

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

Submission date 20/09/2017	Recruitment status No longer recruiting	☒ Prospectively registered ☒ Protocol
Registration date 26/09/2017	Overall study status Completed	☐ Statistical analysis plan ☒ Results
Last Edited 22/03/2021	Condition category Surgery	☐ 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 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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Additional identifiers**Protocol serial number**

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

Primary study design

Interventional

Study design

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

Study type(s)

Treatment

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(s)

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

Key secondary outcome(s)

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

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

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 Years

Sex

All

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

United Kingdom

Scotland

Study participating centre**University of Glasgow**

Institute of Cardiovascular and Medical Sciences

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Sponsor information

Organisation

NHS Greater Glasgow and Clyde

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

Trusts, charities, foundations (both public and private)

Location

United Kingdom

Funder Name

Darlinda's Charity for Renal Research

Results and Publications

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?
Results article	protocol	01/03/2021	22/03/2021	Yes	No
Protocol article		01/07/2020	25/11/2020	Yes	No
HRA research summary			28/06/2023	No	No