Keele UNIVERSITY
Impact Accelerator Unit

Keele Critically Appraised Topic (CAT Form)

Clinical Question:

In preterm and neonatal patients with secretion retention, does the use of mucoactive nebulisers improve clinical outcomes compared to usual care?

Clinical bottom line

There is currently a lack of high-quality evidence to determine whether nebulised mucoactive drugs improve clinical outcomes in neonatal patients with secretion retention. Based on the available literature, our clinical practice remains unchanged, as there is insufficient evidence to support the routine use of nebulisers in this patient group at present. We plan to explore this further through benchmarking with other neonatal units within the UK.

Plain language summary

In our neonatal unit, some babies struggle with thick, sticky mucus in their lungs. In older children and adults, medication can be given as a mist by a nebuliser machine and used to loosen this mucus. At present, there isn't strong evidence to show clear benefits of using these same medicines in premature or newborn babies.

Most of the research so far has been based on very small studies, so more large, high-quality research is needed to properly understand how helpful these treatments may

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be. Because there are relatively few babies in neonatal units who might need this treatment, it can be difficult to run such studies and will likely need a number of units to work together in a multi-centre trial.

Some medicines may have benefits in specific situations. For example, a drug called rhDNase may help clear collapsed areas of the lung (atelectasis), and another medicine called hypertonic saline may help babies with certain lung infections like RSV bronchiolitis. Another medicine, N-acetylcysteine, has not been shown to be helpful. These medicines work best when combined with treatments that clear mucus from the lungs, such as chest physiotherapy.

Looking ahead, we plan to continue carefully offering these treatments to selected babies, always in discussion with the wider healthcare team. We will record case studies to review outcomes and work with physiotherapists from other neonatal units to share experiences and build a clearer picture of when these treatments are most helpful.

Why is this important?

In our clinical practice, several neonatal patients have experienced secretion retention due to thick, tenacious secretions. In paediatric and adult populations, nebulised mucoactive agents such as hypertonic saline or recombinant human deoxyribonuclease (rhDNase) are commonly used to aid secretion clearance. However, in neonates this approach is limited by the lack of appropriate nebulisation equipment and the practical challenges of delivering therapy effectively. Addressing this question would help determine whether investment in nebulisation equipment is justified and whether nebulised mucoactive drugs represent a viable and beneficial adjunct for secretion management in this population.

Search timeframe (e.g. 2013-2013)

2011-2025

This timeframe was selected to capture advances in neonatal care, particularly improved outcomes for extremely preterm infants, while excluding older studies that may not reflect current practices.

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Search criteria

Population Intervention Comparison Outcomes (PICO) themes	**Description**	**Search terms**
Population and Setting E.g. adults with OA, primary care	Neonates (infants up to 44 weeks gestational age) This reflects the mix of preterm and term infants as seen on our neonatal unit	Preterm infants (less than 37 weeks) Neonates Newborn up to 1 month premature
Intervention or Exposure (i.e. what is being tested) e.g. manual therapy	Nebulised mucoactive drugs	nebuliser nebulizer nebulizer treatment aerosol treatment aerosol
Comparison, if any e.g. usual care, leaflet	Usual care	
Outcomes of interest e.g. Visual analogue scale, Range of motion	Safety Effectiveness – deposition of drug Improved outcome – e.g. resolution of CXR findings, improved respiratory function, decreased length of stay	Harm Adverse events negative effects negative impacts negative outcomes negative consequences efficiency productivity

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		therapy or treatment effect length of stay improved respiratory function chest x-ray resolution
Types of studies e.g. Randomised Controlled Trails, Systematic reviews	All	

Databases searched

- Cochrane Library
- Directory of Open Access Journals
- EBSCOhost
- Embase
- Gale Health and Wellness
- Gale OneFile: Health and Medicine
- HMIC Health Management Information Consortium
- Ovid Emcare
- PubMed
- Web of Science

