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Laminar airflow in severe asthma for exacerbation reduction

Submission date 15/01/2014	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 22/01/2014	**Overall study status** Completed	
Last Edited 09/08/2019	**Condition category** Respiratory	

Plain English summary of protocol

Background and study aims
Acute attacks of asthma (asthma exacerbations) are common and cause a great deal of suffering in asthmatic patients. Current treatments for asthma are not completely effective and new and better treatments are needed. We would like to test whether a new device that reduces the number of allergy particles in the air (which are known to cause asthma) can help reduce these asthma attacks and improve asthma patients' quality of life. The device is known as a Temperature Controlled Laminar Airflow (TLA) device or Airsonett® device. The TLA device is installed in the participant's bedroom and will automatically switch on each night. The machine filters the air, removing allergy particles from the patient's breathing zone to allow the lungs to 'rest' overnight.

Who can participate?
Adults (aged 18-75) with severe, poorly-controlled asthma will be approached to take part in the study.

What does the study involve?
Initially participants will be invited to attend information events to hear what is involved with the study. Thereafter if participants are willing to take part they will be invited to attend a screening visit where various tests will be performed, including breathing, blood tests, allergy testing as well as completing several questionnaires. Half of the participants will be given a TLA machine that is working, and the other half will be given a machine which has been inactivated (the filtering process will be switched off, although the participants will not be able to tell that this has occurred). Which participant receives the working or deactivated machine will be decided by a random process and will be unknown to the researcher and the participant. An engineering team from the manufacturer will install the machine in the participants home at the beginning of the study and will be available throughout the study period to deal with any queries. Participants will be in the study for 12 months, and will be asked to report their asthma attacks to the study team whenever they occur, in addition to visiting the study team 4 times over the 12 months to assess their asthma control and quality of life. At the end of the study all participants, regardless of their initial study group, will be offered the opportunity to keep a working machine in their home free of charge for a further four years.

What are the possible benefits and risks of participating?
By performing this study it is hoped it will improve the treatment of asthma in the future. There are no known risks associated with this treatment.

Where is the study run from?
The study is currently being running the following sites in the UK: Southampton General Hospital, Glenfield Hospital, Heartlands Hospital, Bradford Hospital, St Georges, Churchill Hospital, Maidstone Hospital, Queen Elizabeth, Birmingham, Belfast City Hospital, Chester Hospital, Aintree, Liverpool, Royal Liverpool Hospital, Castle Hill Hospital, Queen Alexandra Hospital.

When is the study starting and how long is it expected to run for?
December 2013 - July 2018

Who is funding the study?
The study is being funded by the National Institute for Health Research (NIHR), (UK).

Who is the main contact?
Dr Will Storrar
William.storrar@porthosp.nhs.uk

Study website
http://www.asthma-treatment.org.uk/

Contact information

Type(s)
Scientific

Contact name
Prof Anoop Chauhan

Contact details
Queen Alexandra Hospital
Cosham
Hants
United Kingdom
PO6 3LY
-
anoop.chauhan@porthosp.nhs.uk

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number
NCT03058497

Secondary identifying numbers
HTA 12/33/28

Study information

Scientific Title
A multi-centre randomised, double-blind, placebo-controlled, parallel-group trial of the effectiveness of the nocturnal use of a Temperature Controlled Laminar Airflow (TLA) Device (Airsonett®) in adults with poorly-controlled, severe allergic asthma

Acronym
LASER

Study objectives
To determine whether nocturnal TLA treatment reduces the frequency of severe asthma exacerbations (defined as an acute deterioration in asthma requiring treatment with systemic corticosteroids).

More details can be found at: http://www.nets.nihr.ac.uk/projects/hta/123328
Protocol can be found at: http://www.nets.nihr.ac.uk/__data/assets/pdf_file/0006/97359/PRO-12-33-28.pdf

Ethics approval required
Old ethics approval format

Ethics approval(s)
South Central - Berkshire, 26/02/2014, ref: 14/SC/0092

Study design
Multi-centre randomised double-blind placebo-controlled parallel group trial of 12 months duration with a 4-month internal pilot

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
http://www.asthma-treatment.org.uk/wp-content/uploads/2015/03/LASER-Patient-Information-Leaflet-v1.0-5.2.14.pdf

