ORIGINAL REPORT

Antibiotic prescribing for otitis media: how well does it match published guidelines?

Laura N. McEwen MPH, Rand Farjo MD and Betsy Foxman PhD*

University of Michigan, Ann Arbor, MI 48109, USA

SUMMARY

Otitis media (OM) accounts for \sim 31 million physician visits annually, and is typically treated with antibiotics. Amoxicillin is the recommended first-line treatment; appropriate antibiotic use slows the development of resistance. We analyzed insurance claims from families of employees working at a single company to determine if OM treatments (1) matched published standards; and (2) varied by patient characteristics, type of physician practice or geographic location. Persons diagnosed with OM between 1996 and 1999 were matched to prescription drug claims for those who filled an antibiotic prescription within 3 days of diagnosis. Physicians prescribed amoxicillin for only 31% of acute cases and 19% of recurrent cases. For acute infections in children \leq 2 years the prescribed duration often matched the standard of 10 days, but for persons >2 years the prescribed duration was often longer than the suggested duration of 5–7 days. For persons of all ages with recurrent infections, the prescribed duration was often shorter than suggested (10 days versus \geq 14 days). There were only modest variations by urban/rural location or provider type. Copyright © 2002 John Wiley & Sons, Ltd.

KEY WORDS — otitis media; antibiotics; treatment guidelines

INTRODUCTION

Otitis media (OM) is the single most common bacterial infection diagnosed in children younger than 15 years who visit physicians on an outpatient basis. More than 24 million cases are seen annually in the United States, and the number of cases has increased substantially during the last 2 decades. Sixty percent of all children have at least one office visit for acute otitis media by age 1 year, 75% have one visit by age 3 years, and 33% have three or more episodes by age 3 years. Among adults OM also occurs frequently; overall, OM accounts for ~31 million physician visits annually, and results in 20–25% of all orders for oral antibiotics prescribed yearly in the United States.

OM frequently recurs. Therefore, prophylatic duration of therapy is recommended for recurring OM, usually defined as four or more episodes in a 12-month period. Since OM is a frequent complaint, and most physicians vary in their approach to treating OM, even small variations in diagnosis and treatment can account for large differences in expense when aggregated over millions of cases. The medical and nonmedical costs of OM episodes are high: \$114 and \$131, respectively, for a simple episode and \$404 and \$327, respectively, for a complex relapsing episode.²

Over the last 10 years, primary OM pathogens, *Streptococcus pneumoniae* and *Haemophilus influenzae* and *Moraxella cataralis*, have become resistant to the majority of antibiotic drugs used in the treatment of OM. For example, the SENTRY Antimicrobial Surveillance Program (1997–1999) detected the following rates in the US for respiratory isolates of *Streptococcus pneumoniae*: 3.2% were amoxicillinresistant and 26.2% were cefaclor-resistant; *Haemophilus influenzae*: 31.5% were amoxicillin-resistant

E-mail: Bfoxman@umich.edu

Contract/grant sponsor: Michigan Antibiotic Resistance Reduction Coalition (MARRC).

^{*}Correspondence to: Betsy Foxman, 109 Observatory Street, 2010 SPH I, Ann Arbor, MI 48109-2029, USA.

and 14.6% were trimethoprim-sulfamethoxazole resistant; *Moraxella cataralis*: 0.1% were amoxicillin-clavulanate resistant and 96.8% were clindamycin-resistant.⁴

Because of the high incidence of OM, antibiotic therapy has a large potential to increases the risk of resistance development. In order to preserve their effectiveness, judicious use is required.1 Treatment guidelines are intended to reduce pressures for antibiotic resistance. OM is almost always diagnosed clinically; the symptoms are frequently caused by viruses rather than bacteria. Further, OM is often self-limiting. Because of the high incidence and self-limiting nature, antibiotic treatment for OM has a large potential to increase population pressure for the development of antibiotic resistance.⁵ Thus, watchful waiting is suggested in some countries; most published US guidelines recommend using amoxicillin as the first-line antibiotic. 6-16,18 The recommended duration for treatment with amoxicillin varies by patient characteristics.

