ISRCTN65344386 https://doi.org/10.1186/ISRCTN65344386

Safe withdrawal of inhaled steroids in mild or moderate COPD

Submission date
04/12/2017

Recruitment status
No longer recruiting

Registration date
14/12/2017

Overall study status
Completed

Last Edited
17/06/2020

Condition category
Respiratory

[_] Prospectively registered
[_] Protocol
[_] 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 the group of lung conditions that cause breathing problems. Patients with severe or very severe COPD may benefit from using high-dose inhaled corticosteroid drugs (anti-inflammatory medicines). There is evidence of widespread overprescribing of these drugs to patients with mild or moderate COPD in many countries. These drugs can increase the risk to patients of developing pneumonia (an estimated extra 3000 cases per year in England), fractures and cataracts. In most patients with mild or moderate COPD there is no evidence of any benefit from high dose inhaled corticosteroids. The drugs prescribed to patients with mild or moderate COPD are costly. In the NHS in England more than £122 million is spent each year in prescribing high-dose inhaled corticosteroids in mild and moderate COPD, approximately 20% of the total spending on these drugs. Little is known of patients' perceptions of the proposed withdrawal of these drugs when prescribed outside guidelines. This research will examine the feasibility of carrying out a trial of withdrawing these high-dose inhaled corticosteroids in patients with mild or moderate COPD. In this study for which this is a feasibility study the effect of the withdrawal of high-dose inhaled corticosteroids will be assessed for impact on patients' quality of life, lung function, exacerbation frequency, markers of inflammation in the blood, or evidence of interference with breathlessness. The acceptability of this research to patients and practices and its safety will also be assessed. In preparation for their use as outcome measures in any future trial the distribution of the outcome measures will be examined. Finally the ability to test the safety of withdrawing high dose inhaled corticosteroids by assessing the frequency of exacerbations of the disease will be assessed. Success in these aims will enable a definitive cluster randomised controlled trial of the withdrawal of high-dose inhaled corticosteroids to be proposed and conducted at a later date.

Who can participate?
Adults aged 45 and older who have COPD.

What does the study involve?
Participants are asked about their views on high-dose ICS (inhaled cortico-steroids) that are prescribed against guideline advice. Participants are then randomly allocated to one of two groups as to when they are withdrawn from ICS. Those in the first group have ICS withdrawn over two months and the effects of the withdrawal are reviewed at three and six months. Those

in the second group continue with ICS for those six months and are then withdrawn from the ICS the same way as those in the first group.

What are the possible benefits and risks of participating?
Most participants in this study will benefit from the withdrawal of high-dose inhaled corticosteroids for which there is no good evidence of beneficial effect in patients of the type to be recruited. They are also likely to benefit from the reduced risk of the side effects of high dose inhaled corticosteroids. Participants in the intervention phase of this study will all have the opportunity to withdraw from high-dose inhaled corticosteroids and to see if the withdrawal leads to any undesirable effects. This will apply to those randomised initially and to those not randomised.

Where is the study run from?
Manor Place Surgery (UK)

When is the study starting and how long is it expected to run for?
January 2016 to July 2019

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

Who is the main contact?
Dr Gill Gilworth (Scientific)

Contact information

Type(s)
Scientific

Contact name
Dr Gill Gilworth

Contact details
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Additional identifiers

EudraCT/CTIS number
2016-001876-31

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

32059

Study information

Scientific Title
Feasibility of the Safe Withdrawal of inhaled corticosteroids in Patients with mild to moderate COPD prescribed outside guidelines

Acronym
SWAP

Study objectives
The aim of this study is to examine the feasibility of carrying out a trial of withdrawing high dose inhaled corticosteroids in patients with mild or moderate COPD by assessing whether withdrawal of high dose inhaled corticosteroids has any impact on patients' quality of life, lung function, exacerbation frequency, markers of inflammation in the blood, or evidence of interference with breathlessness. This study will also assess whether patients and practices find this research acceptable and safe in proceeding with a definitive trial of the withdrawal of high dose inhaled corticosteroids.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Londonbridge NRES Committee, 26/10/2016, ref: 16/LO/1696

Study design
Randomised; Both; Design type: Treatment, Screening, Process of Care, Drug, Management of Care, Cross-sectional

Primary study design
Interventional

Secondary study design
Randomised cross over trial

Study setting(s)
GP practice

Study type(s)
Treatment

Participant information sheet
See additional files

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

Interventions

This is an unblinded feasibility study of the withdrawal of high-dose inhaled cortico-steroids (ICS) prescribed for patients with COPD. There are two phases to the study.

The first phase is a qualitative interview study of the views of patients on high-dose ICS, who were prescribed them against guideline advice, of their possible withdrawal.

