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# Vitamin D and vascular health of chronic fatigue syndrome patients

**Submission date**
10/02/2010

**Recruitment status**
No longer recruiting

**Registration date**
18/03/2010

**Overall study status**
Completed

**Last Edited**
01/11/2017

**Condition category**
Nervous System Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] 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
Dundee
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# Additional identifiers

### EudraCT/CTIS number
2010-019096-29

### IRAS number

### ClinicalTrials.gov number

### Secondary identifying numbers
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)
Fife & Forth Valley Research Ethics Committee 2 (now called East of Scotland Research Ethics Service REC 2), 15/02/2011, REC ref: 10/SO501/61

## Study design
Randomised double-blind placebo-controlled parallel-group study

## 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
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 measure
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.

## Secondary outcome measures

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)

### Overall study start date
01/04/2010

### 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

### Age group
Adult

### Lower age limit
18 Years

### Sex
Both

### Target number of participants
50

### 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
Scotland

United Kingdom

### Study participating centre
**Ninewells Hospital**
Dundee
United Kingdom
DD1 9SY

## Sponsor information

### Organisation
University of Dundee

### Sponsor details
c/o Catrina Forde PhD
Tayside Medical Science Centre
Ninewells Hospital & Medical School

Research & Development Office
Residency Block, Level 3
George Pirie Way
Dundee
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**Sponsor type**
University/education

**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**
Other non-profit organizations

**Location**
United Kingdom

# Results and Publications

**Publication and dissemination plan**
Not provided at time of registration

**Intention to publish date**

**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. Faisel 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 |