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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

**Protocol serial number**
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).

## Primary study design
Interventional

## Study design
Randomised repeated period crossover trial design

## Study type(s)
Other

## 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(s)
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

### Key secondary outcome(s)
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

### Completion date
30/08/2012

## Eligibility

### Key inclusion criteria
Healthy individuals aged between 18 to 60 years

### Participant type(s)
Patient

### Healthy volunteers allowed
No

### Age group
Adult

### Lower age limit
18 Years

### Upper age limit
60 Years

### Sex
Not Specified

### 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
United Kingdom

Northern Ireland

**Study participating centre**
**Consultant/Senior Lecture in Cardiology**
Belfast
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# Sponsor information

**Organisation**
Royal Group of Hospitals Trust (UK)

**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

**Individual participant data (IPD) sharing plan**

**IPD sharing plan summary**
Not provided at time of registration