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Comparison of lower airway sampling strategies in children with protracted bacterial bronchitis

Submission date
03/11/2021

Recruitment status
No longer recruiting

Registration date
08/11/2021

Overall study status
Completed

Last Edited
03/07/2024

Condition category
Respiratory

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Protracted bacterial bronchitis (PBB) is a type of chest infection in young children. It causes a persistent cough which can affect school performance, limit activity and disrupt sleep. It is treated with antibiotics but prolonged and/or multiple courses are often required. Knowing which bug is causing the infection guides antibiotic choice and reduces the risk of antibiotic resistance, but this requires a lower airway sample. Unfortunately, lower airway samples are difficult to collect in children with PBB as they rarely cough up sputum. It is done by taking a washing (bronchoalveolar lavage [BAL]) during a camera test of the lungs (flexible bronchoscopy [FB]). This is invasive and requires a general anaesthetic. Although safe, it is only available at specialist centres and causes significant disruption to families. Therefore, FB-BAL is only used in PBB if the cough does not improve with treatment or frequently relapses. The aim of this study is to find out if two non-invasive methods of obtaining lower airway samples (cough swab and induced sputum) are useful alternatives to FB-BAL. Both are commonly used and usually well tolerated in children with other lung conditions.

Who can participate?
Children aged 1-10 years with PBB referred for a bronchoscopy at five UK hospitals

What does the study involve?
Participating children will have two extra samples taken (a cough swab and an induced sputum sample) when they attend the hospital for their bronchoscopy. The study does not need any extra hospital visits and does not require any blood tests.
The cough swab will be taken by a paediatric (children's) physiotherapist while the child is in the hospital waiting for their bronchoscopy. The child will be asked to tilt their head back and open their mouth wide. A sterile cotton swab will be placed at the back of the throat and the child will be asked to cough. If the child is too young to cough on command, the swab will be gently placed further back in the throat to encourage your child to cough. This should take no more than 2 minutes. This procedure is performed frequently in children with other chest problems and is very well tolerated. After the cough swab has been collected parents will be asked to complete a questionnaire on behalf of their child (with their input if appropriate) to score how tolerable the procedure was. It should not take any more than 5 minutes to complete this.
The induced sputum sample will also be taken by a paediatric (children's) physiotherapist whilst

the child is waiting to have their bronchoscopy. This procedure involves breathing in a saltwater mist (nebulised saline). While this happens, the physiotherapist will perform chest physiotherapy. This involves patting on the chest or breathing into a special device. This will help the child to cough up a sputum sample. If the child is unable to spit it out, a suction tube may be used to collect the sample from the back of the mouth. This procedure should take no more than 20 minutes. This procedure is performed frequently in children with other chest problems and is very well tolerated. Parents will be asked to complete another questionnaire to assess the tolerability of this procedure. This includes the same questions as the cough swab questionnaire and will also take no more than 5 minutes to complete.
FB-BAL is not part of the study as the child would be having this regardless of their participation in the study. All the information about this procedure provided by the hospital should be followed. This includes the fasting instruction and post-procedure care.
Before their child is discharged parents will be asked to complete the FB-BAL tolerability questionnaire (with their child's input if appropriate). Once this final questionnaire has been filled out the child's participation in the study is complete.

What are the possible benefits and risks of participating?
Participants will be contributing to the scientific and medical effort to find a non-invasive, child-friendly alternative to bronchoscopy in children with PBB. This may help improve the treatment provided to children with PBB in the future.
If the researchers find any extra information about the bugs or type of bug in the child's study samples, the doctors will consider this when managing the child's PBB condition. There is no payment for participating in this study.
The researchers have taken care to design this study to reduce the risk to all participants in this study. Although no extra visits are required for this study, the child may be asked to attend the hospital on the day of their bronchoscopy slightly earlier than if they were not part of the study. This will enable the cough swab and induced sputum samples to be collected without affecting the timing of the bronchoscopy. Breathing in the salt mist for the induced sputum sample is likely to cause the child to cough. This helps them produce the sample and settles quickly. It may also cause the child to wheeze. If this happens the child may be treated with some puffs of a blue inhaler. The child may be given some puffs of the blue inhaler before the induced sputum sample is taken if the study team think that this is needed. Completing the three questionnaires will take about 5 minutes each. These can be completed whilst in the hospital and should not delay discharge.

