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Evaluation of Adherence to Guidelines for Treatment of Acute Pharyngitis and Sinusitis in US Outpatient Settings

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Abstract

The aim of this study was to look at the appropriateness of prescribing patterns for acute sinusitis and acute pharyngitis and compare with treatment guidelines issued by the Center for Disease Control and Prevention (CDC). 2015 National Ambulatory Medical Care Survey (NAMCS) data were used to determine antibiotic prescribing practices of providers treating the two conditions. Inclusion criteria were primary diagnosis of acute sinusitis and acute pharyngitis. Amoxicillin or penicillin, as recommended first-line treatment, were considered appropriate agents for the purposes of this study. Demographic variables, such as gender, age and race were examined along with prescribing variables, including insurance type, geographic area and physician type. In 46 (23.8%) cases, inappropriate agent was chosen. General doctors (14), pediatricians (12) and otolaryngologists (10) were prescribed most of inappropriate prescriptions. Inappropriate antibiotics were often prescribed for patients under 15 (11) and 45 to 64 (11) years of age (X_2=0.318), white patients (27) (X_2=0.411), those with private insurance (30), (X_2=0.726) and from South (13) and West (16) regions (X_2 =0.410). Chi-square test found no correlation amongst gender, age, race, insurance type, geographic area or physician type being predictors of appropriate or inappropriate prescribing patterns. Binary logistic regression did not show strong interactions amongst the variables in terms of prescribing pattern, and R2 was found to be significant. Adherence to CDC guidelines to treat acute pharyngitis and sinusitis can decrease the risk of bacteria developing resistance and translate into better clinical outcomes. Future research should continue identifying antibiotic prescribing trends for subsequent years.

Keywords: Prescribing patterns; Antibiotic resistance; Upper respiratory tract infections; Pharyngitis; Sinusitis; Adherence; Guidelines

Introduction

According to Center for Disease Control and Prevention (CDC), antibiotic resistance has risen in the last decade. Current antibiotics on the market are losing their effects at an alarming rate, while the development of new agents isn't keeping pace with it. More than a dozen agents were discovered between 1930 and 1970, but only 2 new classes have developed since then. [1] When looking at antibiotic prescribing trends from southeastern US physicians in private practice form the years 2000-2012 on primary or secondary diagnosis of an upper viral RTI that doesn't require antibiotic therapy per evidence-based practice guidelines [2], we see that antibiotic use has decreased form 56% to about 45% in 2007, and rose again to 62% in 2012. [3]

Acute RTIs are the condition for which Americans seek medical attention most frequently. Despite the release of several practice guidelines, providers continue prescribing antibiotics for influenza and other viral infections with no secondary diagnosis. High influenza-associated morbidity and mortality results in productivity loss and have a direct as well as indirect economic impact on the US healthcare. [4] An estimated 2 million people are infected with drug-resistant organisms annually in the United States, resulting in 23,000 deaths and over 20 billion dollars in excess costs.[5] According to US ambulatory care visit data from years 1997-2001, inappropriate antibiotic prescribing cost was estimated to be 92.9 million dollars over the 5-year period, and an average of 18.6 million dollars annually as a result of data analysis from 5 years. [6] When assessing actual empiric antibiotic prescribing and the cost of inappropriate prescribing in influenza patients enrolled in managed care plans in the US from US Impact National Benchmark Database for the years 1997-2009, inappropriate antibiotic prescribing for flu costs the US healthcare about 211 billion dollars per annum. [7]

Acute respiratory tract infections, including sinusitis and pharyngitis, are the most common diagnoses for which antibiotic is being prescribed. Sinusitis affects about 1 in 8 adults in the US, resulting in over 30 million annual diagnoses with direct annual managing cost of over 11 billion dollars, not including expenses from lost productivity, reduced job effectiveness and impaired quality of life. [8] This is a symptomatic inflammatory condition of the paranasal sinuses and nasal cavity, which usually affects patients 18 or older. The term rhinosinusitis almost always replaces sinusitis. Uncomplicated rhinosinusitis is defined as rhinosinusitis not extending outside the paranasal sinuses and nasal cavity at the time of diagnosis. Acute rhinosinusitis can be acute, lasting less than 4 weeks, and chronic, lasting longer than 12 weeks, with or without acute exacerbations, and recurrent, having 4 or more annual episodes. Distinguishing bacterial from viral rhinosinusitis is important as antibiotic therapy is inappropriate for the latter. [8]

