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A study of the mechanics of breathlessness and how these change following drainage of a pleural effusion

Submission date
02/05/2017

Recruitment status
No longer recruiting

Registration date
03/05/2017

Overall study status
Completed

Last Edited
15/11/2023

Condition category
Respiratory

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
The lining of the lung (called the pleura) produces a small amount of fluid to lubricate the lungs. Disease of this lining increases the production of fluid, known as a pleural effusion. This causes breathlessness and significant impact on quality of life. The majority of patients with pleural effusion have advanced cancerous disease, with an average hospital length of stay of 6 days therefore an appropriate management decision is crucial in this particular group. Doctors can try to provide symptom relief by draining off the fluid. Some people are very breathless with small amounts of fluid whereas others feel well with a large collection of pleural fluid by inserting a needle between the ribs (thoracentesis). This procedure can make an immediate difference in symptoms or very little difference at all. There is no method for doctors to reliably predict who will benefit most from drainage, with the only option of giving patients a "trial of treatment" As such patients may undergo an unnecessary and invasive procedure which carries substantial risks. There is a need to provide patients with personalised and accurate information to help them to make the right choice as part of a shared decision making process. Use of a physiological biomarker (natural indicator in the body) to determine who will benefit most from an invasive procedure will transform management by preventing unnecessary admissions and procedures in some patients. The aim of this study is to will investigate the mechanics of breathing in patients with pleural effusion. In particular, it will assess the electrical activity of the breathing system during drainage of an effusion as well as the pressure within the pleura, movement of diaphragm (the main breathing muscle).

Who can participate?
Adults with pleural effusion.

What does the study involve?
At the start of the study, all participants complete questionnaires about their breathlessness, a walking test to assess their exercise capacity, and some lung function tests, which involve breathing into a machine. Ultrasound scanning is then used to identify a safe site for inserting needle for draining gluid. A small oesophageal catheter (thin tube) containing the electrodes and pressure balloons is passed through the nose into the stomach. It is the "gold standard"

approach offering the clearest and most accurate data. As well as this, electrode stickers are also placed on the patient's chest, belly and neck muscle which offer a non-invasive way of measuring the electrical activity of the breathing muscles. The patient then undergoes an ultrasound scan of their diaphragm to measure its movement. Pleural pressure is measured with a handheld device called an electronic manometer. The fluid is then drained and at every 200mls, the pleural pressure readings and ultrasound measurements are repeated. 24 hours later, the initial tests are repeated.

What are the possible benefits and risks of participating?
Patients are expected to benefit from an improvement in their symptoms after having the drainage. The tests in this study are widely used and shown to be safe but there are a few small risks. Some patients experience some pain after having the fluid drained when the local anaesthetic (numbing medication) wears off. There is a very small risk of infection both during the procedure and afterwards as well as a small risk of air to leak from the lung (pneumothorax). Some patients may also experience nausea when the thin tube is inserted through the nose into the stomach.

Where is the study run from?
St Thomas' Hospital (UK)

When is the study starting and how long is it expected to run for?
March 2016 to September 2020 (updated 04/02/2021, previously: January 2020)

Who is funding the study?
Rocket Medical PLC (UK)

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
34053

Study information

Scientific Title
A study to investigate the effect of thoracocentesis on neural respiratory drive in pleural effusion

Acronym
SINE

Study objectives
The aim of this study is to test the hypothesis that neural respiratory drive improves following thoracocentesis.

Ethics approval required
Old ethics approval format

Ethics approval(s)
South East Coast - Brighton & Sussex Research Ethics Committee, 28/04/2017, ref: 17/LO/0463

Study design
Non-randomised; Interventional; Design type: Process of Care, Management of Care, Active Monitoring

Primary study design
Interventional

Secondary study design
Non randomised study

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 effusion

Interventions
Potentially eligible patients will be invited by the direct care team to speak to the research team. The research team will provide information about the trial as well as perform an ultrasound evaluation of the chest to ensure no evidence of loculations or contraindications to therapeutic thoracocentesis.

Once eligible participants have signed the consent form, they will have a baseline assessment. This will comprise of measurements of their height, weight as well a number of physiological measurements including heart rate and blood pressure. The depth of effusion on ultrasound as well as diaphragmatic thickness will be measured. They will then be provided with an appointment to have their procedure performed.

On arrival to their appointment for the study, patients will undergo a 6 minute walk test to ascertain exercise tolerance and be asked to complete a breathlessness questionnaire comprising the Multidimensional Dyspnea Profile (MDP) and 100mm Visual Analogue Scale for breathlessness. They will also undergo body plethysmography to determine lung function.

Ultrasound guidance will be used to select the most dependent site in a position anterior to the posterior axillary line. A thoracocentesis catheter will be inserted.

M-mode ultrasonagraphic evaluation of the diaphragm will be performed placing the probe between the midclavicular and anterior axillary lines, in the subcostal area, and directing it medially, cranially, and dorsally, so that the ultrasound beam reaches perpendicularly the posterior third of the hemidiaphragm. If diaphragmatic movement is paradoxical to respiration, this will be recorded as a negative (-) value. Recordings will be taken over three respiratory cycles.

