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The role of aldosterone in cardiovascular disease in chronic renal failure

Submission date 30/09/2005	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 30/09/2005	**Overall study status** Completed	
Last Edited 28/03/2012	**Condition category** Circulatory System	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N0265155244

Study information

Scientific Title

Study objectives
1. To determine the effect of spironolactone, an agent that blocks the action of the hormone aldosterone, on measures of heart size and function (left ventricular hypertrophy, diastolic function, heart rate variability), blood vessel function (arterial stiffness, endothelial dysfunction) and adverse blood test results (plasma oxidant and inflammatory markers) in patients with mild chronic kidney disease. All these measures are associated with a higher rate of heart attacks and strokes.
2. To determine the safety and tolerability of spironolactone in patients with mild chronic kidney disease.
3. To determine the importance of aldosterone as a cause of heart and arterial disease in patients with mild chronic kidney disease.

The demonstration of an important pathophysiological role for aldosterone in the cardiovascular disease associated with renal failure would be a major advance in the understanding of this problem and have important implication for treatment. Because the cardiac and vascular parameters to be studied are prognostically significant markers in chronic renal failure, a positive effect would suggest that aldosterone inhibition in renal failure might be of prognostic value and provide a rationale for a large clinical trial with mortality as the end-point.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Randomised double-blind placebo-controlled study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Not Specified

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
Cardiovascular: Associated with renal failure

Interventions

The study has been designed after extensive consultation with our very experienced multidisciplinary renal research team. This will be a randomised, double-blind, placebo-controlled study of the effects of aldosterone inhibition with spironolactone in 200 patients with mild chronic kidney disease (glomerular filtration rate 40-80 ml/min). Following informed consent, all patients will be entered into active run-in phase consisting of spironolactone 25 mg daily for 4 weeks. This will allow an early evaluation of patient safety and tolerability. Patients will have blood samples on day zero and at weeks 1, 2 and 4 to monitor serum potassium and renal function. In the event of hyperkalaemia, or any other adverse event, patients will be either withdrawn or tried on a lower dose of spironolactone. Patients tolerating spironolactone for 4 weeks will be randomised to receive spironolactone 25 mg (or a lower dose) or matching placebo for a further 36 weeks. Patients will continue to take the rest of their medications as usual. Over 40 weeks there will be 3 main visits to the Renal Unit and 5 very short visits. We will try and combine these visits with any existing Outpatient Appointments.

The end-points of the study will be:
- Left ventricular mass by echocardiography (and magnetic resonance imaging in a subset of patients).
- Left ventricular systolic and diastolic function by echocardiography
- Arterial stiffness by pulse wave analysis and pulse wave velocity
- Heart rate variability by 24-hour ECG recordings
- Blood markers of inflammation and oxidative stress.

The 5 short visits (to see the Study Nurse) will be for a simple blood test (5 ml; 1 teaspoon) to monitor blood potassium levels and should take no longer than 10 minutes. The 3 main visits will each last approximately 2 hours. They will happen right at the beginning, after 4 weeks and at the end of the study. The first thirty minutes will be spent resting in a quiet temperature controlled room. An echocardiogram will then be performed. Following this patients will have their blood pressure taken. Patients will then have their arterial stiffness measured by taking their pulse at the radial artery (augmentation index), carotid and femoral arteries (pulse wave velocity) with a tonometer, which looks like a pen. This takes approximately 15 minutes. After this endothelial function will be measured in the skin circulation. This is done by applying extremely small amounts of drugs (acetylcholine and sodium nitroprusside) onto the skin that dilate blood vessels. The increased blood flow through the skin is measured by using a monitor applied to the finger tip. This whole process takes about 30 minutes. After this a blood test is taken. An extra 10 ml (2 tablespoons) of blood is taken to measure the concentrations of aldosterone and other hormones (angiotensin II, renin) as well as markers of inflammation (CRP and 8-isoprostane). Before leaving the renal unit three ECG (heart monitor) leads are attached to the patient's chest. These are connected to a heart monitor that fits into a little pocket that can be attached to a belt. A 24-hour blood pressure monitor will also be fitted. These will be worn for the next 24 hours. At the end of the 2 hours the patient will leave the renal unit. There will be no side-effects or discomfort from any of the measurements made and the patient should therefore be able to get on with the rest of their day as normal. Arrangements will be made for collection of the 24-hour ECG and blood pressure monitors.
Some of the patients will be asked to attend on two further visits of about 30 minutes each at the start and end of the study. These will be to allow as to perform a cardiac magnetic resonance study. This is a special scan of the heart which will allow us to make a more detailed and accurate measurements of the heart. It will involve lying down on a table which is then pushed into the scanner that looks like a small tunnel. The whole process takes about 15 minutes. No X-rays are used and there is therefore no exposure to radiation. A small amount of contrast will be injected into a vein. Efforts will be made to time these extra visits with either other study visits or clinic

visits to minimise inconvenience. After the third main visit the spironolactone or placebo tablets will be stopped and there will be no further visits or tests to be done. Patients will continue to attend the renal clinics as usual.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
aldosterone

Primary outcome measure
1. Arterial stiffness after 40 weeks of spironolactone/placebo
2. Left ventricular mass, systolic & diastolic dysfunction, heart rate variability, endothelial dysfunction, plasma oxidant and inflammatory markers

Secondary outcome measures
Not provided at time of registration

Overall study start date
23/03/2005

Completion date
23/03/2008

Eligibility

Key inclusion criteria
Not provided at time of registration

Participant type(s)
Patient

Age group
Not Specified

Sex
Not Specified

Target number of participants
200

Key exclusion criteria
Not provided at time of registration

Date of first enrolment
23/03/2005

Date of final enrolment
23/03/2008

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
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Funder(s)

Funder type
Government

Funder Name

University Hospital Birmingham NHS Trust (UK)

Funder Name
NHS R&D Support Funding

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	04/08/2009		Yes	No