Health condition(s) or problem(s) studied
Asthma

Interventions
The active TLA device (Airsonett®) significantly reduces nocturnal allergen exposure by filtering ambient air through a high efficiency particulate air filter, slightly cooling (5-8°C) and 'showering' it over the participant during sleep. The reduced temperature allows the filtered air to descend in a laminar stream, displacing allergen-rich air from the breathing zone, reducing allergen exposure without creating draft or dehydration. The device is installed next to the participant's bed and is easy to use with no identified safety concerns in previous trials. The device is CE marked and licensed for use in the UK for allergic asthma. The device uses the same amount of electricity as a 60W light bulb and has an anticipated life-span of 5 years with filter changes required every 6 months.

The placebo devices are adjusted to deliver isothermal air, instead of slightly cooled air, and holes in the filter effectively bypass it whilst still maintaining an equivalent sound and airflow level to an active device. This allows the placebo device to deliver a laminar flow of non-filtered, non-descending, isothermal air which, when mixed with the warm body convection, will ascend towards the ceiling and thus have no effect on the normal air flow pattern around the breathing zone. There is no difference in the air delivery rate, perceived air movements or sound level between an active or placebo device. The human body is not able to detect an absolute temperature difference of 0.75 deg C and as such there is no perceptible temperature difference sleeping beneath an active or a placebo device. Electricity usage is the same as for active devices and the filter is changed at 6-month intervals.

Intervention Type
Device

Primary outcome measure
The primary efficacy end point in this study, the rate of clinically significant exacerbations over the 12-month period, will be modelled as a Poisson random variable. A Poisson regression model with an adjustment for over-dispersion will be used to compare the rate of asthma exacerbations between the two groups with log of time used as an offset variable. Further analysis will adjust for the baseline characteristics including the ACQ score, age, BMI and sex. Intention to treat (ITT) analysis will be performed on the primary outcome on all participants who will be randomised. The study results will be reported in accordance with the CONSORT (Consolidated Standards of Reporting Trials) 2010 statements. Stata (or equivalent stats package) will be used for all the analyses. All the tests will be done at a 5% two-sided significance level.

Secondary outcome measures
Kaplan-Meier curves and log-rank test will be used to compare the time to first asthma exacerbation between the two groups. In addition, Cox proportional hazards models will be used to evaluate the effect of the TLA device on the time to first asthma exacerbation, adjusting for the same covariates as in the primary analysis. Since the analysis of only time to first exacerbation leaves out much of the data, analysis incorporating multiple time-to-event (recurrent exacerbations) methods will also be carried out. Andersen-Gill (1982) extension of the Cox proportional regression will be used to analyze recurrent exacerbations. Using this model, the problem reduces to the analysis of time to first exacerbation, time to second exacerbation, and so on. Poisson regression will be used to compare the incidence of severe exacerbations, and incidence of moderate exacerbations between the two groups over the 12-month period. The proportion of participants experiencing severe, moderate, or any exacerbations over the 12-month period will be compared using a continuity-corrected Chi-squared test. The duration of severe and moderate exacerbations, the total number of days with an exacerbation over the 12-

month period, and the number of health care utilisations will be compared between the two groups using a two-sample independent t-test. We will utilise longitudinal analysis methods for the continuous secondary endpoints, which involve repeated measures at baseline, 3, 6, 9, and 12 months follow-ups (measures of airflow obstruction, composite asthma control scores, symptom measures, and health-related quality of life measures). Mixed effect models will be used to determine whether there is an effect of the TLA device over time in these measures. Changes from baseline to 12 months in markers of allergy will be analysed using ANCOVA (analysis of covariance) models, with the corresponding baseline measurement used as a covariate and treatment group as a factor.

