ISRCTN11746266 https://doi.org/10.1186/ISRCTN11746266

The bronchiolitis endotracheal surfactant study

Submission date 24/09/2018	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [X] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 01/10/2018	**Overall study status** Ongoing	
Last Edited 02/01/2026	**Condition category** Respiratory	

Plain English summary of protocol

Background and study aims
Bronchiolitis is a winter viral chest infection that causes breathing difficulties in babies. It is the single most common reason for hospital admission of babies in the UK. Over 25,000 babies are admitted to hospital in England each year. There is no vaccine or specific treatment. Breathing fails in very severe cases, and these babies need intensive care to go on a breathing machine called a mechanical ventilator. Surfactant is in the liquid produced in healthy lungs that allows the lungs to inflate more easily. Surfactant therapy is safe and established for use in premature babies for over 30 years. The aim of this study is to find out whether surfactant reduces the time critically ill babies with bronchiolitis spend on a mechanical ventilator.

Who can participate?
Babies aged under 6 months with bronchiolitis

What does the study involve?
Babies are randomly allocated to either be treated with surfactant or undergo a dummy procedure. Tests are carried out to measure how much surfactant the babies are making, how much of the surfactant given stays in the lungs, which virus and bacteria are infecting the airways and how much inflammation is in the airways. Babies that have severe bronchiolitis often have more episodes of chestiness and wheeze in the months after their illness than those that do not have bronchiolitis. It is possible that the surfactant given in this study may help reduce these symptoms. Parents are asked to complete a questionnaire at 6 and 12 months after their baby goes home to tell us about any breathing symptoms they notice in their baby.

What are the possible benefits and risks of participating?
Surfactant has been used in preterm babies for over 30 years and is a safe treatment for breathing problems caused by prematurity. There is some information suggesting that surfactant might help babies with bronchiolitis, but not enough evidence to give doctors confidence that it should be used routinely. Some doctors do use surfactant when treating babies in intensive care with bronchiolitis, but others don’t. It is not known how well surfactant works in these babies, which is why this study is needed. A potential benefit of this treatment might be a reduced period of time spent on the mechanical ventilator, which could reduce the risk of complications associated with being on the mechanical ventilator and in intensive care. Before surfactant or air is given, the baby will have a respiratory toilet to reduce the risk of thick secretions blocking the tube into the baby’s lungs. Even with the respiratory toilet, there are

some temporary side effects that often occur in the first few minutes after surfactant is given, such as a slowed heart rate (bradycardia), low blood pressure (hypotension), or a drop in blood oxygen level (desaturation). These problems are commonly seen in babies in intensive care with bronchiolitis who are not given surfactant just because they are so unwell. The hospital team caring for your baby will look out for these problems and will make sure the baby gets extra support if needed. The results from the study will help doctors and nurses in the future decide whether they should or should not treat babies with bronchiolitis with surfactant.

Where is the study run from?
University of Liverpool (UK)

When is the study starting and how long is it expected to run for?
April 2018 to September 2026

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

Who is the main contact?
Laura Price
bess@liverpool.ac.uk

Contact information

Type(s)
Scientific

Contact name
Mrs Laura Price

Contact details
Liverpool Clinical Trials Centre
University of Liverpool
Block C, Waterhouse Building
Brownlow Street
Liverpool
United Kingdom
L69 3GL
+44 (0)151 795 8757
bess@liverpool.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
2018-001169-18

Integrated Research Application System (IRAS)
220853

Protocol serial number
39520

Study information

Scientific Title
The efficacy and mechanism of surfactant therapy for critically ill infants with bronchiolitis: the Bronchiolitis Endotracheal Surfactant Study (BESS)

Acronym
BESS

Study objectives
The aim of this study is to find out if surfactant reduces the time critically ill babies with bronchiolitis spend on a mechanical ventilator.

