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Airway and Increasing Airflow to the Lungs to Breathe Easier

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Abstract

Most physicians recommend mucus clearance as the mainstay of therapy in bronchiectasis. Consensus guidelines recommend that all patients with bronchiectasis receive some instruction in physiotherapy, even if for very mild patients, they only perform physiotherapy during exacerbations. There are a wide range of techniques and, in the author's opinion, the chosen technique should be tailored to the patient preference, taking into account that simple and quicker techniques will encourage patient adherence. The evidence for physiotherapy interventions in bronchiectasis is weak. Murray performed a randomised crossover trial in patient's not currently practicing chest clearance, and compared use of the acapella oscillatory positive expiratory pressure device for few months with no chest physiotherapy for few months.

Keywords: COPD; Lung function; Resource; Glucocorticoids; Cross-study interpretation; Reported outcomes

Introduction

At completion of the study, cough improved as measure by the Leicester Cough Questionnaire, with increases in spontaneous 24-h sputum volume and exercise capacity. The effect on quality of life was excellent and well above the clinically important difference of few points. The poor state of evidence in this area, however, is illustrated by the associated Cochrane review. This review found the body of evidence for physiotherapy in bronchiectasis constituted five trials with few participants. They concluded that airway clearance techniques were safe and that the limited data suggested improvements in sputum expectoration, reduced hyperinflation and improved health-related quality of life in stable patients [1]. One of the most effective forms of chest physiotherapy, in the authors' opinion, is exercise. Pulmonary rehabilitation is recommended for patients with bronchiectasis and although studies to date have been small, they have clearly demonstrated the benefits of rehabilitation are at least as great in bronchiectasis as in COPD. In a retrospective study, Ong studied patients with bronchiectasis, demonstrating a mean improvement in 6-min walk distance which was sustained. A subsequent pilot randomised controlled trial showed improvements in LCQ and SGRQ sustained after treatment. In a recent randomised controlled trial, an 8-week supervised exercise training schedule that includes airway-clearance techniques was compared with standard care. 43 patients were randomised to exercise training and standard care. At the end of treatment, patients in the exercise group had an increase in their incremental shuttle walk distance, improved dyspnoea and a reduced time to the next exacerbation and total number of exacerbations over months [2]. This study clearly demonstrates a benefit of exercise to patients with bronchiectasis, but most of the benefits were not sustained to 6 or 12 months suggesting this kind of intervention needs to be continuous to achieve long-term benefits. A variety of agents, such as nebulised hypertonic saline solution, mannitol and mucolytic agents, have been developed to help patients to clear airway secretions.

Discussion

Hypertonic saline may improve forced expiratory volume when used in combination with chest physiotherapy but a recent trial could not clearly establish it was superior to saline. A large trial of hypertonic saline is needed. Recombinant DNase is effective in CF but has been shown to be potentially harmful in a randomised controlled trial in bronchiectasis. It is therefore not advised for use in this group of patients, and highlights the different pathophysiology in bronchiectasis, compared with CF-associated bronchiectasis. The mucolytics, for example carbocisteine and N-acetylcysteine, are widely used as evidenced by the BTS audit, but there are no controlled trials to demonstrate if this practice is beneficial. Inhaled dry powder mannitol has been the subject of two recent phase randomised controlled trials [3]. The first study included few patients on mannitol twice daily or placebo twice daily for few weeks followed by open label extension. The study found an increased sputum weight in favour of mannitol with no significant difference in quality of life using the SGRQ. It was not clear if the differences in sputum weight were due to higher antibiotic use in the placebo group. Therefore a further trial was conducted focussing on exacerbations. This study randomised patients to inhaled mannitol or control mannitol for weeks. The population was tightly defined, requiring two exacerbations in the previous year. The primary outcome was the rate of pulmonary exacerbations over 1 year. The study failed to meet its primary end-point, with a rate ratio for exacerbations. Among secondary endpoints there was an increase in time to next exacerbation and a small improvement in SGRQ with mannitol treatment. Therefore, despite two large trials the role of mannitol in bronchiectasis treatment remains unclear. Macrolides have been widely used for bronchiectasis for many years but there was a lack of evidence until three game-changing studies, which now provide robust evidence to support their use [4]. All three trials used the frequency of exacerbations as the primary outcome, but used different macrolides, different doses and had slightly difference inclusion and exclusion criteria. The Bronchiectasis and Long Term Azithromycin Treatment trial used azithromycin daily and required patients in addition to a computed tomography diagnosis of bronchiectasis to have had three exacerbations in the previous year and a positive sputum culture for bacteria. Improvements were also observed in the SGRQ, with small changes in