Where is the study run from?
University Hospitals of North Midlands NHS Trust (UK)

When is the study starting and how long is it expected to run for?
March 2021 to July 2024

Who is funding the study?
National Institute for Health Research (NIHR) (UK)

Who is the main contact?
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Contact information

Type(s)

Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
299341

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 50504, IRAS 299341

Study information

Scientific Title
A multi-centre, prospective, cross-sectional cohort study comparing the microbiology yields of cough swab and induced sputum samples with that of bronchoalveolar lavage samples obtained during flexible bronchoscopy, in children with protracted bacterial bronchitis

Acronym
CLASSIC PBB

Study objectives
Is a cough swab or an induced sputum a useful alternative to bronchoalveolar lavage samples obtained during flexible bronchoscopy (FB-BAL) as a method of identifying lower airway pathogens in children with protracted bacterial bronchitis (PBB)?

Primary objectives:
1. To compare pathogen yield in children with PBB between induced sputum and FB-BAL samples
2. To compare pathogen yield in children with PBB between a cough swab and FB-BAL samples

Secondary objectives:
1, To calculate the sensitivity of each sampling technique (cough swab, induced sputum and FB-BAL) to correctly identify all pathogens isolated from the lower airway in children with PBB
2. To report the success rate of obtaining a usable induced sputum sample in children with PBB
3. To report the tolerability of the three sampling techniques (cough swab, induced sputum and FB-BAL) in children with PBB

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 19/10/2021, London - Central Research Ethics Committee (3rd Floor, Barlow House, 4 Minshull Street, Manchester, M1 3DZ, UK; +44 (0)207 104 8225, +44 (0)207 104 8221, +44 (0)207 104 8208; londoncentral.rec@hra.nhs.uk), REC ref: 21/LO/0689

Study design
Non-randomized; Both; Design type: Diagnosis, Other, Cross-sectional

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 to request a participant information sheet

Health condition(s) or problem(s) studied
Protracted bacterial bronchitis

Interventions
Participants will have two extra samples taken (a cough swab and an induced sputum sample) when they attend the hospital for their bronchoscopy.
The study does not need any extra hospital visits and does not require any blood tests. A participant's in the study can be broken up into the following stages:

1. Screening and Consent:
The participant's consultant or a member of the study team will talk to the parent/guardian /child about the study, answer any questions and confirm if the child is eligible to take part. If the parent/guardian/child would like to take part they will be asked to sign a form to confirm

this (written consent). This can be done while they are in clinic or when they come to hospital for the child's bronchoscopy if more time is needed to think about it. This would give them the opportunity to talk to their friends, family, and General Practitioner (GP) if they wish. If appropriate, the child will also be given the opportunity to sign a form to say they would like to take part (written assent). Once written consent is given the study team will collect some brief background information required for the study about the child. This may include date of birth, weight, height, duration of cough and details of recent antibiotic use.

2. Cough Swab Sample:
The cough swab will be taken by a Paediatric (Children's) Physiotherapist while the child is in the hospital waiting for their bronchoscopy. The child will be asked to tilt their head back and open their mouth wide. A sterile cotton swab will be placed at the back of the throat and the child will be asked to cough. If the child is too young to cough on command, the swab will be gently placed further back in the throat encourage the child to cough. This should take no more than 2 minutes. This procedure is performed frequently in children with other chest problems and is very well tolerated. After the cough swab has been collected the parent/guardian will be asked to complete a questionnaire on behalf of their child (with their input if appropriate) to score how tolerable the procedure was. It should not take any more than 5 minutes to complete this.

3. Induced Sputum Sample:
The induced sputum sample will also be taken by a Paediatric (Children's) Physiotherapist whilst the child is waiting to have their bronchoscopy. This procedure involves breathing in a saltwater mist (nebulised saline). While this happens, the Physiotherapist will perform chest physiotherapy. This involves patting on the chest or breathing into a special device. This will help the child to cough up a sputum sample. If the child is unable to spit it out, a suction tube may be used to collect the sample from the back of the mouth. This procedure should take no more than 20 minutes. This procedure is performed frequently in children with other chest problems and is very well tolerated. The parent/guardian will be asked to complete another questionnaire to assess the tolerability of this procedure. This includes the same questions as the cough swab questionnaire and will also take no more than 5 minutes to complete.