Infectious Disease Society of America 2012 guidelines and Centers for Disease Control and Prevention 2018 guidelines on antibiotic use encourage watchful waiting for up to 10 days for acute uncomplicated rhinosinusitis when a reliable follow-up is available. If the condition is

not eliminated after watchful waiting, amoxicillin or amoxicillin with clavulanate is recommended as first line therapy. For penicillin-allergic patients, doxycycline or a respiratory fluoroquinolone, such as levofloxacin or moxifloxacin are recommended. Macrolides, such as azithromycin are not recommended due to high levels of Streptococcus pneumoniae resistance (40%).[9 – 11]American Academy of Otolaryngology-Head and Neck Surgery Foundation 2015 guidelines sate the importance of distinguishing between acute bacterial, viral and chronic rhinosinusitis. Antibiotics should be prescribed only in bacterial sinusitis cases with a duration of therapy being 5-10 days. They also stress the importance of watchful waiting. Their antibiotic recommendations are consistent with the sources mentioned above. As for viral rhinosinusitis, nasal saline irrigation, intranasal corticosteroids and analgesics are recommended for symptomatic relief. [8,11]

Acute pharyngitis is also very common illness caused by viruses or bacteria. When caused by Streptococcus pyogenes, also called group A streptococcal (GAS), acute pharyngitis is known as strep throat. GAS can occur in all ages, but commonly in children 5 through 15 years of age and is rare in children less than 3. Group A streptococcal pharyngitis is a significant cause of community-associated infections. According to the guidelines mentioned above, penicillin or amoxicillin is the antibiotic of choice to treat group A strep pharyngitis. Resistance to macrolides, such as azithromycin and clarithromycin is not common, but can happen in some communities. Penicillin-allergic patients are recommended to be treated with narrow-spectrum cephalosporins, such as cephalexin and cefadroxil, as well as clindamycin, azithromycin and clarithromycin. The duration of treatment is 10 days for all oral beta lactams, except azithromycin, which is required for 5 days. [11–13]

Despite universal agreement that antibiotic overprescribing is of major concern, this trend still continues. Acute respiratory tract infections, such as pharyngitis, sinusitis, tonsillitis, common cold, bronchitis and others, are the most common conditions making up to 40% of prescribing inappropriate. Sinusitis and pharyngitis are the diagnoses associated with greatest proportion of inappropriate and appropriate antibiotic prescribing. [14,15] Active Bacterial Core surveillance (ABCs) program, a part of the Centers for Disease Controls and Prevention Emerging Infections Program (EIP), was launched in 1995 to assess the extent of invasive bacterial infections of public health importance. This is a large, population-based, geographically diverse and active laboratory-based identification of epidemiologic information that allows for more in-depth monitoring of antimicrobial drug resistance, and the response to public health emergencies and other emerging infections.[16] Perhaps, active implementation of this program along with patient education can reduce inappropriate antibiotic prescribing and drug resistance. This is why it is also important to use narrow-spectrum agents, such as amoxicillin, cephalexin or trimethoprim-sulfamethoxazole when possible.[11] Between 2006 and 2008, pediatric patents were given broad-spectrum agents 50% of the time, of which macrolides were the most commonly prescribed. [17]

Antibiotic overprescribing affects not only gut microbiome and decreases the diversity of gut bacteria, resulting in C. difficile infections and $6.3 billion annually, but also leads to drug resistance. [18] The reason for inappropriate prescribing has been discussed in a systematic review. It found that patient demand, pharmaceutical company marketing activities, limited up-to-date information sources, as well as physician fear of losing patients are major reasons for unnecessary prescribing. [19] Patient demand and their satisfaction are the main drivers of unnecessary prescribing. Both patients and parents reported higher satisfaction with physicians explaining why antibiotics were not indicated, and such explanations didn't even take a lot of time. [20]

The aim of this study was to look at prescribing patterns for two types of upper respiratory tract infections: acute sinusitis and acute pharyngitis-conditions that usually don't require antibiotic treatment.