Ethics approval required
Old ethics approval format

Ethics approval(s)
South Central – Berkshire REC, 08/10/2018, ref: 18/SC/0427

Study design
Randomized; Interventional; Design type: Treatment, Drug

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Mechanical ventilation in infants with bronchiolitis

Interventions
Current interventions as of 25/03/2024:

All potential patients (infants) admitted to participating PICUs receiving mechanical ventilation to help treat severe bronchiolitis will be screened for eligibility. Screening and full eligibility assessment will be completed so that patients can be randomised within 48 hours of intubation. Patients will be reviewed for eligibility once they have been intubated for MV, or as soon as they arrive to a PICU if they already intubated.

The study concept will be introduced to the parent (or person with parental responsibility) by members of the usual care team who will make a further introduction to members of the research team if appropriate. The infant may only be enrolled into the trial once eligibility has been confirmed by a medically qualified doctor and the parent has provided legal written informed consent on the trial-specific REC approved consent form.
Parents of potential participants will be offered the opportunity to take part in a study of parent experiences of consent and participation, and may take part in this aspect even if they decline participation in the main trial.

Participants will be randomised to either treatment with surfactant (poractant alfa) or air (placebo) in a 1:1 ratio. Patients, their parents and their usual care team will be blinded to the treatment allocation where possible.

Participants will be randomised locally using a secure web-based randomisation system; a unique study number and treatment allocation will be generated for each patient. The randomising staff member will be able to select the patient weight category so the system can allocate the required number of vials to the patient. Participants will be randomised equally to receive either endotracheal poractant alfa or air in a sham procedure. Patients randomised to receive endotracheal poractant alfa will receive a first dose of 200 mg/kg, and if still intubated this will be repeated 12 hourly at 100 mg/kg, to a total of 3 doses. This is in line with the manufacturer's summary of product characteristics (SPC). Patients randomised to the placebo will receive an identical series of three procedures (while intubated) using air as the placebo. 200 mg/kg is 200 milligrams of poractant alfa per kilogram of body weight. 100 mg/kg is 100 milligrams of poractant alfa per kilogram of body weight. The participant's weight will be detailed on the prescription in kilograms and the prescribing clinician will calculate the appropriate dose for the participant.

Prior to administration of any intervention, infants in both the treatment and placebo arms of the trial will have 0.9% sodium chloride "normal saline" tracheal toilet immediately prior to administration of the intervention. This can cause immediate transient desaturation, need for increased sedation but also and more often rapid improvement in gas exchange when obstructing secretions are removed. Tracheal toilet can also lead to creamy secretions appearing in the endotracheal tube, and this will be observed in both treatment and placebo groups.

Tracheal toilet is usually required for babies with bronchiolitis and will be done as recommended in the Summary of Product Characteristics (SPC) before administration of poractant alfa. Tracheal toilet is done by catheter access to the trachea by one of two methods (at the attending Respiratory Physiotherapist's decision based on patient status) either; A) via the endotracheal suction port without disconnecting the infant from the ventilator or B) by disconnecting the infant from the ventilator and performing hand-bagging while a catheter is placed into the trachea via a side-port with one-way valve.

The intervention will be given per either method described in the SPC; either keeping the infant connected to the ventilator or momentarily disconnecting and performing hand-bagging (at the attending Respiratory Physiotherapist's decision based on patient status). The intervention will be delivered as a single slow bolus over 0.5-3 minutes directly into the lower trachea and will be dispersed through ventilation breaths.

Participants will be assessed for any safety issues until 24 hours after their last trial intervention (including placebo)is given, various other items of data will be collected and blood gas samples will be taken. At 12 hours, the intervention will be administered again (unless the infant does not require further mechanical ventilation) and more blood gas samples will be taken and data collected. At 24 hours the process will be repeated again (unless the infant does not require further mechanical ventilation). Thus safety assessment will be conducted throughout the intervention period. Blood gas sampling and data collection will be conducted daily until the patient is extubated. Some of these procedures are done as part of routine care.

To minimise disturbance of the babies and minimise blood sampling, our sampling schedule and training will emphasise the use of data from routinely collected blood gas samples when these have been or are planned to be taken within an acceptable window of the intended sample time.

The unblinded staff involved in the administration of the BESS intervention (study respiratory physiotherapist or nurse practitioner or other qualified person and one usual care PICU nurse) and parents who may be observing, will not be involved in decisions to wean respiratory support provided by mechanical ventilation and will not be involved in decisions to extubate.

