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Vitamin K in kidney transplant organ recipients: Investigating the effect on vessel stiffness

Submission date
20/09/2017

Recruitment status
No longer recruiting

Registration date
26/09/2017

Overall study status
Completed

Last Edited
22/03/2021

Condition category
Surgery

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Reduced kidney function (sometimes called chronic kidney disease) is common, especially as people get older. Kidney problems don't just affect the kidney, but can affect the health of blood vessels and the heart, leading to an increased risk of heart disease or strokes. After a kidney transplant, this risk of heart disease is reduced a little bit, but patients with kidney transplants are still at higher risk compared to the general population. Kidney problems also lead to blood vessels becoming stiffer than usual, due to a build-up of calcium (rather like chalk) in the wall of the blood vessel. There are no good treatments for this problem yet. Some recent research suggests that vitamin K—a vitamin present in vegetables and dairy foods—might be able to slow down or stop this build-up of calcium in blood vessels. The aim of this study is to examine whether giving extra vitamin K, which is also known as menadiol diphosphate, can affect blood vessel stiffness (which is linked to improving cardiovascular health and survival) and other measures of heart and vessel health.

Who can participate?
Adults aged 18 and older in the Glasgow area who have had a functioning kidney transplant for a year or more will be taking part.

What does the study involve?
Participants are randomly allocated to one of two groups, to receive either a vitamin K or placebo capsule three times per week. There are up to five visits to the hospital in this time, and up to two additional, brief meetings to hand out more study medication, like collecting a prescription. Most participants have have a screening visit combined with a baseline visit, and if happy to participate, have blood and urine tests taken, blood vessel stiffness measured using a small, plastic pencil-shaped device and inflatable cuffs placed on the arm and the leg, and they will attend for an MRI and CT scan of the heart, to measure blood vessel stiffness and calcification. They have transplant function and immunosuppression levels checked one month after starting to ensure the medication is not interfering with their renal transplant (this is not expected). Participants attend for a review - without any additional tests - at 6 months, when they are given more study medication. The final review takes place at 12 months when all the baseline tests are repeated.

What are the possible benefits and risks of participating?
The dose of vitamin K has been used before and is known to be safe. There is a small excess risk of jaundice (yellow appearance of your skin), more common in participants with a particular genetic condition, and people with this condition will not be able to participate in the study. Some participants may experience some bruising or discomfort when having blood tests taken. Some people find the blood pressure cuff a little uncomfortable. The MRI scan is conducted in a narrow tunnel that can be quite noisy, and some people may find this claustrophobic. We ask for two CT scans of the heart and large vessels during the study. These CT scans expose participants to a small amount of radiation, equivalent to the amount the average person is exposed to in 4-6 months from natural sources in the environment. The excess radiation exposes you to a tiny increased risk of developing cancer of 1 in 9000. This is equivalent to the risk of dying from an insect bite.

Where is the study run from?
University of Glasgow, Scotland (UK)

When is the study starting and how long is it expected to run for?
September 2017 to August 2018

Who is funding the study?
1. Kidney Research UK (UK)
2. Darlinda's Charity for Renal Research (UK)

Who is the main contact?
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Contact information

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Public

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
GN16RE696

Study information

Scientific Title
Vitamin K in kidney Transplant Organ Recipients: Investigating vEssel Stiffness

Acronym
ViKTORIES

Study objectives
Hypothesis:
1. Vitamin K supplementation in renal transplant patients will reduce markers of vascular stiffness and calcification in prevalent renal transplant patients compared with placebo.
2. There will be secondary beneficial effects on transplant function and LV mass/cardiac fibrosis as assessed by magnetic resonance imaging.

Ethics approval required
Old ethics approval format

Ethics approval(s)
West of Scotland Research Ethics Committee 4, 22/06/2017, ref: 17/WS/0101

Study design
Single-centre parallel-group randomised double-blind placebo-controlled trial of vitamin K4 (Menadiol diphosphate) versus placebo

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format. Please use contact details to request a participant information sheet.

Health condition(s) or problem(s) studied
Renal transplant recipients

Interventions
Most participants have a screening visit combined with a baseline visit, and if happy to participate, have blood and urine tests taken, blood vessel stiffness measured using a small, plastic pencil-shaped device and inflatable cuffs placed on the arm and the leg, and they will attend for an MRI and CT scan of the heart, to measure blood vessel stiffness and calcification.

