Reversal Of Arterial Disease by modulating Magnesium and Phosphate

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON27899

Source
Nationaal Trial Register

Brief title
ROADMAP-study

Health condition

Chronic Kidney Disease, Cardiovascular Disease

Sponsors and support

Primary sponsor: VU University Medical Center
Source(s) of monetary or material Support: Health Holland, Dutch Kidney Foundation (DKF LSH-TKI)

Intervention

Outcome measures

Primary outcome

Pulse Wave Velocity (PWV): the difference in PWV over 24 weeks between groups

Secondary outcome

Calcification propensity (T50): the difference in plasma T50 and CPP concentrations over 24 weeks between groups

Study description

Background summary

This study is also registered through: https://www.clinicaltrialsregister.eu EudraCT Number: 2019-001306-23

Background: Cardiovascular disease (CVD) is the leading cause of death in patients with chronic kidney disease (CKD). Accumulating evidence suggests that CVD and mortality are partially driven by inflammation and an increased calcification, both features that affect arterial stiffness. Recently, clinical quantification of calcification propensity, i.e. the tendency to develop calcifications, has become feasible by measuring calciprotein particle (CPP) maturation time in-vitro from patient samples (T50). Besides their direct effect on vascular mineralization, CPP's seem to induce inflammation, that contributes to vascular calcification and endothelial dysfunction, contributing to increased arterial stiffness as well. Importantly, both magnesium deficiency and excess phosphate are associated with increased arterial stiffness as can be measured by pulse wave velocity (PWV). The influences of lower magnesium and higher phosphate concentrations on arterial stiffness are possibly explained by their modulating, detrimental effect on endothelial function and their ability to aggravate CPP formation, respectively. Moreover, multiple observational studies among CKD patients have linked magnesium deficiency to cardiovascular events and mortality.
This study focuses on the role of magnesium as a powerful endogenous calcification inhibitor, examining the effect of magnesium supplementation on arterial stiffness and calcification propensity. In addition, we will determine whether phosphate-binding therapy in CKD patients without overt hyperphosphatemia can amplify the presumed beneficial effect of magnesium. By focusing on the role of magnesium and phosphate as targets that can modulate arterial stiffness, this research aims to improve cardiovascular outcomes in the CKD population. Moreover, the hypothesis will be tested, if the effects on arterial stiffness and inflammation are mediated by changes in calcification propensity. If this hypothesis can be confirmed, this will enable personalized medicine on this aspect of CKD, by directing interventions on the T50 score.

Primary Objective:
- Determine the effect of 24 weeks of oral magnesium supplementation and/or the phosphate binder sucroferric oxyhydroxide on arterial wall stiffness in CKD patients, as measured by pulse wave velocity.
Secondary Objectives:
- Determine the effect of 24 weeks of oral magnesium supplementation and/or the phosphate binder sucroferric oxyhydroxide on calcification propensity and vascular inflammation in CKD patients, measured by markers including T50, CPP concentrations, FGF-23, Klotho and hsCRP.
- Explore the effect of 24 weeks of oral magnesium supplementation and/or the phosphate

binder sucroferric oxyhydroxide on vascular calcification and vascular inflammation, assessed by 18F-NaF-PET scans and 18F-FDG-PET, respectively, in a subsample of 40 participants.

Methods: A Randomized Controlled Trial, with a double blind magnesium citrate intervention and an open label sucroferric oxyhydroxide (phophate-binder) intervention in adult non-dialysis dependent CKD patients.

Intervention & Comparator:
- Magnesium 117mg 3dd (350 mg elemental magnesium a day, supplemented as magnesium citrate)
- Magnesium placebo (Mg-placebo) 3dd
- Magnesium 117mg 3dd + sucroferric oxyhydroxide (SFOH) 2dd 500mg
- Mg-Placebo 3dd + SFOH 2dd 500mg

Country of recruitment: The Netherlands

Study objective

We hypothesize that 24 weeks of oral magnesium supplementation in patients with chronic kidney disease can improve vascular stiffness, through inhibiting calcification propensity and inflammation. In addition, we test the hypothesis that phosphate-binding therapy in these patients without overt hyperphosphatemia, amplifies the beneficial effects of magnesium.

Study design

- week 0, 12 and 24 measurement of PWV
- week 0, 12, 24 and 28 measurement of calcification propensity and additional laboratory measurements
- week 0 and 24 weeks biobank material storage (plasma, serum and urine)

Intervention

Magnesium Citrate and Sucroferric Oxyhydroxide

Contacts

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Eligibility criteria

Inclusion criteria

In order to be eligible to participate, a patient must meet all of the following criteria:
- Aged between 18-80 years and a life expectancy of > 1 year
- Provide informed consent
- CKD patient with an eGFR 10-45 ml/min/1.73m2
- Plasma magnesium concentration 0.5-1.4 mmol/L
- Plasma phosphate concentration 0.8-1.6 mmol/L

Exclusion criteria

A potential participant who meets any of the following criteria will be excluded from participation:
- Any phosphate binding therapy
- Unwilling to discontinue over-the-counter magnesium supplementation (for the study duration)
- Renal transplantation in medical history or expected transplantation within 6 months
- Prolongation of QTc interval of > 500 ms, 2nd or 3rd degree atrio-ventricular block on ECG or bradycardia (heart rate below 60 bpm on screenings ECG)
- Pacemaker implantation
- Atrial fibrillation or atrial flutter
- Known unstable carotid plaques (carotid imaging report check in case of CVA or TIA in medical history)Hemochromatosis or other causes of iron overload, or hemoglobin >10.5 mmol/L
- Chronic diarrhea
- Chronic use of antibiotics
- Active malignancy
- Pregnancy or lactation
- Inability to measure PWV or to take blood samples for any reason, inability to swallow medication

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	28-01-2020
Enrollment:	180
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Plan description
N/A

Ethics review

Positive opinion

Date:	23-12-2019
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 55005
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL8252
CCMO	NL69613.029.19
OMON	NL-OMON55005

Study results

Summary results
N/A