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Pleural Infection Trial (PIT-1)

Submission date	Recruitment status	[_] Prospectively registered
16/05/2012	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
22/05/2012	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
20/05/2016	Respiratory	

Plain English summary of protocol

Background and study aims

Pleural infection (infection between the two linings of the lung) is a common and serious medical condition. It frequently follows pneumonia although rarely occurs as a primary disease. While pleural infection can occur at any age, within the adult population, it is most common in the elderly and in patients with other diseases such as diabetes. Up to 15% of patients with pleural infection do not survive the episode.

Currently, the best available primary treatment is a combination of antibiotics (given into a vein, usually for at least 7 days) and drainage of fluid/pus from the pleural space via a tube that remains in place for some days (a chest drain). This treatment is not fully effective for a significant proportion of patients, resulting in worsening or ongoing grumbling infection or persistent breathlessness after the initial illness due to residual scarring and thickening of the lining of the lung. In these cases (up to 40%) patients require a surgical procedure. Decortication procedures are performed by cardiothoracic surgeons under general anaesthetic with the aim of clearing all infected and abnormal tissue from the lining of the lung. The best timing and patient factors that indicate the need for surgery are not known and practice amongst respiratory physicians varies. Surgical procedures are associated with a risk of serious complications and many patients with pleural infection are unfit for a general anaesthetic, leaving them with limited options.

The most common cause of failure of simple treatment with antibiotics and a chest tube (resulting in the need for a surgical procedure) is inadequate drainage of thick pleural fluid (fluid in between the linings of the lung). This issue has been the subject of significant research which has told us that larger tubes and drugs (fibrinolytics) that break down pockets within the fluid do not improve drainage.

There may be a simpler solution. European centres are increasingly using saline irrigation into chest drains in the primary treatment of pleural infection. Although success rates are impressive, avoiding the need to operate on most patients, there have been no published trials to allow it to be extended into global clinical practice. Irrigation has been used after operations in patients with pleural infection and published results suggests that it may reduce the need for second surgical procedures.

Irrigation is a simple and inexpensive treatment that has not been associated with serious side effects. It employs 0.9% saline (commonly used as a physiological solution to rehydrate patients and to clean and irrigate wounds) which is infused into the chest cavity via the chest drain every six hours to effectively wash out the pleural space and thin pleural fluid so it drains more easily.

Who can participate?
This study will recruit 40 patients with pleural infection.

What does the study involve?
Participants will be randomly allocated to receive either saline irrigation through their chest drain or standard chest drain management with small volume saline flushes. Each patient will receive nine doses of either irrigation or flushes over a three-day period. Patients will undergo a CT and ultrasound scan at the beginning and the end of the trial to look for any improvement. Blood tests (including measurement of a blood protein, procalcitonin, which may be a marker of severity of the infection), patient experience and need for surgery for pleural infection will also be monitored. Patients will be followed up for 4 months after trial entry.

What are the possible benefits and risks of participating?
If the patient is allocated to saline irrigation, it is possible that they will benefit from this promising treatment. Whichever group a patient is allocated to, they will be contributing to our understanding and development of new, better ways to treat pleural infection which will benefit patients in the future. The pilot study data will allow the development of a multicentre trial. Positive results would change clinical practice, potentially leading to reduced death rates, especially in those not fit enough for surgery. There are no specific risks associated with saline irrigation but trial involvement does involve one extra CT scan, which is associated with exposure to additional radiation equivalent to about 4-5 years of background radiation.

Where is the study run from?
North Bristol NHS Trust (UK).

When is the study starting and how long is it expected to run for?
The study opened to recruitment in November 2009 and will close in July 2012.

Who is funding the study?
The study is funded by a small grants award from North Bristol NHS Trust and the company, Biomerieux, who supplied the equipment to measure procalcitonin levels.

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
NBT Rand D number: 2224

Study information

Scientific Title
A randomised controlled pilot study comparing intrapleural saline irrigation with simple tube drainage in the management of pleural infection

Acronym
PIT-1

Study objectives
1. Is saline irrigation superior to standard care in the management of pleural infection as measured by early radiological and clinical improvement?
2. Is saline irrigation superior to standard care in the management of pleural infection as measured by reduction in the need for surgical referral?
3. Are serum and pleural fluid procalcitonin levels useful in monitoring the progress of patients with pleural infection and can they predict outcome?
4. Is procalcitonin a superior marker to serum C reactive protein (CRP) in this setting?
5. Does the microbiology of throat swabs taken at presentation predict bacterial growth from pleural fluid?

