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Medical management of severe aortic regurgitation in asymptomatic patients with normal left ventricular function with valsartan - a study to assess disease progression

Submission date 29/09/2006	**Recruitment status** Stopped	[ ] Prospectively registered [ ] Protocol
Registration date 29/09/2006	**Overall study status** Stopped	[ ] Statistical analysis plan [ ] Results
Last Edited 06/03/2015	**Condition category** Circulatory System	[ ] Individual participant data [ ] Record updated in last year

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
N0265170217

Study information

Scientific Title

Medical management of severe aortic regurgitation in asymptomatic patients with normal left ventricular function with valsartan -a study to assess disease progression

Study objectives
Treatment with valsartan reduces the adaptive increase in LV mass to chronic moderate-severe AR in asymptomatic patients (NYHA II or less) with normal EF >50% and preserved LV dimensions (LVIDs less than 5.5cm) to a greater extent than short-acting nifedipine.

Updated 06/03/2015: the trial was stopped due to lack of recruitment.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Primary study design
Interventional

Study design
Randomised controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Cardiovascular: Severe Aortic Regurgitation

Interventions
Patients will be randomised in a single blind fashion to Valsartan 80 mg twice daily or modified release nifedipine 20 mg bd continued for one year.

In all patients at entry, a full clinical assessment will be performed and clinical details including cause of AR, presence of vascular disease, risk factors for vascular disease and drug therapy will be recorded. Blood pressure, heart rate and body mass index will be recorded. NYHA and CSA status will be recorded. A 12 lead ECG will be recorded. Routine haematological and biochemical parameters including plasma lipids will be recorded. Renal function will be measured at two weeks following randomisation. If creatinine has risen by more that 10% or >150 micromol/l or potassium >5.9 mmol/l then the study drug will be withdrawn. Exercise capacity will be assessed using the six minute walk test. At baseline, the following measurements will be made:

CMR
LV mass, LV volumes and LV function will be calculated using serial contiguous short axis TrueFISP cine sequences with 7 mm slice thickness and 3 mm gap using a 1.5-Tesla magnet as previously described (Bellenger and Pennell 2002). Analysis will be performed off-line using the semi-automated Siemens ARGOS software. In addition, regurgitant fraction and regurgitant volumes will be calculated from LV and RV volumetric analysis, together with velocity-encoded flow mapping.

ECHOCARDIOGRAPHY
The following parameters will be obtained:
Assessment of AR:
- Regurgitant jet size on CF Doppler (%LVOT)
- Vena contracta
- PISA radius and effective orifice quantification
- Diastolic jet deceleration (pressure half-time)
- Regurgitant fraction by stroke volume (AV / PV)
- Doppler flow reversal aorta
- Subjective assessment
LV mass (ASE): 0.80 . 1.05 . [(IVS+PW+LVID)3 - LVID3]
LV systolic (and diastolic) function:
- LVEF by modified Simpsons rule
- Tei index

REPEATED MEASURES
Clinical, biochemical, echo and CMR assessment will be repeated at 12 months.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Valsartan, nifedipine

Primary outcome(s)
The primary end-point will be a comparison in the reduction in LV mass assessed with cardiac MR at one year between Valsartan 80mg bd and modified release nifedipine 20mg bd.

Quality of measurement will be enhanced by assessment by two independent assessors at different sittings. Studies will be performed to confirm inter- and intra-observer variability of assessments.

Key secondary outcome(s)
1. Change in LV ejection fraction
2. Change in LV volume
3. Change in regurgitant fraction
4. Reduction in progression to the combined end-point of symptoms (NYHA >II)
5. LV systolic dysfunction (LVEF<50%)
6. Requirement for AVR
6. Death over the study period

Completion date
10/04/2008

Reason abandoned (if study stopped)
Participant recruitment issue

Eligibility

Key inclusion criteria
Subjects are to be recruited from patients either under active follow-up or active referral as in-patients or out-patients to the Department of Cardiology, University Hospital Birmingham.
Inclusion criteria:
1. Asymptomatic or mildly symptomatic patients with moderate - severe AR (NYHA II or less; CSA <2)
2. Normal LVEF >50%
3. Preserved LV dimensions (LVIDs <5.5cm)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Not Specified

Sex
Not Specified

Key exclusion criteria
1. Acute, severe AR or rapid deterioration of AR (within the preceding six months)
2. Mixed aortic stenosis and regurgitation (valve stenosis > mild defined as peak gradient above 20 mm Hg)
3. Evidence of additional valvular or congenital heart disease on echocardiographic study sufficient to require surgical intervention
4. Abnormal left ventricular ejection fraction (<50 percent)
5. Contra-indications to Angiotensin II receptor antagonist therapy (previous intolerance; known or suspected renovascular hypertension; creatinine >150 umol/L, serum potassium > 5.9 mmol/l) or to treatment with nifedipine
6. Contra-indication to cardiac MRI

Date of first enrolment
10/04/2005

Date of final enrolment
10/04/2008

Locations

Countries of recruitment
United Kingdom

England

Study participating centre

Selly Oak Hospital
Birmingham
United Kingdom
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Sponsor information

Organisation
Record Provided by the NHSTCT Register - 2006 Update - Department of Health

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
University Hospital Birmingham NHS Trust

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