The trialists will wean respiratory support provided by mechanical ventilation and extubate according to a standardised protocol that will form part of the site-specific training packages.

Readiness for a spontaneous breathing test (SBT) will be identified by the patient meeting specified physiological targets of gas exchange at a given level of ventilation and/or the treating clinician believes the child to be ready for SBT.

The time at which a child is deemed ready for SBT must be recorded in their notes/electronic health record. The time that a child is extubated must be recorded in their notes/electronic health record.

Clinical follow-up (daily data collection) will take place for the period of time between randomisation and the discharge from hospital of the patient.
All adverse events will be collected until 24 hours after the patient receives their final trial intervention; please note that this may not be their third dose if less than 3 doses are required before the patient meets the criteria to be ready for weaning (see section 10 for full safety reporting information).

Adverse events occurring after 24 hours post-final intervention but before 90 days post-randomisation/discharge home/death should be reported if the local Investigator believes that they may be related to the intervention. Any serious events identified at any time will be reported.

———

Previous interventions:

All potential patients (infants) admitted to participating PICUs receiving mechanical ventilation to help treat severe bronchiolitis will be screened for eligibility. Screening and full eligibility assessment will be completed so that patients can be randomised within 48 hours of intubation. Patients will be reviewed for eligibility once they have been intubated for MV, or as soon as they arrive to a PICU if they already intubated.

The study concept will be introduced to the parent (or person with parental responsibility) by members of the usual care team who will make a further introduction to members of the research team if appropriate. The infant may only be enrolled into the trial once eligibility has been confirmed by a medically qualified doctor and the parent has provided legal written informed consent on the trial-specific REC approved consent form.
Parents of potential participants will be offered the opportunity to take part in a study of parent experiences of consent and participation, and may take part in this aspect even if they decline participation in the main trial.

Participants will be randomised to either treatment with surfactant (poractant alfa) or air (placebo) in a 1:1 ratio. Patients, their parents and their usual care team will be blinded to the treatment allocation where possible.

Participants will be randomised locally using a secure web-based randomisation system; a unique study number and treatment allocation will be generated for each patient. The randomising staff member will be able to select the patient weight category so the system can allocate the required number of vials to the patient. Participants will be randomised equally to receive either endotracheal poractant alfa or air in a sham procedure. Patients randomised to receive endotracheal poractant alfa will receive a first dose of 200 mg/kg, and if still intubated this will be repeated 12 hourly at 100 mg/kg, to a total of 3 doses. This is in line with the manufacturer's summary of product characteristics (SPC). Patients randomised to the placebo will receive an identical series of three procedures (while intubated) using air as the placebo. 200 mg/kg is 200 milligrams of poractant alfa per kilogram of body weight. 100 mg/kg is 100 milligrams of poractant alfa per kilogram of body weight. The participant's weight will be detailed on the prescription in kilograms and the prescribing clinician will calculate the appropriate dose for the participant.

Prior to administration of any intervention, infants in both the treatment and placebo arms of the trial will have 0.9% sodium chloride "normal saline" tracheal toilet and 0.9% sodium chloride bronchoalveolar lavage (BAL) immediately prior to administration of the intervention. Both can cause immediate transient desaturation, need for increased sedation but also and more often rapid improvement in gas exchange when obstructing secretions are removed. Tracheal toilet and BAL can also lead to creamy secretions appearing in the endotracheal tube, and this will be observed in both treatment and placebo groups.

Tracheal toilet is usually required for babies with bronchiolitis and will be done as recommended in the Summary of Product Characteristics (SPC) before administration of poractant alfa. BAL sampling with 0.9% sodium chloride (2x1mL/kg) will be done if scheduled for research purposes. Both tracheal toilet and BAL sampling is done by catheter access to the trachea by one of two methods (at the attending Respiratory Physiotherapist's decision based on patient status) either; A) via the endotracheal suction port without disconnecting the infant from the ventilator or B) by disconnecting the infant from the ventilator and performing hand-bagging while a catheter is placed into the trachea via a side-port with one-way valve.