Overall study start date
01/12/2013

Completion date
01/07/2018

Eligibility

Key inclusion criteria
Current inclusion criteria as of 24/07/2015:
1. Adults (aged 16-75 years inclusive)
2. A clinical diagnosis of asthma for ≥6 months supported by evidence of any one of the following:
2.1. Airflow variability with a mean diurnal peak expiratory flow (PEF) variability >15% during the baseline 2-week period or a variability in FEV1 of >20% across clinic visits within the preceding 12 months, with concomitant evidence of airflow obstruction (FEV1/FVC ratio <70%);
2.2. Airway reversibility with an improvement in FEV1 by ≥12% or 200 ml after inhalation of 400 µg of salbutamol via a metered dose inhaler and spacer at first study visit or within the preceding 12 months;
2.3. Airway hyper-responsiveness demonstrated by Methacholine challenge testing with a provocative concentration of Methacholine required to cause a 20% reduction in FEV1 (PC20) of ≤8mg/ml or equivalent test (See Appendix 3).
3. Severe asthma:
3.1. Requirement for high-dose inhaled corticosteroids (ICS) (≥1000µg/day beclomethasone (BDP) or equivalent – see Appendix 4) plus a second controller (long-acting ß2-agonist or anti-muscarinic, theophylline, or leukotriene antagonist), and/or systemic corticosteroids.
3.2. If on maintenance corticosteroids, the maintenance dose must have been stable for 3-months– this excludes any interim need for short-term steroid bursts to treat exacerbations.
4. Poorly controlled asthma demonstrated by BOTH:
4.1. ≥2 severe asthma exacerbations, requiring systemic corticosteroids ≥30mg prednisolone or equivalent daily (or ≥50% increase in dose if maintenance 30mg prednisolone or above), for 3 or more days, during the previous 12 months, despite the use of high-dose inhaled corticosteroids (ICS) and additional controller medication;
4.2. ACQ (7-point) score >1 at Screening Visit 1 and Randomisation Visit 2.
5. Atopic status:
5.1. Sensitisation to ≥1 perennial indoor aeroallergen[2] (including House Dust Mite, domestic pet or fungi) to which they are likely to be exposed during the study, demonstrated by a positive skin prick test (wheal diameter ≥3mm more than negative control) or specific IgE ≥0.35 IU/L).
6. Exacerbation free and taking stable maintenance asthma medications (not including short-acting bronchodilator or other reliever therapies) for at least 2-weeks prior to Screening Visit 1
7. Exacerbation free and taking stable maintenance asthma medications (not including short-

acting bronchodilator or other reliever therapies) in the period between Screening Visit 1 and Randomisation Visit 2.(the Screening Period). Participants suffering a severe exacerbation during the Screening Period can be rescreened 2 weeks after returning to their maintenance asthma medications (See 11.3.2)
8. Able to use the TLA device during sleep on at least five nights per week (excluding holidays)
9. Able to understand and give written informed consent prior to participation in the trial and able to comply with the trial requirements

Previous inclusion criteria:
1. Adults (aged 18-75 years inclusive)
2. A clinical diagnosis of asthma for ≥6 months prior to trial entry supported by evidence of either:
2.1. Airflow variability with a maximum diurnal peak expiratory flow (PEF) variability >15% during the baseline 2-week period or a variability in FEV1 of >20% across clinic visits within the preceding 12 months, with concomitant evidence of airflow obstruction (FEV1/FVC ratio <70%)
2.2. Airway reversibility with an improvement in FEV1 by ≥12% or 200 ml after inhalation of 400 µg of salbutamol via a metered dose inhaler and spacer at first study visit or within the preceding 12 months
2.3. Airway hyper-responsiveness with a provocative concentration of Methacholine required to cause a 20% reduction in FEV1 (PC20) of ≤8mg/ml within the preceding 12 months
3. Severe asthma (GINA Steps 4-5 and BTS Steps 4-5)
3.1. Requirement for high-dose inhaled corticosteroids (≥1500 µg/day beclomethasone or equivalent), with or without maintenance oral corticosteroids and the need for daily treatment with a controller medication (long-acting ß2-agonist or anti-muscarinic, theophylline, or leukotriene antagonist)
3.2. If on maintenance corticosteroids, the maintenance dose must have been stable for 3 months prior to trial entry - this excludes any interim need for short-term steroid bursts to treat exacerbations
4. Poorly controlled asthma demonstrated by BOTH:
4.1. ≥2 severe asthma exacerbations, requiring systemic corticosteroids ≥30 mg prednisolone or equivalent daily (or ≥50% increase in dose if maintenance 30 mg prednisolone or above), for 3 or more days, during the previous 12 months, despite the use of high-dose inhaled corticosteroids (ICS) and additional controller medication
4.2. ACQ (7-point) score >1.5 at Screening Visit 1 and Baseline Visit 2
5. Atopic status
5.1. Sensitisation to ≥1 perennial indoor aeroallergen (including House Dust Mite, domestic pet or fungi) to which they are likely to be exposed during the study, demonstrated by a positive skin prick test (wheal diameter ≥3 mm more than negative control) or specific IgE ≥0.35 IU/L)
6. Participants must have remained exacerbation free and have been taking their current asthma medications for at least 4 weeks prior to Screening Visit 1
7. Participants must also be able to give written informed consent prior to participation in the study and be able to comply with the study requirements and restrictions