Pleural manometry will be performed. An opening pressure measurement will be measured, recording the end expiratory, end inspiratory pressures. Diaphragmatic EMG and parasternal EMG will be performed. A multipair oesophageal electrode catheter comprising of five pairs of electrodes will be used. This also contains an oesophageal and gastric balloon when attached to a transducer is capable of measuring pressure. The oesophageal electrode will passed through the nose and swallowed into the oesophagus. Following satisfactory oesophageal electrode placement, parasternal, sternocleidomastoid and abdominal EMG electrodes will be applied to the patient. EMG and oesophageal pressures will be acquired during quiet breathing for at least 2 minutes until 1 minute of stable breathing is recorded. Recordings will then be acquired for four inspiratory manoeuvres:

1. Maximal inspiration to total lung capacity
2. Maximal static inspiration at functional residual capacity against a closed valve
3. Maximal sniff from functional residual capacity
4. Maximal voluntary ventilation for 15 seconds (sprint MVV)

Manoeuvres 1-3 will be repeated at least three times until satisfied that a truly maximal effort has been performed. Sprint MVV will only be performed once.

Following this, fluid will be drained in increments of 250ml. After 250mls of fluid has been drained, ultrasound using M-mode will be used to measure diaphragmatic movement. Markers will be placed on the EMG recording software to indicate the timepoints for each 250ml increment. Pleural pressure measurements will also be recorded as above.

The whole process will be repeated at 250ml increments until one of three criteria is met:
1. Effusion fully drained
2. Patient symptomatic with pain, cough or presyncope
3. End-expiratory pleural pressure drops below -20 cmH20 or pleural elastance greater than 19 (pleural elastance is calculated by dividing the change in pleural pressure by the volume (in litres) removed)

Criteria b) and c) are included to ensure the risk of re-expansion pulmonary oedema is minimised

If the effusion is fully drained or patient is symptomatic, final pleural pressure and ultrasound readings will be taken (if feasible in the context of symptoms) prior to pleural catheter removal. Total volume drained will be recorded. The patient will then undergo continuous EMG and oesophageal recording for 10 minutes post procedure during which they will repeat manoeuvres 1-3 outlined above.

The thoracocentesis catheter will be removed and the patient will then be observed clinically for one hour to ensure no complications. They will be encouraged to be mobile. Patients will then undergo body plethysmography and be asked to complete the VAS and MDP breathlessness questionnaires exactly one hour post termination of the procedure.

They will be asked to complete an MDP and VAS score for breathlessness 24 hours post procedure. If the patient is unable to attend this appointment (for medical, personal reasons or if this falls on the weekend) they can complete this at home with the data posted or brought back to the research department. Patients will also be asked to return to hospital for a 6 minute walk test which should be completed 24hrs (+72hrs to account for weekend if required) post procedure. It will be made clear that this test is at the patient's discretion.

If for any reason either EMG placement fails or there is poor diaphragmatic visualisation on ultrasound at the time of procedure patients will still undergo pleural drainage and pleural manometry if they wish to continue. Dyspnoea scores will be recorded.

Intervention Type
Other

Primary outcome measure
Neural respiratory drive is measured by diaphragmatic EMG at baseline, continuously during thoracocentesis and up to 10 minutes post procedure.

Secondary outcome measures
1. Diaphragmatic excursion is measured by M-mode ultrasonography at baseline and every 250mls to the end of thoracocentesis procedure
2. Pleural pressure is measured using pleural manometry at baseline and every 250mls to the end of thoracocentesis procedure
3. Change in breathlessness measured by the Multidimensional Dyspnea Profile and 100mm visual analogue scale (VAS) at baseline, 1 hour post thoracentesis and 24 hours post-thoracentesis

4. Exercise tolerance measured using the 6 minute walk test at baseline and 24 hours post-thoracocentesis

Overall study start date
01/03/2016

Completion date
16/09/2020

Eligibility

Key inclusion criteria
1. Unilateral pleural effusion requiring thoracentesis on clinical grounds
2. Aged 18 years and over

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 10; UK Sample Size: 10

Total final enrolment
8

Key exclusion criteria
1. Age less than 18 years old
2. Any contraindications to thoracocentesis
3. Evidence of loculation on ultrasound
4. Unable to undergo procedure comfortably for up to one hour
5. Allergy to lidocaine
6. Unable to tolerate oesophageal catheter placement
7. Suspected trapped lung based on clinical suspicion
8. Pre-existing lung disease
9. Any previous pleural intervention on ipsilateral side excluding previous thoracocentesis
10. Past medical history of diaphragmatic paralysis

Date of first enrolment
01/06/2017

Date of final enrolment
16/06/2020

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
St Thomas' Hospital
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Sponsor information

Organisation
Guy's And St Thomas' NHS Foundation Trust

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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/00j161312

Funder(s)

Funder type
Industry

Funder Name

Results and Publications

Publication and dissemination plan
Presentation at international conferences as well as planned publication in a high-impact peer reviewed journal within one year of overall trial end date.

Intention to publish date
27/01/2021

Individual participant data (IPD) sharing plan
The current data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Abstract results	This abstract was presented at the 2021 ERS International Congress, in session “Prediction of exacerbations in patients with COPD”.	25/11/2021	15/11/2023	No	No