MUCOACTIVE DRUGS AND AIRWAY HYGIENE

Dr. Trình Thị Ngà
Respiratoiry Deparment

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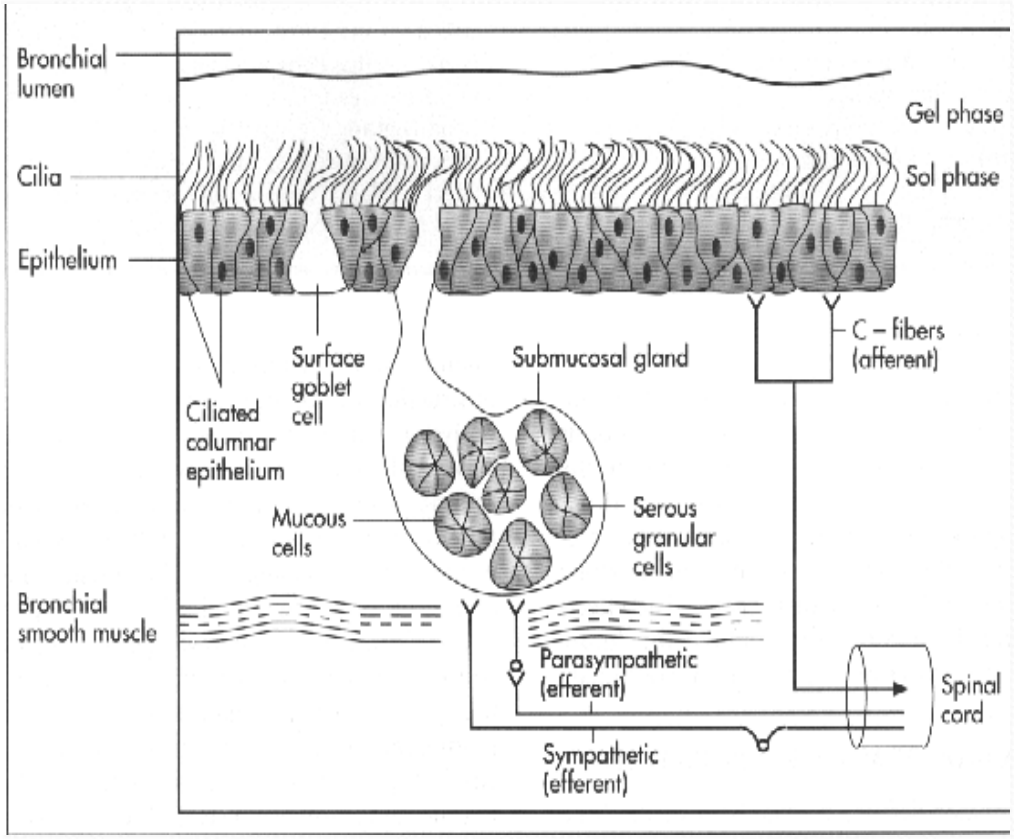
MUCOACTIVE DRUGS

Muco-ciliary Blanket



95% water, 2% glycoproteins

Gel layer-high viscosity from goblet cells

Sol layer – low viscosity from submucosal bronchial glands

- neutrophil-derived DNA
- filamentous actin (F-actin), dead/apoptotic cells,
- bacteria and cell debris

→ mucus purulence = sputum

TABLE 1 Mucoactive drugs and their potential mechanisms of action

Mucoactive drugs	Potential mechanism of action
Expectorants	
Hypertonic saline	Increases secretion volume and/or hydration
Guaifenesin	Stimulates secretion and reduces mucus viscosity
Mucoregulators	
Carbocysteine	Metabolism of mucus producing cells, antioxidant and anti-inflammatory effects, modulates mucus production
Anticholinergic agents	Decreases secretion volume
Glucocorticoids	Reduces airway inflammation and mucin secretion
Macrolide antibiotics	Reduces airway inflammation and mucin secretion
Mucolytics	
N-Acetylcysteine	Breaks disulphide bonds linking mucin polymers Antioxidant and anti-inflammatory effects
N-Acystelyn	Increases chloride secretion and breaks disulphide bonds
Erdosteine	Modulates mucus production and increases mucociliary transport
Dornase alfa	Hydrolyses the DNA in mucus and reduces viscosity in the lungs
Gelsolin	Severs actin filament cross-links
Thymosin β_4	Severs actin filament cross-links
Dextran	Breaks hydrogen bonds and increases secretion hydration
Heparin	Breaks both hydrogen and ionic bonds
Mucokinetics[#]	
Bronchodilators	Improves cough clearance by increasing expiratory flow
Surfactants	Decreases sputum/mucus adhesiveness
Ambroxol	Stimulates surfactant production and inhibits neuronal sodium channels

