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Management of Bronchiectasis for the Community Respirologist

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Introduction

Bronchiectasis is a common chronic lung disease that remains undertreated and under serviced, likely in part due to its heterogenous nature and diversity in clinical presentation. Bronchiectasis is characterized by the permanent dilation of the airways visible on radiographic imaging, characterized by decreased function of the mucociliary transport mechanism. This dysfunction leads to recurrent infections secondary to increased bacterial invasion and mucus accumulation. It is defined as a syndrome marked by chronic cough, sputum production, and repeated lower respiratory tract infections.[1,2] Bronchiectasis is an important area of respiratory medicine given its increasing prevalence. It affects an estimated 566 individuals per 100,000, making it the third most common chronic airway disease, after chronic obstructive pulmonary disease and asthma.[3] While it can develop in childhood, particularly during the pre-antibiotic era,[4] it can occur at any age, with prevalence increasing with advancing age. This increase in prevalence may be secondary to greater awareness amongst healthcare professionals.

Bronchiectasis is a treatable but rarely curable condition. Identifying and treating the underlying cause is recommended. Bronchiectasis can be caused by many underlying etiologies, including infectious, inflammatory, genetic, or immunological causes. Despite this wide range of etiologies, idiopathic bronchiectasis accounts for 32%–66% of all causes.[5] Treatment goals include managing any underlying systemic conditions, preventing lung infections, and implementing chest physiotherapy. Surgery may be recommended for localized bronchiectasis with refractory infections and hemoptysis. This article will review the chronic management of bronchiectasis, with a focus on chest physiotherapy techniques and the use of inhaled antibiotics.

Chest physiotherapy helps expectorate sputum and is the mainstay of therapy. It should be recommended for all patients irrespective of the etiology of bronchiectasis. It includes techniques such as postural drainage, deep breathing exercises, percussion, and the use of positive expiratory pressure devices. Postural drainage relies on gravity to drain mucous from the uppermost lung lobes, while deep breathing followed by forced expiratory manoeuvres, known as the "active cycle of breathing" technique, allows secretions in the dilated bronchi to gravitate toward larger airways for clearance. Percussion of the chest wall, performed manually with cupped hands or using oscillating devices,

aids in loosening and dislodging sputum. These techniques should be performed for a minimum of 5 to 10 minutes twice daily. When efficiently performed, chest physiotherapy can reduce cough and sputum production, thereby reducing the risk of pulmonary infections.

Pseudomonas aeruginosa (Pa) is the most common pathogen isolated in the sputum of patients with bronchiectasis airways.[6,7] Chronic infection, defined as isolation of Pa in sputum cultures on at least two or more occasions, spaced at least 3 months apart over a one-year period,[8] is difficult to eradicate even with the use of broad spectrum intravenous (IV) antibiotics.[9] Once established, chronic Pa forms biofilms, which are thin layers of bacteria within an extracellular polymeric matrix. They form colonized surfaces in airways, which are associated with greater airway inflammation and an increased risk of exacerbations that potentially require hospitalization, and increased mortality compared to non-pseudomonas.[6,7] This infectious process perpetuates the bronchiectasis cycle. Biofilms inhibit the clearance of bacteria by the host immune system and reduce antibiotic penetration, favouring microbial persistence.[10] As a result, international guidelines recommend long-term antibiotic treatment for patients with chronic Pa infection and frequent exacerbations.[1]