Date of search

10.09.2025

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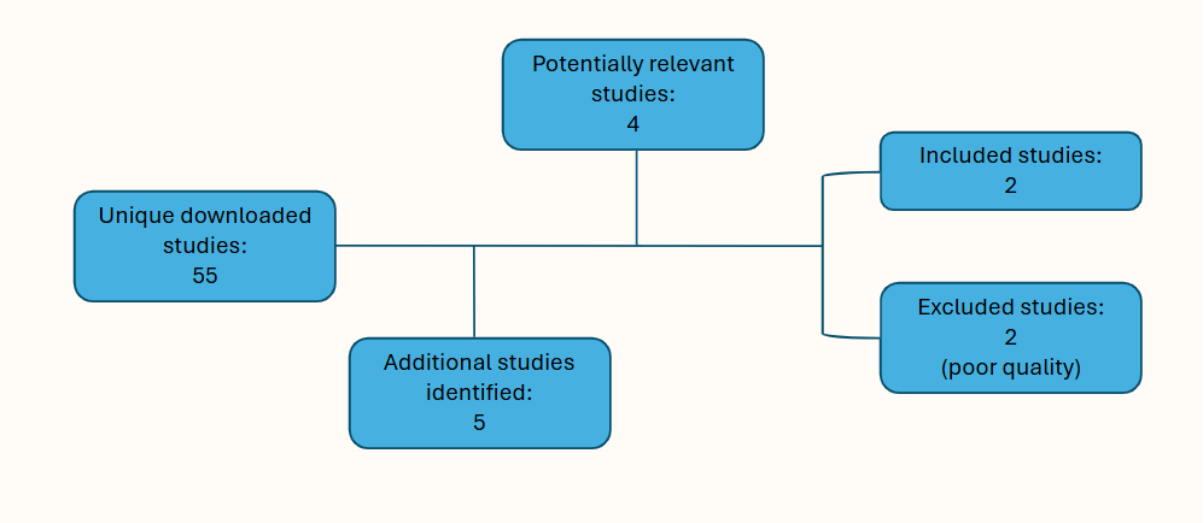

Results of the search:

There were fifty-five unique downloaded studies. Further searches and discussion with colleagues revealed an additional five papers. There were four potentially relevant studies. There were two included and their critical appraisal is included in Table 1. The other two were two excluded.

Table 1- Detail of included studies

First author, year and type of study	Population and setting	Intervention or exposure tested	Study results	Assessment of quality and comments
McGoven 2021 Literature review	Mix of pre-term and term infants Literature search completed in May 2021	Identifying evidence reviewing safety analysis of preterm infants receiving rhDNase with atelectasis, both	95 studies screened, 8 identified and discussed, only 2 randomised controlled trials (RCTs) included following	Poor quality case studies included with limited evidence and population size Population sizes likely to be

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	Cochrane and Medline databases searched	nebulised and instilled Studies included if objectively measuring clinical improvement following rhDNase with a control In the studies included chest x-ray (CXR) changes and clinical parameters were used as objective outcomes	inclusion criteria The two studies included a total of 30 preterm infants and 13 term infants Limited evidence. In both RCTs there was significant improvement in CXR scores and partial pressure of carbon dioxide (PC02). One RCT also reported significant improvement in respiratory rate (RR) and fraction of inspired oxygen (Fi02) requirement 2 cases of increased atelectasis, and 1 case of increased secretion retention reported however in this case rhDNase not used	limited due to rarity of patients Variation in dosage and delivery method Clear inclusion/ exclusion criteria

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			alongside chest physiotherapy	
First author, year and type of study	**Population and setting**	**Intervention or exposure tested**	**Study results**	**Assessment of quality and comments**
Boogaard 2007 Literature review	Mixture of ages (children 0-18 years, including preterm) MEDLINE database and Cochrane library utilised, search strategy fully broken down in method section	Aim of review was to summarize published literature on mucoactive agents most frequently used and studied in children with non-cystic fibrosis lung disease, this is, N-acetylcysteine (NAC) and other sulfhydryl compounds, rhDNase, and hypertonic saline (HTS). Focused on literature reporting effects of mucoactive agents on clinical outcome measures e.g. length of stay, symptom severity, and CXR changes.	Total of 34 relevant articles retrieved, 21 articles reported RCTs, 22 reported uncontrolled clinical observations Authors suggest that use of mucoactive drugs should be in conjunction with effective airway clearance to minimise risk of mucus plugging and improve effectiveness **NAC and other Sulfhydryl compounds:** -No solid evidence to support use of inhaled or oral NAC or other sulfhydryl compounds, in children with	Predominantly uncontrolled observations that suggest beneficial effects of mucoactive agents in different lung diseases Likely effect of publication bias, as uncontrolled observations of unfavourable findings are rarely published Discusses both instilled and nebulised mucolytics – at points unclear as to method of delivery For most disease no RCTs have been conducted to confirm or