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FEV1 which are unlikely to be of clinical significance. The main concern of macrolide therapy is a marked increase in macrolide resistance in oropharyngeal and other bacteria. The BAT trial showed macrolide resistance in the treatment group compared on placebo. A recent secondary analysis of the BLESS trial has suggested that erythromycin therapy was associated with the emergence, using molecular techniques. No patients became colonised with P.aeruginosa by culture and so the clinical importance of this finding is not clear. Azithromycin was associated with increased gastrointestinal side effects in the BAT trial, although erythromycin appeared to be better tolerated in BLESS, There have been other concerns regarding macrolides including an increased incidence of cardiovascular events although no cardiovascular complications were observed in these small RCT's [5]. Additional concerns over macrolides include the possibility of inducing resistance in NTM, hepatotoxicity and decreased hearing. The authors recommend warning patients regarding hearing loss and to perform electrocardiogram and sputum culture for NTM prior to commencement of macrolide therapy. Macrolides should be avoided in patients with a prolonged QT interval. How macrolides achieve their beneficial effects is unclear. Alongside their antimicrobial effects, macrolides have anti-inflammatory effects including inhibition of inflammatory cell migration, cytokine secretion and possible attenuation of the production of reactive oxygen species. Other mechanisms that have been proposed to explain macrolide benefit include reduction of biofilms surrounding virulent Gram-negative organisms such as P. aeruginosa and promotion of gastric emptying that may reduce potential for acid reflux. Several meta-analyses of the evidence for macrolides in bronchiectasis have recently been reported. For example, demonstrated a pooled effect of macrolides that equated to a reduction of exacerbation per patient per year, an overall reduction in SGRQ compared with placebo, small but significant improvements in dyspnoea and sputum volume and a clinically insignificant improvement in FEV [6]. Macrolides are therefore effective, but the key question is in which patients they should now be used. BTS guidelines recommend consideration of long-term oral antibiotics for patients with exacerbations per year or those chronically colonised with P. aeruginosa. These guidelines were written before the publication of the three recent trials and, given that the EMBRACE trial showed benefit in patients with one or more exacerbations per year, these recommendations may change. In clinical practice, macrolides are most frequently used in patients with three or more exacerbations per year, in patients with P. aeruginosa and also in patients with less frequent exacerbations who continue to have significant impairment of quality of life despite standard treatment. Further research needs to explore the best dosage and schedule for macrolide therapy with a clear aim of optimising benefits and reducing adverse events. There is a lack of evidence for alternative long-term oral antibiotics, and controlled trials are needed [7]. Agents used frequently in clinic practice include β-lactams and tetracyclines. The role of inhaled corticosteroids in bronchiectasis is less clear. They have an established role in asthma and COPD, and are used in patients with bronchiectasis complicating these two disorders. Some studies have shown that regular high-dose inhaled steroids reduce 24-h sputum volume, reduce inflammatory markers in sputum and improve quality of life. However, they have not shown any significant improvement in lung function, or exacerbation frequency. In a small randomised controlled trial in bronchiectasis patients with chronic airflow limitation, the combination of inhaled formoterol plus budesonide was compared with inhaled budesonide alone. The combination group experienced improved dyspnoea, coughing and health-related quality of life without alteration in sputum pathogens or an increase in adverse effects. As pointed out in a recent Cochrane review, the absence of high-quality evidence means that decisions to use or discontinue combined ICS and long-acting β-adrenoceptor agonist in people with bronchiectasis may need to take account of the presence or absence of co-existing airway hyper-responsiveness and consideration of potential adverse events associated with combined ICS-LABA. These adverse effects include the recently noted increase in pneumonia risk in COPD patients [8]. Whether this same risk applies to patients with bronchiectasis is unclear and requires further study. Holme also reported in a study of patients with bronchiectasis that nearly inhaled steroid users with bronchiectasis had evidence of adrenal suppression and that this correlated with poorer health status. There is no role for oral corticosteroids in bronchiectasis out with the treatment of ABPA or for acute exacerbations of bronchiectasis that are accompanied by wheezing suggestive of concomitant asthma. Inhaled antibiotics have theoretical advantages over oral therapies by delivering higher concentrations of drug to the airway, they may reduce systemic absorption and side effects and perhaps reduce collateral damage, for example through resistance development in gastrointestinal microorganisms. Commonly used agents in clinical practice are primarily those used to target P. aeruginosa, such as tobramycin, gentamicin and colomycin. Inhaled antibiotics reduce airway bacterial load and recent data clearly demonstrate that reductions in bacterial load are associated with reduced airway inflammation, providing theoretical rationale for clinical use of inhaled antibiotics [9]. Until recently, however, there have been little supporting data with clinically important end-points, and most have been extrapolated from the CF population in which inhaled antibiotics suppress bacterial load, reduce exacerbations and hospital admissions. Currently, however, no inhaled antibiotic agents are approved for use in bronchiectasis by any regulatory agency either in Europe or North America. Trial evidence has been mixed. Several open label studies in the late 1980's, testing nebulised β-lactams, demonstrated reduced sputum purulence, sputum volume and improvements in inflammatory markers. In an early phase II double-blind placebo-controlled study, nebulised tobramycin significantly reduced the primary outcome of P. aeruginosa bacterial load but was poorly tolerated by some patients. Increased cough, dyspnoea,chest pain and wheeze were reported in the tobramycin group. This phase II study has therefore never been followed by a larger phase III trial. Subsequently a single-blind randomised controlled trial of nebulised gentamicin for 12 months reported significant benefits. The study enrolled patients with chronic bacterial colonisation, two exacerbations in previous year, and excluded smokers and patients receiving other long term antibiotics. After few months there was a significant reduction in bacterial density in the gentamicin group. Four out of few patients colonised with P.aeruginosa at baseline were negative at follow-up, and patients colonised with other pathogens were negative by quantitative sputum culture at the end of treatment. In addition, quality of life, as measured by the SGRQ and LCQ, was improved and exacerbations were reduced [10]. Tolerance was generally better with this dose of gentamicin compared with the previous tobramycin study, although bronchospasm requiring bronchodilator treatment, only two patients were withdrawn for this reason. No nephrotoxicity or ototoxicity was reported.