Participant type(s)
Patient

Age group
Adult

Lower age limit
16 Years

Upper age limit
75 Years

Sex
Both

Target number of participants
222

Total final enrolment
240

Key exclusion criteria
1. Current smokers or ex-smokers abstinent for <6 months
2. Ex-smokers with ≥15 pack year smoking history
3. Partner who is a current smoker and smokes within the bedroom where the TLA device is installed
4. TLA device cannot be safely installed within the bedroom, intending to move out of study area within the trial period or unable to use the TLA device for at least 8 hours on at least 5 nights per week
5. Documented poor treatment adherence
6. Occupational asthma with continued exposure to known sensitising agents in the workplace
7. Previous bronchial thermoplasty within 12 months
8. Maintenance treatment with Omalizumab (anti-IgE) within 3 months
9. Using long-term oxygen, Continuous Positive Airway Pressure (CPAP) or Non-Invasive Ventilation (NIV) routinely overnight as this will impair the effect of the TLA device
10. Uncontrolled symptomatic gastro-oesophageal reflux that may act as a persistent asthma trigger
11. Presence of clinically significant lung disease other than asthma, including smoking-related chronic obstructive pulmonary disease (COPD), bronchiectasis associated with recurrent bacterial infection, allergic bronchopulmonary aspergillosis (mycosis), pulmonary fibrosis, sleep apnoea, pulmonary hypertension, or lung cancer
12. Patients with clinically significant co-morbidity (including cardiovascular, endocrine, metabolic, gastro-intestinal, hepatic, neurological, renal, haematological and malignant conditions) that remains uncontrolled with standard treatment
13. Patients currently taking part in other interventional clinical trials

Date of first enrolment
01/05/2014

Date of final enrolment
11/01/2016

Locations

Countries of recruitment
England

Northern Ireland

United Kingdom

Study participating centre
Queen Alexandra Hospital
Hants
United Kingdom
PO6 3LY

Study participating centre
Southampton General Hospital
Southampton
United Kingdom
SO16 6YD

Study participating centre
Glenfield Hospital
Leicester
United Kingdom
LE3 9QP

Study participating centre
Heartlands Hospital
Birmingham
United Kingdom
B9 5SS

Study participating centre
Bradford Hospital
Bradford
United Kingdom
BD9 6RJ

Study participating centre
St Georges, London
London
United Kingdom
SW17 0QT

Study participating centre
Churchill Hospital
Oxford
United Kingdom
OX3 7LE

Study participating centre
Queen Elizabeth, Birmingham
Birmingham
United Kingdom
B9 5SS

Study participating centre
Maidstone Hospital
Maidstone
United Kingdom
ME16 9QQ

Study participating centre
Belfast City Hospital
Belfast
United Kingdom
BT9 7AB

Study participating centre
Chester Hospital
Chester
United Kingdom
CH2 1UL

Study participating centre
Aintree University Hospital
Liverpool
United Kingdom
L9 7AL

Study participating centre

Royal Liverpool Hospital
Liverpool
United Kingdom
L7 8XP

Study participating centre
Castle Hill Hospital
Hull
United Kingdom
HU16 5JQ

Sponsor information

Organisation
Queen Alexandra Hospital (UK)

Sponsor details
c/o Alison Mortlock
Research Office
1st Floor Gloucester House
Cosham
Hants
England
United Kingdom
PO6 3LY
+44 (0)23 9228 6000 Ext 4271
Alice.Mortlock@porthosp.nhs.uk

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/04rha3g10

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

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

Intention to publish date
31/12/2018

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from:
Research & Quality Manager
1st Floor Lancaster Building
Queen Alexandra Hospital
Southwick Hill Road
Portsmouth
PO6 3LY

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	08/01/2016		Yes	No
Results article	results	01/06/2019	25/06/2019	Yes	No
HRA research summary			28/06/2023	No	No