ISRCTN15717783 https://doi.org/10.1186/ISRCTN15717783

Can vitamin D supplementation in patients with Crohn's disease improve symptoms as an adjunct therapy

Submission date
28/01/2019

Recruitment status
No longer recruiting

Registration date
01/03/2019

Overall study status
Completed

Last Edited
14/04/2023

Condition category
Digestive System

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

Plain English summary of protocol

Background and study aims
About half to three-quarters of people with Crohn’s Disease may develop vitamin D deficiency (very low levels of vitamin D in the body). Vitamin D is very important to help maintain healthy bones. Recent research has found that for people with Crohn’s Disease, having normal levels of vitamin D might also help to improve the symptoms of their disease. Despite this vitamin D levels are not routinely checked for people with Crohn's Disease. There are many different doses and types of vitamin D available on prescription and over the counter but there is no standard treatment for vitamin D deficiency in Crohn's Disease. The aim of this study is to compare two different doses of vitamin D capsules to treat vitamin D deficiency in adults with Crohn's Disease. The aims of the study are to:
Understand what proportion of people with Crohn's Disease have vitamin D deficiency at the end of the winter and during the summer months.
Understand any specific factors that might contribute to vitamin D deficiency in people with Crohn's Disease.
Find out if it is possible to carry out the study with a large number of people to see which dose of vitamin D is best at treating vitamin D deficiency in people with Crohn's Disease

Who can participate?
Vitamin D Screening studies: Adult patients with Crohn’s Disease who have their usual care at one of the participating hospitals
Vitamin D Supplementation trial: Adult patients with Crohn’s Disease who have been found to have vitamin D deficiency in the winter vitamin D screening study

What does the study involve?
Vitamin D Screening studies: Participants have a finger-prick blood test to measure their vitamin D levels. They also answer questions about their diet and lifestyle that might influence their vitamin D levels.
Vitamin D Supplementation trial: All participants receive a vitamin called D3 (cholecalciferol). The capsule is taken once a day by mouth. Participants in one group get a different treatment than participants in another group. There are two treatment groups: one group receive vitamin

D3 400 iu, one capsule daily for24 weeks. The other group receive vitamin D3 3,200 iu one capsule daily for 12 weeks and then vitamin D3 800 iu one capsule daily for 12 weeks. A number of blood samples and a stool sample are taken to monitor the safety and effectiveness of the treatment. Blood tests and stool samples are taken at the start, after 12 weeks and then at the end of 24 weeks. Participants complete questionnaires at the start of the study and at the end of 24 weeks and keep a diary of when they have taken their vitamin D capsules each day. It is expected that each study appointment may take up to 40 minutes to complete. Appointments are carried out at the hospital participants usually attend for their Crohn's Disease follow-up.

What are the possible benefits and risks of participating?
Vitamin D Screening studies: It is hoped that the results from the study will help doctors and patients in the future when making decisions about treatment. There should not be any risks involved in taking part in the Vitamin D Screening Study. Some people may find the finger-prick blood test uncomfortable. Four large spots of blood are needed for the test. If it is difficult to get enough drops of blood from the first finger prick it may need to be repeated. The researchers will try to take the samples from the least sensitive part of the fingertip.
Vitamin D Supplementation trial: It is hoped that the results from the study will help inform a large study that will help doctors and patients in the future when making decisions about treatment for people with Crohn's Disease. Both treatments have been shown to treat or prevent vitamin D deficiency, but it cannot be guaranteed that either treatment will make any difference to the symptoms of Crohn's Disease. The main risk of taking any vitamin D supplement is developing too much calcium in the blood (hypercalcaemia). Hypercalcaemia may also lead to calcium in the urine (hypercalciuria). This risk is classed as 'uncommon' but if this happened the main symptoms would be: nausea, vomiting, passing large amounts of urine, loss of appetite, weakness, apathy, thirst, constipation. For this reason calcium blood levels will be checked at the beginning of the study to ensure they are normal, and at the 12 week and 24 week appointments along with other safety blood measures to ensure they remain within safe limits. Rarely some people report developing a rash when they take a vitamin D capsules. Participants will need to have three sets of blood tests over the whole study duration. Some people may find these uncomfortable and there may be some bruising afterwards but samples will be taken by an appropriately trained person.

