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The effects of vitamin D supplementation on glycemic control and oxidative stress parameters in patients with type 2 diabetes mellitus

Submission date
26/11/2019

Recruitment status
No longer recruiting

Registration date
02/12/2019

Overall study status
Completed

Last Edited
17/01/2023

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
Vitamin D is a fat-soluble vitamin that our body gets mainly when we expose the skin to sunlight. Its primary role is to maintain adequate blood levels of calcium and phosphorus needed for keeping our bones healthy. Beside its skeletal effects, increasing evidence shows that vitamin D could play an important role in developing some chronic conditions like type 2 diabetes mellitus (T2DM). Patients with T2DM usually have a lack of vitamin D but it is still unknown if this is a coincidence or low levels of vitamin D may cause the disease. This could mean that giving vitamin D to patients with T2DM might help them in better control of their disease. Unfortunately, there is a lack of evidence to clarify if vitamin D could be used with the standard pharmacological treatment. In order to help clarify its role in treating patients with T2DM the aim of this study is to compare patients using vitamin D supplements and antidiabetic drugs with patients using antidiabetic drugs only.

Who can participate?
Patients from Primary Health Care Center Podgorica, diagnosed with T2DM, aged 30 and older with good metabolic control of the disease (HbA1c≤7 %)

What does the study involve?
Participation in this study is completely voluntary. Half of the participants are randomly allocated to receive the vitamin D supplement in addition to standard antidiabetic treatment (metformin and lifestyle advice) while the other half of the participants continue using antidiabetic treatment only. Vitamin D supplements are given in the form of oil drops (Vigantol oil). Dosing is carried out according to the available clinical practice guideline in relation to vitamin D baseline levels. If their starting levels of vitamin D are 50 nmol/L or less participants are asked to take 15 drops of Vigantol oil daily (equal to 50,000 IU weekly) for the first 3 months, and 4 drops of Vigantol oil (equal to 14,000 IU weekly) for the next 3 months. Participants whose vitamin D levels are more than 50 nmol/L are asked to take 4 drops of Vigantol oil (equal to 14,000 IU weekly) during their participation in the study (6 months). All participants are given

recommendations regarding nutrition and sunlight exposure, where the compliance is carefully controlled by medical staff. During the study all participants are asked to provide a small amount of blood at the start of the study and after 3 and 6 months. The purpose of the blood test is to check each participant's vitamin D levels when they enter the study and again at the 3 and 6 month assessment points. From the same blood sample the researchers also check general blood chemistry, including calcium levels and hormones that are linked to glycemic control (insulin) as well as oxidative stress markers. To monitor their physical health the researchers ask each participant's permission to measure their weight, height, waist and blood pressure measurements at the start of the study and after 3 and 6 months.

What are the possible benefits and risks of participating?
Participants using vitamin D supplements will have benefit for their bone and muscle health. The researchers will closely monitor their vitamin D and calcium levels in blood in order to prevent the negative effects of excessive vitamin D supplementation. All participants will benefit from their close and regular contact with the medical team regarding their disease control.

Where is the study run from?
Primary Health Care Center Podgorica (Montenegro)

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

Who is funding the study?
Investigator initiated and funded

Who is the main contact?
Dr Milena Cojić
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Contact information

Type(s)
Public

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Additional identifiers

Protocol serial number
05/01-E.K.-5989/1

Study information

Scientific Title
The effects of vitamin D supplementation on insulin resistance, Castelli Risk Index I and TG/TBARS Index in patients with type 2 diabetes: a 6-month follow-up randomized controlled study

Acronym
EVID T2DM

Study objectives
Six-month vitamin D supplementation will improve insulin resistance, atherogenic risk index and oxidative stress parameters in patients with type 2 diabetes mellitus treated with metformin and lifestyle advice.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 10/04/2019, Ethical Committee of Primary Health Care Center in Podgorica (Trg Nikole Kovačevića 6, Podgorica, Montenegro; Tel: +382 (0)20481900; Email: domzdravljapdg@t-com.me), ID number 05/01-E.K.-5989/1

Primary study design
Interventional

Study design
Prospective randomized controlled open-label study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Type 2 diabetes mellitus

Interventions
The eligible participants recruited consecutively were randomly assigned to two groups in 1:1 ratio. The serum level of 25(OH)D (marker of vitamin D status) was measured at baseline in all participants. Half of the patients (n=65) were randomly prescribed vitamin D3 therapy and continued their prescribed metformin therapy for 6 months, while the other group (n=65) continued their prescribed metformin therapy only. The dosing was carried out according to the Endocrine Society's clinical practice guidelines as for the vitamin D baseline levels. The participants in the first group who were vitamin D deficient [defined as serum levels of 25(OH)D ≤ 50 nmol/L] were asked to take 50 000 IU of vitamin D3 weekly (equal to 15 drops of vitamin D supplement-Vigantol oil daily) during the first 3 months and 14 000 IU weekly (4 drops daily) for the next 3 months. The participants in the same group whose 25(OH)D levels were > 50 nmol/L were asked to take 14 000 IU weekly (4 drops daily) until the end of the study.

Intervention Type
Supplement

Primary outcome(s)
1. Glycemic control measured through assessing blood levels of glycated hemoglobin (HbA1c) immunoturbidimetrically at baseline, 3 months and 6 months.
2. Insulin resistance measured using levels of HOMA-IR (the homeostasis model assessment of insulin resistance calculated by the formula: HOMA–IR=Fasting Blood Glucose (mmol/L)×Fasting Insulin (μIU/L)/22.5) at baseline, 3 months and 6 months

Key secondary outcome(s)
1. Atherogenic risk index is determined through the total cholesterol/HDL cholesterol ratio (Castelli risk I) at baseline, 3 months and 6 months
2. Oxidative stress is measured in plasma through markers of:
2.1. Lipid peroxidation measured in plasma and expressed as the Thiobarbituric acid-reactive substances (TBARS) biomarker malondyadehide (MDA) at baseline, 3 months and 6 months
2.2. Advanced oxidation protein product level (AOPP) measured in plasma spectrophotometrically, expressed as chloramine-T equivalents at baseline, 3 months and 6 months

Completion date
15/12/2018

Eligibility

Key inclusion criteria
1. Diabetes mellitus type 2
2. ≥ 30 years of age
3. Good metabolic control (HbA1c ≤ 7 %)
4. Treated with metformin and lifestyle advice

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
130

Key exclusion criteria
1. Use of vitamin D supplements and any diabetes pharmacotherapy other than metformin
2. Use of drugs which affect the metabolism of vitamin D (corticosteroids and anticonvulsants)
3. Severe anemia

4. Chronic liver or kidney failure
5. Alcoholism
6. Pregnancy
7. Malabsorption
8. Urolithiasis
9. Hypercalcemia
10. Body mass index (BMI) ≥ 40 kg/m2
11. Presence of acute or chronic inflammatory conditions

Date of first enrolment
03/05/2018

Date of final enrolment
31/05/2018

Locations

Countries of recruitment
Montenegro

Study participating centre
Primary Health Center Podgorica
trg Nikole Kovacevica 6
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Montenegro
81000

Sponsor information

Organisation
Primary Health Care Center Podgorica

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

Individual participant data (IPD) sharing plan

All data generated or analysed during this study will be included in the subsequent results publication.

IPD sharing plan summary

Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		19/08/2021	17/01/2023	Yes	No