14.3% to 18.4% ($p < 0.001$).

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TABLE 1. Multivariate assessment of amoxicillin-clavulanate prescriptions for ARS

Variable	n	Proportion of sample	OR	CI	p value
Age (years)					
18-98	1637	100%	0.999	0.995–1.003	0.653
Year					
2014–2019	1637	100%	1.132	1.089–1.175	<0.001
Medical history					
Asthma or COPD	468	29%	0.916	0.805–1.041	0.179
Current smoker	298	18%	0.985	0.845–1.146	0.844
Diabetes	283	17%	1.058	0.898–1.244	0.499
Antibiotics 30 days earlier	228	14%	0.976	0.822–1.155	0.776
Heart disease	203	12%	0.892	0.741–1.071	0.225
Kidney disease	188	11%	1.001	0.825–1.211	0.989
Fever at presentation	31	2%	1.349	0.855–2.089	0.187
Encounter location					
Outpatient, primary care	1258	77%	Reference		
Emergency department	232	14%	1.326	1.105–1.589	0.002
Otolaryngology clinic	147	9%	0.719	0.587–0.875	0.001

ARS = acute rhinosinusitis; CI = confidence interval; COPD = chronic obstructive pulmonary disease; OR = odds ratio.

Multivariate analysis

Amoxicillin-clavulanate use increased by each year (odds ratio [OR], 1.132; 95% confidence interval [CI], 1.089–1.175; $p < 0.001$) after including age, medical history, and encounter location as covariates (Table 1).

Amoxicillin-clavulanate use by diagnosis

With year as the predictor, amoxicillin-clavulanate use increased slightly with pharyngitis (OR, 1.005; 95% CI, 1.0007–1.0087; $p = 0.0208$), but not with CRS (OR, 1.041; 95% CI, 0.980–1.087; $p = 0.062$). In contrast, amoxicillin-clavulanate increased the most with ARS (OR, 1.131; 95% CI, 1.090–1.174; $p < 0.001$) on univariate analysis. The lower limit of the 95% CI of the per-year increase for ARS (1.090) was higher than that of the upper limit of the 95% CI for pharyngitis (1.0087) (Fig. 1).

Discussion

CPGs bring the evidence of medical research into clinical practice, yet concordance is less clear. Although in this study we have examined only a single institution, the medical record system allowed for compilation of thousands of encounters.

The justification for amoxicillin as a first-line therapy for ABRS relates to its safety, efficacy, low cost, and narrow microbiologic spectrum.¹ The harms of amoxicillin-

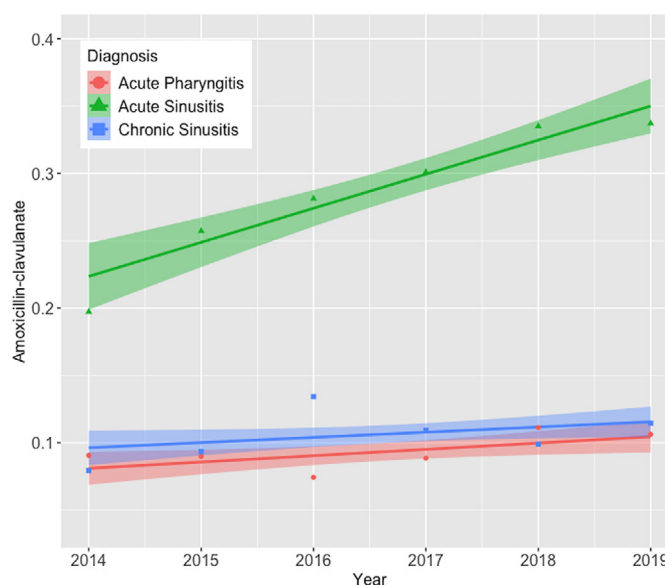


FIGURE 1. Rate of amoxicillin-clavulanate associated encounters by year and diagnosis. Shaded areas represent 95% confidence interval.

clavulanate over amoxicillin alone include cost and adverse effects including diarrhea and hypersensitivity.

There is weak evidence that some may benefit from high-dose amoxicillin-clavulanate over amoxicillin alone.³ Although the causative organisms are known, culture-directed antibiotic therapy is rarely performed for ABRS.

Therefore, in 2015 the AAO-HNS described risk factors for ABRS caused by an organism with likely resistance to amoxicillin.¹ The guideline is intentionally vague to allow for clinician discretion.¹ Before the update, the 2007 AAO-HNS guideline recommended amoxicillin alone as first-line treatment, coinciding with increased use.⁷

The data presented indicate a significant per-year rise of amoxicillin-clavulanate use in ARS, independent of the risk factors that would lead a clinician to prescribe amoxicillin-clavulanate. Therefore, it does not appear that the population has changed significantly to warrant the increased utilization. Furthermore, the rise appears isolated to ARS, higher than the change associated with acute pharyngitis and CRS. Taken together, the shift appears to be prescriber behavior, and this coincides with

the updated CPG on adult sinusitis in 2015 along with the 2012 the Infectious Diseases Society of America guidelines recommending amoxicillin-clavulanate over amoxicillin alone. Furthermore, AAO-HNS guidelines reach a wide audience and were reaffirmed through guideline publications by the American Academy of Family Physicians in 2016 and by *UpToDate* in 2017.^{8,9} Although this effect was likely not the intent, CPG ambiguity may reduce clinician adherence.¹⁰ Future, straightforward recommendations may curtail the rise in amoxicillin-clavulanate use.

There are several limitations to this study. ABRS complicates a fraction of viral sinusitis episodes, and many patients with acute sinusitis likely did not meet criteria for ABRS. Furthermore, these data represent new medication orders, not medications dispensed.

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