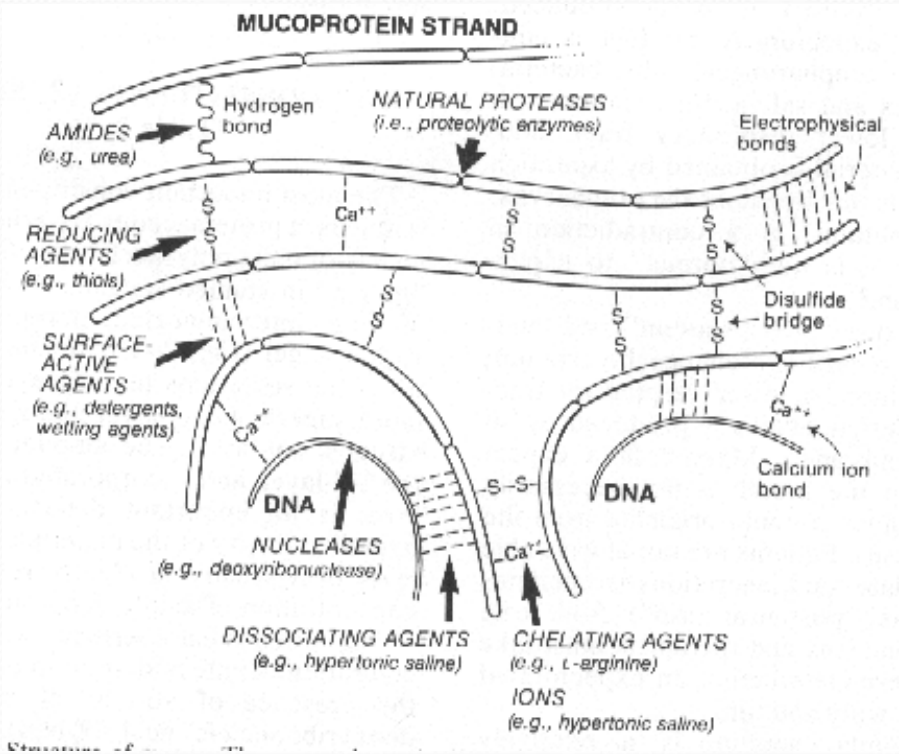
[#]: also referred to as cough clearance promoters.

Mucolytics

- Acetylcystein, bromhexin
- Recombinant human DNase (DNase, Pulmozyme)
- Endosteine

- Mucolytics: orally or parenterally.
- RhDNase: nebulisation and inhalation.

Mucolytics: Mucomyst (N-Acetylcysteine)



- 10 or 20% solution (hypertonic and alkaline pH)
- Breaks disulfide bonds (most effective form of mucolysis)
- Also breaks mucoprotein bonds and hydrogen bonds
- Bronchorrhea

Mucolytics: Pulmozyme (Dornase Alpha or DNAse)

- Excellent aerosol mucolytic for cystic fibrosis patients
- Lyses the DNA bonds in the sputum of cystic fibrosis patients
  - These patients have a lot of these bonds!

THE STUDIES

Available online http://ccforum.com/content/9/4/R351

Research

Open Access

DNase and atelectasis in non-cystic fibrosis pediatric patients

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nebulised or endotracheally instilled DNase

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- a retrospective descriptive study.
- n = 30
- nebulised or endotracheally instilled DNase

Conclusion:

- rapid clinical improvement was observed within 2 h and radiologic improvement was documented within 24h in the large majority of children.
- DNase may be an effective treatment for infectious atelectasis in non-cystic fibrosis pediatric patients.

Cochrane Library

Cochrane Database of Systematic Reviews

Mucolytics for bronchiectasis (Review)

Wilkinson M, Sugumar K, Milan SJ, Hart A, Crockett A, Crossingham I

COCHRANE 2014

- Bronchiectasis is a disease characterised by excessive mucus production and retention.

- Retained sputum could potentially act as a culture medium for bacteria leading to recurrent or persistent chest infection.

- 4 RCTs = 528 participants (adult)
- Bromhexine (n= 88): 30mg orally three times per day,

→ improving sputum expectoration after ten days' treatment, reduced sputum production at 7, 10 and 16 days.

COCHRANE 2014

- Erdosteine + physiotherapy(n = 30) slightly improved sputum purulence and small but clinically useful changes in spirometry over a 15-day period.
- Recombinant human Dnase (Rh DNase)(n = 460): 2,5 – 5mg aerosol → no important significant differences versus placebo.

→ Randomised controlled trials are needed.

