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The pharmacogenetics of aspirin resistance

Submission date	Recruitment status	[ ] Prospectively registered
06/10/2006	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
14/03/2007	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
15/04/2016	Injury, Occupational Diseases, Poisoning	[ ] 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

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
RGHT000270

Study information

Scientific Title
The pharmacogenetics of aspirin resistance

Study objectives
The Antiplatelet Trialists' Collaboration meta-analyses (1994) documented a 25% reduction of death, myocardial infarction, and stroke in high-risk patients treated with aspirin. However, some patients continue to experience clinical events despite aspirin therapy, indicating that the anti-platelet effect of aspirin may not be uniform in all patients. Clinical aspirin resistance refers to those patients who have recurrent thrombotic events despite compliance with therapy. Biochemical aspirin refers to inadequate platelet inhibition on formal testing.

The aims of this proposed study are to use a repeated period crossover trial design in order to assess the reproducibility of aspirin resistance in healthy control individuals, using standard optical platelet aggregometry. Additional measures of platelet function will also be assessed using the Platelet Function Analyser (PFA-100) system, and levels of serum thromboxane B2 and urinary 11-dehydro thromboxane B2.

Furthermore, the contribution of genetic polymorphisms in candidate genes to the phenomenon of aspirin resistance will be characterised. Polymorphisms of several contributing genes including the Cyclooxygenase-1 (COX-1), Cyclooxygenase-2 (COX-2), GlycoProtein IIIa (GPIIIA), and adenosine 5-diphosphate receptor genes will be investigated using standard molecular approaches.

01/10/2012: Please note that the anticipated end date of this trial was updated from 01/08 /2009 to 30/08/2012

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approval received from the Office for Research Ethics Committees Northern Ireland (ORECNI) on the 14th June 2006 (reference number: 06/NIR01/44).

Study design
Randomised repeated period crossover trial design

Primary study design
Interventional

Secondary study design
Randomised cross over trial

Study setting(s)
Hospital

Study type(s)
Other

Participant information sheet

Health condition(s) or problem(s) studied
Aspirin resistance

Interventions
The study is a repeated crossover trial design of two treatments and four periods. The aspirin dose will be either 75 mg or 300 mg but will be fixed within individual patients. A subject will be randomised to one of four treatment sequences: ABBA, BAAB, ABAB or BABA, where A is active drug and B is placebo.

Each individual study period will last for three weeks, therefore the total period of study for each patient will be 12 weeks. This type of design allows the study of treatment, subject, period and carry-over effects, and their interactions, specifically the subject-by-treatment interaction.

The individuals will be seen at baseline and once informed consent has been obtained, baseline tests for platelet function tests (optical aggregometry, PFA-100) and serum/urine thromboxane levels will be taken, as will whole blood for later analysis of genetic polymorphisms. Further samples for platelet function testing will be taken at the end of each crossover period.

Intervention Type
Drug

Phase
Not Specified

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

Primary outcome measure
1. Assess the reproducibility of aspirin resistance in healthy control individuals, as defined by standard optical platelet aggregometry
2. Characterise the contribution of genetic polymorphisms in candidate genes, specifically the cyclooxygenase and adenosine 5-diphosphate receptor genes, to the phenomenon of aspirin resistance

Secondary outcome measures
1. The assessment of the reproducibility of aspirin response as defined by other platelet function tests (PFA-100 system, thromboxane levels)
2. The contribution of other genetic polymorphisms to the phenomenon of aspirin resistance
3. The correlation between the various platelet function tests used in this study

Overall study start date
01/08/2006

Completion date
30/08/2012

Eligibility

Key inclusion criteria
Healthy individuals aged between 18 to 60 years

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
60 Years

Sex
Not Specified

Target number of participants
150 (53 participants actually recruited)

Key exclusion criteria
Current exclusion criteria as of 01/10/2012
1. Use of other anti-platelet drugs (thienopyridines, GPIIb/IIIa antagonists, dipyridamole) because these drugs would interfere with platelet function assays
2. Use of other non-steroidal anti-inflammatory drugs, because of the pharmacodynamic interactions
3. History of dyspepsia or peptic ulceration requiring treatment with proton pump inhibitors/H2 antagonists, in view of the increased risk of gastrointestinal haemorrhage
4. History of systemic inflammatory diseases, in view of the need for these patients to take anti-inflammatory drugs
5. History of asthma
6. Use of other aspirin-containing medications (including herbal preparations)
7. Family or personal history of bleeding disorders
8. Use of oral anticoagulants
9. Platelet count outside the normal range (150,000 to 450,000/ml)
10. Significant anaemia (Haemoglobin [Hb] less than 10 g/dl)
11. Recent major surgery
12. Known significant malignant disease
13. known aspirin allergy
14.1 Pregnancy
14.2 Women of childbearing potential except in the following circumstances for the duration of the trial: 'monogamous relationship and partner sterilised' or 'for personal reasons not sexually active' or 'use of double barrier methods of contraception'
15. History of lactose intolerance, as lactose if the primary substance contained in the placebo
16. History of gout, as aspirin can precipitate gout
17. History of severe renal or hepatic dysfunction
18. Planned surgery during participation in trial
19. Excessive alcohol ingestion (more than 40 units per week)
20. Inability to provide informed consent

Previous exclusion criteria until 01/10/2012:
14. Pregnancy/women of childbearing potential

Date of first enrolment
01/08/2006

Date of final enrolment
30/08/2012

Locations

Countries of recruitment
Northern Ireland

United Kingdom

Study participating centre
Consultant/Senior Lecture in Cardiology
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Sponsor information

Organisation
Royal Group of Hospitals Trust (UK)

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Sponsor type
Hospital/treatment centre

Website
http://www.royalhospitals.org/

ROR
https://ror.org/03rq50d77

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Royal Hospitals Trust Clinical Fellowship (UK)

Funder Name
Northern Ireland Chest Heart & Stroke Association (UK)

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