# The effect of reducing heart rate on central aortic blood pressure: a comparative study of ivabradine and atenolol on haemodynamic parameters at rest

Submission date 28/09/2007	<b>Recruitment status</b> Stopped	<ul> <li>Prospectively registered</li> <li>Protocol</li> </ul>
<b>Registration date</b> 28/09/2007	<b>Overall study status</b> Stopped	<ul> <li>Statistical analysis plan</li> <li>Results</li> </ul>
Last Edited 14/09/2012	<b>Condition category</b> Circulatory System	<ul> <li>Individual participant data</li> <li>Record updated in last year</li> </ul>

#### Plain English summary of protocol

Not provided at time of registration

# Contact information

### Type(s)

Scientific

# Contact name

Dr Ian Wilkinson

#### **Contact details**

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# Additional identifiers

EudraCT/CTIS number

**IRAS number** 

#### ClinicalTrials.gov number

Secondary identifying numbers

N0544183629

# Study information

#### Scientific Title

Ethics approval was received from the local Cambridge medical ethics committee before trial recruitment began.

#### **Study objectives**

1. Hypothesis: heart rate reduction per se leads to an accentuation of central aortic pressure irrespective of the mechanism of heart rate reduction or changes in peripheral blood pressure. 2. Aims: we aim to test the above hypothesis by employing a pharmacological approach: comparing the haemodynamic effects of a beta-blocker (atenolol) and a heart rate limiting drug (ivabradine) in a placebo-controlled crossover trial (ie all participants will get placebo, atenolol and ivabradine at some stage). Heart rate, central and peripheral blood pressure, cardiac output and arterial stiffness (the 'haemodynamic parameters') will be assessed at baseline and up to 4 hours after each acute dosing.

**Ethics approval required** Old ethics approval format

**Ethics approval(s)** Not provided at time of registration

**Study design** Placebo controlled crossover trial

**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

Cardiovascular: Haemodynamic parameters at rest

#### Interventions

#### STUDY DESCRIPTION

Up to 24 healthy people will be recruited in to the study via a poster asking for volunteers. The study will consist of 4 visits.

14/09/2012: Please note that this trial was stopped due to poor recruitment

#### INCLUSION AND EXCLUSION CRITERIA

Visit 1 - Volunteers will be interviewed, examined and formal consent obtained. Height and weight will also be taken and a 12 lead electrocardiogram (ECG) performed. The GP will be informed with the subjects agreement.

Visit 2, 3 and 4 - Subjects will be asked to have a light breakfast (excluding tea, coffee, alcohol) and arrive by 8.30am. They will lie down and an intravenous cannula will be inserted into the forearm through which we will take blood. They will also be connected to a heart monitor. After an hour, baseline measurements will be taken. This involves applying a probe to the surface of the neck and the wrist. Via a computer and software programme, we can then assess central aortic pressure too. Haemodynamic parameters to be measured include: augmentation index, aortic and radial pulse wave velocity and analysis. These will be measured using the SphygmoCor system 2-Atcor Medical, Sydney, Australia. This will allow assessment of central aortic blood pressure using a validated transfer function. Electrodes placed on the chest will record heart rate. This will allow us to determine heart rate variability during specific times during the study with the SphymoCor HRV system. Similarly, cardiac output, stroke volume and cardiac index will be determined. Peripheral blood pressure will also be measured using a sphygmomanometer. Following this, we will take about 10-15ml of blood (approximately a tablespoonful) and send it for the measurement of sodium, potassium, calcium, creatinine, renin and aldosterone and catecholamines.

Then, subjects will be dosed with one of 3 pills orally: either atenolol 50mg, ivabradine 20mg or placebo (a dummy pill), but neither the volunteer nor the person doing the measurements will know which. Blood pressure readings will be repeated hourly and the blood tests at 4 hours. The final measurements will be made 4 hours post dosing, after which participants will be given food and drink and if the blood pressure and heart rate is acceptable, let home. Note that subjects are not permitted to eat or drink during the period of study. There will be a minimum 'washout' period of 3 days post which volunteers will attend for 2 more visits like the one described above but with different drugs (ie they will get all three types of pill during the course of the study).

#### ADVERSE EVENTS

Participants will be encouraged to report any adverse events and to contact members of the research team if they experience any problems. All serious adverse events will be reported to the Research and Development Department at Addenbrookes Hospital and other authorities as appropriate.

#### **TERMINATION OF STUDY**

The study will be ended when the last subject completes the study. Participants will be offered notification as to when any results might be published in the form of a scientific publication.

Intervention Type Drug

**Phase** Not Specified

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

ivabradine and atenolol

**Primary outcome measure** Assessing change in central blood pressure

**Secondary outcome measures** Assessing change in haemodynamic parameters

Overall study start date 01/06/2006

**Completion date** 01/07/2009

**Reason abandoned (if study stopped)** Participant recruitment issue

# Eligibility

#### Key inclusion criteria

- 1. Volunteers aged 18-65
- 2. Subjects able to give informed consent
- 3. Normal blood pressure (< 140/90 mmHg but = 110/70 mmHg)
- 4. Resting heart rate = 50 beats per minute

**Participant type(s)** Patient

**Age group** Adult

**Lower age limit** 18 Years

**Upper age limit** 65 Years

**Sex** Not Specified

Target number of participants

24 healthy volunteers

#### Key exclusion criteria

- 1. Subjects with a history of hypertension or diabetes mellitus
- 2. Volunteers with a conduction defect on the ECG
- 3. Resting heart rate < 50 beats per minute and blood pressure < 110/70 mmHg
- 4. Pregnant women or those of childbearing age taking inadequate contraception
- 5. Volunteers with a history of asthma, cardiovascular disease or arrhythmias
- 6. Participants with a history of intolerance to beta-blockers or ivabradine

Date of first enrolment 01/06/2006

Date of final enrolment 01/07/2009

# Locations

**Countries of recruitment** England

United Kingdom

**Study participating centre Lecturer and Honorary Consultant** Cambridge United Kingdom CB2 2QQ

### Sponsor information

**Organisation** Record Provided by the NHSTCT Register - 2007 Update - Department of Health

**Sponsor details** The Department of Health, Richmond House, 79 Whitehall London United Kingdom SW1A 2NL +44 (0)20 7307 2622 dhmail@doh.gsi.org.uk

**Sponsor type** Government

Website http://www.dh.gov.uk/Home/fs/en

# Funder(s)

**Funder type** Government

#### Funder Name

Cambridge Consortium - Addenbrooke's (UK), Departmental Funds, NHS R&D Support Funding

# **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