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A randomised controlled trial to test whether active vitamin D can improve the clinical response to steroids in asthmatic patients

Submission date 17/03/2009	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 07/05/2009	**Overall study status** Completed	
Last Edited 01/09/2014	**Condition category** Respiratory	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
Protocol 08

Study information

Scientific Title
Does 1-alpha, 25-dihydroxyvitamin D3 (calcitriol) enhance corticosteroid activity in steroid refractory asthma? A randomised controlled trial

Acronym
VitD1/08

Study objectives
We hypothesise that the administration of the active form of vitamin D (calcitriol) improves the clinical response to systemic corticosteroid therapy in patients with moderate to severe asthma whose symptoms fail to improve on steroid therapy.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Guys Research Ethics Committee, 01/08/2008, ref: 08/H0804/84

Study design
Randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
Screen visit 1:
Informed consent will be obtained before screening starts. Suitable subjects will undergo full assessment of their medical history (including a complete smoking history) and laboratory evaluation for safety haematology and biochemistry profile. Up to 100 ml of venous blood will also be drawn for ex-vivo experiments. Spirometry will be performed and the FEV1 and forced vital capacity (FVC) obtained. Reversibility would be assessed by giving the subject a short acting beta agonist and measuring the FEV1 pre- and 15 - 30 minutes post-bronchodilator. We will measure fractional exhaled nitric oxide (FeNO) using an Aerocrine NIOX MINO® monitor following the American Thoracic Society (ATS)/European Respiratory Society (ERS) guidelines. A peak flow meter and a diary card will be given to the subject to record morning and evening peak flows throughout the study. All these procedures are done in accordance with departmental Standard Operating Procedures.

Eligible subjects would be entered into the second part of the screening process. These subjects would be given prednisolone 40 mg/1.73 m^2/day as a single dose in the morning for 14 days, to be taken at home.

Screen visit 2:
The subject's medical history and adverse events would be reviewed at the start of the screening visit 2. Spirometry will be performed and the FEV1 and FVC obtained. Subjects who demonstrate an increase of greater than 15% in the FEV1 when compared to baseline (screen visit 1) would be excluded. Subjects who are still eligible would be entered into the main part of the trial. We will repeat FeNO in exhaled air. Up to 100 ml of venous blood will be taken for safety haematology and biochemistry and for ex-vivo experiments.

Treatment visit day 1:
Following a 4-week washout period (from screen visit 2) participants would attend treatment visit day 1. The subjects' medical history and adverse events would be reviewed at the start of this visit. Up to 100 ml of venous blood would be taken for safety haematology and biochemistry and for ex-vivo experiments. Participants would be randomised to receive either calcitriol 0.25 mg twice daily or matching placebo. The first dose would be done under supervision. Subjects would be discharged following first dosing and would take the subsequent doses at home.

Treatment visit day 15:
On day 15 of treatment subjects would attend treatment visit day 15. Subjects are to withhold their day 15 treatment dose prior to attending. The subjects medical history and adverse events would be reviewed at the start of this visit. Prior to dosing up to 100 ml of venous blood would be taken for safety haematology and biochemistry and for ex-vivo experiments. Subject would perform spirometry and fraction of nitric oxide in exhaled air (FeNO) pre-dose. These would be done in accordance with departmental standard operating procedures. A standard Asthma Control Questionnaire (ACQ) would also be completed by the subject pre-dose.

FeNo measurements are highly correlated with eosinophilic airway inflammation; eosinophilic inflammation is correlated with response to steroid treatment. We will measure FeNO using a Aerocrine NIOX MINO® monitor, following the ATS/ERS guidelines.

Subjects who are still eligible to continue in the study would be commenced on prednisolone 40 mg/1.73 m^2/day as a single dose for 14 days. The first dose of prednisolone and day 15 dose of treatment article would be done under supervision. Subjects would be discharged following dosing and would take subsequent doses of treatment and prednisolone at home.

Treatment visit day 28:
On day 28 of treatment subjects would attend treatment visit day 28. Subjects would have completed a 28-day dosing period of treatment article and a 14-day dosing period of prednisolone. The subject's medical history and adverse events would be reviewed at the start of this visit. Following this up to 100 ml of venous blood would be taken for safety haematology and biochemistry and for ex-vivo experiments. Subject would perform spirometry, and fraction of nitric oxide in exhaled air (FeNO). A standard Asthma Control Questionnaire (ACQ) would also be completed by the subject. A physical examination would also be performed.

Follow-up day 56:
After 1 month subjects will be interviewed either during a routine visit to the asthma clinic or via telephone call to check medical history and adverse events. Following all these procedures subjects would be discharged from the study.

Intervention Type
Supplement

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Vitamin D3 supplementation

Primary outcome(s)
Change in FEV1 at baseline compared to the end of the treatment period.

Key secondary outcome(s))
1. Level of the ex-vivo production of interleukin-10 (IL-10) and other surrogate biomarkers of outcome or drug effects/process by T-cells, measured at screen visit 1, screen visit 2, treatment visit day 1, treatment visit day 15 and treatment visit day 28
2. Serological markers of inflammation, measured at screen visit 1, screen visit 2, treatment visit day 1, treatment visit day 15 and treatment visit day 28
3. Fraction of nitric oxide in exhaled air, measured at screen visit 1, screen visit 2, treatment visit day 15 and treatment visit day 28
4. Asthma Control Questionnaire (ACQ) score, measured at treatment visit day 15 and treatment visit day 28

Completion date
30/09/2011

Eligibility

Key inclusion criteria
1. Male or female adults aged between 18 to 65 years
2. Documented history and typical symptoms of asthma for greater than or equal to 6 months prior to screening
3. Pre-bronchodilator forced expriatory volume in one second (FEV1) less than 70% predicted and greater than 15% reversibility to beta 2-agonist or diurnal peak flow variability of greater than 20%
4. Corticosteroid refractory asthma, as defined by a less than 15% improvement in FEV1 following a 14-day course of prednisolone 40 mg/1.73 m^2/days 29 - 31
5. Written informed consent received

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Past or present disease, which, as judged by the investigator, may affect the study outcome (other than asthma, rhinitis or eczema)
2. Serum corrected calcium greater than 2.66 mmol/l
3. Clinically significant deviation from normal (physical examination or laboratory parameters) as judged by the investigator at the screening visit
4. Current smoker or an ex-smoker of less than 5 years with a greater than 5 pack year history

5. Pregnant or lactating females or those at risk of pregnancy (women of childbearing age may be offered a pregnancy test prior to recruitment)
6. History of a respiratory tract infection and/or exacerbation of asthma within 4 weeks of the screening visit requiring oral corticosteroid tablets
7. Participation in a study involving an investigational medicinal product in the previous 3 months or blood donation within the last year
8. Participants taking regular medications for diseases other than those for asthma or rhinitis
9. Current or previous allergen immunotherapy
10. Concomitant treatment with a thiazide diuretic or calcium supplement
11. Inability to understand or comply with the research protocol

Date of first enrolment
01/04/2009

Date of final enrolment
30/09/2011

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Department of Asthma, Allergy and Respiratory Allergy
London
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Sponsor information

Organisation
Kings College London (UK)

ROR
https://ror.org/0220mzb33

Funder(s)

Funder type
Charity

Funder Name
Asthma UK (UK)

Alternative Name(s)
asthmalunguk, Asthma UK, Asthma + Lung UK

Funding Body Type
Private sector organisation

Funding Body Subtype
Research institutes and centers

Location
United Kingdom

Funder Name
Friends of Guy's Hospital (UK)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/06/2014		Yes	No