The development of a guideline for the use of Dornase Alfa (DNase) in non CF patients on PICU

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Introduction

It is common for mucolytics to be used alongside chest physiotherapy to aid clearance of thick secretions and alveolar recruitment. Mucolytic selection varies and at Great Ormond Street Hospital there were no guidelines to support the use of DNase on PICU.

Aim

DNase is an accepted treatment option for asthma exacerbations on PICU but outside this population evidence is limited. A guideline was necessary to standardise treatment with this unlicenced mucolytic in a non CF population.

Method

- Database search of DNase use in the non CF population.
- Collaboration between Pharmacy, Physiotherapy and PICU Consultant producing a prescribing guideline and formulary submission.
- Physiotherapy guidance for patient positioning when instilling DNase optimising deposition, timing and treatment (Figure 1).

Results

- Clinical studies and case reports support the use of DNase (nebulised or endotracheal) as a second-line treatment in paediatric patients with persistent atelectasis.
- Guideline approved by Drugs and Therapeutics Committee.

Guideline Details

- **Indication** - Mucous plugging/atelectasis resistant to standard therapy (sodium chloride 0.9% lavage, nebulised hypertonic sodium chloride 3% or 7%) and Chest Physiotherapy.
- **Dosage & administration** –

Nebulised: Consider nebulised before endotracheal for neonates. 2.5mg OD for up to 3 days. Consider BD after 6-12 hrs if no response.
ETT administration: <20kg: 0.25mg/kg (to max 5mg) instilled via ETT.
≥20kg: 5mg instilled via ETT.
Repeat once 6-8 hrs later if necessary.

- Dilute each 2.5mg vial with 7.5ml sodium chloride 0.9% to get total volume of 10ml (0.25mg/ml).
- Draw up required dose of solution whereby
  - 0.25mg/kg (max 5mg) = 1ml/kg (max 20ml).
- Non-asthmatic/unstable patients who may not tolerate this volume; dilute each vial with 2.5ml sodium chloride 0.9%, to get a total volume of 5ml (0.5mg/ml).

Figure 1 – Reverse postural drainage for DNase instillation


Left Upper Lobe – Bed flat, patient slightly tilted to left, head turn to right


Left Lower Lobe – Bed elevated to approximately 35 degrees, patient left side lying, head turn to right


Right Middle Lobe – Bed elevated to approximately 15 degrees, patient right side lying, head turn to left


Left Lingula – Bed elevated to approx. 15 degrees, patient left side lying, head turn to right


Right Upper Lobe – Bed flat, patient slightly tilted to right, head turn to left


Right Lower Lobe – Bed elevated to approximately 35 degrees, patient right side lying, head turn to left

N.B. For a larger child elevate the head of the bed, flexion at the hips.

Case Study

Day 10 of life

Male, 40+5 weeks gestation, 3.9kg meconium aspiration.

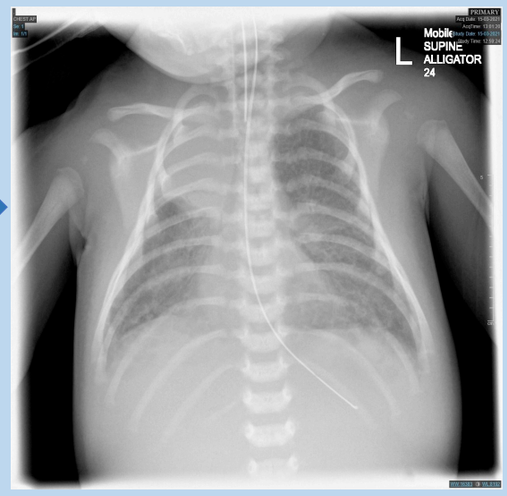
- ECMO referral for poor oxygenation and pulmonary hypertension.
- HFOV, inhaled nitric oxide, paralysis, inotropes.

Days 16 - 19

- Developed R UL collapse.
- Directed sodium chloride 0.9% lavage added to Chest Physio as above BD for 2 days.
- CXR unchanged: hypertonic sodium chloride 3% nebulised BD pre Physio for 1 day.

Once daily Chest Physio assessment and OD treatment:

- Positioning.
- ETT sodium chloride 0.9% instillation.
- manual lung inflation with expiratory vibrations
- ETT suction.

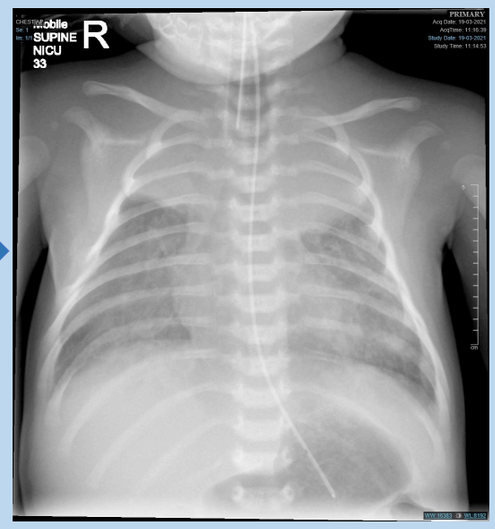


Day 20

- Persistent R UL collapse on auscultation.
- DNase nebulisation BD and Physio BD.

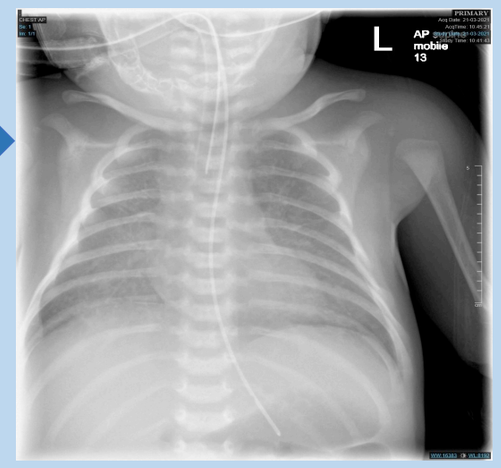
Day 21

- Ongoing persistent R UL collapse and new L UL collapse.
- DNase administered via ETT; 2.5mg diluted with 2.5ml sodium chloride 0.9%; 0.25mg/kg divided between each lung.
- Physio performed 45 mins later in supported sitting.



Day 22

- Follow up CXR demonstrates resolution of bi-apical collapse.
- Ventilation weaning.



Day 23

- Successful extubation.
- Transferred back to local following day self ventilating in room air.

Discussion

- Retained pulmonary secretions are associated with the development of atelectasis in paediatric patients and is associated with poor clinical outcomes, including prolonged mechanical ventilation.[1]
- Using the evidence found and expert clinical opinion a guideline for the use of DNase was developed. This has been incorporated into daily PICU practice, providing support for junior members of staff in mucolytic selection and standardising care.
- Case study illustrates how the guideline was followed in a critically ill neonate demonstrating the use of DNase as a successful adjunct to Physiotherapy. Escalation of mucolytic use was as per guideline and clinical stability, however earlier escalation to DNase via ETT may have expediated extubation.

References

1. Thornby K, Johnson A, Axtell S, Dornase Alfa for Non-Cystic Fibrosis Pediatric Pulmonary Atelectasis. *Annals of Pharmacotherapy* 2014 Vol 48(8) 1040-1049

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