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A comparison of the effects of rosiglitazone on endothelial function and arterial stiffness in insulin resistant individuals and normal controls

Submission date 12/09/2003	**Recruitment status** Stopped	[ ] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 12/09/2003	**Overall study status** Stopped	
Last Edited 27/09/2011	**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

Protocol serial number
N0544093589

Study information

Scientific Title

Study objectives
Rosiglitazone: endothelial function and arterial stiffness.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Randomised controlled trial

Primary study design
Interventional

Study type(s)
Not Specified

Health condition(s) or problem(s) studied
Cardiovascular: Endothelial function and arterial stiffness

Interventions
Rosiglitazone has been noted to have effects on the vasculature. We hypothesise that it may improve endothelial function and reduce arterial stiffness. We believe that the effects may be greater in people who are overweight as they tend to have insulin resistance and the actions of rosiglitazone may occur via its insulin-sensitizing effects. The effects may also be partially mediated via nitric oxide dependent mechanisms. We propose to study 12 obese and 12 non-obese subjects. They will be required to attend for three visits, the first of which will last for 30 min and the second and third for around 3 h each. The first visit will be a screening visit during which informed consent will be obtained and inclusion and exclusion criteria checked. Physical examination and medical history will be performed to ensure that it is safe for inclusion in the study. On the second and third visits, measurements of blood pressure, bio-impedance, forearm blood flow and arterial stiffness will be made (all non-invasive). Subjects will then be given a single oral dose of either rosiglitazone 8 mg or placebo. Two hours later, measurements of endothelial function will be made. A 27 gauge needle will be inserted into the left brachial artery under local anaethesia (1% lignocaine). Saline or drugs will be infused at a constant rate of 1.0 ml /min by means of a constant rate infusion pump throughout the duration of the study. Basal blood flow will be recorded after 18 min of 0.9% saline infusion. Acetylcholine will then be co-infused with saline at a dose of 7.5 and 15 ug/min, each dose at 1.0 ml/min for 6 min. There will then be a 18 min washout period during which saline infusion will be given. Sodium nitroprusside will then be co-infused with saline at a dose of 3 and 10 ug/min, each dose at 1.0 ml/min for 6 min. There will then be a further 18 min washout period with saline. L-NG-monomethyl-arginine (L-NMMA) will then be co-infused with saline at a dose of 4 then 8 umol/min, each dose at 1.0 ml /min for 6 min. Further measurements of forearm blood flow will be made during the last 2 min of each infusion period by venous occlusion plethysmography over 1 min. Blood flow will be measured every alternate 3 min for a 3 min period by intermittent inflation of a blood pressure cuff around the upper arm to 40 mmHg. A second cuff will be inflated around the wrist to a pressure of 200 mmHg during measurements of blood flow (maximum duration 3 min) in order

to exclude the hand from the circulation during measurements. At the first visit subjects will also undergo measurement of Minimum Forearm Vascular Resistance (MFVR). In order to measure MFVR, a cuff will be inflated around the upper arm to a pressure of 300 mmHg to occlude arterial flow to the forearm for 13 min and then deflated and a measurement of forearm blood flow made by venous occlusion plethysmography. Arterial stiffness will be measured non-invasively using Pulse Wave Analysis (SphygmoCor, PWV Medical, Australia). This involves holding a small pressure sensitive probe against the skin overlying the radial, carotid and femoral arteries in turn. Following the assessment of endothelial function on the second and third visits, subjects will have baseline measurements of arterial stiffness repeated. They will then receive 400 micrograms of salbutamol by inhalation and after values have returned to baseline 500 micrograms of glyceryl trinitrate (GTN) sublingually, with repeat measurements of arterial stiffness immediately after each drug is given. This will allow endothelial function in the large arteries to be assessed. The study will be conducted according to International Conference on Harmonisation (ICH)-Good Clinical Practice (GCP) guidelines.

This trial has stopped due to lack of funding

Intervention Type
Drug

Phase
Not Specified

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

Primary outcome(s)
Not provided at time of registration

Key secondary outcome(s))
Not provided at time of registration

Completion date
30/09/2003

Reason abandoned (if study stopped)
Lack of funding

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
26/01/2001

Date of final enrolment
30/09/2003

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Clinical Pharmacology Unit
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Sponsor information

Organisation
Department of Health (UK)

Funder(s)

Funder type
Government

Funder Name
Cambridge Consortium - Addenbrooke's (UK)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration