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Study of Shufeng Jiedu® (SFJD) capsules to aid antibiotic use reduction in acute exacerbations of chronic obstructive pulmonary disease

Submission date
09/06/2021

Recruitment status
No longer recruiting

Registration date
01/07/2021

Overall study status
Completed

Last Edited
06/10/2023

Condition category
Respiratory

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

Plain English summary of protocol

Background and study aims
Chronic obstructive pulmonary disease (COPD) is the name for a group of lung conditions that cause breathing difficulties.
Patients with COPD commonly experience flare-ups (“acute exacerbations”) and antibiotics are often prescribed. However, only one in three flare-ups are caused by bacterial infections and are helped by antibiotics. The remaining two out of three flare-ups are caused by viruses or environmental factors and in these cases, antibiotics will not help. If you take antibiotics, you are more likely to suffer from an infection from drug-resistant bacteria in the future, so it is important to find a safe and effective way to control the symptoms of COPD flare-ups without using antibiotics. There is evidence, based on studies conducted in China, that a herbal combination treatment called Shufeng Jiedu could help control symptoms of COPD flare-ups. We would like to know whether the herbal combination, Shufeng Jiedu, could be an alternative to antibiotics. As this study is a feasibility study, it will not answer this question but this will help us to plan a large, full-scale trial.

Who can participate?
COPD patients aged 40 years or older who present at their GP Practice with an acute exacerbation of COPD will be invited to take part in the EXCALIBUR trial.

What does the study involve?
Eligible patients (participants) will be randomly allocated to Shufeng Jiedu (SFJD) capsules or matched placebo (dummy capsule), and will take 4 capsules, 3 times a day for 14 days. Participants will be asked to complete a participant diary for 28 days, recording their COPD flare-up symptoms in a symptom questionnaire and any medication they have taken for their flare-up (including the trial treatment). The participants will receive a final questionnaire mailed to them at 12 weeks post-randomisation. Research sites will perform a review of the participant's notes 12 weeks post-randomisation to record any further GP visits or hospital admissions. Participants will also be interviewed at 4 weeks to give their views on the trial documents, design, and herbal treatment.

What are the possible benefits and risks of participating?
It is not known whether you will have any additional benefit from taking part in this trial. However, your participation will give important information about how best to treat people with flare-ups of their COPD.
You may experience mild side effects from taking the trial medication.

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

When is the study starting and how long is it expected to run for?
June 2019 to December 2022

Who is funding the study?
Innovate UK

Who is the main contact?
Tom Oliver, EXCALIBUR@soton.ac.uk

Study website
http://www.southampton.ac.uk/ctu

Contact information

Type(s)
Scientific

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Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
268737

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 45360, Grant Codes: 104983, IRAS 268737

Study information

Scientific Title
Treating Acute EXacerbation of COPD with Chinese HerbAL MedIcine to aid AntiBiotic Use Reduction (EXCALIBUR) - Study of Shufeng Jiedu® (SFJD) capsules to aid antibiotic use reduction in acute exacerbations of chronic obstructive pulmonary disease: a mixed-methods, double blind, randomised placebo-controlled feasibility trial

Acronym
EXCALIBUR

Study objectives
We hypothesise that SFJD will improve symptoms in people with AECOPD, and will therefore reduce the necessity for antibiotics, the risk and duration of admission to hospital, and the risk of relapse. This trial will be a feasibility study in patients treated for AECOPD in primary care in the UK, in preparation for a full trial to assess whether adding SFJD to standard treatment will enable patients to improve faster, thus reducing the necessity for antibiotics and reducing their risk of admission to hospital. If successful, this would pave the way for a full-scale clinical trial in the UK. The addition of SFJD to antibiotics has the potential to significantly reduce healthcare costs associated with COPD and to reduce the risk of development of antimicrobial resistance, by reducing the number of antibiotic prescriptions and reducing the risk and duration of hospital admission.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 30/11/2020, London - Surrey Research Ethics Committee (Wates Room, Wates House, University of Surrey, Guildford, Surrey, GU2 7XH, United Kingdom; +44 (0)207 104 8088, (0)207 104 8131; surrey.rec@hra.nhs.uk), ref: 20/LO/0580

Study design
Interventional randomized controlled feasibility study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
GP practice

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
Chronic obstructive pulmonary disease

Interventions
OVERVIEW
This is a multicentre, double blind placebo-controlled feasibility trial of Shufeng Jiedu® in treating symptoms of acute exacerbations of COPD (AECOPD). This trial will also contain nested qualitative interviews of patients who choose to take part and those who don't, in order to help aid the design of the large, full-scale trial.