We used insurance claims from persons treated in a preferred provider organization in order to describe the frequency and duration of amoxicillin prescribing to treat OM infections; and to determine if the likelihood of receiving a prescription for amoxicillin varied by patient characteristics, type of physician practice or geographic location.

METHODS

Study population

The subjects of this study were employees and dependents of a large Midwestern manufacturing organization with preferred provider organization (PPO) coverage who had (1) out-patient claims records for a physician visit from 1996–1999; (2) a billed diagnosis of OM; and (3) pharmacy claim for antimicrobial or anti-infective prescriptions filled within 3 days of the office visit for OM. Diagnosis of OM was indicated by the ICD-9 codes of 381.0, 381.3, 381.4, 381.00–381.06, 381.10 and 381.19. With the exception of 1999, all data were pulled as incurred in the specific calendar year with a 3 month paid run-out. The average age of the source PPO population was 38 years with a nearly equal gender distribution.

Our data included 13 511 claims with a diagnosis of OM and a pharmacy claim filled within 3 days. We then excluded 4881 claims (36%) where we could not determine whether or not it was an acute or recurrent infection, 50 claims for topical antimicrobial agents, two claims for antibiotics that must be administered intravenously, and 1312 claims (9%) that had

a missing value for either the provider group, drug name or provider zip code. This gave us a final study population of 7266 claims.

Definition of recurrent infections

Recurrent episodes were separated from nonrecurrent episodes since the recommended duration of therapy differs. We defined a recurrence as four or more physician visits for OM within a 12-month period where a pharmacy claim was filled within 3 days. ^{7,9,11,16–19} We used 1996 data to define recurring infections in 1997. Therefore, only cases from claims filed during 1997–1999 were included in the analysis. This ensured that the 'first' diagnosis recorded for the 1997 calendar year was the first infection after at least a 12-month period in which the subjects were free of infection.

Recommended OM treatment

Health care professionals, including the Center for Disease Control and Prevention, Institute for Clinical Systems Improvement and individual physicians suggest oral amoxicillin as the first-line treatment for OM. 6-16,18 For uncomplicated acute infections, a 5-7 day duration of amoxicillin is recommended. The Drug-resistant Streptococcus pneumoniae Therapeutic Working Group states, 'In addition to excellent pharmacokinetic and pharmacodynamic properties, amoxicillin has a long record of safety and clinical efficacy in treating OM, has a narrower spectrum of activity than many of the alternative agents and is inexpensive.' For children at high risk, i.e. age <2 years, the recommendation is for a 10 day amoxicillin prescription. Because dosage of the antibiotic varies widely with each individual patient's weight and metabolism, and that information was not included in these data, it will not be addressed in this study.

Recurrent OM infections are not specifically addressed in the reviewed literature, but most literature suggests that a prophylactic duration of therapy, i.e. 2–4 weeks of a low dose, is needed for effective treatment. For the purposes of this study, we assumed a duration of 14 days or longer to be appropriate.

Type of physician practice

We grouped physician practices noted on the claims data into five categories: family/general practice, internal medicine, pediatrics, ear–nose–throat (ENT) specialists, and other. Emergency room physicians were not included as a code on the claims data, so that group is not considered separately.

Geographic location (urban versus rural)

To determine if a provider was located in a rural or urban area, zip code data were correlated to 1990 census information. If the 1990 census classified more than 50% of the area within the zip code as urban, then it received an urban designation for this study, otherwise it was classified as rural.²⁰

Statistical analysis

We described the prescriptions filled for acute and recurrent OM by age, gender, provider type and geographic location using simple descriptive statistics. We estimated the association of these variables with the probability of amoxicillin being prescribed using odds ratios with 95% Cornfield or Exact confidence intervals. In order to simultaneously assess the impact of gender, recurrence, age, geographic location and provider type on prescribing amoxicillin we fit a logistic regression model. Analyses were conducted using SAS (SAS Institute, Cary, NC, version 8.2). We calculated odds ratios and their confidence intervals using EpiInfo 2000 (Center for Disease Control and Prevention, version 1.1.2).

