Randomized placebo-controlled pilot study to determine the effect of probiotics on vitamin K status in renal transplant recipients

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To investigate the effect of a daily sachet of probiotics for 12 weeks vs placebo on vitamin K status in renal transplant recipients.

Ethical review	Not approved
Status	Will not start
Health condition type	Coagulopathies and bleeding diatheses (excl thrombocytopenic)
Study type	Interventional

Summary

ID

NL-OMON56610

Source
ToetsingOnline

Brief title
Probiotics and vitamin K2 status

Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)
- Bone, calcium, magnesium and phosphorus metabolism disorders
- Embolism and thrombosis

Synonym
Osteoporose

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Health Holland,Winclove

Intervention

Keyword: Probiotics, Renal transplant recipients, Vitamin K2

Outcome measures

Primary outcome

The main study parameter is the difference in vitamin K status as assessed by plasma dp-ucMGP between the 2 groups after 12 weeks.

Secondary outcome

1. To determine the effect of a daily sachet of 4 gram freeze-dried probiotics producing 180 µg vitamin K2 in 24-hour urine on vitamin K metabolites 5C and 7C-aglycone, and vitamin K1 and MK4 and MK-7 in stool samples after 12 weeks in participants.

2. Impact of the probiotic on the composition of the gut microbiome.

3. Assess the affect of the probiotic on serum markers for low grade inflammation (high-sensitivity C-reactive protein) and endothelial dysfunction (soluble vascular endothelium adhesion molecule 1 and soluble intercellular adhesion molecule 1) will also be assessed

Study description

Background summary

Since its discovery in 1929, vitamin K has been primarily considered for its role as a coagulation cofactor, but the last decades it became clear that vitamin K insufficiency plays a significant role in cardiovascular health as

well as in bone health. Vitamin K insufficiency is highly prevalent in the Western general population, particularly in older individuals and in certain patient groups, including patients with type 2 diabetes and kidney disease. With respect to the latter patient group, we have found that more than 90% of renal transplant recipients have a vitamin K deficiency independent of adequate dietary intake, which likely adds to the very high rate of cardiovascular events and high frequency of osteopenic fractures in these patients. Also, we recently found that renal transplant recipients suffer from gut microbial dysbiosis, which might contribute to an impaired vitamin K status. Vitamin K is a fat-soluble vitamin, present in two forms in our diet, namely phylloquinone (vitamin K1), which is mainly provided by green leafy vegetables and menaquinone (vitamin K2), mainly provided by fermented food such as cheese, yoghurt and buttermilk. In addition to dietary sources, vitamin K2 is produced by gut bacteria. Recently it has been discovered that certain probiotic strains that are already on the market have the ability to produce vitamin K2 in vitro. These probiotics are currently approved as over-the-counter supplements and are safe according to EFSA. We aim to administer probiotic formulations with vitamin K2-producing bacteria to renal transplant recipients to investigate whether this improves vitamin K status. The aim of the project is to better understand the potential of these newly developed formulations in vivo, by assessing whether vitamin K production can be stimulated by probiotic bacteria in renal transplant recipients. This probiotic has the potential to improve vitamin K status, gut health in general and improve cardiovascular and bone health.

Study objective

To investigate the effect of a daily sachet of probiotics for 12 weeks vs placebo on vitamin K status in renal transplant recipients.

Study design

This intervention study is a double-blind, randomized, placebo-controlled pilot study. During 12 weeks, participants will either take a probiotic or a placebo. Participants will be randomized into two equal groups, of which one group will receive a probiotic with bacteria that produce vitamin K2. The duration of the present study is 12 weeks, study visits will take place at baseline, after 6 weeks and after 12 weeks.

Intervention

Participants will take one dose of oral probiotic or placebo daily for 12 weeks. The daily dose will consist of 1 sachet of 4 gram probiotics or placebo per day dissolved in 200 ml luke warm water.

Study burden and risks

Before the start of the study, subjects will attend the research facilities for a screening visit. During this visit, anthropometric measurements (weight, length, body mass index) will be performed and blood pressure will be determined. For the study, 3 visits to the UMCG will take a total time of 3 hours. Before each test day, 24-hour urine samples and faecal samples will be collected. After 6 and 12 weeks, measurements will be repeated. No direct health benefit for the participants is expected. Subjects assigned to active treatment will receive probiotics with strains that are thoroughly tested and are currently approved as over-the-counter supplements and safe according to EFSA. The probiotics can induce changes in bowel frequency and bowel movement, which will likely stabilize after 2 weeks. At each visit a total amount of up to 18 ml blood will be collected by means of vena puncture. Vena puncture can cause discomfort and can result in bruising that continues up to a few days after the examinations. Also during the visits, participants will hand in a 24-hour urine collection and a frozen stool sample. Participants gain no individual benefit from their participation in the study. The study will provide pilot data for the design of a larger intervention study, which is expected to contribute to reducing the high prevalence of vitamin K deficiency and thereby the high burden of cardiovascular disease and osteopenic fractures in renal transplant recipients.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Adult renal transplant recipient >1 year post transplantation
2. Signed informed consent

Exclusion criteria

1. Renal transplant recipient <1 year post transplantation
2. Consuming probiotic supplements in the past 3 months
3. Patients receiving any form of antibiotic treatment in the past 3 months
4. Any supplementation of Vitamin K (e.g. multivitamin)
5. Medical history of blood clotting disorders (hypercoagulable states) and increased risk of thrombosis (history of myocardial infarction, percutaneous transluminal angioplasty/stenting of coronary of peripheral arteries, bypass operation, intermittent claudication, amputation for vascular reasons, transient ischemic attack (TIA) or ischemic cerebrovascular accident).
6. Gastrointestinal disorders or undergone digestive tract surgery (except appendectomy)
7. Use of medication that would interfere with the study parameters: Vitamin K antagonists or fytomenadion
8. Reported slimming or medically prescribed diet
9. Pregnancy, lactation or a female planning to conceive within the study period (a pregnancy test will be performed if there is any doubt regarding a potential pregnancy).

Study design

Design

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

Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	20
Type:	Anticipated

Ethics review

Not approved

Date:	30-01-2024
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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
CCMO	NL70202.042.20