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Insulin action and hypertension: effects of hyperaldosteronism and its treatment

Submission date	Recruitment status	[_] Prospectively registered
30/07/2008	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
23/09/2008	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
06/06/2016	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
RGHT 000298

Study information

Scientific Title
Insulin action and hypertension: effects of hyperaldosteronism and its treatment

Study objectives
Many common conditions such as type two diabetes and hypertension, as well as less common conditions such as hypopituitarism and secondary hypertension are associated with insulin resistance. All are associated with increased vascular risk to which insulin resistance may contribute. The study seeks to determine how to characterise and treat hypertensive patients with special reference to the influence of insulin action.

The link between increased insulin resistance, diabetes and essential hypertension has prompted concern regarding deleterious effects of antihypertensive therapy on glucose and lipid metabolism. Evidence that commonly prescribed agents may increase insulin resistance and that this may lessen the beneficial impact of tight blood pressure control on cardiovascular endpoints has led to much debate regarding appropriate choice of drug treatment. The continued use of older agents, in particular thiazide diuretics, has been supported by one recent large trial but shown to be associated with a less favourable outcome in another.

Recent trials have also demonstrated a protective effect of aldosterone antagonist therapy in heart failure and left ventricular dysfunction after myocardial infarction. Despite these advances little is known of the effect on insulin resistance of aldosterone antagonist drugs such as spironolactone or the new agent, eplerenone.

The first study outlined seeks to determine the effect of eplerenone on insulin action in essential hypertension using a double blind, cross-over protocol.

Ethics approval required
Old ethics approval format

Ethics approval(s)
The Office for Research Ethics Committee in Northern Ireland (ORECNI), 13/05/2008, ref: 08 /NIR01/12

Study design
Randomised controlled crossover double-blind trial

Primary study design
Interventional

Secondary study design
Randomised cross over trial

Study setting(s)
Hospital

Study type(s)
Treatment

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
Hypertension and insulin resistance

Interventions
A randomised double-blind control crossover design will be employed. All antihypertensive agents will be withdrawn and placebo substituted for six weeks. During this period blood pressure will be monitored every two weeks. There will be two study periods of 12 weeks during which blood pressure will be measured after two weeks and then every four weeks, separated by a six-week washout during which blood pressure will be measured every two weeks. It is no longer ethical to compare with placebo and so we will compare with doxazosin, which has been shown to be neutral in its effect on insulin action. Patients will be started on eplerenone 25 mg twice daily or doxazosin 1 mg twice daily for the first week, 2 mg twice daily thereafter.

Insulin action will be assessed at the end of the placebo run in and after each of the two study periods. Twenty-four hour ambulatory blood pressure monitoring will be performed in the last week of placebo run-in and each treatment period. If, during the study (including during placebo run-in or wash-out), systolic blood pressure rises above 160 mmHg or diastolic blood pressure rises above 100 mmHg on any occasion, or above 160 and 95 mmHg on two occasions, additional therapy with doxazosin will be given, with the addition of up to 12 mg of doxazosin. Serum creatinine and potassium will be measured at baseline and every four weeks during the active treatment periods.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Insulin (eplerenone), doxazosin

Primary outcome measure
Insulin action will be measured by performing a hyperinsulinaemic, euglycaemic clamp, measured at the end of weeks 6, 18 and 36.

Secondary outcome measures
Blood pressure will be measured using a standard automated blood pressure machine, measured at the end of weeks 2, 4, 6, 8, 12, 16, 18, 20, 22, 24, 26, 30, 34 and 36.

Overall study start date
15/08/2008

Completion date
15/08/2010

Eligibility

Key inclusion criteria
1. Patients aged under 70 years, either sex
2. Mild essential hypertension

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
16

Key exclusion criteria
1. Presence of diabetes mellitus
2. Significant obesity (body mass index [BMI] exceeding 35 kg/m^2)
3. Cardiac, renal or hepatic disease
4. A history of gout
5. Any treatment that may affect insulin action
6. Hyperkalaemia
7. Taking potassium sparing diuretics, potassium supplements or strong inhibitors of CYP 34A
8. Women who are pregnant or breastfeeding
9. Secondary hypertension
10. Diastolic blood pressure outside 80 - 105 mmHg range after placebo run-in of six weeks
11. Not capable of giving informed consent

Date of first enrolment
15/08/2008

Date of final enrolment
15/08/2010

Locations

Countries of recruitment
Northern Ireland

United Kingdom

Study participating centre
Royal Victoria Hospital
Belfast
United Kingdom
BT12 6BA

Sponsor information

Organisation
Belfast Health and Social Care Trust (UK)

Sponsor details
Royal Research Office
First Floor, Education Centre
Royal Victoria Hospital
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Sponsor type
Hospital/treatment centre

Website
http://www.belfasttrust.hscni.net/

ROR
https://ror.org/02tdmfk69

Funder(s)

Funder type
Government

Funder Name
Northern Ireland Research and Development Office (UK) - Recognised Research Group Funding (ref: RRG 5.46)

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	01/10/2014		Yes	No