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Oxidative stress in patients with chronic kidney disease

Submission date	Recruitment status	[_] Prospectively registered
29/10/2013	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
18/12/2013	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
22/01/2019	Urological and Genital Diseases	

Plain English summary of protocol

Background and study aims
We already know that the blood vessels in patients with chronic kidney disease (CKD) do not function properly, and that this can contribute to a higher blood pressure and to stiffer blood vessels. It has been suggested that increased oxidative stress is an important cause for the impaired function of blood vessels in CKD, but this has not been studied in detail. In this context, oxidative stress means an increased production of highly reactive oxygen molecules that have the potential to impair the function of blood vessels. In this research project, we are investigating whether infusing the antioxidant vitamin C, which can reduce oxidative stress, improves blood vessel function in CKD patients and in a group of healthy volunteers. In future this knowledge could lead to therapies that improve blood vessel function and reduce blood pressure in CKD patients.

Who can participate?
People with chronic kidney disease stages 3 5, people with chronic kidney disease requiring dialysis, and people with hypertension and normal kidney function.

What does the study involve?
Study visit 1 will be during one of your regular visits to the renal clinic. We will check whether you are eligible for this study, give you information about the study and take some blood and urine samples. Visit 2 will be at the Clinical Research Facility for the actual test of blood vessel function, including the intravenous infusion of vitamin C.
On each occasion, we ask you to come fasted (from midnight for a morning appointment and after breakfast for an afternoon appointment) and not to take any caffeine for 12 hours beforehand.
Visit 1
After you have read the project information sheet, we will answer any questions that you might have about this study. This will take about 15 minutes.
We will perform a brief clinical examination, measure height and weight and ask you some simple questions about your health and the medication you are taking.
We will measure your blood pressure using a machine (similar to the one used at the renal clinic and at the GP practice). Clinical examination and blood pressure measurement should take no longer than 15 minutes.

We will also look at the results of the blood and urine taken at your renal clinic appointments (no additional samples are required for visit 1).
Visit 2
We will put two cannulas in the veins of your arms, one for infusions and one for drawing bloods. We will first infuse normal saline over duration of 10 minutes. We will wait 10 minutes and then take a blood sample (about 15 ml, about two teaspoonfuls). The blood will be stored in our lab to be analysed at a later date, to look at markers of oxidative stress.
We will then examine the blood vessels in your wrist. This examination involves assessment of your pulse with a pencil-like probe. It is carried out at the artery in your wrist and enables us to look at the pulse waveform, which gives us useful information about the blood vessels. This will take about 15 minutes.
We will then measure changes in the diameter of your main artery of your arm with an ultrasound probe. We will apply a jelly-like substance to the skin and the probe will be gently pressed against your upper arm to visualise the main artery. A blood pressure cuff will be placed around your forearm and inflated for 5 minutes. We can then measure the changes in the diameter of the upper arm artery after deflation of the blood pressure cuff. The final part of the test involves a spray of a medication called GTN spray under the tongue. GTN is a very short acting medication which dilates the blood vessel. Overall, this will take about 20 minutes.
We will then infuse vitamin C at a dose of 2 grams over 10 minutes. Subsequently, we will take another blood sample (about 15 ml, about two teaspoons), and repeat the examinations of the blood vessels in your wrist and arm, as described above. We will then take a third blood sample (about 15 ml, about two teaspoons).
The total time for these tests will be about 160 minutes (60 minutes for the infusions and 70 minutes for the above described tests of blood vessel function, 30 minutes to take consent, assess basic parameters, and move you through the study process).

