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An investigation into why people with kidney disease lose muscle and feel weak

Submission date
30/11/2015

Recruitment status
No longer recruiting

Registration date
10/02/2016

Overall study status
Completed

Last Edited
18/09/2023

Condition category
Urological and Genital Diseases

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

Plain English summary of protocol

Background and study aims
Chronic kidney disease (CKD) is a long-term condition where the kidneys do not work properly. In a healthy person, the kidneys are vital for filtering out the waste products and excess water in the blood, and converting them into urine. In patients suffering from CKD, the kidneys are unable to do this, and so the body is unable to get rid of the waste products building up in the blood. A common feature of CKD is muscle wasting (when the muscles waste away). This can start early on in the disease, and is thought to play an important role in the way the disease progresses, and even the patients' ultimate chance of survival. It inevitably leads to a poor quality of life and an inactive (sedentary) lifestyle, which in itself can be bad for general health. Currently, the exact cause of muscle wasting in CKD is not really known, and so further research is needed so that it can be better understood and treated. The aim of this study is to grow small pieces of muscle taken from the legs of adult CKD sufferers and healthy adults in the laboratory, in order to find out what is different in the muscle of CKD patients and what the cause of their muscle loss may be. These muscles will also be stretched in the lab to simulate exercise, in order to find out if exercise could have any positive effects.

Who can participate?
Adults suffering from severe CKD and healthy adults of the same age, sex and race.

What does the study involve?
All participants have a small sample of muscle tissue taken from their thigh (biopsy) using a needle. They also provide a blood sample and a urine sample at this time. Information about their condition is gathered using a questionnaire at the start of the study, and then again at 6, 12 and 24 months.

What are the possible benefits and risks of participating?
There are no direct benefits for participants taking part in this study. The muscle biopsy carries with it a small risk of bleeding and infection, but to minimise these risks participants taking blood thinners are not able to take part and the procedure will be performed under sterile conditions. The area will ache for a day or so afterwards.

Where is the study run from?
Leicester General Hospital (UK)

When is the study starting and how long is it expected to run for?
March 2015 to May 2016

Who is funding the study?
Kidney Research UK (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
187619

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
Nil known

Study information

Scientific Title
Mechanisms of muscle wasting in advanced chronic kidney disease

Acronym
Explore CKD

Study objectives
The aim of this study is to investigate the mechanisms of muscle wasting in human CKD and their potential to be manipulated by exercise.

Main research questions:
1. How is the molecular control of muscle protein synthesis and degradation modified in CKD and affected by exercise?
2. How is the process of myogenesis modified in CKD and affected by exercise?
3. Is there a molecular role of microRNA in muscle loss in CKD?

Ethics approval required
Old ethics approval format

Ethics approval(s)
NHS East Midlands - Leicester South Research Ethics Committee, 28/11/2015, ref: 15/EM/0467

Study design
Mechanistic observational laboratory-based study

Primary study design
Observational

Study type(s)
Other

Health condition(s) or problem(s) studied
Chronic kidney disease

Interventions
A one-off muscle sample will be collected from the leg of CKD patients and matched controls as well as a blood and urine sample. These samples will be used in laboratory experiments to understand the mechanisms of muscle loss in this disease. We will also collect clinical information at 6, 12 and 24 months.

Intervention Type
Other

Primary outcome(s)
Muscle fibre size is measured using immunohistochemistry.

Key secondary outcome(s))
1. Differences in the processes of myogenesis measured using flow cytometry, immunohistochemistry and PCR
2. Differences in protein turnover measured using uptake and release labelling experiments
3. MicroRNA expression and involvement in any dysregulation seen above measured using next generation sequencing and PCR
4. Amino acid transport and intracellular concentrations
5. Muscle architecture
6. Metabolic flexibility and mitochondrial function measured using high resolution respirometry at baseline, 6, 12 and 24 months
7. Differences in physical activity levels between groups determined using patient questionnaires at baseline, 6, 12 and 24 months

Completion date
02/11/2020

Eligibility

Key inclusion criteria
CKD patients:
1. Over 18 years of age
2. Diagnosed CKD stage 3b-5
3. If diabetic, good control - HbA1c <9%

Matched controls - will be matched to CKD patients for age, sex and race.
1. Over 18 years of age
2. Kidney function < 80mL/min/1.73m2
3. Good general health

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
73

Key exclusion criteria
CKD patients:
1. Aged under 18 years
2. Uncontrolled diabetes mellitus (HbA1c >9%)
3. Inability to give consent for any reason

Matched controls:
1. Aged under 18 years
2. Presence of CKD (eGFR>80mL/min/1.73m2)
3. Presence of other diseases known to cause muscle wasting (some cancers, sepsis, burns and HIV)
4. Inability to give informed consent for any reason.

Date of first enrolment
01/01/2015

Date of final enrolment
02/11/2020

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Leicester General Hospital
Gwendolen Road
Leicester
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LE5 4PW

Sponsor information

Organisation

University Hospitals of Leicester (UK)

ROR
https://ror.org/02fha3693

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

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		25/04/2022	18/09/2023	Yes	No
Results article		06/12/2019	18/09/2023	Yes	No
Results article		14/01/2022	18/09/2023	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Plain English results		18/09/2023	18/09/2023	No	Yes