Hypertonic saline for the treatment of Non-CF bronchiectasis

Whilst the specific clinically relevant mechanisms has not been elucidated, hyperosmolar agents are used principally to reduce sputum viscosity and therefore ease chest clearance. When inhaled they are deposited in the airway, and the consequence of their hyperosmolarity in theory is that they draw fluid from the airway epithelium onto the mucosal surface and hence into contact with the mucous (Wills 2006). This then has the effect of both loosening the mucous and making it less viscous (Shibuya 2003; Wills 1997) which (particularly when used together with effective chest clearance techniques) will facilitate expectoration (Daviskas 2001; Kellett 2005).

One potential disadvantage of such agents occurs where there might be an asthmatic element to the bronchiectasis, such as in allergic bronchopulmonary aspergillosis. Inhaled hyperosmolar agents also have the effect of desiccating airway inflammatory cells, disrupting the cell membrane and causing release of bronchoconstricting and pro-inflammatory mediators, such as histamine and leukotrienes. This may cause significant acute bronchoconstriction, and hence it is recommended that a supervised test dose be administered with spirometry or peak expiratory flow (PEF) measurements before and after (Pasteur 2010). Those at risk of bronchial hyperresponsiveness should be pre-treated with an inhaled bronchodilator (Pasteur 2010).

Wording in guidelines:

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Link</th>
<th>Wording on hypertonic saline</th>
<th>Additional information</th>
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<tbody>
<tr>
<td>BTS Guideline 2010, UK</td>
<td><a href="https://www.brit-thoracic.org.uk/document-library/clinical-information/breathing/bronchiectasis/bts-guideline-for-non-cf-bronchiectasis/">https://www.brit-thoracic.org.uk/document-library/clinical-information/breathing/bronchiectasis/bts-guideline-for-non-cf-bronchiectasis/</a></td>
<td>The use of nebulised hypertonic saline prior to airway clearance could be considered to increase sputum yield, reduce sputum viscosity and improve ease of expectoration. [B]</td>
<td>Are inhaled corticosteroids a useful treatment for bronchiectasis?  &lt; Inhaled steroids should not be used routinely in children with bronchiectasis (outside of use for those patients with additional asthma) (see comments below). [D]  &lt; In adults, current evidence does not support routine use of inhaled corticosteroids in bronchiectasis (outside of use for those patients with additional asthma). [B]</td>
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<tr>
<td>Pasteur</td>
<td></td>
<td>In concentrations of 3e14%, hypertonic saline has been shown to improve tracheobronchial clearance in patients with chronic bronchitis, CF, asthma and normal individuals.393</td>
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<tr>
<td>NICE 2013, UK</td>
<td></td>
<td>These treatments should not be used for the treatment of bronchiectasis:</td>
<td>These treatments should not be used for the treatment of bronchiectasis:</td>
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<tr>
<td></td>
<td></td>
<td>• Corticosteroids (inhaled or oral) — unless there is coexistent asthma.</td>
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<td>• Mucolytics.</td>
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<td>• Leukotriene receptor antagonists.</td>
<td>• Leukotriene receptor antagonists.</td>
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Research articles:

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<tr>
<th>Author</th>
<th>Year</th>
<th>Publication</th>
<th>Result</th>
<th>Conclusion</th>
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<tr>
<td>Yap VL†</td>
<td>2015</td>
<td>New therapeutic options for noncystic fibrosis bronchiectasis.</td>
<td>Inhaled hyperosmolar agents such as hypertonic saline and mannitol are promising but study results have been mixed. There is limited evidence of benefit of other therapies, including inhaled antibiotics and pharmacologic agents to enhance mucus clearance</td>
<td>REVIEW Hypertonic saline is promising for the therapy of NCFB, but more studies are necessary</td>
</tr>
<tr>
<td>Hart A†</td>
<td>2014</td>
<td>Inhaled hyperosmolar agents for bronchiectasis.</td>
<td>Four studies (combined N = 113) compared hypertonic saline versus isotonic saline. On most outcomes there were conflicting results and the</td>
<td>REVIEW No benefit over isotonic saline measurable, but</td>
</tr>
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</table>
opportunities for the statistical aggregation of data from studies was very limited. It is not possible to draw robust conclusions for this comparison and judgments should be reserved until further data are available. The data suggest that it is unlikely to have benefit over isotonic saline in patients with milder disease.