Conclusion

Evidence for an anti-inflammatory effect of combination therapy came from bronchial biopsies, whereas sputum analysis revealed little evidence of an anti-inflammatory effect.

Acknowledgement

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Conflict of Interest

None

References

1. Pisarski K (2019) The global burden of disease of zoonotic parasitic diseases: top 5 contenders for priority consideration. Trop Med Infect Dis EU 4:1-44.
2. Kahn LH (2006) Confronting zoonoses, linking human and veterinary medicine. Emerg Infect Dis US 12:556-561.
3. Slifko TR, Smith HV, Rose JB (2000) Emerging parasite zoonosis associated with water and food. Int J Parasitol EU 30:1379-1393.
4. Bidaisee S, Macpherson CNL (2014) Zoonoses and one health: a review of the literature. J Parasitol 2014:1-8.
5. Cooper GS, Parks CG (2004) Occupational and environmental exposures as risk factors for systemic lupus erythematosus. Curr Rheumatol Rep EU 6:367-374.
6. Parks CG, Santos ASE, Barbhaiya M, Costenbader KH (2017) Understanding the role of environmental factors in the development of systemic lupus erythematosus. Best Pract Res Clin Rheumatol EU 31:306-320.
7. M Barbhaiya, KH Costenbader (2016) Environmental exposures and the development of systemic lupus erythematosus. Curr Opin Rheumatol US 28:497-505.
8. Gergianaki I, Bortoluzzi A, Bertsias G (2018) Update on the epidemiology, risk factors, and disease outcomes of systemic lupus erythematosus. Best Pract Res Clin Rheumatol EU 32:188-205.
9. Cunningham AA, Daszak P, Wood JLN (2017) One Health, emerging infectious diseases and wildlife: two decades of progress? Phil Trans UK 372:1-8.
10. Sue LJ (2004) Zoonotic poxvirus infections in humans. Curr Opin Infect Dis MN 17:81-90.