RESULTS

The majority (96%) of the 7266 claims for OM in 1997–1999 were for acute infections (Table 1). Both

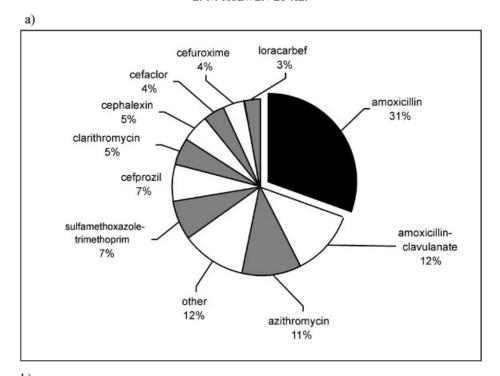
acute and recurrent infections occurred equally often among males and females (46% males and 54% females). Seventeen percent (17%) of the claims were for children ≤2 years. The majority (47%) of the claims were filled for patients who saw a family/general practitioner (Table 1). Otherwise there was a large variation in the physician's specialties. For each category of claim, over 85% of those cases lived in an urban area (Table 1).

Amoxicillin, the recommended first-line OM therapy, was prescribed for only 31% of persons with acute OM and 19% of those with recurring OM [Figures 1(a) and (b)]. The remainder were prescribed a wide variety of antibiotics. Eighty-two percent (82%) of acute OM in children \leq 2 years was prescribed the recommended 10 day duration of therapy of amoxicillin, and 18% of recurrent OM in children \leq 2 years was prescribed the recommended 14 or more days of therapy of amoxicillin (Table 2). For persons >2 years, 8% of acute OM was prescribed the recommended 5–7 day duration of therapy of amoxicillin, and 7% of recurrent OM was prescribed the recommended 14 or more days of therapy of amoxicillin (Table 2).

After fitting a logistic regression model including gender, recurrence, age, geographic location and provider type, gender was not associated with amoxicillin prescription. Persons with recurrence, younger ages and seen at Internal Medicine or ENT provider (using Family Practitioners as the reference group) were significantly less likely to be prescribed amoxicillin, while those living in urban areas were more likely (Table 3).

Table 1. Characteristics of persons with acute and recurrent otitis media filling antibiotic prescriptions within 3 days of diagnosis, and percent of claims for amoxicillin (7266 claims from persons or dependents working at a single company, receiving care from a preferred provider organization, 1997–1999)

Characteristic	Acute OM ($N = 6997$)		Recurrent $(N=269)$	
	N with characteristic	% claims for amoxicillin	N with characteristic	% claims for amoxicillin
Age				
≤2 years old	1107	39	146	16
>2 years old	5890	29	123	23
Gender				
Female	3758	30	134	18
Male	3239	32	135	20
Provider type				
Family practice	3367	31	75	23
Internal medicine	607	24	6	0
Pediatrics	1717	39	143	17
Ear, nose and throat	1107	21	43	21
Other	199	36	2	50
Geographic location				
Urban	6095	31	242	19
Rural	902	28	27	15



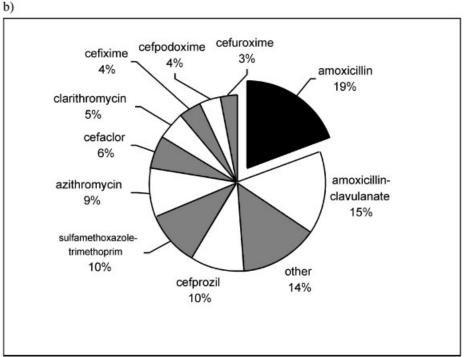


Figure 1. (a) Percent distribution of antibiotic therapies prescribed to treat acute otitis media and filled within 3 days of physician visit (6997 claims from persons or dependents, of all ages, of a single company, receiving care from a preferred provider organization, 1997–1999). (b) Percent distribution of antibiotic therapies prescribed to treat recurrent otitis media and filled within 3 days of physician visit (269 claims from persons or dependents, of all ages, of a single company, receiving care from a preferred provider organization, 1997–1999)

