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Urinary biomarkers of aminoglycoside-induced nephrotoxicity in children with cystic fibrosis

Submission date
06/03/2012

Recruitment status
No longer recruiting

Registration date
08/05/2012

Overall study status
Completed

Last Edited
21/01/2019

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and study aims
Children with the genetic disease cystic fibrosis (CF) are prone to chest infection with a bacterium called Pseudomonas aeruginosa. Treatment with a type of antibiotic called an aminoglycoside can improve survival in these patients. However, exposure to these antibiotics can lead to reduced kidney function in around one third of patients by the time theyre adults. Currently we measure a substance called creatinine in blood tests to check how well the kidneys are working. However, creatinine is slow to respond to any damage to the kidney, so we may not find out that damage has occurred until it is too late to reverse it. A number of substances, called biomarkers, can be measured in the urine. We think that some of these biomarkers might be useful at telling us how well a childs kidneys are working, and whether any damage is occurring as a result of treatment with aminoglycosides.

In this study we aim to measure these biomarkers in the urine of children with CF at regular intervals (routine outpatient clinic appointments), and during treatment with an aminoglycoside called tobramycin.

We expect that this research will help us to develop non-invasive urine biomarker tests which can identify kidney damage from aminoglycosides early. We aim to build upon this study to develop new methods of preventing kidney damage from this important group of antibiotics. Our ultimate aim is to improve the long-term outlook for children with CF by ensuring that far fewer develop kidney problems as a result of their treatment, and allow doctors to have access to the antibiotics they require to treat such patients. Ultimately we may be able to replace some uncomfortable blood tests with non-invasive urine tests, therefore reducing the burden on patients.

Who can participate?
Children and young adults with CF aged 0 to 20 years.

What does the study involve?
All participants will provide a urine sample on the day of recruitment (at a CF outpatient clinic) and each time they subsequently come to the clinic. Ideally the sample will be collected by asking the child to go into a toilet cubicle and pass urine into a sterile container. Parents may

need to give their child some help with this. If the child is too young or not able to pass urine on demand, there are other ways we can collect the sample. None of these are invasive or painful, and these will be discussed with parents.
If the child has a course of intravenous tobramycin in hospital, or at home with daily community nurse visits, we will collect one urine sample on the same day but before the first dose of tobramycin, and a further urine sample each day during the treatment.
If the child has tobramycin at home without daily community nurse visits we will collect one urine sample on the same day but before the first dose of tobramycin, and a further urine sample on each day that monitoring blood tests are done, and on the final day of treatment.
We will provide parents with the sample pots required. We will also collect a follow-up sample 5-10 days after the last dose of tobramycin. We will arrange either to go and collect this sample, or for parents to bring it to the hospital.
Each child will be involved in the study for at least 1 year, and possibly up to 2 years.
We will store the urine samples in a freezer, and test for different biomarkers at different times. We will keep the sample until it is used up.

What are the possible benefits and risks of participating?
We do not anticipate any problems. We will choose an appropriate urine collection method for each child. There are no immediate benefits.

Where is the study run from?
University of Liverpool and Alder Hey Childrens NHS Foundation Trust

When is study starting and how long is it expected to run for?
The study is starting in April 2012 and is expected to run until October 2014

Who is funding the study?
Medical Research Council.

Who is the main contact?
Dr Steve McWilliam
S.Mcwilliam1@liverpool.ac.uk

Contact information

Type(s)
Scientific

Contact name
Dr Stephen J McWilliam

Contact details
University of Liverpool
Molecular and Clinical Pharmacology
1-3 Brownlow Street
Liverpool
United Kingdom
L69 3GL
+44 151 794 2000
S.Mcwilliam1@liverpool.ac.uk

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
11815

Study information

Scientific Title
URinary Biomarkers of Aminoglycoside-induced Nephrotoxicity in children with Cystic Fibrosis

Acronym
URBAN CF

Study objectives
The aim of this study is to measure these biomarkers in the urine of children with cystic fibrosis (CF) at regular intervals (routine outpatient clinic appointments), and during treatment with an aminoglycoside called tobramycin.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee North West Liverpool East, 27/02/2012, ref: 12/NW/0122

Study design
Observational clinical laboratory study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Diagnostic

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

Cystic fibrosis / kidney injury

Interventions
In this study children and young adults with CF will be asked to provide a number of urine samples. They will provide routine urine samples when they attend outpatient appointments, and they will also provide more frequent urine samples if they receive one or more courses of treatment with tobramycin.

Participants will be involved in the study for at least 1 year, and possibly up to 2 years. The urine samples will be analysed for a number of urine biomarkers. The primary aim of the study is to identify whether there are elevations in these urine biomarkers during treatment with tobramycin.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
The mean difference in urinary biomarker value between samples collected during tobramycin treatment, and samples collected when not receiving tobramycin. This will be calculated for each biomarker measured over the time course of each participants involvement in the study.

Secondary outcome measures
1. The association between urinary biomarker values and conventional measures of renal function [serum urea and creatinine, estimated glomerular filtration rate (eGFR)]
2. The association between urinary biomarker values and cumulative lifetime aminoglycoside exposure, compared to biomarker values in children with CF who have never received aminoglycosides and to a healthy children cohort
3. An analysis of changes in urinary biomarker values in the same patient with repeated courses of tobramycin

Overall study start date
01/03/2012

Completion date
01/10/2014

Eligibility

Key inclusion criteria
1. Age 0-20 years, either sex (Some patients with CF will continue to be seen in a Paediatric CF clinic beyond the age of 16 and will therefore be included by having a higher upper age limit)
2. Diagnosis of cystic fibrosis (established by sweat test or genotype)

Participant type(s)
Patient

Age group

Child

Lower age limit
0 Years

Upper age limit
20 Years

Sex
Both

Target number of participants
Planned Sample Size: 120; UK Sample Size: 120

Key exclusion criteria
Does not meet inclusion criteria

Date of first enrolment
01/03/2012

Date of final enrolment
01/10/2014

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University of Liverpool
Liverpool
United Kingdom
L69 3GL

Sponsor information

Organisation
University of Liverpool

Sponsor details
Whelan Building
Quadrangle
Brownlow Hill

Liverpool
England
United Kingdom
L69 3GL

Sponsor type
University/education

Website
http://www.liv.ac.uk/

ROR
https://ror.org/04xs57h96

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council [MRC] (UK) ref: G1000417, 94909

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	23/03/2018	21/01/2019	Yes	No