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# Effects of vitamin D supplementation in type 1 diabetes mellitus patients

**Submission date**
06/03/2017

**Recruitment status**
No longer recruiting

**Registration date**
31/07/2017

**Overall study status**
Completed

**Last Edited**
18/03/2024

**Condition category**
Nutritional, Metabolic, Endocrine

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

## Plain English summary of protocol

Background and study aims
Diabetes mellitus is a life-long condition where a person is unable to control their blood sugar levels. There are two main types of diabetes, type 1 (around 10% of cases) and type 2. In type 1 diabetes (T1DM) the immune system attacks specialised cells in the pancreas called beta-cells (which are responsible for producing the hormone insulin). This means that the sufferer is unable to produce enough insulin to effectively control their blood sugar levels and so regularly inject insulin in order to keep their blood sugar levels in a healthy range (glycaemic variability). Some studies have shown that taking vitamin D supplements can help to reduce fluxuations in blood sugar levels. The aim of this study is to find out whether vitamin D supplementation can help improve glycaemic variability in patients with T1DM.

Who can participate?
Adults aged 18-50 who have T1DM.

What does the study involve?
Participants attend an initial study visit at which they have a sample of blood taken to measure their vitamin D levels, have body measurements taken, and have a device called a continuous glucose monitoring system (CGMS) fitted to their belly. This device consists of a small sensor inserted into the skin to measure sugar levels in the tissue. It is connected to a transmitter that sends readings to a monitoring and display device. Participants then attend another study visit at which they are given vitamin D supplements to take for three months. After three months, information about glycaemic variability, vitamin D levels and diabetes complications are collected from the CGMS, physical examination and blood analysis.

What are the possible benefits and risks of participating?
Participants who have an underlying vitamin D deficiency benefit from having this discovered and being able to take vitamin D supplements to correct the deficiency. There is a small risk of pain or bruising when blood samples are taken.

Where is the study run from?
University Hospital João de Barros Barreto, Federal University of Pará (Brazil)

When is the study starting and how long is it expected to run for?
February 2015 to December 2018

Who is funding the study?
Investigator initiated and funded (Brazil)

Who is the main contact?
Dr João Soares Felício
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# Contact information

### Type(s)
Scientific

### Contact name
Dr João Felício

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# Additional identifiers

### EudraCT/CTIS number

### IRAS number

### ClinicalTrials.gov number

### Secondary identifying numbers
005/12

# Study information

### Scientific Title
Effects of vitamin D supplementation in type 1 diabetes mellitus patients: a non-randomised study

### Study objectives
The trialists hypothesize that vitamin D supplementation can bring benefits to type 1 diabetes mellitus patients, especially with regard to its complications.

## Ethics approval required
Old ethics approval format

## Ethics approval(s)
University Hospital João de Barros Barreto ethics committee, 13/02/2012, ref: 005/12

## Study design
Prospective non-randomized placebo-controlled study

## Primary study design
Interventional

## Secondary study design

## Study setting(s)
Hospital

## Study type(s)
Treatment

## Participant information sheet
No participant information sheet available

## Health condition(s) or problem(s) studied
Type 1 diabetes mellitus (DM1)

## Interventions
All participants attend three scheduled study visits. At the first visit, participants undergo a physical examination, have blood samples taken and have a continuous glucose monitoring system (CGMS) fitted. At the second visit, participants receive either vitamin D to take at a dose of 10000 IU/day or placebo for 3 consecutive months, in order to achieve serum levels of at least 30 ng/ml. Those with 25(OH)D levels between 30 and 60 ng/ml are treated with 4000 IU/day of VD or placebo for 3 months, in order to maintain serum levels above 30 ng/ml and less than 100 ng/ml. Three months later, participants attend a third study visit at which the initial assessments are repeated. Glycemic variability (GV) is evaluated throughout the study using the CGMS taking into account all glycemias measured during all days in each patient. Standard deviation of glucose (SDG) is calculated using CGMS data and used to evaluated GV.

24 hours ambulatory blood pressure monitoring is also performed by the oscillometric method. It is installed in the morning and withdrawn after 24 hours, and patients are instructed to maintain their usual activities and write them down in a diary, which should include the time and description of each activity performed. The device is programmed to perform a measurement every fifteen minutes, and the arithmetic mean of systolic and diastolic blood pressure was established for each hour, during the waking period, during sleep and at 24 hours.

The evaluation of autonomic cardiovascular neuropathy (ACN) is performed in patients according to the following protocol: patients were submitted to a questionnaire, where the following symptoms are investigated: dizziness, visual disturbances or pre-syncope in orthostatism, dyspnea, nausea, sweating and precordial pain during physical activity, diarrhea, fecal incontinence, intestinal constipation, post-eating vomiting, erectile dysfunction or vaginal

lubrication, urinary incontinence, polaciuria, urinary urgency, urinary retention, repetitive urinary tract infection, anhydrosis, hyperhidrosis, heat intolerance and gustatory sweating.

Forms of neuropathies secondary to vitamin B12 deficiency, hypothyroidism, alcoholism and chronic renal failure, diagnosis of leprosy or HIV infection are excluded.

Autonomic tests for ACN are performed in the morning after capillary glycemia, whose value should be between 70 and 250 mg/dL. Patients are instructed to stop drinking alcohol and caffeine, in addition to smoking cessation for at least 8 hours before the test; not to perform vigorous physical exercise in the 24 hours prior to the exam, and if they present with fever (Tax ≥ 37.8) in the last two days, major emotional stress on the previous day or hypoglycemia in the 8 hours prior to the exam, the patients are instructed to reschedule autonomic tests.