We found only 2 papers and 2 reviews on the use of rhDNase in children, and in adults 3 trials on HS, 5 on mannitol powder and 2 on rhDNase. In conclusion, no observational or randomized controlled trials (RCT) have been published on the use of these drugs in children with nCFb, while the few conducted on adult patients report some evidence of their effects. Further studies are needed on inhaled mucoactive drugs for the treatment of children with nCFb.


There are no approved pharmacologic agents to enhance mucus clearance in non-cystic fibrosis (CF) bronchiectasis. Evidence supports the use of hyperosmolar agents in CF, and studies with inhaled mannitol and hypertonic saline are ongoing in bronchiectasis.


This concise clinical review focuses on the major etiologies, diagnostic testing, microbiology, and management of patients with adult non-cystic fibrosis bronchiectasis. Systematic evaluation identifies a specific cause in the majority of patients and may affect subsequent treatment. We outline current therapies and review the data that support their use.


Lung function (%change from baseline) improved in HS vs. IS (FEV1: 15.1, 1.8 p<0.01; FVC: 11.2, 0.7 p<0.01. SGRQ improved significantly from baseline (HS 6.0, IS 1.2; p<0.05). There were reductions in annualised antibiotic usage (HS 2.4, IS 5.4 courses per patient per year), annualised emergency health care utilisation visits were reduced (HS 2.1, IS 4.9 events per patient per year). There were also improvements in sputum viscosity and ease of expectoration (visual analogue scale).

Positive: Regular use of 7% hypertonic saline improves lung function, quality of life and health care utilisation in non-cystic fibrosis bronchiectasis patients.

**Rademacher** 2011 Bronchiectasis-- Hypertonic saline is often used because


An advanced practitioner in respiratory medicine at Salford Royal Foundation Trust identified nebulised hypertonic saline (HTS) as a treatment that could potentially improve service provision. She developed and evaluated a safe drug challenge and monitoring service for nebulised HTS.

Positive: Quality of life increased in 59% of patients; Breathlessness-symptoms improved


Preliminary data regarding inhaled hyperosmolar agents such as hypertonic saline and mannitol are also promising, but these therapies cannot yet be recommended for routine therapy of patients with bronchiectasis

Not yet recommended, new studies necessary


Clinical studies using radioaerosols, and imaging with a gamma camera, have demonstrated that hypertonic saline (HS; 3-14.4%) and mannitol (300-400 mg) increase clearance of mucus acutely in patients with mild asthma, bronchiectasis, and cystic fibrosis (CF). Inhalation of 7% HS, four times daily, over 2 weeks improved significantly the baseline mucus clearance rate and lung function in CF patients. In addition, inhalation of 7% HS twice daily over 12 months showed similar results to the short-term studies without a change in the bacterial load in CF patients

Positive: Augmented mucus clearance rate


Sputum weights were significantly higher after HS than IS (P = 0.002). Ease of expectoration also differed overall (P < 0.0001) and was significantly lower with HS than with IS (P = 0.0005). Sputum viscosity differed between treatment phases, with a significant linear trend to reduced sputum viscosity with HS (P = 0.0002). These changes were associated with small but statistically significant differences in FEV1 (P = 0.043) and FVC (P = 0.011) between treatment phases. Nebulised hypertonic saline can be used safely and effectively as an adjunct to physiotherapy in selected patients.

Positive: Additional therapy with HS is beneficial in: > Ease of expectoration > Higher sputum weights

Useful links:
https://www.bronchiectasis.eu/latest-news