ISRCTN15513131 https://doi.org/10.1186/ISRCTN15513131

Optimising salbutamol dose for wheezy preschool children

Submission date 08/04/2015	**Recruitment status** No longer recruiting	[_] Prospectively registered [X] Protocol
Registration date 08/04/2015	**Overall study status** Completed	[_] Statistical analysis plan [X] Results
Last Edited 03/09/2021	**Condition category** Respiratory	[_] Individual participant data

Plain English summary of protocol

Background and study aims
Wheezing is a whistling sound caused by breathing through narrowed airways. It is a common problem in young children. Many preschool children have repeated wheezy episodes, and share characteristics with older children who have asthma. Like them, they are often treated with inhaled salbutamol. However, in the preschool years it is difficult to make a definite diagnosis of asthma, and there is much less consensus about treatment. The correct dose of inhaled salbutamol has been determined in adults and older children by studying their response to a range of doses. This has not been possible in children below 7 years of age who are unable to cooperate with the tests. Doctors commonly ask parents to use any dose between 200 to 1000 micrograms of salbutamol to help their child's wheezy spells. Recently, however, a lung function test that could be used for this purpose has been validated in young children. This study proposes to use this test (Rint) to find the correct dose range that produces an adequate response in most young children. Recent work also suggests that even large doses of salbutamol may not be effective in relieving symptoms in some children. We will define the extent of this problem, as there are alternative 'relievers' that could then be used to help these children. We will also explore whether a simple genetic test that could predict this lack of response.

Who can participate?
Children aged 2 years 6 months to 6 years 11 months, with recurrent wheeze (at least 3 episodes of wheezing over the previous 12 months)

What does the study involve?
Participants are randomly allocated to inhale one of four different doses of salbutamol. Lung function is tested before and 20 minutes after inhaling salbutamol. Saliva and urine samples are also collected. The one-off study visit lasts for around two and half hours and there is no follow up.

What are the possible benefits and risks of participating?
Involvement in the study and the resulting discussions may provide the parent/carer and child with a greater understanding of the processes causing wheeze. This study does not have any risk of physical or psychological harm, and there are no painful procedures. Some young children are bothered by the clicking sounds during the breathing test, so we spend a little time beforehand

getting them used to the equipment. The researchers work with the parents to distract them during the measurements. The collection of the urine and saliva samples does not involve any risks to the child. Travel expenses to the hospital (up to £20) for the research study visit can be reimbursed.

Where is the study run from?
Royal Sussex County Hospital (UK)

When is the study starting and how long is it expected to run for?
January 2014 to June 2017

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

Who is the main contact?
Dr Akshat Kapur, akshat.kapur@nhs.net

Contact information

Type(s)
Scientific

Contact name
Prof Somnath Mukhopadhyay

Contact details
Academic Department of Paediatrics
Royal Alexandra Children's Hospital
Level 6, Room 601, Eastern Road
Brighton
United Kingdom
BN2 5BE
+44 (0)1273 696955 x62409
S.Mukhopadhyay@bsms.ac.uk

Type(s)
Public

Contact name
Dr Akshat Kapur

Contact details
University Hospitals Sussex NHS Foundation Trust
Kemptown
Brighton
United Kingdom
BN2 1DH
+44 (0)1273 641469
akshat.kapur@nhs.net

Type(s)

Scientific

Contact name
Prof Somnath Mukhopadhyay

Contact details
Academic Department of Paediatrics
Royal Alexandra Children's Hospital
Level 6, Room 601
Eastern Road
Brighton
United Kingdom
BN2 5BE
+44 (0)1273 696955 (x62397)
somnath.mukhopadhyay@nhs.net

Additional identifiers

EudraCT/CTIS number
2014-001978-33

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
16931

Study information

Scientific Title
How can we optimise inhaled beta2 agonist dose as 'reliever' medicine for wheezy preschool children?

Acronym
OpSal

Study objectives
The study will help develop the evidence for the correct dose of salbutamol in younger children with recurrent wheeze who have been prescribed salbutamol by their doctor. It is possible that a small dose of salbutamol, such as 2 puffs (200 µg) is adequate for most of these children. If this is the case, larger doses such as 1000 µg, should not be prescribed (as is current practice) as they may be inducing side-effects in these children. Secondly, some younger children who currently prescribed larger doses of salbutamol may in fact be 'poor‘ or 'non-responders' to salbutamol due to their genetic constitution. Such children may benefit from alternative 'reliever' medicines, such as ipratropium or montelukast. We intend to investigate whether an effective marker can be identified for poor salbutamol efficacy in these younger children.

Ethics approval required
Old ethics approval format

Ethics approval(s)
East of Scotland Research Ethics Service REC 2 , 21/07/2014, ref: 14/ES/0072

Study design
Randomised; Interventional; Design type: Treatment

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 contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Topic: Children; Subtopic: All Diagnoses; Disease: All Diseases

Interventions
1. Collection of DNA sample using non-invasive Oragene DNA Collection kits
2. Collection of urine sample after each of the two doses of salbutamol will be attempted
3. Data Collection
4. Rint Measurements: At baseline and 20 minutes after each of the two doses of salbutamol
5. Salbutamol Doses: No control group. Participants are randomised to 1 of 4 dosage schedules:
5.1. 100 µg Salbutamol +300 µg = 400 µg Salbutamol
5.2. 100 µg Salbutamol +500 µg = 600 µg Salbutamol
5.3. 200 µg Salbutamol +600 µg = 800 µg Salbutamol
5.4. 200 µg Salbutamol +200 µg = 400 µg Salbutamol
The one off study visit lasts for around two and half hours. No follow up.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Salbutamol

Primary outcome measure
Bronchodilator response to salbutamol using lung function test (interrupter resistance Rint) at baseline and 30 minutes after each dose of salbutamol.

Secondary outcome measures

N/A

Overall study start date
01/01/2014

Completion date
30/06/2019

Eligibility

Key inclusion criteria
1. Age 2 years 6 months to 6 years 11 months
2. Recurrent wheeze, defined as at least 3 episodes of wheeze over the previous 12 months by the parent

Participant type(s)
Patient

Age group
Child

Lower age limit
2 Years

Upper age limit
6 Years

Sex
Both

Target number of participants
Planned Sample Size: 155; UK Sample Size: 155

Total final enrolment
84

Key exclusion criteria
1. Other major airway or lung disease, e.g. chronic lung disease of prematurity, cystic fibrosis, and abnormal airway anatomy
2. Recent (within 2 weeks) treatment with systemic corticosteroids or leukotriene inhibitors
3. Participants involved in other research currently or recently

Date of first enrolment
15/12/2014

Date of final enrolment
30/06/2017

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Royal Sussex County Hospital
Clinical Investigation and Research Unit, Eastern Road
Brighton
United Kingdom
BN2 5BE

Sponsor information

Organisation
Brighton and Sussex University Hospitals NHS Trust

Sponsor details
Royal Sussex County Hospital
Eastern Road
Brighton
England
United Kingdom
BN2 5BE

Sponsor type
Hospital/treatment centre

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
A research summary will be provided to participants if they request to be made aware of this. Trial results will be communicated to healthcare professionals, the public and other relevant groups at conferences, press releases, through published papers and via parent groups. The full protocol will be published on the online journal www.trialsjournal.com.

Intention to publish date
31/12/2022

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	11/11/2016		Yes	No
Basic results			09/06/2021	No	No
Basic results		09/06/2021	19/07/2021	No	No
HRA research summary			28/06/2023	No	No