Literature Review

The use of antibiotics for viral-associated upper respiratory infections contributes to the spread of antibiotic resistance [9]. National Hospital Ambulatory Medical Care Survey data from 2001-2010 suggests there were 126 million ED visits in the US with a diagnosis of acute RTI, and antibiotics were prescribed in 61% of the cases. Inappropriate antibiotic prescribing decreased for patients younger than 5 years of age but remained unchanged for patients aged 20 to 64 years. Quinolone prescribing rates increased from 83 per 1,000 visits in 2001-2002 to 105 per 1,000 in 2009-2010. This suggests that despite significant reduction of antibiotic utilization for pediatric patients with acute respiratory tract infections (ARTI), its utilization still remains common in adult population [10].

Despite the National Action Plan for Combatting Antibiotic-Resistant Bacteria goal of reducing inappropriate outpatient antibiotic use by 50% by 2020, but the extent of in appropriate prescribing remains large. When combing diagnosis and ages, 30% of the prescriptions prescribed from 2010 to 2011 in ambulatory care settings throughout the US were inappropriate. This restates the importance of having an outpatient antibiotic stewardship [11].

URTIs can be caused by RSV, PIV, hMPV, Rhino/enterovirus, adenovirus, coronavirus, etc [12]. It is estimated that direct and indirect costs if influenza and other acute RTIs combined is over 100 billion dollars annually [4,13]. CDC says about 58% of the antibiotics prescribed in the doctors' offices in 2007-2008 were for 5 commonly diagnosed acute respiratory infections that don't require antibiotic treatment [14]. A study conducted in a number of European countries focusing on the factors affecting antibiotic prescribing found that patient demand represents a huge one. Patient pressure, such as explicit requests, self-diagnosis based on previous consultations along with lack of appropriate alternatives makes doctors more likely prescribe antibiotics [15]. According to NHAMCS 2007 and 2008 data, there were 2.2 million adult uncomplicated URI, such as bronchitis, acute RTI with no specified site, nasopharyngitis, laryngitis and influenza visits with no other concurrent diagnoses in EDs in the US. About 52% were given antibiotics and about one-third were macrolides. The study concluded that bronchitis, fever at presentation, older age, male gender, longer waiting time and metropolitan areas were associated with higher probability of prescribing antibiotics accounting for other confounding factors [16].

When looking at the population most likely to be prescribed antibiotic therapy, NAMCS and NHAMCS data from 1995-2006 on antibiotic prescription rates suggest that ARTI visit rates decreased by 17% for children younger than 5 in 2005-2006. OM visits for the same population decreased by 36% with a decrease in ARTI-associated antibiotic prescriptions. Despite stable ARTI visits for patients younger than 5, antibiotic prescription rates decreased by 18% [17]. However, in the years 2004 to 2010, about 27% of children used at least one antibiotic a year with 12.8% being broad-spectrum and 18.5 percent being narrow spectrum. Among those who were prescribed antibiotic

agents, more than two-thirds were for respiratory tract infections [18]. While prescription rates for penicillin, cephalosporin, sulfonamide/tetracycline for non-OM ARTI decreased by 41%, azithromycin prescribing rates were increased, becoming the most commonly prescribed macrolide for ARTI and OM. Overall, narrow spectrum antibiotic prescription was replaced by broad-spectrum agents [17].

2010 to 2011 NAMCS/NHAMCS data found that physicians used first-line recommended agents 52% of the time, although it would have been appropriate in 80% of the time, and that paediatric patients were more likely to receive appropriate first-line therapy compared to adults [19]. Macrolides, and azithromycin specifically, were the most common non-first line agents [19,20].

Methodology

The study was retrospective in nature and analysed NAMCS database for the year 2015 to evaluate appropriateness of antibiotic prescribing for 2 respiratory conditions: acute sinusitis and acute pharyngitis. We used NAMCS ICD-9 codes 461 for acute sinusitis and 462 for acute pharyngitis to extract the cases with primary diagnoses of the conditions above mentioned. After selecting the cases, we analysed the data on SPSS looking whether antibiotics were prescribed or in the cases prescribed, whether they were first-line and compliant with 2012 IDSA and 2018 CDC guidelines. The 2 conditions have very similar guidelines regarding first line-treatment. According to these guidelines, amoxicillin or amoxicillin/clavulanate for 10 days are recommended first-line therapy for both conditions along with watchful waiting with no antibiotic therapy. However, the second-line treatments were different. For the purposes of this study, amoxicillin or penicillin, as recommended first-line treatment, were considered appropriate agents.