Table 2. Percent distribution of duration of therapy of amoxicillin prescribed for otitis media by recurrance and age group (7266 claims from persons or dependents of a single company, receiving care from a preferred provider organization, 1997–1999). The optimal durations (boldface) for children <2 years with acute infections is 10 days, and with recurrent infections 14+ days. The optimal durations (boldface) for persons >2 years with acute infections is 5–7 days, and with recurrent infections 14+ days

Duration of therapy prescribed (in days)	Children <2 years		Persons >2 years	
	Acute (N = 433) % claims for amoxicillin	Recurrent $(N=23)$ % claims for amoxicillin	Acute $(N = 1710)$ % claims for amoxicillin	Recurrent (N=28) % claims for amoxicillin
<u></u> ≼4	0	0	0.5	0.0
5	1.6	0.0	1.2	3.6
6	0.2	0.0	0.5	0.0
7	1.6	4.4	6.4	3.6
8	0.5	0.0	0.9	3.6
9	0.0	0.0	0.3	0.0
10	82.2	78.2	82.6	78.6
11	1.4	0.0	0.4	0.0
12	1.2	0.0	0.2	0.0
13	3.0	0.0	0.4	3.6
14	3.7	4.4	2.1	0.0
15	1.4	0.0	1.4	0.0
16+	3.2	13.1	3.2	7.1

Table 3. Logistic regression model predicting receiving and filling a prescription for amoxicillin among persons with acute and recurrent otitis media filling antibiotic prescriptions within 3 days of diagnosis (7266 claims from persons or dependents working at a single company, receiving care from a preferred provider organization, 1997–1999)

Variable	Odds ratio	(95% CI)	Pr > Chi-square
Female	0.96	(0.86–1.06)	0.413
Recurring OM	0.41	(0.30-0.56)	< 0.0001
Age of patient (in years)	0.98	(0.98-0.99)	< 0.0001
Urban versus rural residence	1.24	(1.05-1.45)	0.009
Specialty of treating physician			
Internal medicine	0.73	(0.60-0.90)	0.003
Pediatrics	0.93	(0.81-1.07)	0.290
Ear, nose and throat	0.54	(0.46-0.63)	< 0.0001
Other	1.12	(0.83-1.52)	0.457

DISCUSSION

Physician prescribing patterns have a major impact on the development of antibiotic resistance. Unlike diseases where lengthy treatment leads to development of individual resistance, e.g. tuberculosis, common OM therapies are more likely to lead to the development of resistance on a population level. We sought to determine if physicians were prescribing amoxicillin, the recommended first-line antibiotics for treatment of OM. ^{6–16,18} In general, most physicians serving the study population did not do so.

Our finding is consistent with prescribing for OM in a pediatric Medicaid population.²¹ Amoxicillin was most frequently prescribed for a new OM episode, but cephalosporins were prescribed to at least one child at an index visit by 55% of the physicians.²¹ Further, more expensive antibiotics were not associated with a better outcome. Our finding is also consistent with a NAMCS review of antibiotic prescribing from 1980–1992, among children under 15 years of age diagnosed with OM. That study observed an increasing trend for prescribing amoxicillin and cephalosporins and no trend for prescribing trimethoprim-sulfmethaxazole or erythromycins.²²

Physicians take into account patient history in making a determination of what antibiotic to prescribe, for which we had no information, such as (1) drug allergies, (2) drug intolerance, (3) poor compliance because of taste or dosing schedule, (4) suspected resistant pathogens or (5) prior treatment failure. However, only 1–10% of the US population is allergic

to penicillin or other β -lactams.²³ Further, even among children attending day care, at highest risk of both otitis media and antibiotic resistance, amoxicillin resistance among Haemophilus influenzae and Streptococcus pneumoniae does not exceed one-third.² Thus, it seems unlikely that more than half of all OM patients have some other factor that would preclude amoxicillin use. Study participants were all members of a single PPO that has minimal prescription co-pays, maximizing the possibility that a prescription is filled. Some may have been treated by free samples or information or not given an antibiotic at all. We have no information on this group. Since the physicians in our sample do not exclusively see PPO patients we can assume that the same physician would use the same decision-making algorithm for treating all of his/her other patients. This would make our study most likely generalizable to physicians in the Midwest.

