

Pharmacotherapy for Non-Cystic Fibrosis Bronchiectasis



Results From an NTM Info & Research Patient Survey and the Bronchiectasis and NTM Research Registry

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BACKGROUND: Non-cystic fibrosis bronchiectasis (“bronchiectasis”) is a chronic inflammatory lung disease often associated with nontuberculous mycobacteria (NTM) infection. Very little data exist to guide bronchiectasis management decisions. We sought to describe patterns of inhaled corticosteroid (ICS) and antibiotic therapy in the United States.

METHODS: We invited 2,000 patients through NTM Info & Research (NTMir) to complete an anonymous electronic survey. We separately queried baseline clinical and laboratory data from the US Bronchiectasis and NTM Research Registry (BRR).

RESULTS: Among 511 NTMir survey responders with bronchiectasis, whose median age was 67 years, 85 (17%) reported asthma and 99 (19%) reported COPD. History of ICS use was reported by 282 (55%), 171 (61%) of whom were treated 1 year or longer, and 150 (53%) were currently taking ICSs. Fewer reported ever taking azithromycin for non-NTM bronchiectasis (203 responders [40%]) or inhaled tobramycin (78 responders [15%]). The median age of 1,912 BRR patients was 69 years; 528 (28%) had asthma and 360 (19%) had COPD. Among 740 patients (42%) without NTM, 314 were taking ICSs at baseline. Among patients without NTM who were taking ICSs, only 178 (57%) had a concurrent diagnosis of COPD or asthma that could explain ICS use. Fewer were taking suppressive macrolides (96 patients [13%]), and of the 70 patients (10%) taking inhaled suppressive antibiotics, 48 (68%) had chronic *Pseudomonas aeruginosa* infection.

CONCLUSIONS: ICS use was common in two national samples of patients with bronchiectasis, with relatively few patients taking suppressive antibiotic therapies. Further research is needed to clarify the safety and effectiveness of these therapies in patients with bronchiectasis.

CHEST 2017; 152(6):1120-1127

KEY WORDS: bronchiectasis; inhaled antibiotics; inhaled corticosteroids; macrolides

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ABBREVIATIONS: aOR = adjusted OR; BRR = Bronchiectasis and NTM Research Registry; ICS = inhaled corticosteroid; LABA = long-acting beta agonists; NTM = nontuberculous mycobacteria; NTMir = NTM Info & Research

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Non-cystic fibrosis bronchiectasis (“bronchiectasis”) is a chronic slowly progressive inflammatory pulmonary disease that is characterized by airway inflammation and excess sputum production. The prevalence of this orphan disease increased 8.7% per year between 2000 and 2007, affecting 100,000 to 200,000 patients in the US Medicare population.¹ Associated infections (eg, nontuberculous mycobacteria [NTM], *Pseudomonas aeruginosa*, *Haemophilus influenzae*) worsen inflammation and damage to lungs.² The goals of treatment are to improve symptoms, reduce airway inflammation, limit further bronchiectasis progression, and prevent infections. There are no US guidelines for the selection of therapies. The British Thoracic Society published guidelines in 2010 highlighting a lack of evidence for safety and effectiveness of chronic pharmacotherapy.³ Drugs with anti-inflammatory

properties, for example, corticosteroids, have been studied in COPD and other lung diseases, but their safety and effectiveness in bronchiectasis remains unproven.⁴ Macrolides (eg, erythromycin, azithromycin) have both antimicrobial and immunomodulatory properties.⁵ Historically, inhaled antibiotics are prescribed primarily to control *P aeruginosa* in patients with frequent exacerbations.³ What is unknown is how many patients with bronchiectasis are taking inhaled corticosteroids (ICSs), macrolide monotherapy, or inhaled antibiotics in the United States or elsewhere. To provide background for a proposed comparative effectiveness and safety study in US patients, we sought to describe the current and past use of ICSs, oral macrolides, and inhaled antibiotics in patients with bronchiectasis and explore patient characteristics associated with each therapy.

Methods

Our first data source was an anonymous electronic 20-question SurveyMonkey survey (e-Appendix 1) developed by several study authors. The survey link was e-mailed by NTM Info & Research (NTMir), a nonprofit NTM patient advocacy organization, to 2,000

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A portion of this work was presented orally at the American Thoracic Society International Conference, May 15-20, 2015, Denver, CO.

FUNDING/SUPPORT: The Bronchiectasis and NTM Research Registry was funded by the COPD Foundation and, in part, by the Intramural Research Program of the National Heart, Lung, and Blood Institute of the National Institutes of Health (to K. N. O.).

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DOI: <http://dx.doi.org/10.1016/j.chest.2017.04.167>

patients in December 2013. Responses were collected through January 2014. Patients self-identified as having bronchiectasis. Patients reported whether they had ever taken or were currently taking inhaled tobramycin, oral azithromycin for NTM treatment, oral azithromycin for other infections or exacerbation prevention, oral steroids, or ICSs with or without long-acting beta agonists (LABA). We also asked patients to estimate the cumulative lifetime duration of treatment with azithromycin or ICSs as < 4 weeks, 4 weeks to < 1 year, or 1 year or longer. The survey was anonymous and was conducted as “preparatory to research.”

The second data source was the national Bronchiectasis and NTM Research Registry (BRR), managed by the COPD Foundation.⁶ The BRR is actively enrolling from 13 sites and includes detailed clinical and microbiological data for > 2,000 patients with bronchiectasis or patients who meet the American Thoracic Society/Infectious Diseases Society of America 2007 case criteria for NTM disease.⁷ For this analysis, any patient with a history of or current NTM isolation was classified as having NTM infection (“NTM”), regardless of whether or not they met American Thoracic Society/Infectious Diseases Society of America disease criteria. The BRR collects data from chart review, including patient demographics, current pharmacotherapy, COPD or asthma diagnosis, history of *P. aeruginosa* or *Staphylococcus aureus* isolation, exacerbation in prior 2 years, or hospitalized exacerbation in prior 2 years. BRR data captured current “suppressive” macrolide and inhaled antibiotic therapy, indicating use other than for acute exacerbations. Oral steroids were marked as “continuous” or “intermittent” and combined into a single variable to describe current use. The BRR was approved by each site’s institutional review board.

First, we described the characteristics of the survey and registry populations. For both data sets, we reported the proportion of patients taking each class of therapy, stratified by NTM in BRR patients. Next, in patients without NTM in the BRR, we separately compared “current users” of (1) inhaled corticosteroids, (2) macrolides, and (3) inhaled antibiotics to “nonusers” of each group. We performed statistical comparisons using the χ^2 test for categorical variables and the Student *t* test for continuous variables. Finally, in BRR patients without NTM, we conducted separate multivariate logistic regression analysis to evaluate factors associated with current use of each class of drug (compared with nonuse of each). Multivariate models included patient

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