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			respiratory tract disease. The few published RCTs in non-CF pts were of crossover design and short duration. They showed no effects at all or futile effects of doubtful clinical significance. Despite this lack of supporting literature, NAC is widely prescribed for children with various respiratory diseases. **RhDNase:** Two RCTs in infants with moderate-to-severe respiratory syncytial virus (RSV) bronchiolitis and one RCT in children with mod-to-severe asthma	refute these positive findings Larger studies needed to confirm results

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			exacerbation demonstrated NO clinical benefits of rhDNase One RTC showed reduction in length of stay on Intensive care unit (ITU) and lower incidence of atelectasis in post-operative ventilated patients Anecdotal evidence suggests that rhDNase could be beneficial in childhood lung diseases with impaired mucociliary clearance during mechanical ventilation **HTS:** Efficiency of HTS in non-CF patients has been studied in only 3 small RCTs in infants with RSV	

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			bronchiolitis (all completed by the same research group). - They reported a beneficial effect on length of stay and symptoms. These results need confirming in larger trial	

Summary

There is a lack of high-quality evidence supporting the clinical benefit of nebulised mucoactive drugs in neonatal and preterm populations. Existing evidence is largely limited to small observational studies or low-quality randomised controlled trials, highlighting the need for larger, more robust studies to confirm these findings. However, recruitment to such trials is likely to be challenging due to the relatively small pool of eligible preterm and neonatal patients.

The available evidence suggests some potential benefit from the use of rhDNase in resolving atelectasis and from hypertonic saline in the treatment of RSV bronchiolitis. In contrast, there is little evidence to support the use of NAC. It was also highlighted that mucoactive drugs should ideally be used in conjunction with effective airway clearance methods such as chest physiotherapy.

The studies identified included a mixture of preterm and term infants. While this reflects the typical patient population in our neonatal unit, the anatomical and physiological differences between these groups mean that a clearer separation of data would have been valuable. Unfortunately, many studies did not provide a detailed breakdown of gestational age, or combined preterm and term infants within their analyses, limiting the ability to assess outcomes separately. Where possible, we have specified whether each included study applied to preterm, term, or mixed populations.

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During this literature search and service development project, guidance was sought from Emma Foulerton (Lead Physiotherapist within the West Midlands Neonatal network) with clinical expertise in respiratory neonatal Physiotherapy.

Implications for practice

More high-quality evidence is needed around the clinical benefits of nebulised mucoactive drugs within the neonatal and preterm populations. There is some evidence that certain nebulised mucoactive drugs such as rhDnase and hypertonic saline may improve clinical outcomes in certain situations. Due to the limited nature of the research, there is no evidence to support the routine use of these interventions in our neonatal population. However, they may present a viable treatment option, alongside other chest clearance techniques, in some cases following discussion with the multidisciplinary team.

Following an audit of respiratory physiotherapy input on a level three neonatal unit carried out over a period of a year, one infant was identified to benefit from use of nebulised mucolytics. The infant was born at 23+1 weeks gestational age and seen at 32+ 6 corrected gestational age. The infant presented intubated and ventilated with a right sided collapse and consolidation on CXR, secretion retention and difficulty clearing, on 100% FiO2. Nebulised 7% hypertonic saline was delivered via a manual hyperinflation circuit by physiotherapists alongside positioning, manual techniques and airway clearance. No adverse effects were identified, the infant's CXR resolved, oxygen demand decreased, and they were eventually extubated onto non-invasive ventilation.

Moving forward we plan to continue to scope delivering nebulised mucolytics to suitable individuals on the neonatal unit, in discussion with the multidisciplinary team. Written case studies will then be completed to review clinical impact on an individual case basis. We aim to seek further clinical experience and cases from respiratory physiotherapists working in other level three neonatal units and discuss findings within the specialist interest group.

What would you post on social media?

No high-quality evidence evaluating clinical outcomes with the use of mucoactive nebulisers in preterm & neonatal patients compared to usual care.

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We are interested in the views and outcomes of any respiratory neonatal physiotherapists that have experience in using nebulised mucoactives in the preterm or term population.

CAT image	Evidence quality	Checkbox
	Good quality evidence to support use....	☐
	Insufficient and poor-quality evidence OR substantial harms suggest intervention used with caution after discussion with patient...	☐ x
	No good quality evidence, do not use until further research is conducted OR Good quality evidence to indicate that harms outweigh the benefits....	☐

If you require this document in an alternative format, such as large print or a coloured background, please contact health.iau@keele.ac.uk

Acknowledgements

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