The intervention will be given per either method described in the SPC; either keeping the infant connected to the ventilator or momentarily disconnecting and performing hand-bagging (at the attending Respiratory Physiotherapist's decision based on patient status). The intervention will be delivered as a single slow bolus over 0.5-3 minutes directly into the lower trachea and will be dispersed through ventilation breaths.

Participants will be assessed for any safety issues until 24 hours after their last trial intervention (including placebo)is given, various other items of data will be collected and blood gas samples will be taken. At 12 hours, the intervention will be administered again (unless the infant does not require further mechanical ventilation) and more blood gas samples will be taken and data collected. At 24 hours the process will be repeated again (unless the infant does not require further mechanical ventilation). Thus safety assessment will be conducted throughout the intervention period. Blood gas sampling, data collection and BAL will be conducted daily until the patient is extubated. Some of these procedures are done as part of routine care.

To minimise disturbance of the babies and minimise blood sampling, our sampling schedule and training will emphasise the use of data from routinely collected blood gas samples when these have been or are planned to be taken within an acceptable window of the intended sample time.

The unblinded staff involved in the administration of the BESS intervention (study respiratory physiotherapist or nurse practitioner or other qualified person and one usual care PICU nurse)

and parents who may be observing, will not be involved in decisions to wean respiratory support provided by mechanical ventilation and will not be involved in decisions to extubate.

The trialists will wean respiratory support provided by mechanical ventilation and extubate according to a standardised protocol that will form part of the site-specific training packages.

Readiness for a spontaneous breathing test (SBT) will be identified by the patient meeting specified physiological targets of gas exchange at a given level of ventilation and/or the treating clinician believes the child to be ready for SBT.

The time at which a child is deemed ready for SBT must be recorded in their notes/electronic health record. The time that a child is extubated must be recorded in their notes/electronic health record.

Clinical follow-up (daily data collection) will take place for the period of time between randomisation and the discharge from hospital of the patient.
All adverse events will be collected until 24 hours after the patient receives their final trial intervention; please note that this may not be their third dose if less than 3 doses are required before the patient meets the criteria to be ready for weaning (see section 10 for full safety reporting information).

Adverse events occurring after 24 hours post-final intervention but before 90 days post-randomisation/discharge home/death should be reported if the local Investigator believes that they may be related to the intervention. Any serious events identified at any time will be reported.

At two sites, Liverpool & Southampton, in addition to the Trial and Parent experience work packages, and then only with written informed consent, infants will receive a single intravenous injection of labelled Choline and additional, BAL and small volume blood samples. This will allow translational exploratory work on surfactant synthesis. Choline is natural part of Vitamin B. The labelling process used the naturally occurring safe stable (non-radioactive) isotope of Hydrogen.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Poractant alfa

Primary outcome(s)
Total duration of Mechanical Ventilation (MV), in hours, from randomisation to final extubation. This will include time off MV due to failed extubation.

Key secondary outcome(s))
1. Duration of post-extubation non-invasive respiratory support (all forms of non-invasive ventilation: e.g. nasal CPAP and nasal high low oxygen)
2. Duration of oxygen supplementation
3. Number of trial interventions given (both poractant and placebo)
4. Use of steroids to assist extubation (at final extubation – yes or no to whether steroids were

used)
5. Duration of stay on PICU and in hospital
6. Change over time from baseline of Ventilation Index (VI), Oxygenation Index (OI) and Oxygenation Saturation Index (OSI) while mechanically ventilated, & SpO2/FiO2 (SF) ratio
7. The score (value) of parent reported outcome measure of respiratory symptoms the Liverpool Respiratory Symptom Questionnaire (LRSQ) at 6 months (+/-1 months) and 12 months (+/-1 month)
8. Time from randomisation to meeting study criteria for readiness for Spontaneous Breathing Test
9. Failure to administer the intervention due to any adverse event during preparatory processes (tracheal toilet or BAL)
10. Failure to complete administration of the intervention due to any adverse event during administration of the intervention (regardless of which arm of allocation)
11. Incidents of 'air leak' (pneumothorax and pneumomediastinum) occurring before discharge from PICU (number of incidents)
12. Other adverse events and serious adverse events associated with the intervention
13. Any need to replace the endotracheal tube
14. Parent reported readmission to hospital (all causes) up to 90 days post randomisation
15. Death during PICU admission
16. All-cause mortality at 90 days post randomisation

