Keele UNIVERSITY

Impact Accelerator Unit

Keele Critically Appraised Topic (CAT Form)

Clinical Question:

In preterm and neonatal patients, does nebulisation of mucoactive drugs result in effective lung deposition?

Clinical bottom line

Effective lung deposition of mucoactive drugs can be achieved in preterm and neonatal patients via a nebuliser system. Lung deposition is however, reduced in neonates and preterm infants compared with adults, owing to their unique physiological characteristics. Lung deposition can be optimised by using vibrating mesh nebulisers, while additional factors such as ventilator settings, nebuliser placement within the circuit, and the presence of significant air leaks may also influence drug delivery. Further high-quality evidence is required. We will look at the feasibility of introducing a vibrating mesh nebuliser system on our unit following discussion with the multi-disciplinary team.

Plain language summary

In our neonatal unit, we sometimes see babies who have trouble clearing thick, sticky mucus from their lungs. In older children and adults, medication can be given as a mist by a nebuliser machine to loosen this mucus. However, in newborn babies, especially those born early, using nebulised medicines is more complicated. The equipment is not always designed for this age group, and it can be difficult to make sure the medicine reaches the lungs effectively.

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At the moment, there is very little high-quality research in this area. The existing evidence suggests that medicines delivered by nebulisers do reach the lungs of these smaller babies, but not as well as in adults. This is because babies have smaller lungs and breathe less regularly. Special nebuliser machines called *vibrating mesh nebulisers* can produce a finer mist that reach the lungs better than standard *jet nebulisers*. Other factors, such as how the nebuliser is connected to the breathing machine, the settings used on the ventilator, and the presence of leaks, may also affect how much medicine gets into the lungs.

More good quality studies are needed to understand whether these medicines really help newborns and premature babies and how best to deliver them.

Based on this work our unit is planning to explore whether buying a vibrating mesh nebuliser machine would improve care, as this type of device can deliver these medicines better than the equipment we currently use.

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 as they can deliver drugs directly to the target organ with a decreased risk of systemic toxicity. 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 therapy or treatment effect

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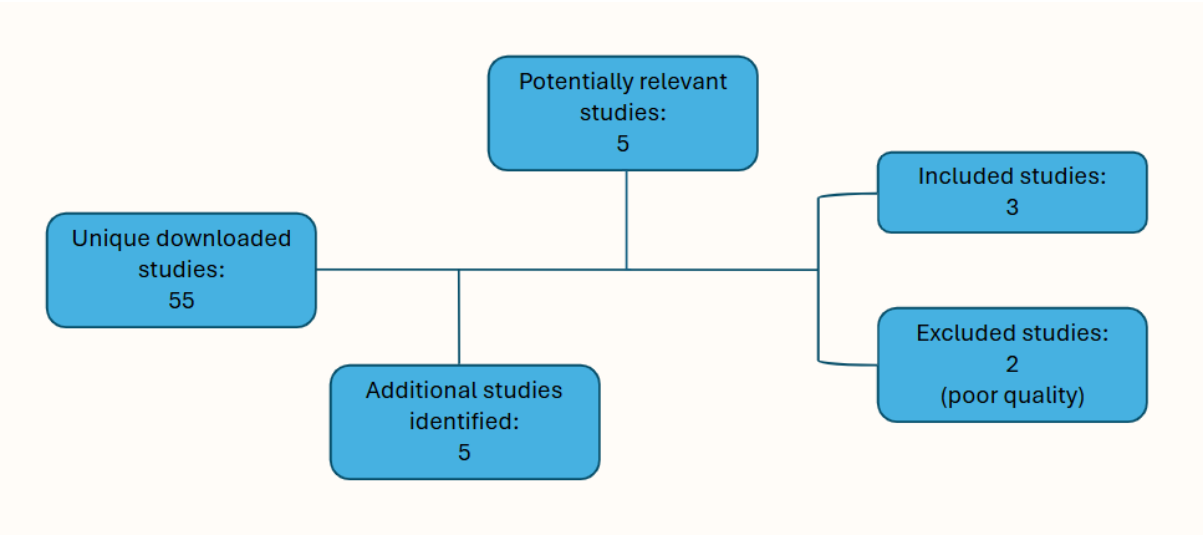
		length of stay improved respiratory function chest x-ray resolution
Types of studies e.g. Randomised Controlled Trails, Systematic reviews	All	

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 five potentially relevant studies. There were three included and their critical appraisal is included in Table 1. There were two excluded studies.

