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# A brief review of non-acute medical management of bronchiectasis

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## Introduction

Pertussis is re-emerging in patients aged between 1-6 months old.[1] Another study reported high incidence of bronchiectasis in New Zealand children, nearly twice the rate for cystic fibrosis. Incidence varied substantially between ethnicities. Most cases of bronchiectasis developed in early childhood and had delayed diagnosis.[2] The prevalence of bronchiectasis may increase in the near future. The current review was undertaken to look at the medical management of non-cystic fibrosis bronchiectasis.

## Medical management of bronchiectasis

### Inhaled mannitol (dry powder inhalation, ~400 mg in adult)

Adult study showed that coughing and inspiratory manoeuvres alone increased clearance only in the central region of the lung. Mannitol doubled the clearance of mucus compared with control in both the central and intermediate regions.[3] A significant reduction in retained mucus at 24 hours was observed but there was no effect on spirometry.[4]

### Prolonged antibiotics (=>4 weeks)

A placebo controlled study in children showed that roxithromycin (4 mg/kg BD) for 12 weeks showed a significant improvement in sputum purulence and leucocyte scores, as well as a significant reduction in airways responsiveness to methacholine compared to baseline.[5] Koh et al concluded that the reduction in airway responsiveness can be due to both the anti-inflammatory and antimicrobial effect. However, follow-up data were not available for the duration of the beneficial effect. The anti-inflammatory properties of the macrolides are multifactorial. Macrolides inhibit the production of many proinflammatory cytokines, such as interleukin (IL)-1, IL-6, IL-8, and tumor necrosis factor-alpha by suppressing the transcription factor nuclear factor-kappaB or activator protein-1. Inhibition of cytokine production was seen in bronchoalveolar lavage fluid, which contained less IL-8 and fewer neutrophils after treatment with macrolides. Macrolides also inhibit formation of leukotriene B4, which attracts neutrophils, and inhibit the release of superoxide anion by neutrophils that may be present in the airway.[6]

Adult study showed nebulized tobramycin for 4 weeks led to a significant reductions in *Pseudomonas aeruginos*a density compared to placebo after 4 weeks of treatment and eradication of the organism in 35% of actively treated patients after 6 weeks, with no differences in FEV1.[7,8] Drobnic et al also showed decreased *Pseudomonas aeruginosa* density after nebulized tobramycin, 300 mg BD for 6 months with a 1 month wash out period.[9] Other study showed that sputum volume was reduced to 20% of pre-treatment volume with amoxycillin 3 gram BD during the treatment period. There was a significant reduction in numbers of patients with positive sputum culture of Haemophilus species after treatment with amoxicillin. However, the incidence of resistant *Haemophilus* species was higher in those who remained positive.[10]

Nebulization of 80 mg gentamicin in saline was reported to be safe in children and sputum gentamicin concentration was reported to attain satisfactory level.[11] In our own experience, gentamicin nebulization was helpful in our patients colonized with *Pseudomonas aeroginosa*.

### Inhaled steroid

Inhaled fluticasone 500 mcg BD for four weeks is beneficial in adult bronchiectasis patients in terms of sputum volume but not in lung function although there was a trend toward an improvement in some lung function indices.[12] However, follow-up data were not available in the study. A recent placebo controlled study showed that bronchiectasis patients with Pseudomonas

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aeruginosa infection receiving fluticasone, 500 mcg BD for 12 months, had improvement in 24-hour sputum volume and exacerbation frequency.[13]

**Respiratory muscle training devices** (Figure 1)
In inspiratory muscle training, the patient inspires through a mouthpiece with a two-way valve and a resistance in the inspiratory line.[14] Inspiratory muscle training for eight weeks showed improved quality of life and improvement of maximal inspiratory pressure. The effect on exercise tolerance remained controversial.[15,16]

Use of flutter in adult patients was reported as effective as active cycle of breathing technique (Figure 2).[17] However, there was no significant change in peak expiratory flow rate or in breathlessness.

**Beta 2 agonist and ipratropium bromide**
Hassan et al (a non RCT) showed that a subset of patients responded significantly to bronchodilators.[18] Lung function test was done 30 and 60 minutes after bronchodilator. 45.8% of patient showed good response, i.e. FEV1 >15% improvement. Overall, femoterol 5 mg nebulisation or 400 mcg MDI improved peak flow rate by 14% and 8.6% respectively. The use of bronchodilator should be individualised and the response may be dose dependent.

**Figure 1**. Inspiratory muscle training device.

**Figure 2**. Flutter.

**Mucolytics**
Bromhexine 30 mg tds for 10 days was reported to decrease sputum volume.[19] The use of aerosolised DNase is controversial and may worsen the situation.[20,21] Use of DNase 5 mg did not improve dyspnoea, quality of life score, FEV1 or FVC at day 15 and there were significant number of patients having an influenza type syndrome.[20] Acetylcysteine is a common "mucolytic" but clinical trial on its use in bronchiectasis is not available.

**Non-steroidal anti-inflammatory drugs (NSAIDs)**
In vivo study showed reduction in peripheral neutrophil chemotaxis to N-formyl-methionyl-leucyl-phenylalanine (FMLP) and a reduction in fibronectin degradation both by resting and FMLP-stimulated neutrophils after 4 weeks of therapy (25 mg tds).[22] We found iburprofen useful in an open-label N-of-1 trial in reducing the daily sputum volume in an adolescent with brochiectasis secondary to ciliary dyskinesia. (unpublished data)

**Nutrition**
Dogru et al suggested that improved nutrition in developing countries may prevent bronchiecatsis.[23] As bronchiectasis is a chronic disease, good nutrition to maintain growth is mandatory. A diet rich in fresh fruit and fish was reported to be associated with a beneficial effect on lung health.[24] Detailed description of diet beneficial to patient with bronchiectasis is not available. In children with bronchiectasis, regular nutritional assessment should be performed which may include the standard weight, height, skin-fold calibres and bioimpedence measurements. Study in cystic fibrosis patients showed that the high resolution CT scan score, the FEV1 and the resting energy expenditure were positively correlated.[25] So, we have to be particularly careful in monitoring the nutritional status of patients with impaired lung function. In our department, indirect calorimetry is done to estimate the resting energy expenditure and patients are referred to dietitian to estimate the daily intake. By combining the data, a suitable diet for anabolism can be prescribed. If the patient had severe impaired pulmonary function or the patient is wasted, high fat, high protein diet may help.

## Conclusion

In children with bronchiectais, chest physiotherapy, respiratory muscle training and good nutrition are accepted as standard management. Randomized controlled trial on drug treatment are limited on non-CF bronchiectasis, particularly in children, only one randomized controlled trial (patient with a mean age of ~13 years old) investigating the effect of macrolide was available. As *Pseudomonas aerugenosa* is associated with poor outcome, use of nebulized tobramycin or gentamicin and inhaled corticosteroid should be considered in patient with sputum that grew *Pseudomonas aerugenosa*. The case series[11] and our own experience suggested that nebulized gentamicin is safe and effective. However, the duration and frequency of nebulized therapy in non-cystic fibrosis bronchiectasis is to be defined. Lung function test with reversibility should be done and long acting β2 agonist can be offered in positive cases. In cases with troublesome sputum volume, inhaled mannitol, inhaled corticosteroid, oral bromhexine may be useful.

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