POPULATION
We aim to recruit 80 adults, 40 years and over, presenting to their GP with an acute exacerbation of their COPD and with at least one of the Anthonisen criteria (increased pus in sputum; increased sputum volume; increased breathlessness), and the GP is considering use of antibiotics.

IDENTIFICATION
Potential participants will be made aware of the EXCALIBUR trial via mail-out from the 8 recruiting GP sites. The criteria for receiving a mail-out pack will be for patients to have experienced an acute exacerbation (flare-up) of their COPD (AECOPD) in the last two years. This mail out pack will inform the patient about the trial and to contact their GP next time they suffer an AECOPD, before taking any AECOPD treatment.

ELIGIBILITY
On presentation at a GP Practice with an AECOPD, the patient will be assessed for eligibility from the patient notes and by clinical assessment of their symptoms.

TREATMENT
Eligible participants will be randomised to active or placebo IMP in a 1:1 allocation, on top of usual care for AECOPD (such as antibiotics and oral corticosteroids). Participants will be asked to

take the trial medication of 4 capsules, 3 times a day, preferably after meals, for 14 days. GPs will be given the option to prescribe immediate; delayed; or no antibiotics on the trial based on the clinical assessment of the patient and their symptoms.

PARTICIPANT DIARY
Participants will be asked to complete daily diary data for up to 28 days after presentation at their GP practice. This diary collects information on the patients' symptoms as well as any treatment taken for the AECOPD. The diary may be completed early if the participant's exacerbation has ended for 7 days and the diary has been completed for at least 14 days. Patients will receive follow up phone calls or text messages from the research team at the Southampton Clinical Trials Unit (SCTU) at 2-3; 14; and 28 days following randomisation to prompt diary completion and return.
A final COPD Assessment Test (CAT) questionnaire will be mailed to the participant at 12 weeks post-randomisation, after which their involvement in the trial will be complete.

NOTES REVIEW
A notes review will be undertaken 12 weeks after randomisation to document return visits to the GP for repeat COPD consultations, antibiotic prescriptions, other medications prescribed for treatment of AECOPD and hospital attendances (both inpatient and outpatient).

NESTED QUALITATIVE SUBSTUDY
As part of the EXCALIBUR trial, we would like to talk to both people who entered the trial and those who chose not to enter. We will ask patients about their views on herbal medicine and delayed prescriptions of antibiotics in the treatment of flare-ups of COPD. Additionally, we wish to learn about their experience of taking part in the EXCALIBUR trial or their reasons for not doing so.
These interviews will range from 15-60 minutes long and be conducted over the telephone.

Intervention Type
Drug

Pharmaceutical study type(s)
Not Applicable

Phase
Phase III

Drug/device/biological/vaccine name(s)
Shufeng Jiedu Capsules (SFJDC)

Primary outcome measure
1. Number and proportion of patients on the COPD register who present with AECOPD measured using: Onsite screening logs – proportion of patients on the COPD register who present to their GP practice with AECOPD and are considered for eligibility into EXCALIBUR
2. Proportion of patients presenting with AECOPD that are eligible and ineligible (plus reasons) for the trial measured using: Onsite screening logs – proportion of patients approached who agreed to be assessed for eligibility and are found eligible for inclusion
3. Proportion of eligible patients recruited measured using: Onsite screening logs – proportion of eligible patients who are recruited to the trial and eligible patients refusing to enter the trial (plus reasons why) and patient feedback from qualitative interviews.
4. Recruitment rate per site per month open measured using: Onsite enrolment logs – number of