Where is the study run from?
1. Queen Elizabeth Hospital Birmingham (UK)
2. Birmingham Heartlands Hospital (UK)
3. Good Hope Hospital (UK)

When is the study starting and how long is it expected to run for?
Vitamin D Screening will be starting in March 2019 and will continue for about 2 months. The participants in the vitamin D supplementation study will be in the study for a total of 36 weeks.

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

Who is the main contact?
Dr Jane Fletcher
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Study website
www.dcode-trial.org.uk

Contact information

Type(s)
Scientific

Contact name
Dr Jane Fletcher

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Additional identifiers

EudraCT/CTIS number
2018-003910-42

IRAS number

ClinicalTrials.gov number
NCT03718182

Secondary identifying numbers
40194

Study information

Scientific Title
Can vitamin D supplementation in patients with Crohn's disease improve symptoms as an adjunct therapy: D-CODE feasibility study

Acronym
D-CODE Feasibility Study version 1.0

Study objectives
Treating vitamin D deficiency with oral supplementation in people with Crohn’s Disease may help to improve the symptoms of their disease.

Ethics approval required

Old ethics approval format

Ethics approval(s)
Current ethics approval as of 20/09/2019:
Approved 08/03/2019, Newcastle and North Tyneside 2 Research Ethics Committee, NHS BT Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ, Tel: +44 (0)207 1048082, Email: nrescommittee.northeast-newcastleandnorthtyneside2@nhs.net, ref: 19/NE/0019.

Previous ethics approval:
Newcastle and North Tyneside 2 Research Ethics Committee, NHS BT Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ, Tel: +44 (0)207 1048082, Email: nrescommittee.northeast-newcastleandnorthtyneside2@nhs.net, ref: 19/NE/0019 - approval pending

Study design
Randomised; Interventional; Design type: Treatment, Screening, Drug, Dietary

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 the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Crohn's disease

Interventions
There will be two parts to the planned research involving three hospitals in Birmingham. Part 1 is a vitamin D screening study, where adults will be asked to have a finger-prick blood test to check their vitamin D levels. They will asked to answer dietary and lifestyle questions. Adults found to have vitamin D deficiency in part 1 may be invited to join part 2 of the research.

Part 2 is a vitamin D supplementation study where participants will be given a daily vitamin D capsule to take by mouth for 24 weeks. They will be randomly allocated to 2 different groups with each group receiving a different dose of vitamin D. Web randomisation will be carried out. This will be stratified by site in a ratio of 1:1.

Arm A: Fultium D3 Daily 400iu, one to be taken daily for 24 weeks
Arm B: Fultium D3 3,200iu, one to be taken daily for 12 weeks followed by Fultium D3 800iu one to be taken daily for 12 weeks.

There is no control group. Participants will have blood tests at the start,12 weeks and 24 weeks. They will complete quality of life questionnaires at the start and after 24 weeks. The last appointment will be a final follow-up appointment after 36 weeks.

Intervention Type
Other

Phase
Phase IV

Primary outcome measure
Screening studies:
25(OH) vitamin D results measured using finger-prick blood test to determine prevalence of vitamin D deficiency <50nmol/l during winter and summer months

Feasibility trial:
Feasibility assessed at the end of the trial when the final participant has had their final follow up appointment:
1. Consent rate
2. Compliance rate
3. Retention rate
4. Completion rates of efficacy outcomes
5. Adverse events

The following success criteria will be applied:
1. At least 50% of all eligible patients can be recruited and consented to join the vitamin D supplementation feasibility trial
2. At least 80% participant compliance with the intervention measured by a treatment diary.
3. Retention and follow up in at least 80% of all recruited participants at 6 months
4. Completion of all trial processes in at least 80% of recruited participants.
5. Absence of adverse reactions and causative adverse events in at least 80% of participants.

Outcomes will be either:
Feasible with no modifications
Feasible with modifications
Main study not feasible

All criteria must be met to deem the study feasible without modifications. At least criteria 1 must be met to deem the study feasible with modifications. If none of the criteria are met then the study is not feasible.