4. FB-BAL:
This procedure is not part of the study as the child would be having this regardless of their participation in the study. All the information about this procedure provided by the hospital should be followed. This includes the fasting instruction and post-procedure care. Before the child is discharged the parent/guardian will be asked to complete the FB-BAL tolerability questionnaire (with your child's input if appropriate). Once this final questionnaire has been filled out the child's participation in the study is complete.

All samples will be processed locally as per local policies and procedures. The remaining induced sputum and FB-BAL samples will be anonymised and sent to the UoB for additional research purposes (UHNM site only and if the parent/guardian has consented to this). There is no follow-up in this study.

Intervention Type
Other

Primary outcome measure
1. Discordance of pathogen yield between induced sputum and FB-BAL approximately 48-72 hours post-procedure. If the same organisms are not identified in both samples the pathogen yield is discordant. Discordance will be classified as CS+/FB-BAL- when an organism is isolated on

cough swab but not on FB-BAL or CS-/FB-BAL+ when an organism is isolated on the FB-BAL but not on the cough swab.
2. Discordance of pathogen yield between cough swab and FB-BAL approximately 48-72 hours post-procedure. If the same organisms are not identified in both samples the pathogen yield is discordant. Discordance will be classified as IS+/FB-BAL- when an organism is isolated on induced sputum but not on FB-BAL or IS-/FB-BAL+ when an organism is isolated on FB-BAL but not on induced sputum.

Secondary outcome measures
1. The sensitivity of each sampling technique calculated from triplicate (CS/is/BAL) culture results approximately 48-72 hours post-procedure.
2. Success of sputum induction collected via the case report form (CRF) on the day of sample collection
3. Tolerability of sampling techniques using Tolerability Questionnaire on the day of sample collection

Overall study start date
22/03/2021

Completion date
30/07/2024

Eligibility

Key inclusion criteria
1. Aged 1-10 years
2. Have a clinical diagnosis of PBB
3. Referred for a clinically indicated FB-BAL
4. Parent/guardian willing and able to give fully informed consent
5. Willing and able to comply with the study procedures

Participant type(s)
Patient

Age group
Child

Lower age limit
1 Years

Upper age limit
10 Years

Sex
Both

Target number of participants
Planned Sample Size: 131; UK Sample Size: 131

Total final enrolment

137

Key exclusion criteria
1. Diagnosis of bronchiectasis, cystic fibrosis or immunodeficiency
2. FB-BAL being performed for a therapeutic indication (i.e. lobar collapse) rather than for lower airway
3. Currently taking part in another interventional study
4. Non-English speaker where translation facilities are insufficient to guarantee informed consent

Date of first enrolment
29/10/2021

Date of final enrolment
31/03/2023

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Freeman Hospital
Freeman Road
High Heaton
Newcastle upon Tyne
United Kingdom
NE7 7DN

Study participating centre
Royal Stoke University Hospital
Newcastle Road
Stoke-On-Trent
United Kingdom
ST4 6QG

Study participating centre
Sheffield Children's Hospital
Western Bank
Sheffield
United Kingdom
S10 2TH

Study participating centre
Manchester Royal Infirmary
Oxford Road
Manchester
United Kingdom
M13 9WL

Study participating centre
Alder Hey Hospital
Eaton Road
West Derby
Liverpool
United Kingdom
L12 2AP

Sponsor information

Organisation
University Hospitals of North Midlands NHS Trust

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Research and Innovation Directorate, Courtyard Annexe – C Block
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Sponsor type
Hospital/treatment centre

Website
http://www.uhnm.nhs.uk/Pages/Home.aspx

ROR
https://ror.org/03g47g866

Funder(s)

Funder type

Government

Funder Name
NIHR Central Commissioning Facility (CCF); Grant Codes: NIHR202272

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal

Intention to publish date
31/12/2024

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication

IPD sharing plan summary
Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		01/11/2022	17/01/2023	Yes	No
HRA research summary			28/06/2023	No	No