participants recruited per site per 1000 registered patients per month open.
5. Compliance with medication according to diary data and returned medication measured using: Medication adherence collected from medication diary and returned medication.
Qualitative: Patient experiences of taking SFJD from qualitative interviews
6. Average no. of capsules taken per day per patient measured using: Number of capsules recorded in medication diary and in returned medication.
7. Duration of treatment per patient measured using: Number of days trial medication taken as per medication diary and in returned medication.
8. % of patients correctly guessing treatment/placebo allocation and reasons why measured using % of patients who correctly guessed whether they had been allocated to SFJD or placebo and reasons why (as reported in medication diaries and qualitative interviews).
9. % of patients returning trial diaries measured using: Percentage of patients returning diaries and patient experiences of completing the diary
10. % of diary completion measured using: Percentage of diary completion per patient and patient experiences of completing the diary
11. % of patients who took antibiotics in each group measured using: Antibiotic prescribing from baseline CRF and self-reported antibiotic use (number of days on which antibiotics were consumed) from the patient diary
12. % of patients given immediate and delayed antibiotic prescriptions measured using % receiving delayed and immediate antibiotic prescriptions from baseline CRF and self-reported antibiotic use (number of days on which antibiotics were consumed) from the patient diary

Secondary outcome measures
There are no secondary outcome measures

Overall study start date
01/06/2019

Completion date
30/12/2022

Eligibility

Key inclusion criteria
1. Has a current acute exacerbation of COPD with at least one of the following:
1.1. Increased sputum purulence;
1.2. Increased sputum volume;
1.3. Increased breathlessness.
2. The current acute exacerbation has lasted for at least 24 hours and no longer than 21 days.
3. The responsible clinician is considering use of antibiotics for the acute exacerbation.
4. Diagnosis of COPD in clinical record.
5. Age 40 years or more.
6. Able to provide informed consent.
7. Able to provide the primary outcome data at 2 and 4 weeks within the expected windows.

Participant type(s)
Patient

Age group
Adult

Lower age limit
40 Years

Sex
Both

Target number of participants
Planned Sample Size: 80; UK Sample Size: 80

Total final enrolment
19

Key exclusion criteria
1. The responsible clinician feels urgent referral to hospital is necessary.
2. Severe illness (e.g. suspected pneumonia or pulmonary embolism or lung cancer; necessity for emergency admission to hospital).
3. Patient has a primary diagnosis of bronchiectasis, lung cancer or other active chronic respiratory disease.
4. Currently on or has previously had antibiotics or corticosteroids for this AECOPD.
5. Patient is on a maintenance dose of antibiotics for treatment of COPD.
6. Known or suspected pregnancy.
7. Women of childbearing potential who are at risk of pregnancy and not using an effective form of contraception.
8. Currently breast-feeding.
9. Chronic kidney disease stage 4 or 5.
10. Severe liver disease.
11. Cannot read or understand the study materials.
12. Previously recruited into this “EXCALIBUR” trial.
13. Previously been recruited into another drug trial within the last 6 weeks.

Date of first enrolment
30/07/2021

Date of final enrolment
31/07/2022

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
NIHR CRN Wessex
Unit 7
Berrywood Business Village
Tollbar Way
Hedge End

Southampton
United Kingdom
SO30 2UN

Sponsor information

Organisation
University of Southampton

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Sponsor type
University/education

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ROR
https://ror.org/01ryk1543

Funder(s)

Funder type
Government

Funder Name
Innovate UK

Alternative Name(s)
innovateuk

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
31/12/2023

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available because the participants did not consent for their data to be used in further research. Access to this data is strictly controlled by the Southampton Clinical Trials Unit and no third parties will be granted access to the Medidata servers holding research data. For any queries please contact ctu@soton.ac.uk.

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		19/12/2022	20/12/2022	Yes	No
HRA research summary			28/06/2023	No	No
Basic results			06/10/2023	No	No
Results article		25/09/2023	06/10/2023	Yes	No
Statistical Analysis Plan	version 1.0	09/11/2022	06/10/2023	No	No