Secondary outcome measures
Outcomes that will be used to assess efficacy in future definitive trial:
Primary outcome: health related quality of life measured using the Inflammatory Bowel Disease Questionnaire (IBDQ) at baseline and 24 weeks

Overall study start date
01/05/2018

Completion date

31/12/2021

Eligibility

Key inclusion criteria
Screening study:
1. Confirmed diagnosis of Crohn's Disease (CD)
2. > = 18 years of age
3. Written informed consent

Intervention study:
1. Confirmed diagnosis of CD
2. Identified as having Vitamin D deficiency < 50 nmol/L in the Winter screening study
3. > = 18 years of age
4. Already receiving treatment for CD as per National Institute for Health and Care Excellence (NICE) Guidance or those in remission and not currently receiving treatment but who continue to attend hospital out-patient appointments
5. Written informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 300; UK Sample Size: 300

Total final enrolment
172

Key exclusion criteria
Screening study:
Does not meet inclusion criteria

Intervention study:
1. Currently taking over the counter vitamin D, fish oil or multi-vitamin supplementation and unwilling to stop this to participate in the intervention study
2. Currently receiving:
2.1. Vitamin D containing supplements prescribed by a healthcare professional
2.2. Bisphosphonates
2.3. Digitalis or other cardiac glycosides
2.4. Phenytoin
2.5. Barbituates (e.g. Amylobarbitone, Butobarbitone, Methyl Phenobarbitone, Pentobarbitone,

Quinalbarbitone, Amylobarbitone)
2.6. Actinomycin
2.7. Imidazole
3. With known hyperparathyroidism
4. With known sarcoidosis
5. With known renal disease or kidney stones
6. With known hypercalcaemia (corrected serum calcium > = 2.60 mmol/L)
7. With known underlying liver disease
8. With known hypersensitivity to vitamin D supplements or any of the trial medication excipients
9. Who are pregnant, breastfeeding, trying to conceive or women of child-bearing capacity who decline to have a pregnancy test where applicable and/or decline to take effective contraceptive measures during the intervention period
10. Individuals who have participated in a trial testing a medicinal product within 6 months preceding screening

Date of first enrolment
19/09/2019

Date of final enrolment
31/01/2021

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University Hospitals Birmingham, Queen Elizabeth Hospital (lead site)
Mindelsohn Way
Edgbaston
Birmingham
United Kingdom
B15 2WB

Study participating centre
University Hospitals Birmingham, Birmingham Heartlands Hospital
Bordesley Green East
Birmingham
United Kingdom
B9 5SS

Study participating centre

University Hospitals Birmingham, Good Hope Hospital
Rectory Road
Sutton Coldfield
United Kingdom
B75 7RS

Sponsor information

Organisation
University Hospitals Birmingham NHS Foundation Trust

Sponsor details
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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/014ja3n03

Funder(s)

Funder type
Government

Funder Name
NIHR Academy; Grant Codes: ICA-CDRF-2017-03-083

Results and Publications

Publication and dissemination plan
Results will be disseminated via publication and presentation at clinical and scientific conferences. In addition, the trial website will be updated in a timely manner to ensure progress

reports and results are easily accessible to a wide audience. Results will be disseminated regardless of the magnitude or direction of effect.

Key target audiences are nurses and medics working in gastroenterology areas. These practitioners are key in influencing changes in everyday practice in terms of screening for vitamin D deficiency in patients with CD. Publications will include findings from:
1. Vitamin D deficiency screening and prevalence study
2. The feasibility trial
3. Patient and public involvement in the study
Publications will be in peer-reviewed journals. In order to maximise impact, journals that are most likely to be read by practitioners involved in the management of patients with CD will be selected. In addition, specific results, such as the role of vitamin D and hepcidin monitoring in the feasibility trial, will be of interest to scientists and endocrinologists who specialise in the field of vitamin D research. Publication is intended at one year after the overall trial end date

Intention to publish date
31/10/2022

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available due to the study being a feasibility study only.

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		20/03/2021	22/03/2021	Yes	No
Basic results			14/04/2023	No	No
HRA research summary			28/06/2023	No	No