What are the possible benefits and risks of participating?
We will take blood from the vein in your arm which in rare cases results in a small bruise. The amount of blood taken for this research does not place you at any risk. The other tests are non-invasive the probes are attached to the skin and no needles are involved. Assessment of the pulse waveform has no specific side effects or risks. Inflation of the blood pressure cuff during the examination of your main arm artery may lead to some discomfort and numbness in the fingers. This will disappear when the cuff is deflated. A small bruise on your forearm may result from the cuff but will disappear within a couple of days. Some studies have suggested that administration of vitamin C may cause kidney stones. To minimize any such risk, you should not take part in this study if you previously had a kidney stone or if you are already taking daily vitamin C supplements. GTN spray is very short acting. In some people it can cause a headache which is short lived and will disappear within a few minutes.

Where is the study run from?
The British Heart Foundation Glasgow Clinical Research Centre (UK)

When is study starting and how long is it expected to run for?
February 2012 February 2015

Who is funding the study?
NHS Greater Glasgow and Clyde Renal Unit Endowment Fund (UK)

Who is the main contact?
Dr Keith Gillis, Clinical Research Fellow
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Contact information

Type(s)
Scientific

Contact name
Dr Patrick Mark

Contact details
BHF GCRC
126 University Place
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G12 8TA

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
GN11RE311

Study information

Scientific Title
Oxidative stress in patients with chronic kidney disease: a cross over study of vitamin C versus normal saline

Acronym
Renox

Study objectives
Vitamin C will improve endothelial function and markers of oxidative stress in patients with chronic kidney disease.

Ethics approval required
Old ethics approval format

Ethics approval(s)
West of Scotland Research Ethics Service, 15/05/2012, 11/WS/0045

Study design
Single centre, non-randomised, cross over study

Primary study design

Interventional

Secondary study design
Non randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Renal Chronic kidney disease, Cardiovascular disease

Interventions
Participants are given ascorbic acid 2000mg in 100ml 0.9% saline given intravenously by peripheral cannula over 10 minutes. There is no randomisation and follow up is for the duration of the study visit, that is around 1.5 hours.

Intervention Type
Supplement

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Vitamin C

Primary outcome measure
Change in flow mediated dilatation assessed by brachial artery ultrasound, after saline and after ascorbic acid

Secondary outcome measures
1. Arterial stiffness assessed by pulse wave analysis using the Sphygmocor system.
2. Biomarkers of oxidative stress both measured after saline and then at 0 and 60 minutes after ascorbic acid:
2.1 Total antioxidant capacity measured by colorimetric assay
2.2 Rate of reactive oxygen species generation measured by electron paramagnetic resonance

Overall study start date
21/05/2012

Completion date
01/02/2015

Eligibility

Key inclusion criteria
1. Aged over 18 years
2. Written informed consent
3. CKD - patients with chronic kidney disease recruited from local clinic. eGFR 15 - 30ml/min on recent bloods.
4. ESRD - patients with end stage renal disease recruited from local service. Currently receiving renal replacement therapy
5. HTN - patients with hypertension recruited from local clinic. Normal renal function but diagnosis of hypertension

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
60

Key exclusion criteria
1. Known liver disease (alcoholic liver disease, hepatitis, cirrhosis)
2. Known HIV infection
3. Known i.v. drug or alcohol abuse
4. Clinical signs of acute infection
5. Known pregnancy
6. Women of childbearing age are who are at risk of pregnancy
7. Subjects with a history of kidney stones
8. Subjects taking daily vitamin C supplements

Date of first enrolment
21/05/2012

Date of final enrolment
01/02/2015

Locations

Countries of recruitment
Scotland

United Kingdom

Study participating centre
BHF GCRC
Glasgow
United Kingdom
G12 8TA

Sponsor information

Organisation
NHS Greater Glasgow and Clyde (UK)

Sponsor details
c/o Dr Maureen Travers
R&D Management Office
Western Infirmary
Tennent Institute
1st floor 38 Church Street
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United Kingdom
G11 6NT

Sponsor type
Government

ROR
https://ror.org/05kdz4d87

Funder(s)

Funder type
Charity

Funder Name
NHS Greater Glasgow and Clyde Renal Unit Endowment Fund (UK)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/08/2018	22/01/2019	Yes	No