COCHRANE 2014

PLOS | ONE

RESEARCH ARTICLE

Mucolytic Effectiveness of Tyloxapol in Chronic Obstructive Pulmonary Disease - A Double-Blind, Randomized Controlled Trial

Martin Koppitz[1], Charlotte Eschenburg[1], Emilia Salzmann[2], Martin Rosewich[1], Ralf Schubert[1], Stefan Zielen[1]*

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* Stefan.Zielen@kgu.de

Design:

- A randomized, placebo-controlled, double-blinded crossover; n = 28.
- Patient: inhale 5 ml Tyloxapol 1% or saline 0.9% solution 3 times daily for 3 weeks.
- Tacholiquin(Germany): 1% Tyloxapol, 5% glycerine and 2% sodium hydrogen carbonate in a sterile aqueous solution and saline 0.9% solution.

Conclusion:

- Our study demonstrated that inhalation of Tyloxapol by patients with COPD is safe and superior to saline and has some anti-inflammatory effects.

PLOS ONE | DOI:10.1371/journal.pone.0156999 June 16, 2016

van der Hoeven *et al. Trials* (2015) 16:389
DOI 10.1186/s13063-015-0865-0

TRIALS

STUDY PROTOCOL Open Access

Preventive nebulization of mucolytic agents and bronchodilating drugs in invasively ventilated intensive care unit patients (NEBULAE): study protocol for a randomized controlled trial

Sophia M. van der Hoeven[1*], Jan M. Binnekade[1], Corianne A. J. M. de Borgie[3], Frank H. Bosch[4], Henrik Endeman[5], Janneke Horn[1,2], Nicole P. Juffermans[1,2], Nardo J. M. van der Meer[6,9], Maruschka P. Merkus[3], Hazra S. Moeniralam[7], Bart van Silfhout[7], Mathilde Slabbekoorn[8], Willemke Stilma[5], Jan Willem Wijnhoven[6], Marcus J. Schultz[1,2] and Frederique Paulus[1]

- This RCT, multicenter, open-label, Netherlands.
- n = 950 intubated and ventilated ICU patients
- nebulization of acetylcysteine(300mg) and/or salbutamol(2.5mg)/6h
- Outcome: the number of ventilator-free days, surviving on day 28; ICU and hospital length of stay, ICU and hospital mortality…

- NEBULAE *is the first randomized controlled trial sufficiently powered* .(22/7/2014 → 1/6/2016)

AIRWAY HYGIENE

Review

Clinical review: Airway hygiene in the intensive care unit

Sanja Jelic, Jennifer A Cunningham and Phillip Factor

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Published: 31 March 2008
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This article is online at http://ccforum.com/content/12/2/209

Table 1

Recommendations for airway hygiene in critically ill patients for reduction in health-care-associated pneumonia

Strategies	Recommended for clinical use	Grade	Reduction in HCAP	Reduction in mortality
Effective strategies				
Chlorhexidine gluconate oral rinse	Yes	A	Yes	No
Endotracheal suctioning on 'as needed' basis (compared with routine suctioning)	Yes	A	No increased incidence of HCAP	No
Kinetic therapy	Yes[a]	A	Inconclusive	No
Ineffective strategies				
Selective digestive decontamination	No	A	Inconclusive	No
Oral topical iseganan	No	B	No	No
Aerosolized mucus-controlling agents	No	U	N/A	N/A
Endotracheal instillation of saline	No	C	N/A	N/A
Chest physiotherapy	No	A	Inconclusive	No
Strategies of equivocal or undetermined effectiveness				
Continuous subglottic suctioning	Yes[b]	A	Yes	No
Bronchoscopy	Yes[c]	B	N/A	N/A
Closed (in-line) endotracheal suctioning (compared with open suctioning)	Yes[d]	A	Inconclusive	No

- Bronchoscopy should be reserved primarily for patients with acute atelectasis involving more than a single lung segment in the absence of air bronchograms who remain symptomatic after 24 hours of chest physiotherapy.

Critical Care, 2008, Vol 12 No 2 Jelic et al.

Thorax
AN INTERNATIONAL JOURNAL OF RESPIRATORY MEDICINE

Guideline for non-CF Bronchiectasis

British Thoracic Society
Bronchiectasis (non-CF) Guideline Group

THORAX.2010

Are adjuncts to airway clearance techniques useful?

- *Sterile water inhalation* may be used before airway clearance to facilitate clearance. [B]
- The use of *nebulised normal saline* prior to airway clearance could be considered to increase sputum yield, reduce sputum viscosity and improve ease of expectoration. [B]
- The use of *nebulised hypertonic saline* prior to airway clearance could be considered to increase sputum yield, reduce sputum viscosity and improve ease of xpectoration. [B]
- Consider using nebulised b2 agonists prior to treatment to enhance sputum clearance. [B]

- Recombinant human DNase should not be used in adults with bronchiectasis. [A]
- Recombinant human DNase should not be used in children with bronchiectasis. [D]

CONCLUSION


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LOT 49-132-EV


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