Ethics approval required
Old ethics approval format

Ethics approval(s)
Southmead Hospital Research Ethics Committee, October 2009, ref: 09/H0102/58

Study design
Randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Pleural infection

Interventions
Patients will undergo blood tests at baseline and daily during the trial. They will receive antibiotics for pleural infection as per hospital guidelines and will have a 12-14Fr chest tube inserted as treatment for infection. This will be flushed 3 times per day with 20ml 0.9% saline and meticulous records will be kept of drainage volumes. Pleural fluid will be sent for culture.

12-72 hours following drain placement patients will undergo a CT thorax with pleural contrast (Trial scan). Patients with no fluid or thickening present on CT will be excluded from randomisation at this stage and the chest drain removed (standard care). They will also have a bedside ultrasound performed.

Patients will be randomised to saline irrigation or standard care with minimisation for volume of pleural fluid on CT scan (< 25% hemithorax or < 25% hemithorax occupied by pleural fluid), and presence or absence of septation/loculation on bedside pleural ultrasound. Day 1 begins at randomisation.

Saline irrigation group
250ml 0.9% saline will be administered to the pleural space via the patients chest drain 3 times per day for 3 days (9 doses). Patients will complete a visual analogue scale (VAS) comfort score following 2 irrigations.

Standard care group
20 ml 0.9% saline flushes administered via the patients chest drain 3 times per day for 3 days (9 doses). Patients will complete a VAS comfort score following 2 flushes.

Daily monitoring day 1-6
Observations: Temperature and blood pressure.
Blood tests: Full blood count (FBC), albumin, C-reactive protein (CRP), procalcitonin level.
Chest x-ray alternate days.

After nine irrigations or flushes
Pleural phase contrast CT thorax scan done on day 4-6 (standard care). Clinical decision whether to refer for surgical intervention. If not referred, chest tube removed and discharged with 14 days oral antibiotics as per NBLC protocol (standard care).

Clinic follow-up at 4 and 12 weeks post discharge (standard care), which will include a chest x-ray, FBC, CRP, serum albumin.
Simple spirometry at 12 weeks (standard care).
Serum procalcitonin at 4 and 12 weeks (trial test).

Intervention Type
Procedure/Surgery

Primary outcome measure
Change in volume of pleural fluid between 12 - 72 hours and 4-9 days post chest drain placement (before and after 9 irrigations/flushes) as assessed on CT scan with volumetric reporting.

Secondary outcome measures
1. Change in volume of pleural thickening between 12-72 hours and 4-9 days post chest drain placement as assessed on CT with volumetric reporting
2. Percentage of patients requiring surgery at 4 and 12 weeks post trial entry
3. Percentage of patients referred for surgery at 6 days post chest drain placement
4. Length of in-patient hospital stay
5. Mortality at 12 weeks
6. Change in volume of pleural thickening between 12-72 hours and 12 weeks post drain placement as assessed by chest x-ray
7. Change in volume of pleural fluid and thickening between baseline and completion of 9 irrigations/ flushes on chest x-ray
8. Change in loculation score on ultrasound (see annex 4) between 12-24 hours post drain placement and completion of 9 irrigations
9. Time for CRP to fall to 50% of day 0 value
10. Time for CRP to fall to less than 100 mg/l
11. Serial serum and pleural fluid procalcitonin levels with correlation to surgical referral rates and CRP
12. Spirometry (Forced vital capacity) as percentage predicted at 12 weeks (patients with previously diagnosed respiratory disease excluded from this analysis)

Overall study start date
23/11/2009

Completion date
16/07/2012

Eligibility

Key inclusion criteria
1. Clinical presentation consistent with pleural infection requiring chest tube drainage
2. Pleural fluid is:
2.1. Purulent
2.2. Gram stain or culture positive
2.3. pH >7.2

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
40

Key exclusion criteria
1. Inability to give informed written consent
2. Pregnancy or lactation
3. Age < 18 years
4. Previous thoracic surgery for pleural infection
5. Drain size > 14F already placed or drain placed >72 hours ago

Date of first enrolment
23/11/2009

Date of final enrolment
16/07/2012

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
North Bristol NHS Trust
Bristol
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Sponsor information

Organisation
North Bristol NHS Trust (UK)

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Sponsor type
Hospital/treatment centre

Website
http://www.nbt.nhs.uk/

ROR
https://ror.org/036x6gt55

Funder(s)

Funder type
Government

Funder Name
North Bristol Small Grant Scheme (UK)

Funder Name
Biomerieux Ltd (UK)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/08/2015		Yes	No