Because we linked insurance claims for OM to antibiotic prescriptions we cannot be certain that the antibiotic was in fact prescribed for the OM. To minimize this potential we included only persons filling prescriptions within 3 days of the office visit, and excluded all cases where the prescribed antibiotic was one that could not be given in an out-patient setting or that is used topically. Bacterial OM is difficult to accurately diagnose²⁵ and is difficult to distinguish from OM caused by viral agents. Short of requiring culture—which is not a standard practice—we cannot be certain of the diagnosis. We based our diagnosis on billing codes and have made no verification of the diagnosis. Thus, some misclassification in diagnosis could have occurred both via the physician's misdiagnosis and because OM was the stated billing code for convenience or other reasons.

Patient compliance is a major issue that can lead to antibiotic resistance. Duration of therapy prescribed does not necessarily reflect how long the therapy was used. However, as our focus was on what the physician prescribed rather than on compliance, this is not a limitation of our study. We acknowledge that studies on the impact of emerging resistance attributed to the use of different classes of antimicrobials and different durations are less clear, and, therefore, the 'ideal' prescription is controversial.

OM pathogens are major causes of other, more invasive, diseases such as meningitis. ²⁶ Because of this, preserving their antibiotic sensitivities is a priority. In our study population antibiotics used to treat OM were fairly uniformly prescribed. We did not see strong differences by speciality or geographic location suggesting that while prescribing habits

may not be following first-line suggested therapy, they are at least stable enough to determine if a change in habit will alter the levels of drug resistance in a community.

In conclusion, while amoxicillin was the most commonly prescribed antibiotic for OM, it represents a much lower percentage than might be anticipated based on published guidelines. This might be remedied by educating both physicians and patients on the proper use of antibiotics for OM. As resistance patterns may change rapidly, local surveillance for resistance to common bacterial pathogens would facilitate appropriate treatment and provide needed information for keeping guidelines current.

KEY POINTS

- Physicians prescribe the recommended first-line treatment for OM (amoxicillin) for only 31% of acute cases and 19% of recurrent cases.
- For acute infections in children ≤2 years the prescribed duration often matched the standard of 10 days, but for persons >2 years the prescribed duration was often longer than the recommended optimal duration of 5-7 days.
- For persons with recurrent infections, the prescribed duration was often too short (10 days versus ≥14 days).
- There were only modest variations by urban/rural location or provider type.

ACKNOWLEDGEMENTS

The authors would like to thank Dr Patricia Salber and the Michigan Antibiotic Resistance Reduction Coalition (MARRC) for assistance in making this study possible.

REFERENCES

- Levy SB. The challenge of antibiotic resistance. Sci Am 1998; 278: 46–53.
- Leibovitz E, Dagan R. Otitis media therapy and drug resistance—part 1: management principles. *Infect Med* 2001; 18: 212–216.
- Roche Laboratories, Inc. Acute otitis media. Total Res Utilization Conspectus 1999; 1: 1–56.
- Hoban DJ, Doern GV, Fluit AC, Roussel-Delvallez M, Jones RN. Worldwide prevalence of antimicrobial resistance in Streptococcus pneumoniae, Haemophilus influenzae, and Moraxella catarrhalis in the SENTRY antimicrobial surveillance program, 1997–1999. Clin Infect Dis 2001; 32(Suppl. 2): S81–S93.