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**
Chartrand 2022 Scoping review	No breakdown of preterm vs term Research question ran twice (2021 and 2022) Medline, CINAHL and EMBASE databases searched	Identify evidence and literature gaps regarding delivery of aerosolized medication to paediatric and neonatal patients receiving mechanical ventilation	248 articles screened – total of 5 included after applying exclusion criteria and full text screening Evidence is limited Large variation in practice – no standardised protocols/guidance Mesh nebulizers shown to be superior to jet nebulisers	Clear methodology and exclusion/inclusion criteria 5 studies included The methodology and methods used across the included studies varies a lot so may account for inconsistencies across results and make interpretation difficult

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			Optimal placement of nebuliser in circuit unclear as results inconsistent May be optimal vent settings but few studies and outdated. Flow rate and inspiratory: expiratory ratio (I:E) seem most important variables	The studies used simulated lung models or animal substitutes to gather data – this is likely due to ethical considerations of a very vulnerable patient group and low numbers of eligible patients
First author, year and type of study	**Population and setting**	**Intervention or exposure tested**	**Study results**	**Assessment of quality and comments**
Kohler 2008 Randomised control Trial	All preterm infants at birth, at age of study some participants were greater than 37 weeks 17 Spontaneously breathing oxygen independent male preterm infants (Magdeburg children's	LC star Jet nebuliser+ PARI master compressor, LS 290 ultrasonic nebuliser, and project ultrasonic neb All infants inhaled a solution from each nebuliser over a week period using a face mask. Measuring deposition of solution through urine sample	1. Highest neb deposition with LC star Jet nebuliser (this nebuliser produced the highest number of smaller droplet sizes) 2. All nebs tolerated well, no statistically significant distress scored Results support the notion that	Only relevant to babies self-ventilating on room air, with a mean corrected gestational age (CGA) of 36 weeks nearing term age Small sample size, one hospital Funding not stated

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	hospital Germany)		smaller droplet sizes are needed to maximise lung deposition On average only a very small percentage of total drug dose was delivered to the lungs	
First author, year and type of study	**Population and setting**	**Intervention or exposure tested**	**Study results**	**Assessment of quality and comments**
Bianco 2021 Literature review	Preterm population only	Summary of the intrinsic and extrinsic factors that have been highlighted as affecting drug deposition in preterm infants during NIV	Intrinsic factors: Low lung volumes Reduced lung compliance Irregular respiratory rate (RR) Extrinsic factors: Choice of nebuliser system Placement of nebuliser in circuit Type of drug being delivered	No information on how information was gathered or analysed however, the paper provides a comprehensive summary of factors to consider when using nebulizers with preterm infants therefore was included Only relates to NIV

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			Aerosol particle size Choice of non-invasive ventilation (NIV) Patient interface Suggested <1% lung deposition in pre terms compared to 5-25% in adults	

Summary

There is limited evidence available on this topic. The evidence that is available is mostly based on simulated data and methodology varies, making it hard to compare results. Many of the studies that have been reported are of low quality.

The literature indicates that achieving effective lung deposition remains a significant challenge, particularly in smaller, preterm infants and that lung deposition is reduced compared to the adult population. Evidence highlights the critical role of fine aerosol droplets in maximizing drug delivery to lung tissue. Consequently, vibrating mesh nebulisers, which generate smaller droplet sizes, are considered superior to conventional jet nebulisers. Other extrinsic factors, such as the position of the nebuliser within the ventilator circuit, the presence of air leaks, and ventilator settings, have shown inconsistent effects, making it difficult to draw firm conclusions. In addition, intrinsic factors related to the physiology of neonates and preterm infants, including low lung volumes and irregular respiratory rates, have been identified as further barriers to achieving effective lung deposition.

The studies found looked at a mixture of preterm and term infants, whilst this is a good reflection of our own neonatal unit population, it should be noted that due to anatomical and physiological difference between these patient groups it would have been beneficial to be able to split this question further into specific preterm and term populations. Unfortunately, some of the studies did not give a full breakdown of patients' gestational

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ages or contained a mix of patient ages therefore this was not possible. We have tried to specify for each included paper if it applies to preterm, term or a mixed population.

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 effectiveness of nebulised mucoactive drugs within the neonatal and preterm populations especially related to how drug delivery can be optimised. Moving forward we plan to scope the possibility of using a mesh vibrating nebuliser system (Aerogen) on our neonatal unit as this has been shown to be superior in drug deliver to the jet system that we currently have access to.

What would you post on social media?

Lung deposition of nebulised mucoactive drugs is lower in neonates & preterm infants versus adults. Using vibrating mesh nebulisers could help optimise delivery.

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....	☐

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