The authors looked at the rates of prescribing specific agents, evaluated whether prescribing patterns were dependent on demographic variables, geography, provider type or the type of insurance. For the patients taking two antibiotic agents, we chose the more potent one to include in the analysis. We summarized our findings in the results section and determined the significance of each variable.

Results

The mean for the age was 30 years old. 56% of the sample were females, and 61.7% were white. Most of the sampled visits occurred in the South, followed by West. Most of our sample was under 15 years of age (35.8). The rest of age groups represented similar proportion in the sample. Majority of the patients had private insurance (62.2%) or were paid by Medicaid or other state-based programs (20.7%). Most of the patients were seen by pediatricians (37.3%) and general/family practitioners (28%). Only one patient was seen by a nurse practitioner, and 13 (6.7%) were seen by physician assistant (Table 1).

Demographics	Frequency	Percent
Gender		
Females	108	56
Male	85	44
Age		
Under 15	69	35.8
15-24	34	17.6
25-44	31	16.1
45-64	32	16.6
65-74	18	9.3
75 and older	9	4.7
Race		
White	119	61.7
African American	11	5.7
Asian	5	2.6
Other	58	30
Region		
Northwest	36	18.7
Midwest	48	24.9
South	60	31.1
West	49	25.4
Type of payment		
Private	120	62.2
Medicare	22	11.4
Medicaid, CHIP and another state-based program	40	20.7
Others		
Physician	11	5.7
General/Family	54	28
Internal	19	9.8
Pediatrics	72	37.3
Otolaryngology	30	15.5
Physician Assistant	13	6.7
Other Specialties	5	2.6

Table 1: The mean for the age was 30 years old.

In 147 (76.2%) of the cases, no antibiotic agent or first-line treatment agents were chosen, and so were considered as appropriate. However, in 46 (23.8%) cases, non-first line treatment or inappropriate agent was chosen.

General or family practitioners (14), paediatricians (12) and otolaryngologists (10) were responsible for the majority of inappropriate prescriptions. Paediatricians, however, were also responsible for most of appropriate prescriptions (60), followed by family doctors (40) and otolaryngologist (20). Another finding was that antibiotics deemed inappropriate were often prescribed for patients under 15 years of age and 45 to 64-year-olds (X_2 = 0.318). White patients received inappropriate prescriptions in most of the cases (27) (X_2 =0.411). Most inappropriate prescriptions were given to patients with private insurance (30), followed by Medicaid (8) and

Medicare (7) (X_2 =0.726). Most of inappropriate agents were prescribed in West (16) and South (13) (X_2 =0.410). Individually the demographic variables were not significantly related with inappropriate prescribing. Although pediatricians and otolaryngologists prescribed more appropriately as compared to other specialists (Table 2).

Prescribing Pattern Based on Demographic Variables	Inappropriate prescribing	Appropriate prescribing	Chi-Square
Gender			
Female	29	79	0.265
Male	17	68	
Age			
Under 15	11	58	
15-24	7	27	0.318
25-44	9	22	
45-64	11	21	
65-74	6	12	
75 and older	2	7	
Race			
White	27	92	
African American	3	8	0.411
Asian	0	5	
Other	16	42	
Insurance type			
Private	30	90	
Medicare	7	15	
Medicaid, CHIP and another state-based program	8	32	0.726
Others	1	10	
Region			
Northwest	8	28	
Midwest	9	39	0.41
South	13	47	
West	16	33	
Physician			
General/Family	14	40	
Internal	4	15	
Pediatrics	12	60	0.213
Otolaryngology	10	20	
Physician Assistant	6	7	

Other Specialties	0	5	

Table 2: Comparison of demographic variable with different conditions.

When examining whether the variables, such as gender, age, race, insurance type, geographic area or physician type were predictors of prescribing patterns being appropriate or inappropriate, we found no significant correlation among them (Table 3).

Single Variable vs prescribing pattern	Nagelkerke R2
Provider specialty	0.018
Age range	0.045
Type of payment	0.001
Region	0.013
Gender	0.010

Table 3: The Correlation with single variables.

When performing a binary logistic regression analysis, we found no statistical significance in provider specialty, all other demographic variables versus patterns of prescribing. However, we found a correlation between each individual independent variable and prescribing pattern. Provider specialty, patient age and type of insurance all together correlated with prescribing pattern. Provider specialty, race, and gender was another group of variables correlating to appropriate vs appropriate prescribing. Lastly, age, gender and insurance type were found to be significantly correlated with prescribing pattern of antibiotics as well (Table 4).