Completion date
30/09/2026

Eligibility

Key inclusion criteria
1. Term-born infants < 26 weeks old and preterm-born infants < 26 weeks corrected age†
2. Diagnosis of bronchiolitis (see below)
3. Requires conventional invasive MV via tracheal intubation
4. Parent or person with parental responsibility has given written informed consent for trial participation
†Premature born infants have their age corrected to account for weeks of lost gestation

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
0 weeks

Upper age limit
26 weeks

Sex

All

Total final enrolment
232

Key exclusion criteria
1. Major congenital anomalies, including complex or haemodynamically compromising cardiac anomalies.
2. Congenital neuromuscular disease
3. Already intubated for MV for > 48 hours or likely to have been intubated for MV for > 48 hours by randomisation
4. Have received or are receiving extracorporeal membrane oxygenation (ECMO) or oscillation during this episode of bronchiolitis
5. Have received or are receiving intratracheal administration of any surfactant during this episode of bronchiolitis
6. Receiving MV for primary apnoea rather than respiratory failure
7. A decision to wean to extubation has already been made
8. Clinical judgement of futility

Date of first enrolment
01/11/2018

Date of final enrolment
31/03/2024

Locations

Countries of recruitment
United Kingdom

England

Northern Ireland

Scotland

Study participating centre
Alder Hey Children’s Hospital
Eaton Road
Liverpool
England
L12 2AP

Study participating centre
Southampton Children's Hospital
Southampton General Hospital
Tremona Road

Southampton
England
SO16 6YD

Study participating centre
Royal Hospital for Sick Children
9 Sciennes Road
Edinburgh
Scotland
EH9 1LF

Study participating centre
Royal Hospital for Children,
1345 Govan Road
Govan
Glasgow
Scotland
G51 4TF

Study participating centre
The Royal Belfast Hospital for Sick Children
274 Grosvenor Road
Belfast
Northern Ireland
BT12 6BA

Study participating centre
Great North Children's Hospital
Victoria Wing
Royal Victoria Infirmary
Newcastle upon Tyne
England
NE1 4LP

Study participating centre
Royal Manchester Children's Hospital
Oxford Rd
Manchester
England
M13 9WL

Study participating centre
Leeds Children's Hospital
Clarendon Wing
Leeds General Infirmary
Leeds
England
LS1 3EX

Study participating centre
Royal Stoke University Hospital
Newcastle Rd
Stoke-on-Trent
England
ST4 6QG

Study participating centre
Birmingham Children's Hospital
Steelhouse Ln
Birmingham
England
B4 6NH

Study participating centre
Bristol Royal Hospital for Children
Upper Maudlin St
Bristol
England
BS2 8BJ

Study participating centre
Royal London Hospital
Whitechapel Rd
Whitechapel
London
England
E1 1BB

Study participating centre

John Radcliffe Hospital
Headley Way
Headington
Oxford
England
OX3 9DU

Study participating centre
Nottingham University Hospitals NHS Trust - Queen's Medical Centre Campus
Nottingham University Hospital
Derby Road
Nottingham
England
NG7 2UH

Study participating centre
Leicester Royal Infirmary Laboratory
Leicester Royal Infirmary
Infirmary Square
Leicester
England
LE1 5WW

Sponsor information

Organisation
University of Liverpool

ROR
https://ror.org/04xs57h96

Funder(s)

Funder type
Government

Funder Name
NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC); Grant Codes: 15/21/01

Results and Publications

Individual participant data (IPD) sharing plan

Data sharing will be considered by the Trial Management Group on application after the publication of the final report and not before June 2024.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			20/09/2023	No	No
Other publications	A mixed-method embedded study	02/01/2024	04/01/2024	Yes	No
Participant information sheet	version 5.0	02/02/2023	13/05/2025	No	Yes
Protocol file	version 6.0	09/10/2023	25/03/2024	No	No
Protocol file	version 7.0	19/03/2025	13/05/2025	No	No
Statistical Analysis Plan	version 2.0	16/04/2024	23/04/2024	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes