

Vitamin D and vascular health of chronic fatigue syndrome patients

Submission date 10/02/2010	Recruitment status No longer recruiting	☒ Prospectively registered ☐ Protocol
Registration date 18/03/2010	Overall study status Completed	☐ Statistical analysis plan ☒ Results
Last Edited 01/11/2017	Condition category Nervous System Diseases	☐ Individual participant data

Plain English summary of protocol

Background and study aims

Vitamin D levels are commonly low in patients with chronic fatigue syndrome and these patients can also have poor vascular health. The aim of this study is to test whether high-dose intermittent oral vitamin D therapy given every two months for six months could improve markers of vascular health and fatigue in patients with chronic fatigue syndrome.

Who can participate?

Patients aged 18 - 65 with chronic fatigue syndrome

What does the study involve?

Participants are randomly allocated to receive 100,000 units oral vitamin D3 or a matching placebo (dummy) treatment every 2 months for 6 months. Blood vessel function is assessed using non-invasive methods at a visit before receiving vitamin D3 and at the final 6-month visit. Other tests undertaken by participants are flow-mediated dilatation of the brachial artery; blood pressure, cholesterol, insulin resistance, markers of inflammation and oxidative stress are tested at the start of the study and repeated at 6 months, and each participant completes a fatigue questionnaire before and after 6 months in the study.

What are the possible benefits and risks of participating?

Potential risks of taking part include a risk of low calcium blood levels with high dose vitamin D3 but participants are monitored regularly.

Where is the study run from?

Ninewells Hospital (UK)

When is the study starting and how long is it expected to run for?

April 2010 to April 2011

Who is funding the study?

ME Research UK

Who is the main contact?

Prof. JJF Belch

Contact information

Type(s)

Scientific

Contact name

Prof JJF Belch

Contact details

The Institute of Cardiovascular Research

Ninewells Hospital

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Additional identifiers

Clinical Trials Information System (CTIS)

2010-019096-29

Protocol serial number

2009CV08

Study information

Scientific Title

Vitamin D supplementation in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) patients: a randomised, placebo-controlled, parallel, double-blind study

Study objectives

Serum concentration of 25-hydroxyvitamin D (25[OH]D) levels are associated with important cardiovascular risk factors. Low levels of 25(OH)D are associated with hypertension, increased vascular resistance, increased left ventricular mass index, and increased coronary calcification.

Correlation between levels of inflammation and arterial stiffness has been reported in a population of 41 well-characterised patients with ME/CFS compared to 30 healthy subjects but vitamin D levels were not measured as part of that study done by University of Dundee.

This study will investigate the relationship between vitamin D and arterial stiffness and inflammation and further examine various parts of the vitamin D pathway.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Study design

Randomised double-blind placebo-controlled parallel-group study

Primary study design

Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Myalgic Encephalomyelitis (ME); Chronic Fatigue Syndrome (CFS)

Interventions

In total there will be five visits in this study: screening, baseline visit, and visits during months 2, 4 and 6. The screening visit will involve taking written informed consent, a physical examination, medical history to diagnose CFS and to check inclusion/exclusion criteria. The baseline visit will involve dosing of 100,000 unit of cholecalciferol or matching placebo and taking blood for baseline biomarkers, Peripheral Arterial Tonometry (PAT), blood pressure (BP) and electrocardiography (ECG). The dose of cholecalciferol will be repeated during the 2nd and 4th month visits. Activities during 2nd month and 6th month visit will be identical to the baseline visit. The 4th month visit will involve only dosing and review of adverse events (AE). The total duration of this study is 18 months.

Intervention Type

Supplement

Primary outcome(s)

Arterial stiffness, assessed at baseline, 2 and 6 months:

Blood pressure will be measured in triplicate using an automated blood pressure monitor (Omron705 CPII). Peripheral pressure waveforms will be recorded at the radial, femoral and carotid artery using the validated SphygmoCor pulse waveform analysis system (AtCor Medical). The carotid to femoral and carotid to radial pulse wave velocity will be calculated, and additionally the augmentation index.

