Reversal Of Arterial Disease by modulating Magnesium and Phosphate

Gepubliceerd: 23-12-2019 Laatst bijgewerkt: 19-03-2025

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-…

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON27899

Bron
Nationaal Trial Register

Verkorte titel
ROADMAP-study

Aandoening

Chronic Kidney Disease, Cardiovascular Disease

Ondersteuning

Primaire sponsor: VU University Medical Center
Overige ondersteuning: Health Holland, Dutch Kidney Foundation (DKF LSH-TKI)

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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

Toelichting onderzoek

Achtergrond van het onderzoek

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

Doel van het onderzoek

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.

Onderzoeksopzet

- 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)

Onderzoeksproduct en/of interventie

Magnesium Citrate and Sucroferric Oxyhydroxide

Contactpersonen

Publiek

Amsterdam UMC
Emma Vermeulen

06-16484735

Wetenschappelijk

Amsterdam UMC
Emma Vermeulen

06-16484735

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Placebo

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	28-01-2020
Aantal proefpersonen:	180
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Toelichting
N/A

Ethische beoordeling

Positief advies

Datum:	23-12-2019
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 55005
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

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

Resultaten

Samenvatting resultaten
N/A