Bronchiectasis, part 2: Management

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Systemic antibiotics are the mainstay of the management of acute exacerbations of bronchiectasis. Antibiotic selection should include coverage for *Streptococcus pneumoniae* and *Haemophilus influenzae*; particular attention also should be paid to the presence of *Staphylococcus aureus* and *Pseudomonas* species. There is some evidence that long-term low-dose macrolide therapy can reduce the incidence of acute exacerbations and decrease sputum production. There also may be a role for the use of inhaled antibiotics in the treatment of bronchiectasis. Airway clearance strategies, such as chest percussion and postural drainage, are clearly useful in patients with cystic fibrosis and may be useful in managing bronchiectasis in other patients. Surgical resection can be considered if a patient has localized disease that is refractory to medical management or if he or she is unwilling to undergo long-term medical therapy. (J Respir Dis. 2008;29(1):20-25)

**ABSTRACT:** Systemic antibiotics are the mainstay of the management of acute exacerbations of bronchiectasis. Antibiotic selection should include coverage for *Streptococcus pneumoniae* and *Haemophilus influenzae*; particular attention also should be paid to the presence of *Staphylococcus aureus* and *Pseudomonas* species. There is some evidence that long-term low-dose macrolide therapy can reduce the incidence of acute exacerbations and decrease sputum production. There also may be a role for the use of inhaled antibiotics in the treatment of bronchiectasis. Airway clearance strategies, such as chest percussion and postural drainage, are clearly useful in patients with cystic fibrosis and may be useful in managing bronchiectasis in other patients. Surgical resection can be considered if a patient has localized disease that is refractory to medical management or if he or she is unwilling to undergo long-term medical therapy. (J Respir Dis. 2008;29(1):20-25)

Bronchiectasis is an increasingly common disease that can cause debilitating pulmonary symptoms and have a significant adverse impact on quality of life. The specific factors contributing to this impact include dyspnea, a reduced forced expiratory volume in 1 second (FEV$_1$), increased sputum production, and *Pseudomonas aeruginosa* infection. In the December 2007 issue of *The Journal of Respiratory Diseases*, we discussed the causes and clinical presentation of bronchiectasis. In this article, we review the components of treatment, including antibiotics, airway clearance, antiinflammatories, and surgery.

**TREATMENT**

The treatment of bronchiectasis primarily targets the complications of irreversibly damaged and dilated airways, with a focus on improving mucociliary clearance and treating and preventing infections. In some cases, therapy is aimed at the underlying cause; in others, it is largely supportive.

**Antibiotics**

Systemic antibiotics are the mainstay of management of acute exacerbations of bronchiectasis. There is very little evidence in the current medical literature to guide antibiotic choices. Antibiotic selection should include coverage for *Streptococcus pneumoniae* and *Haemophilus influenzae*. Particular attention also should be paid to the presence of *Staphylococcus aureus* and *Pseudomonas* species.

We generally recommend narrowing the spectrum of coverage whenever possible; however, if the patient is known to have a *Pseudomonas* infection, some clinicians favor treatment with 2 antipseudomonal antibiotics to reduce the risk of antibiotic resistance. The oral fluoroquinolones with pseudomonal coverage are often part of the regimen. The appropriate route of administration of antibiotics is frequently debated. One small study demonstrated equal efficacy of oral levofloxacin and intravenous ceftazidime, which suggests that a
course of outpatient fluoroquinolone therapy can be tried first if a patient does not otherwise require hospitalization.
The duration of antibiotic therapy in patients with bronchiectasis is not well studied. Most clinicians generally recommend a prolonged course of antibiotic therapy, often longer than 3 weeks. A systematic review of the literature suggests that outcomes may be better with a 4-week course than with shorter courses. A strategy of using long-term suppressive therapy with rotating antibiotics has historically been used in select patients, but this has not been well studied. Although we and others use this treatment method in a small number of select patients, the risk of adverse effects and antibiotic resistance, even with antibiotic rotation, precludes recommending this mode of therapy routinely. Long-term low-dose macrolide therapy may have a role in the treatment of bronchiectasis beyond the macrolide's antimicrobial effects. Studies of patients with diffuse panbronchiolitis, another disorder characterized by progressive decline in lung function, copious sputum production, and colonization with *P. aeruginosa*, indicate that long-term macrolide therapy can stabilize disease progression and reduce the incidence of acute flares. This effect may be the result of immunoregulatory actions of macrolides, such as inhibition of neutrophil chemotaxis. In a small study of the use of erythromycin suppressive therapy in patients with bronchiectasis, those who received erythromycin had an improved FEV₁ and 24-hour sputum production after 8 weeks compared with those who received placebo. More recent data suggest that the administration of low-dose azithromycin for 6 months results in a decreased incidence of exacerbations and a decreased sputum volume, without any serious adverse effects; one pediatric study similarly showed improvement in sputum volume with long-term use of clarithromycin. Importantly, long-term macrolide therapy should not be used in patients with known or suspected nontuberculous mycobacterial infection.

