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The effects of spironolactone on endothelial function, autonomic function and glycaemic control in diabetic patients with poor blood pressure control

Submission date 16/07/2007	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 27/07/2007	**Overall study status** Completed	
Last Edited 12/05/2011	**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
SAM 001

Study information

Scientific Title

Study objectives
Patients with diabetes are at particularly high risk of cardiovascular disease. Infact, macrovascular disease accounts for 70 % of the mortality in type 2 diabetes, making heart attacks and strokes two to four times more frequent in these patients compared to controls. The combination of diabetes and hypertension is a particularly strong cardiovascular risk factor. Vascular endothelial dysfunction is a recognised risk factor for cardiovascular mortality. Blocking aldosterone with spironolactone in patients with cardiac failure can reverse endothelial dysfunction in this patient group, as well as improving the prognostic markers of PIIINP, BNP and heart rate variability. Additionally, the RALES (Randomised Aldactone Evaluation Study) and EPHESUS (Eplerenone Postacute myocardial infarction Heart failure Efficacy and Survival Study) studies have shown a dramatic reduction in total mortality (approximately 30%) with aldosterone blockade in patients with heart failure already taking the recognised optimum treatment for this condition. This lends weight to the concept that reducing endothelial dysfunction by spironolactone may be associated with reduction in real cardiovascular events.

The question then arose whether similar benefits might be seen in other diseases. It was therefore somewhat surprising that in a normotensive population of patients with type 2 diabetes, spironolactone actually worsened the key prognostic marker of endothelial function while also worsening glycaemic control. The situation might however be different in diabetics with poorly controlled hypertension where a spironolactone induced fall in BP might instead lead to an improvement in endothelial and autonomic function. We therefore studied whether, in patients with type 2 diabetes mellitus and poorly controlled hypertension, taking low-dose spironolactone in addition to their normal cardiovascular medication, would improve the important prognostic marker of endothelial function, as logic suggests that this should be of benefit. In addition we wish to investigate whether spironolactone treatment also brings about an improvement in the other prognostic markers of PIIINP, BNP and heart rate variability. We also wanted to see if the spironolactone induced worsening of glycaemic control that we saw in a previous study in normotensive diabetics was reproducible.

Ethics approval required
Old ethics approval format

Ethics approval(s)
The Tayside Committee for Medical Ethics, Scotland, approved on 28/09/2004 (ref: 236/03)

Study design
Randomized, placebo-controlled, double-blind, cross-over design.

Primary study design
Interventional

Secondary study design

Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Not Specified

Participant information sheet

Health condition(s) or problem(s) studied
Type 2 diabetes mellitus and hypertension

Interventions
In this cross-over study, each participant was treated with two different drugs and a placebo, one at a time, in addition to his or her standard medication. Each drug / placebo treatment lasted for 4 weeks, and there was a 2-week washout period between each treatment (during the washout period participants took their standard medication only). Therefore, the entire duration of the intervention was 16 weeks. Details of the intervention treatments are as follows:
1. Spironolactone, 25 mg orally per day for 1 week, increased to 50 mg per day for the next 3 weeks if potassium levels were within normal limits (total duration of treatment 4 weeks)
2. Amlodipine, 5 mg orally per day for 4 weeks
3. Placebo for 4 weeks

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Spironolactone, Amlodipine

Primary outcome measure
Improvement in endothelial function, assessed 24 months after the start of the trial.

Secondary outcome measures
The following were assessed 24 months after the start of the trial:
1. Improvement in the other prognostic markers of PIIINP and B-type Natriuretic Peptide (BNP)
2. Improvement in heart rate variability

Overall study start date
01/01/2005

Completion date
31/12/2006

Eligibility

Key inclusion criteria

Patients with type 2 diabetes mellitus and hypertension who were on standard treatment were recruited. All patients were on either Angiotensin Converting Enzyme (ACE) inhibitors or angiotensin receptor blockers.

Participant type(s)
Patient

Age group
Not Specified

Sex
Both

Target number of participants
50

Key exclusion criteria
1. Blood pressure <140 mm Hg systolic and 80 mm Hg diastolic
2. Recent admission to hospital within last 4 weeks
3. History of alcohol abuse
4. Liver or renal impairment
5. Heart failure
6. On potassium sparing diuretics, insulin or warfarin (procedural risks)

Date of first enrolment
01/01/2005

Date of final enrolment
31/12/2006

Locations

Countries of recruitment
Scotland

United Kingdom

Study participating centre
Department of Clinical Pharmacology
Dundee
United Kingdom
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Sponsor information

Organisation
Tenovus Scotland (UK)

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Sponsor type
Charity

Website
http://www.tenovus-scotland.org.uk/TS_homepage.html

ROR
https://ror.org/037866t57

Funder(s)

Funder type
Charity

Funder Name
Tenovus Scotland (ref: T03/21) (UK)

Funder Name
Northwood Trust (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	01/05/2008		Yes	No