Heart rate variability (HRV) is evaluated by computerized system (VNS-MICRO) through seven parameters (the four Ewing tests and the three bands of the spectral analysis). The Valsalva test is performed with the patient in dorsal decubitus (DD) at 30 degrees during 15 minutes of rest, and after this period, the patient performed respiratory effort to maintain a pressure of 40 mmHg for 15 seconds. At the 14th second, there is a maximum physiological tachycardia. After this effort, the sphygmomanometer valve is released and an electrocardiogram (ECG) is performed for 30 to 45 seconds, when a maximum physiologic bradycardia occurred. The reason for Valsalva is the relationship between tachycardia and bradycardia or between the longest and the shortest RR interval.

The orthostatic test (30:15 ratio) is performed by ECG performed in DD under the same conditions above and, after standing up, the relationship between heart rate (HR) or RR intervals corresponding to maximum tachycardia around 15° And the maximum bradycardia around the 30th beat.

The deep breath test (E: I ratio) follows the following protocol: The ECG is performed during a deep breath and expiration lasting at least 5 seconds (each). The E: I ratio is obtained by dividing the maximum HR (inspiration) by the minimum HR (expiration) or the longest RR (E) by the shortest RR (I).

In the orthostatic hypotension (HO) test, the patient remained in DD at 30 degrees for 15 minutes. BP is measured at baseline, one and three minutes after orthostatism. A drop greater than or equal to 20 mmHg in systolic BP was considered altered.

In the study of the HRV by spectral analysis in the three bands (FMB, FB and FA), the patient is in DD at 30 degrees and with spontaneous breathing. An electrocardiographic computerized record is made for 300 seconds. The ECG is analyzed by a mathematical algorithm and expressed in an oscillation amplitude diagram (HR fluctuations per second) versus HR (hertz). The total amplitude of the HRV spectrum consists of three bands: 1) component of very low frequencies or FMB (0.01-0.04 Hz) that is related to the fluctuations of vasomotor tone connected to thermoregulation and sweating (sympathetic control); 2) low frequency components or FB (0.04 to 0.15 Hz) associated with the baroreceptor reflex (sympathetic control with vagal modulation); and 3) components of high frequencies or FA (0.15 to 0.5 Hz), related to the parasympathetic (vagus nerve) control.

Diabetes kidney disease is also evaluated in patients, and to do this, urinary albumin excretion is measured by immunoturbidimetry and patients are classified according to results in

normoalbuminuria (<30 mg/g creatinine), microalbuminuria (≥30 mg/g creatinine and <300 mg/g creatinine), and macroalbuminuria (≥300 mg/g creatinine). Retinopathy is also evaluated through retinographies performed at the first and last visits to patients.

### Intervention Type
Supplement

### Primary outcome measure
Glycemic variability is assessed using continuous glucose monitoring from baseline to three months

### Secondary outcome measures
1. Vitamin D (25(OH)D) levels are measured by immonoassay on blood samples collected at baseline and three months
2. Albuminuria levels are measured by immunoturbidimetry at baseline and three months
3. Autonomic cardiovascular neuropathy is measured by physical examination and ECG at baseline and three months

### Overall study start date
01/02/2015

### Completion date
01/12/2018

## Eligibility

### Key inclusion criteria
1. Diagnosis of type 1 diabetes mellitus
2. Aged between 18 and 50 years
3. Regular follow-up with an Endocrinologist
4. HbA1c ≥7%
5. Treatment with basal-bolus insulin (multiple daily injections) at a stable dose for at least 3 months prior visit 1 (variation of up to 10% of dose was permitted)

### Participant type(s)
Patient

### Age group
Adult

### Lower age limit
18 Years

### Upper age limit
50 Years

### Sex
Both

### Target number of participants

60 in study group and 60 in placebo control group

### Key exclusion criteria
1. Previous and concomitant history of metabolic bone diseases, liver disease, abnormal glomerular filtration rate (GFR) levels
2. Patients that made use of vitamin D or calcium within the last 3 months

### Date of first enrolment
15/02/2015

### Date of final enrolment
01/12/2018

## Locations

### Countries of recruitment
Brazil

### Study participating centre
**University Hospital João de Barros Barreto, Federal University of Pará**
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## Sponsor information

### Organisation
Federal University of Pará

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### Sponsor type
University/education

### ROR
https://ror.org/03q9sr818

## Funder(s)

### Funder type
Other

### Funder Name
Investigator initiated and funded

# Results and Publications

### Publication and dissemination plan
Planned publication in a peer-reviewed journal.

### Intention to publish date
31/12/2017

### Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from João Soares Felicio (felicio.bel@terra.com.br).

### IPD sharing plan summary
Available on request

### Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Results article | results | 01/10/2018 | | Yes | No |
| Results article | results | 19/11/2020 | 18/12/2020 | Yes | No |
| Results article | | 14/08/2017 | 22/08/2022 | Yes | No |
| Results article | | 28/03/2022 | 22/08/2022 | Yes | No |
| Results article | | 06/01/2021 | 22/08/2022 | Yes | No |
| Results article | | 29/07/2020 | 22/08/2022 | Yes | No |
| Results article | | 16/03/2024 | 18/03/2024 | Yes | No |