- Froom J, Culpepper L, Jacobs M, DeMelker RA, Green LA, van Buchem L, Grob P, Heeren T. Antimicrobials for acute otits media? A review from the international primary care network. *BMJ* 1997; 315: 98–102.
- Dowell SF, Butler JC, Giebink GS. Acute otitis media: management and surveillance in an era of pneumococcal resistance—a report from Drug-resistance Streptococcus pneumoniae Therapeutic Working Group. Pediatr Infect Dis J 1999; 18: 1–9.
- Health care guideline: diagnosis and treatment of otitis media in children. Available from Institute for Clinical Systems Improvement via the Internet. www.icsi.org [4 January 2000].
- 8. Klein JO. Otitis media. Clin Infect Dis 1994; 19: 823-833.
- Bluestone CD. Current therapy for otitis media and criteria for evaluation of new antimicrobial agents. *Clin Infect Dis* 1992; 14(Suppl. 2): S197–S203.
- Rosenfeld JA, Clarity G. Otitis media and otitis externa. In Family Medicine: Principles and Practice, Taylor RB (ed.). Springer: New York, NY, 1998; 616–624.
- Feign RD, Chevy JD (eds). Textbook of Ped Inf Dis. Saunders: Philadelphia, PA, 1998; 1; 206–208.
- Hay WH, Hayward AR, Levin MJ, Sondheimer JM (eds). Current Pediatric Diagnosis and Treatment. Appleton & Lange: Stamford, CT, 1999; 14; 398–401.
- Bell N. Implementation of clinical practice guidelines into practice: future strategies. Available from the Alberta Clinical Practice Guidelines Program via the Internet. www.amda.ab. ca/cpg/catalogue/documents/newsletters/september_1999 [12 December 2000].
- Antibiotic management of acute otitis media. Available from Infectious Disease and Immunization Committee, Canadian Paediatric Society via the Internet. www.cps.ca/english/statements/ID/id97-03 [12 December 2000].
- Pediatric Otitis Media. Available from the General Medical Officer Manual: Clinical Section: Pediatrics via the Internet. www.vnh.org/GMO/ClinicalSection/72PedsOtitisMedia [12 December 2000].

- 16. Evidence based clinical practice guideline for medical management of otitis media in children 2 months to 6 years of age. Available from the National Guideline Clearinghouse via the Internet. www.guideline.gov [25 August 2000].
- American Academy of Pediatrics (eds). Red Book. American Academy of Pediatrics: Elk Grove Village, IL; 2000; 647–648.
- Careful Antibiotic Use: Otitis Media. Available from the Center for Disease Control and Prevention via the Internet. www.cdc.gov [12 December 2000].
- Dowell SF, Marcy SM, Phillips WR, Gerber MA, Schwartz B. Otitis media—principles of judicious use of antimicrobial agents. *Pediatrics* 1998; 1: 165–171.
- Master area geographic glossary of terms and MARBLE/Geocorr. Available from the Office of Social and Economic Data Analysis via the Internet. www.census.gov/plue/MARBLE/ Geocorr [10 May 2001].
- Berman S, Byrns PJ, Bondy J, Smith PJ, Lezotte D. Otitis media—related antibiotic prescribing patterns, outcomes, and expenditures in a pediatric Medicaid population. *Pediatrics* 1997; 100: 585–592.
- McCaig LF, Hughes JM. Trends in antimicrobial drug prescribing among office-based physicians in the United States. *JAMA* 1995; 273: 214–219.
- James CW, Gurk-Turner C. Cross-reactivity of betalactam antibiotics. Baylor Univ Med Ctr Proc 2001; 14: 106–107.
- St. Sauver J, Marrs CF, Foxman B, Gilsdorf JR. Genetic diversity of *S. pneumoniae* and *H. influenzae* isolates in children attending Michigan day care centers. *Emerg Infect Dis* 2000; 6: 622–630.
- Finkelstein JA, Metlay JP, Davis RL, Rifas-Shiman SL, Dowell SF, Platt R. Antimicrobial use in defined populations of infants and young children. Arch Ped Adol Med 2000; 154: 395–400.
- Beneson AS. Control of Communicable Disease Manual (16th edn). American Public Health Association: Washington, DC, 1995; 301–310.