Participants are randomised to consuming either identical capsules containing vitamin K4 (menadiol diphosphate) 5mg or placebo to be taken three times per week. Participants are randomised in a 1:1 ratio to vitamin K4 or placebo by a computer-generated randomisation programme (generated by Sealed Envelope: https://sealedenvelope.com/) in random permuted blocks. The total duration of treatment and follow-up is 12 months for both vitamin K4 and placebo groups.

There are up to 5 visits to the hospital in this time, and up to two additional, brief meetings to hand out more study medication, like collecting a prescription.

They have transplant function and immunosuppression levels checked one month after starting to ensure the medication is not interfering with their renal transplant (this is not expected). Participants attend for a review - without any additional tests - at 6 months, when they are given more study medication. The final review takes place at 12 months when all the baseline tests are repeated.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Vitamin K4 (Menadiol diphosphate)

Primary outcome measure

Vascular stiffness is measured using the aortic distensibility on MRI scan at 12 months of treatment.

Secondary outcome measures
1. Carotid-femoral pulse wave velocity is measured using SphygmoCor XCEL PWA & PWV system at 12 months of treatment
2. Left ventricular mass, cardiac fibrosis, left atrial volume, global longitudinal strain, pulse wave velocity are measured using Cardiac MRI at 12 months of treatment
3. Marker of vitamin K status is measured using dp-ucMGP levels, Elastin degradation products (EDPs) at 12 months of treatment
4. Vascular health is measured using office (brachial) blood pressure, electrocardiogram (ECG), augmentation index measured by applanation tonometry at the radial artery at 12 months of treatment
5. Coronary and aortic calcification is measured using cardiac CT scan at 12 months of treatment
6. Bone metabolism and turnover measured using calcium, phosphate, parathyroid hormone, fibroblast growth factor-23 (FGF-23), 25-hydroxyvitamin D, 1,25-hydroxyvitamin D, osteocalcin, fetuin, bone morphogenetic protein (BMP), Tartrate resistant acid phosphatase-5b (TRAP-5b) at 12 months of treatment
7. Cardiovascular markers are measured using high-sensitivity troponin and brain natriuretic peptide at 12 months of treatment
8. Endothelial function is measured using Asymmetric Dimethylarginine (ADMA) at 12 months of treatment
9. Dietary vitamin K content is estimated at baseline using 28-day food diary
10. Transplant function is measured using blood tests for urea and electrolytes at 12 months of treatment
11. Proteinuria is measured using urinary protein to creatinine ratio at 12 months of treatment
12. Quality of life is measured using the EQ-5D at 12 months of treatment

Overall study start date
01/10/2016

Completion date
18/08/2019

Eligibility

Key inclusion criteria
1. Male or female of non-child-bearing potential aged 18 years or over
2. Functioning renal transplant, transplanted > 12 months
3. eGFR >15ml/min by CKD-EPI equation

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex

Both

Target number of participants
90

Total final enrolment
90

Key exclusion criteria
1. Inability to give written informed consent
2. Atrial fibrillation
3. Taking warfarin (vitamin K antagonist)
4. Taking vitamin K or indication for vitamin K
5. Allergy or intolerance to gelatine, lactose or cellulose
6. Breast-feeding or women of child-bearing potential
7. Glucose-6-phosphate dehydrogenase (G6PD) deficiency
8. Life expectancy <12 months
9. Contraindications to MRI scan

Date of first enrolment
26/09/2017

Date of final enrolment
26/06/2018

Locations

Countries of recruitment
Scotland

United Kingdom

Study participating centre
University of Glasgow
Institute of Cardiovascular and Medical Sciences
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Sponsor information

Organisation
NHS Greater Glasgow and Clyde

Sponsor details

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Sponsor type
Research organisation

ROR
https://ror.org/05kdz4d87

Funder(s)

Funder type
Charity

Funder Name
Kidney Research UK

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Funder Name
Darlinda's Charity for Renal Research

Results and Publications

Publication and dissemination plan
We intend to present results at an international renal conference (TBC) and publish in a high-impact journal in approximately November 2020. Protocol available upon request.

Intention to publish date

30/11/2020

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request after study results have been published. Specific data sharing plans to be confirmed and will be made available at a later date.

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	01/07/2020	25/11/2020	Yes	No
Results article		01/03/2021	22/03/2021	Yes	No
HRA research summary			28/06/2023	No	No