Key secondary outcome(s)

1. Endothelial function, assessed at baseline, 2 and 6 months:

Flow-mediated dilation of the brachial artery will be measured according to standard guidelines. The diameter of the brachial artery will be measured using a 7.5-15 MHz linear array transducer. Baseline images are taken for 1 minute. A blood pressure cuff is then placed around the arm and inflated to a suprasystolic pressure for 5 minutes. ECG-triggered images are after captured for 3 minutes after cuff release. Once a stable baseline has been re-established, sublingual nitroglycerine (NTG) (0.4 mg) is administered and endothelium-independent vasodilation is assessed in a similar fashion.

2. Vascular biomarkers, assessed at baseline, 2 and 6 months

2.1. Fasting serum lipid profiles, measured using COBAS Bio Autoanalyser

2.2. Fasting glucose and insulin levels. Estimates of insulin resistance will be calculated using the Homeostasis Model (HOMA) (fasting glucose x fasting insulin/22.5).

2.3. High sensitivity C-reactive protein (CRP), measured by Enzyme Linked Immunosorbent Assay

(ELISA)

2.4. Tumour necrosis factor-alpha (TNF- α), measured by ELISA

2.5. Interleukin-6 (IL-6), measured by ELISA

2.6. Serum 25-hydroxyvitamin D3 (25[OH]D), measured by ELISA

2.7. 1,25-dihydroxyvitamin D3 (1,25-[OH]2D3), measured by ELISA

3. Fatigue, measured using the Piper Fatigue Scale

4. Quality of life, assessed using the Medical Outcomes Study (MOS) SF-36

5. Emotional adjustment, assessed using the Hospital Anxiety and Depression Scale (HADS)

Completion date

01/09/2012

Eligibility

Key inclusion criteria

1. Patients diagnosed with ME/CFS (fulfils the Fukuda [1994] and Canadian [2003] criteria)

2. Serum 25(OH)D levels < 75 nmol/l

3. Male or female, aged 18 - 65

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 years

Sex

All

Key exclusion criteria

1. Patients not diagnosed with ME/CFS

2. Patients already taking Vitamin D supplements (fish oils will be permitted)

3. Estimated Glomerular Filtration Rate (GFR) < 40 ml/min (by MDRD4 method)

4. Adjusted serum calcium < 2.15 or > 2.60 mmol/L

5. Liver Function Test (LFT) > 3x upper limit of normal (ULN)

6. Known metastatic malignancy

7. History of kidney stones

8. History of sarcoidosis or osteoporosis

9. Lying systolic blood pressure (BP) < 80 mm Hg

10. Pregnant, lactating or of childbearing age and not taking reliable contraception

11. Patients diagnosed with psychiatric disorder (including depression) within the past 5 years

12. Patients diagnosed with schizophrenia, mania, substance abuse/dependence, or an eating disorder at any time

13. Patients with other known organic cause for their symptoms

14. Unable to give written informed consent

Date of first enrolment

01/08/2011

Date of final enrolment

01/03/2012

Locations

Countries of recruitment

United Kingdom

Scotland

Study participating centre

Ninewells Hospital

Dundee

United Kingdom

DD1 9SY

Sponsor information

Organisation

University of Dundee

ROR

<https://ror.org/03h2bxq36>

Funder(s)

Funder type

Charity

Funder Name

ME Research UK (UK)

Alternative Name(s)**Funding Body Type**

Private sector organisation

Funding Body Subtype

Research institutes and centers

Location

United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from Prof. Faisal Khan (f.khan@dundee.ac.uk). Access to data will be subject to entering into collaboration with the investigators for non-commercial, bona fide academic analyses; decisions on data access will be made between the investigators and the Sponsor (University of Dundee). Participant consent for unrestricted sharing of individual participant data was not obtained.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/03/2015		Yes	No
Basic results		18/10/2017	01/11/2017	No	No