The use of nebulized antibiotics may have a role in management of bronchiectasis, both acutely and chronically. Nebulized antibiotics deliver high concentrations of medication to the lungs with little or no systemic effects. Suppressive therapy with nebulized antibiotics, especially aminoglycosides, is safe and reduces the number of respiratory flares and hospitalizations in patients with cystic fibrosis (CF). Use of this type of therapy in non-CF bronchiectasis is still under investigation, but preliminary results show similar trends. A short course of inhaled gentamicin has been shown to significantly improve nocturnal oxygenation and walking distance in adults, and it results in limited systemic penetration in children.

Treatment with inhaled tobramycin reduces the burden of *P. aeruginosa* in the sputum of patients with bronchiectasis. One trial showed that in an acute flare, the addition of inhaled tobramycin to ciprofloxacin resulted in a decreased microbiological burden, but it did not result in clinical improvement, perhaps because of increased cough, wheezing, and dyspnea caused by the inhaled medication. However, in a study of patients with severe bronchiectasis with ongoing symptoms, there was a significant improvement in pulmonary symptom severity score and quality of life following treatment with inhaled tobramycin. Another agent gaining popularity is inhaled colistheme, which has been shown to be of some benefit in patients with CF and multidrug-resistant pseudomonal infection. It is our practice to combine inhaled aminoglycosides with a systemic antipseudomonal antibiotic in patients who have ongoing symptoms of respiratory infection with *Pseudomonas* pathogens confirmed by sputum analysis. In the future, dry powder metered-dose inhalers may make the administration of inhaled antibiotics less cumbersome, less costly, and less time-consuming than with the current nebulized techniques.

**Airway clearance**

An important component of the long-term treatment of bronchiectasis is the management of secretions. Enhancing airway clearance is effective and beneficial in CF. Although commonly used in non-CF bronchiectasis, airway clearance strategies have not been well studied. Various options for mechanical enhancement are available, including chest percussion, postural drainage, cough-assist devices, vibration vests, and flutter valves. Although these studies are mostly limited to patients with CF, these treatments are generally well tolerated and may be helpful in managing bronchiectasis in patients who do not have CF. Systemic hydration may also help reduce the viscosity of the secretions, allowing improved clearance. Pharmacological means of improving bronchopulmonary hygiene have been controversial. The use of
recombinant human DNase (rhDNase) as a mucolytic agent in patients with CF has been shown to decrease sputum viscosity\textsuperscript{18} and reduce the frequency of respiratory infections.\textsuperscript{19} However, a randomized controlled trial of rhDNase in patients with idiopathic bronchiectasis demonstrated no improvement and even potential harm.\textsuperscript{20} Some data suggest a benefit from the use of nebulized hypertonic saline in CF patients\textsuperscript{21,22} and non-CF patients with bronchiectasis.\textsuperscript{23} Although the mechanism is not entirely understood, it is thought that hypertonic saline may thin secretions by drawing more fluid into the alveolar spaces. By the same mechanism, inhaled dry powder mannitol is believed to improve tracheobronchial clearance and sputum rheology. It has been studied in small groups of patients, and preliminary data suggest that its use is associated with improvement in subjective assessment of respiratory status and quality of life.\textsuperscript{24} A larger study of dry powder mannitol in non-CF bronchiectasis has been recently completed.