Inhaled antibiotics targeting Pa, such as inhaled colistimethate sodium or inhaled tobramycin, deliver high concentrations of medications directly to the airways, the primary site of infection, providing greater efficacy while minimizing side effects and reducing the risk of antibiotic resistance.[11] A study by Haworth et al., known as PROMIS-I, was a double blind, randomized, placebo-controlled trial evaluating inhaled colistimethate sodium in adults with non-cystic fibrosis bronchiectasis.[12] Conducted across multiple hospitals in 12 countries (Australia, Belgium, Germany, Greece, Israel, Italy, Netherlands, New Zealand, Portugal, Spain, Switzerland, and the UK), the study enrolled patients who had at least two pulmonary exacerbations requiring oral antibiotics or one intravenous antibiotic in the preceding year.[12] Inhaled colistimethate sodium showed a 21% reduction in exacerbations and a 52% reduction in severe exacerbations compared to placebo.[12] Statistically significant improvements were also observed in the frequency of exacerbations, the study's primary outcome, along with a significant reduction in severe exacerbations and a significant improvement in quality of life, measured using the St. Georges Respiratory Questionnaire.[12] These findings have contributed to international guideline recommendations supporting the use of inhaled antibiotics to patients with bronchiectasis, chronic Pa infection, and frequent exacerbations.[1]

Colistimethate sodium, also known as colistin, is supplied as a powder in a vial and can be stored at room temperature. For reconstitution, add 2 mL of sterile water to the vial and 1 mL (equivalent to 75 mg) is drawn for inhalation. To increase volume for nebulization, an additional 2 mL of saline can be added to nebule along with the above mixture. The unused portion should be refrigerated for use in the second dose of the day. The standard dosing regimen is 75 mg inhaled twice daily.

Inhaled tobramycin can also be used to treat or prevent Pa infections, with the main goal of improving or maintaining lung function. As an aminoglycoside antibiotic, tobramycin binds irreversibly to the bacterial 30S ribosomal subunit, thereby inhibiting the initiation of protein synthesis, resulting in bacterial cell death.[13] The 2015 study by Orriols et al. demonstrated that following a 3-month course of inhaled tobramycin, clearance or eradication of Pa was sustained for 12 months in 54.5% of patients.[14] While definitions of eradication vary across studies, it is generally defined as the absence of Pa detection in sputum at a specified time point during the study.[15] Eradicating Pa was associated with a significant reduction in exacerbation frequency, fewer hospitalizations, and shorter hospitalization durations.[15] A literature review of inhaled tobramycin revealed that in five of seven studies, spirometry outcomes remained stable, showing neither significant improvement nor decline.[15] The overall results suggest that eradication, though sometimes transient, was achieved in 22%–55% of patients treated with inhaled tobramycin.[15] Even a simple reduction in Pa density, without complete eradication, can lead to clinical improvement.[13]

Inhaled tobramycin is generally well tolerated by most patients. However, side effects can include hoarseness, increased cough and sputum production, dyspnea, wheezing, pharyngitis, and fatigue.[16] The use of salbutamol may mitigate these side effects. In the study by Loebinger et al. a decline in renal function was observed in 8% of patients, along with reports of mild, transient hearing loss, tinnitus, and occasional cases of

moderate labyrinthitis.[17] For adults with non-cystic fibrosis bronchiectasis, the recommended inhaled dose of tobramycin is 80 mg inhaled twice daily via nebulizer. This can be nebulized along with 0.5 to 1 mL (2.5 mg to 5 mg) of undiluted salbutamol. Prior to initiating therapy, a spirometry test can be carried out before a test dose of inhaled tobramycin. A post spirometry test can be used to evaluate for tolerance and to detect any significant decreases in force expiratory volume in one second (FEV_1) or forced vital capacity (FVC) prior to prescribing inhaled antibiotics. Patients may continue to use inhaled tobramycin as long as it is tolerated and chronic Pa persists in sputum cultures. Once therapy has been initiated, periodic monitoring of sputum cultures and side effects with audiometry tests, blood work (creatinine), and evaluation of symptoms should be implemented.

Conclusion

Improving tracheobronchial clearance should be considered as the mainstay of therapy in bronchiectasis. In cases of chronic Pa, inhaled antibiotics have been incorporated into guidelines for both chronic suppression[18,19] and eradication of Pa.[1] These therapies have become central to improving quality of life for these patients. Facilitating research into the various subtypes of bronchiectasis may help determine the optimal care for these patients and provide a multidisciplinary approach to treatment.

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