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Studies of insulin action in patients at increased vascular risk: modulation by anti-hypertensive and endocrine replacement therapy

Submission date 12/09/2006	**Recruitment status** No longer recruiting
Registration date 25/01/2008	**Overall study status** Completed
Last Edited 17/02/2015	**Condition category** Nutritional, Metabolic, Endocrine

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] 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

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

RGHT000278

Study information

Scientific Title
Studies of insulin action in patients at increased vascular risk: modulation by anti-hypertensive and endocrine replacement therapy

Study objectives
Insulin resistance is present in common clinical conditions including diabetes and hypertension, and in less common ones such as hypopituitarism. Each of these is associated with vascular risk and increasing evidence suggests that insulin resistance may contribute. The studies described aim to define better how treatment interventions in these conditions affect insulin sensitivity.

Studies in the Regional Centre for Endocrinology and Diabetes, Royal Victoria Hospital, Belfast, using detailed assessment of insulin action in carefully controlled protocols have influenced the debate about the most appropriate anti-hypertensive treatment. Our most recent data suggest that combining thiazide diuretics even at low doses with an angiotensin converting enzyme (ACE) inhibitor will increase insulin resistance in hypertensive type two diabetic patients. We plan a similar comparison in nondiabetic hypertensive patients in whom this efficacious combination may be without this adverse effect. We will also compare low dose thiazide/ACE inhibitor with calcium channel blocker/ACE inhibitor, a key choice in current guidelines.

We have previously investigated the impact of hydrocortisone and growth hormone on insulin action in hypopituitarism. Levels of dehydroepiandrosterone (DHEA), an adrenal steroid hormone, are reduced in hypopituitarism. DHEA is available in the United States of America (USA) as replacement therapy and has been shown to improve quality of life in patients with hypoadrenalism. Its effect on insulin sensitivity is controversial and has not been widely researched in patients with hypopituitarism. Using a placebo controlled cross-over trial, we plan to study DHEA replacement in hypopituitarism.

The results of the studies described will influence future therapeutic approaches in these at risk patients.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Office for Research Ethics Committee in Northern Ireland (ORECNI), 29/08/2006, ref: 06/NIR03 /93

Study design
Randomised double-blind placebo-controlled cross-over study

Primary study design
Interventional

Secondary study design
Randomised controlled 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, type 2 diabetes, hypopituitarism

Interventions
Protocols one and two:
Medications will be withdrawn and replaced with placebo for a six week run in. Patients will be randomised to captopril plus study drug (bendroflumethiazide) or captopril plus placebo in protocol one and captopril plus bendroflumethiazide or plus amlodipine in protocol two for 12 weeks. There will be a six week washout, then cross over to the alternative study arm.

Protocol three:
Hydrocortisone therapy will be standardised for four weeks. Patients will receive either dehydroepiandrosterone or placebo for 12 weeks. As for previous protocols, there will be a six week wash out then cross over to the other treatment arm. Insulin action will be assessed after placebo run in and each 12 weeks study period using the hyperinsulinaemic euglycaemic clamp method.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Captopril, bendroflumethiazide, amlodipine

Primary outcome measure
Insulin resistance

Secondary outcome measures
Quality of life following dehydroepiandrosterone replacement

Overall study start date
19/09/2006

Completion date
01/08/2008

Eligibility

Key inclusion criteria

1. Under 65 years old
2. Protocol one: essential hypertension, mild or newly diagnosed
3. Protocol two: type two diabetes and hypertension
4. Protocol 3: hypopituitarism, female, low basal DHEA levels

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
45

Key exclusion criteria
1. Secondary hypertension
2. Obesity
3. Cardiac, renal or hepatic disease
4. History of gout
5. Those in receipt of any additional medications that may affect insulin action
6. Type two diabetics with dipstick positive proteinuria

Date of first enrolment
19/09/2006

Date of final enrolment
01/08/2008

Locations

Countries of recruitment
Northern Ireland

United Kingdom

Study participating centre
Royal Victoria Hospital
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Sponsor information

Organisation
Royal Group Hospitals Trust (UK)

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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/03rq50d77

Funder(s)

Funder type
Government

Funder Name
Research and Development Office (UK) - Department of Health and Social Security

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	01/09/2012		Yes	No
Results article	results	01/04/2013		Yes	No