**Bronchodilators**

Although many patients with bronchiectasis demonstrate obstruction on pulmonary function testing, most do not show significant objective improvement after bronchodilator administration. In addition, the routine use of bronchodilators as part of long-term management has not been well studied in this population. Therefore, we generally do not recommend them for routine use unless there is evidence of bronchial hyperreactivity and a bronchodilator response on pulmonary function testing.

**Anti-inflammatory agents**

Since chronic inflammation is part of the pathophysiology of bronchiectasis, there has been some interest in the use of corticosteroids as part of the long-term management. Although systemic corticosteroids have not been studied in this clinical setting, it is generally accepted that their adverse effects outweigh their potential benefits, and they are not typically used in patients who have bronchiectasis, except for those with allergic bronchopulmonary aspergillosis. Inhaled corticosteroids, however, may have some beneficial effects in patients with bronchiectasis. In one clinical trial, patients with bronchiectasis were given inhaled corticosteroids or placebo and were monitored for 1 year.\textsuperscript{25} The corticosteroid group had a significant improvement in sputum volume, and patients with known pseudomonal infection also had a decreased frequency of exacerbations. There was no improvement in spirometric measurements.\textsuperscript{25} Another study of the use of inhaled corticosteroids in patients with bronchiectasis showed an improvement in the overall subjective evaluation of health-related quality of life, including days without dyspnea, cough, and sputum production, despite no change in frequency of exacerbations or spirometry.\textsuperscript{26}

**Surgery**

Since the first surgery for bronchiectasis was performed in 1901, a variety of techniques have been used for the treatment of this disease, including segmentectomy, lobectomy, and pneumonectomy. Surgical resection can be considered if a patient has localized disease that is refractory to medical management or if he or she is unwilling to undergo long-term medical therapy. At present, the mortality rate associated with surgery in appropriate patients is less than 2%.\textsuperscript{27} A common indication for surgery is massive hemoptysis that is secondary to bronchiectasis and unresponsive to other measures. Another surgical option for patients with severe bronchiectasis is lung transplantation. Although this is a well-established treatment for end-stage CF, there is a paucity of data in the non-CF population. In patients with CF, bilateral lung transplantation is the norm, given the enhanced risk of infection in the native lung in an immunocompromised host. One descriptive study indicates that survival and lung function are similar in the CF and non-CF populations; however, a good outcome is possible in select non-CF patients who undergo single-lung transplantation, particularly those with minimal sputum production, asymmetrical disease, or a history of thoracic surgery.\textsuperscript{28}

**PROGNOSIS**

Before the antibiotic era, the mortality rate associated with bronchiectasis was estimated to be more
than 25%; however, with the advent of antibiotics, survival has undoubtedly improved. In one study of patients with bronchiectasis who were admitted to an ICU with respiratory failure, the ICU mortality rate was 19%, and 1-year mortality rate was 40%. The risk factors for increased mortality were age greater than 65 years and the need for long-term home oxygen therapy. An observational study of 101 patients with bronchiectasis who were admitted to an ICU with respiratory failure, the ICU mortality rate was 19%, and 1-year mortality rate was 40%. Eleven patients (11%) died, and 6 of the deaths were due to progressive respiratory failure. Further investigation is warranted to better understand the natural history of this heterogeneous group of patients.

As we improve our understanding of the pathophysiology and natural history of bronchiectasis, we can develop better tools for the diagnosis and treatment of this potentially devastating disease. Our hope is that with ongoing endeavors, we may continue to improve our care of patients with bronchiectasis.

References: REFERENCES


Links:


[3] [http://www.patientcareonline.com/authors/gregory-tino-md](http://www.patientcareonline.com/authors/gregory-tino-md)