The second phase is a study of the effect of withdrawing high-dose ICS on a number of patient measures including lung function, quality of life, breathlessness, blood biomarkers, fractional exhaled nitric oxide, and neural respiratory drive. Patients are randomised to ICS withdrawal. ICS are withdrawn over 2 months and the effects of withdrawal reviewed at three months and six months. Patients randomised to continue on ICS have the same assessments over six months. At the end of six months patients randomised to ICS withdrawal leave the study. Patients randomised to continue with ICS have their ICS withdrawn according to the same protocol as those patients randomised to withdrawal in the first place. Patients randomised to continue on ICS in the first place remain in the study for one year.

The principle outcome measure of the feasibility of a trial of withdrawal of high-dose ICS will be the proportion of patients who attend the baseline interview who find the invitation to participate acceptable and are willing to submit to randomisation.

Intervention Type
Other

Primary outcome measure
The principle outcome measure of the feasibility of a trial of withdrawal of high-dose ICS will be the proportion of patients who attend the baseline interview who find the invitation to participate acceptable and are willing to submit to randomisation.

Secondary outcome measures
1. Proportion of patients who accept the investigations of the effect of high-dose ICS withdrawal (acceptability of the main trial)
2. Proportion of practices that agreed to participate
3. The distribution of the change in quality of life (SAS-CRQ questionnaire), lung function (spirometry), exacerbation frequency, cellular and molecular biomarkers (FBC, eosinophils, neutrophils, CRP, fibrinogen, periostin) , and neural respiratory drive (experimental assessment of electro-myelogram of afferent electrical impulses in the parasternal muscles), between baseline and six months in patients from whom high-dose ICS were withdrawn (allow the setting of sample sizes for the main trial)
4. Frequency of exacerbations (assessing the safety of the main trial)
5. Proportion of participants in whom evidence of the effectiveness of high-dose ICS was evident from a deterioration in quality of life, lung function, exacerbation frequency, cellular and molecular biomarkers, and neural respiratory drive (assessing sample size for detection of ICS benefits for the main trial)

Overall study start date
01/01/2016

Completion date
31/07/2019

Eligibility

Key inclusion criteria
1. Known diagnosis of mild or moderate COPD (forced expiratory volume in first second (FEV1) ≥50% predicted and FEV1/forced vital capacity (FVC) <0.7) obtained from spirometry within the past 12 months and confirmed at interview
2. Prescribed and have used high-dose ICS (alone or in combination with a long-acting bronchodilator) at a dose of fluticasone propionate ≥250mcg/day, fluticasone furoate ≥92mcg /day, budesonide >400mcg/day or beclomethasone dipropionate >400mcg/day on most days for at least 3 months
3. Age ≥ 45 years
4. <2 exacerbations in the previous year and no admissions to hospital with an exacerbation since the diagnosis of COPD was made
5. BMI of less than 35

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
Planned Sample Size: 106; UK Sample Size: 106

Key exclusion criteria
1. Patients with a BMI greater than 35
2. History of asthma
3. Lung cancer
4. Breathlessness secondary to cardiac disease
5. Moderate or severe osteoarthritis limiting mobility
6. Current severe mental illness (severe depression or psychosis)
7. Current alcohol dependence
8. Dementia
9. Patients who use continuous oral corticosteroids
10. Pregnant females or females of childbearing age not using effective contraception

Date of first enrolment
01/10/2017

Date of final enrolment
13/04/2019

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Manor Place Surgery
1 Manor Place
Camberwell
London
United Kingdom
SE17 3BD

Sponsor information

Organisation
King's College London

Sponsor details
Room 1.8 Hodgkin Building
Guy's Campus
London
England
United Kingdom
SE1 4UL

Sponsor type
University/education

ROR
https://ror.org/0220mzb33

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
Publication of the main findings is planned in a high-impact peer reviewed journal towards the end of 2019. As this is a feasibility study for a trial and not a trial a trial protocol has not been published. At this point there is no intention to do so. All relevant additional documents will be available on request from the trial chief investigator, Dr Patrick White, at patrick.white@kcl.ac.uk

Intention to publish date
30/08/2020

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 numbers will be small (approx. 75) and will be unlikely to representative of the population from which they will have been recruited. The data will be held in anonymised form at King's College, London.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version V2	11/07/2017	14/12/2017	No	Yes
Participant information sheet	version V3	12/07/2017	14/12/2017	No	Yes
Other publications	preliminary research	31/12/2019	17/06/2020	Yes	No
Results article	qualitative results	01/01/2019	17/06/2020	Yes	No
HRA research summary			28/06/2023	No	No