Magnesium Supplementation as a Strategy to Reduce Serum Calcification Propensity and Vascular Stiffness in People with Type 2 Diabetes.

Published: 12-05-2023
Last updated: 21-09-2024

To investigate the effect of daily intake of 350 milligrams of magnesium citrate oral supplementation over a period of six months on calciprotein particle maturation time (T50) in serum, a measure of calcification propensity, and on vascular...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Diabetic complications
Study type	Interventional

Summary

ID

NL-OMON53724

Source
ToetsingOnline

Brief title
Mg-MAC

Condition

- Diabetic complications
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
arterial calcification, Arterial stiffness

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC
Source(s) of monetary or material Support: ZonMW NWO Vidi beurs (91718304)

Intervention

Keyword: Diabetes Mellitus Type 2, Magnesium supplementation, Serum calcium propensity, Vascular stiffness

Outcome measures

Primary outcome

Primary endpoints are serum T50 and carotid-femoral pulse wave velocity (c-f

PWV) at three and six months after baseline.

Secondary outcome

Secondary endpoints are total magnesium, sodium, potassium, calcium, phosphate,

urea, total protein, creatinine, triglycerides, total cholesterol,

LDL-cholesterol, HDL-cholesterol, fasting plasma glucose and HbA1C

concentrations at three and six months after baseline.

Study description

Background summary

Despite therapeutic strategies targeting multiple cardiovascular risk factors, cardiovascular disease (CVD) remains the leading cause of morbidity and mortality in people with type 2 diabetes (T2D). Medial arterial calcification (MAC) is a particular form of calcification that occurs through mineralization of the elastin fibers and precipitation of calcium phosphate in the tunica media, in the absence of lipids. It occurs in approximately 35% of people with T2D and represents an alternative pathophysiological mechanism leading to adverse cardiovascular events than atherosclerosis. It is hypothesized that increased serum calcification propensity leads to MAC and increased vascular stiffness, followed by increased risk of left ventricular hypertrophy and heart failure . While lipoprotein lowering treatment is used to reduce intimal calcification, there is currently no treatment that specifically targets MAC.

The propensity of serum to calcify can be measured using the maturation time of calciprotein particles in serum (T50 test). A shorter T50 has been associated with higher presence of MAC in people with chronic kidney disease and with all-cause and cardiovascular mortality in the general population.
Magnesium is shown to reduce MAC progression in animal models and in people with kidney disease. Oral magnesium supplementation also improved vascular stiffness and cardiac function in people with CVD.
Accordingly, magnesium supplementation could be an effective strategy to tackle MAC by reducing vascular stiffness and serum calcification propensity in people with T2D.

Study objective

To investigate the effect of daily intake of 350 milligrams of magnesium citrate oral supplementation over a period of six months on calciprotein particle maturation time (T50) in serum, a measure of calcification propensity, and on vascular stiffness, in people with T2D.

Study design

A monocenter double-blind, randomized, placebo-controlled parallel trial.

Intervention

Magnesium citrate, 350 mg daily orally for six months, versus placebo.

Study burden and risks

The study involves a total of four visits over a period of six months. Overall, the visits will take approximately 1.5 hours* time. Oral magnesium citrate supplements or placebo supplements have to be taken daily for 6 months. Oral magnesium citrate supplements have a good safety profile and previous studies reported a low rate of adverse events (mainly gastrointestinal such as diarrhea, nausea, and vomiting) that usually only occur when used in very large doses. At screening and at the first follow-up after three months, participants will undergo a blood sampling for plasma magnesium concentrations and measurement of c-f PWV. At baseline and at the second follow-up after six months, participants will undergo blood sampling for magnesium as well as other biomarkers, will hand in a 24-hour urine collection and will undergo measurements of c-f PWV. Additionally, dietary intake of magnesium will be assessed by a short food frequency questionnaire - the Dutch Healthy Diet index Food Frequency Questionnaire - at baseline and the second follow-up after six months. Vena puncture may cause discomfort and may result in bruising that continues up to a few days after the examinations. Determination of c-f PWV is a non-invasive procedure method that measures the propagation of the forward pressure wave traveling along the aorta. Participants gain no individual

benefit from their participation in the study. However, the study is expected to increase our understanding of MAC as a mechanism for increased CVD risk in T2D, and may ultimately lead to a new therapeutic intervention.*

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

age 50-80 years;
Diabetes Mellitus Type 2;
Presence of a predominantly medial arterial calcification pattern on a previously conducted CT scan of the legs;
Carotid-femoral pulse wave velocity higher than 12 meter per seconde;
Ability to provide informed consent prior to initiating screening visit

procedures.

Exclusion criteria

Myasthenia Gravis;
Use of medications that might interact with magnesium supplements (levothyroxine, osteoporosis medications tiludronate and alendronate, warfarin);
Advanced diabetes complications (proliferative retinopathy, disabling polyneuropathy, nephropathy with an estimated glomerular filtration rate (eGFR), calculated with the Jaffé method according to the Chronic Kidney Disease Epidemiology Collaboration equation <15 mL/min/1.73m2 or chronic dialysis, cardiac complications);
Uncontrolled hyperthyroidism or active parathyroid disease;
Chronic diarrheal disease or inflammatory bowel diseases;
Congestive heart failure, bradycardia with a resting heart rate below 60 and systolic blood pressure less than 90 mmHg;
Atrial Fibrillation;
Previous aortic surgery;
Severe hepatic insufficiency;
Malignancy or other non-cardiac conditions limiting life expectancy to <3 years;
Using food supplements that contain magnesium, or unwilling to stop two weeks before randomization;
Mental or legal incapacitation to provide informed consent;
Plasma magnesium concentration*>*2.6*mg/dL or < 1.5 mg/dL at screening.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Basic science

Recruitment

NL
Recruitment status: Recruiting

Start date (anticipated):	06-09-2023
Enrollment:	74
Type:	Actual

Ethics review

Approved WMO Date:	12-05-2023
Application type:	First submission
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ISRCTN	ISRCTNsubmissionreference41701(nognietgepubliceerd,wordtaangepast)
CCMO	NL81281.029.22