Combined Variables *vs* prescribing pattern	Nagelkerke R2
Provider specialty and type of payment	0.019
Provider specialty and age range	0.061
Provider specialty, type of payment and age	0.064
Provider specialty and race	0.025
Provider specialty and gender	0.030
Provider specialty, race and gender	0.037
Race and gender	0.017
Race and insurance type	0.008
Race, gender and insurance type	0.019
Age and gender	0.051
Age and insurance type	0.051
Age, gender and insurance type	0.058

Table 4: The Correlation with combined variables.

Discussion

Females and white patient population received more inappropriate prescriptions. South and West regions had more cases of inappropriate prescribing, which corresponds with data from other studies about South being one of the geographical areas with poor health and wellness. As for the insurance type, the vast majority of the patients were members of private insurance companies, despite the fact that most of the patient population were under 15 years of age and would qualify to be Medicaid members.

More patients under 15 received inappropriate prescriptions compared to other groups mostly because they accounted for most of the sample and because these conditions mainly affect children and young adolescents. Pediatricians who were the most common provider seen by the patients due to same reasons, were also one of the provider specialties prescribing the majority of inappropriate prescriptions.

The decision to prescribe an antibiotic depends on factors, such as patient's explicit demand for an antibiotic, which directly impacts the doctor's decision to prescribe. Antibiotic resistance and negative consequences associated with it are known to many patients. Thus, patient education can play a huge role in reducing antibiotic prescribing, and educational intervention can improve patent understanding of antibiotic resistance [21]. It is hard for the doctors to consult the patient in a few minutes and provide detailed explanations of why antibiotic is inappropriate for self-limiting conditions, especially for the sake of maintaining good doctor-patient relationship [15]. This is why pharmacists are an excellent source to educate adult patients about this topic.

Other factors playing role in inappropriate prescribing of antibiotic agents is diagnostic uncertainty, the level of communication and cooperation between physicians, pharmacists, and other specialists [15].

Assessment of the effects of behavioural interventions on inappropriate antibiotic prescribing among primary care practices has shown that measures, such accountable justification of entering a free-text explanation for prescribing certain antibiotic, along with sending clinicians emails comparing their antibiotic prescribing rates with those of their top peers resulted in lower rates of inappropriate antibiotic prescribing for acute respiratory tract infections [22,23]. Interventions enhancing a physician's contextual awareness can improve antibiotic prescribing pattern [24-26].

The study was retrospective in its nature and relied on the latest reported NAMCS data. It only included visits to physicians in ambulatory care settings for the year of 2015. The data doesn't include all other visits not recorded by providers leading to nonresponse bias [27]. We did not have any access to medical records of NAMCS data [28-31]. We were not able to exclude patients already receiving antibiotic and were not able to distinguish patients with newly diagnosed acute sinusitis from those with recurrent or persistent sinusitis. The data were confounded by providers' biases in their manner of diagnostic coding. For example, one provider may have used ICD-9 465, coded as "acute upper respiratory infection", for patients with infections whom the provider practices watchful waiting,

and may reserve ICD-9 461, coded as "acute sinusitis", for those being prescribed antibiotic. This non-consistency in coding may have resulted in a nondifferential boas over a big number of providers. Another limitation is that we relied on a physician's diagnosis of the condition, and for those being prescribed antibiotic for acute pharyngitis, we assumed to be bacterial rather than viral, and evaluated whether the agent being prescribed was first-line and consistent with current guidelines. We also assumed that the antibiotic agent was for the 2 specific respiratory conditions rather than for other diagnoses [32,33].

For the cases using second-line agent, we were not able to verify whether the selection was due to patient's allergy to first line agents or merely the prescribers' choice based on concomitant bacterial infections.

Antibiotics continue to be overused for patients with mild acute sinusitis and acute pharyngitis. Nonclinical factors can influence use of antibiotics for acute sinusitis and acute pharyngitis [34]. Even though our study did not any correlation among non-clinical factors and prescribing patterns, antibiotic overprescribing is still in issue of concern, and a judicious prescribing practice should be implemented to avoid antibacterial agent resistance and to reach better clinical outcomes.

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