

# The role of aldosterone in cardiovascular disease in chronic renal failure

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		<input type="checkbox"/> Protocol
<b>Registration date</b> 30/09/2005	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
<b>Last Edited</b> 28/03/2012	<b>Condition category</b> Circulatory System	<input type="checkbox"/> Individual participant data

**Plain English summary of protocol**  
Not provided at time of registration

## Contact information

**Type(s)**  
Scientific

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## Additional identifiers

**Protocol serial number**  
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

### **Study type(s)**

Not Specified

### **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 us 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(s)**

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

**Key secondary outcome(s)**

Not provided at time of registration

**Completion date**

23/03/2008

**Eligibility****Key inclusion criteria**

Not provided at time of registration

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Not Specified

**Sex**

Not Specified

**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**

United Kingdom

England

**Study participating centre**

Renal Medicine

Birmingham

United Kingdom

B29 6JD

**Sponsor information**

## Organisation

Department of Health

## Funder(s)

### Funder type

Government

### Funder Name

University Hospital Birmingham NHS Trust (UK)

### Funder Name

NHS R&D Support Funding

## Results and Publications

### 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?
<a href="#">Results article</a>	results	04/08/2009		Yes	No