ADULT PROTOCOL FOR INTRAPLEURAL ALTEPLASE AND DORNASE ALFA FOR THE TREATMENT OF EMPYEMA

Introduction

Reported mortality rates from pleural infection are between 10-20%, and drainage through a chest drain and administration of antibiotics fail in approximately one third of patient, who then require surgical drainage (Farjah et al, 2007). Prompt therapeutic intervention reduces morbidity and mortality as well as healthcare costs (Davies et al, 2010).

Background

The MIST1 trial (Maskell et al, 2005) has confirmed the safety of intra-pleural fibrinolytic use, but has shown that the use of mono-agent streptokinase alone is not sufficient to reduce mortality and the need for surgery in pleural infection.

Intrapleural administration of alteplase and dornase alfa was shown to improve fluid drainage, reduce frequency of surgical referral and decrease the duration of hospitalisation in patients with pleural space infection in one randomised trial by Rahman et al, 2011 (MIST2). This trial included 210 patients that compared dornase alfa plus alteplase vs alteplase vs dornase vs placebo. Use of dornase alfa or alteplase alone were ineffective and comparable to placebo. Following the positive result of this trial for the combination therapy, there have been two single-centre, retrospective descriptive analyses of clinical practice. These suggest that intrapleural alteplase/dornase alfa is an effective treatment by maximising removal of infected pleural fluid therefore avoiding aggressive surgical intervention.

Patient suitability (adapted from MIST 2 criteria, Rahman et al 2011)

Eligible:

- Clinical evidence of infection with pleural fluid macroscopically purulent/turbid or positive on bacterial culture or positive for bacteria on Gram staining, or pleural fluid pH <7.2
- Patients fit for thoracic surgery but transfer delayed and interim measures required
- Patients not fit for thoracic surgery and medical management agreed
- Diagnosis of empyema within four days

Not eligible:

- Previous treatment with intrapleural fibrinolytic agents, dornase or both for empyema
- <18 years of age
- Coincidental stroke

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- Major haemorrhage or trauma
- Major surgery in the preceding 5 days
- Previous pneumonectomy on the infected side
- Pregnancy or lactation
- Documented allergy to alteplase or dornase alfa
- Inability to give informed consent

In all cases, informed consent should be obtained and patients should be informed of the risks and benefits of the procedure as this is an unlicensed treatment.

Prescribing the medication

These medications can only be prescribed by a **consultant chest physician** or by a **specialist registrar on the recommendation by a consultant chest physician**. The following should be prescribed on JAC:

- Alteplase 10mg injection (select the intrapleural route (unlicensed)) twice daily and insert a 3 day course into the appropriate course length box
- Dornase alfa 2500 units nebules (select the intrapleural route (unlicensed)) **5000 units** twice daily and insert a 3 day course into the appropriate course length box

Administration

These medications should be administered by a respiratory registrar or a consultant chest physician with experience in it's use; this is an unlicensed use of alteplase and dornase alfa.

Patients should be managed in areas with registered nurses who are experienced in managing chest drains.

- Ensure Seldinger 18F or large bore surgical chest drain is correctly positioned
- Dilute 10mg alteplase* with 10ml sodium chloride 0.9% and withdraw the full dose from the vial. Dilute with a further 30ml sodium chloride 0.9%. Do not use Water for Injections.
- Instil the diluted alteplase into the chest drain, clamp the drain for 1 hour and then unclamp and allow drainage for 1 hour.
- Draw up 5000 units (the contents of two nebules) of dornase alfa into a syringe and further dilute with 30ml Water for Injections. Do not use sodium chloride 0.9%.
- Instil diluted dornase alfa into the chest drain, clamp the drain for 1 hour and then unclamp and allow to drain for 1 hour.

  *Where alteplase is unavailable, dilute 100,000units of urokinase with 2ml sodium chloride 0.9% and withdraw the full dose from the vial. Dilute with a further 30ml sodium chloride 0.9%. Do no use water for injections.

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Monitoring and follow up

All patients should be monitored for adverse events, such as allergic reactions or signs of bleeding e.g. intrapleural haemorrhage, haemoptysis, gastrointestinal bleeding. All adverse events should be recorded via the DATIX system and reported via the yellow card system monitored by the MHRA.

Treatment should be discontinued in the event the patient clinically deteriorates.

References

Farjah F, Symons RG, Krishnadasan B, Wood DE, Flum DR (2007); Management of pleural space infections: a population based analysis. J Thorac Cardiovasc Surg; 133: 346-51

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Summary of Product Characteristics available at https://www.medicines.org.uk/emc/product/1112 accessed 11/4/2019

Summary of Product Characteristics available at https://www.medicines.org.uk/emc/product/898/smpc accessed 11/4/2019

Luton and Dunstable University Hospital guidelines for intrapleural alteplase and dornase alfa for the treatment of empyema 2017

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