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Genetics of aspirin resistance

Submission date 23/04/2010	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 23/04/2010	**Overall study status** Completed	
Last Edited 23/09/2016	**Condition category** Circulatory System	

Plain English summary of protocol

Background and study aims (to set the scene)
Despite many improvements in the treatment of heart disease and stroke, these conditions remain very common in Western countries, including the UK. One of the main treatments that is used to prevent heart attacks and strokes, in people who are at risk of these, including patients who have previously suffered heart disease or strokes, is aspirin. Aspirin works by inhibiting the activity of certain blood cells, called platelets, which play a role in forming clots in the arteries. However, despite taking aspirin, a number of patients who have previously had heart attacks or strokes experience another such event. These patients have been labelled as 'aspirin resistant', and much research is currently going on to try and find out why aspirin resistance occurs. Recently, several lines of evidence suggest that aspirin resistance may in fact be genetically determined, at least in part, although the genes concerned are presently not clear. This study aims to determine, both in healthy people and in patients with a history of heart disease or stroke, whether variations in certain genes that can affect the functioning of blood platelets may indeed give rise to aspirin resistance.

Who can participate?
Healthy adults aged at least 18.

What does the study involve?
Participants attend the study centre and, after a period of lying down resting, are asked to give a 100 ml blood sample (the equivalent of about 6 tablespoonfuls) from a vein. These samples are used for routine blood tests, to measure the functioning of the blood platelets in the laboratory and to study the DNA (genetic material) of some of the genes that may be important in controlling how platelets respond to aspirin. Participants are also be asked to give a urine sample at this visit, which is analysed to give another measure of how activated platelets are in the bloodstream. Some of the blood is frozen, for subsequent genetic analysis. Subjects are given aspirin 300mg daily for 4 weeks, at the end of which time they re–attend once again under the same conditions as above, for further blood (80 ml blood) and urine testing.

What are the possible benefits and risks of participating?
There are no specific benefit to taking part in the study, and participants treatment will not be affected in any way either by their participation / non-participation or by the results that obtained from them. However, the information that is obtained from this study may help to to treat future patients with (or at risk of) heart disease or stroke better. Participants may

experience slight discomfort in the arm following insertion of a needle for taking blood. Aspirin treatment may give rise to bleeding or bruising, both at the site of blood taking and elsewhere, because aspirin works by thinning the blood slightly. Any such bruising or bleeding is usually minor, but may be more severe if the participant has a reason to bleed easily, for example recent surgery or a blood clotting disorder. Overall, the risk of increased bruising and bleeding (minor and major combined) is approximately 1 in 100. Additionally, aspirin can cause stomach irritation or even ulcers; however, participants who have a history of this will be excluded to minimize the risk of this happening.

Where is the study run from?
King's College London

When is the study starting and how long is it expected to run for?
January 2007 to December 2008

Who is funding the study?
Biotechnology and Biological Science Research Council

Who is the main contact?
Professor Albert Ferro

Contact information

Type(s)
Scientific

Contact name
Prof Albert Ferro

Contact details
King's College London
3.07 Franklin-Wilkins Building
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SE1 9NH

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
4069

Study information

Scientific Title
An investigation into the genes underlying the clinical syndrome of aspirin resistance: a non-randomised interventional treatment trial

Study objectives
1. What is the prevalence of true aspirin resistance in a healthy population?
2. Can a genetic basis be identified for this?

Ethics approval required
Old ethics approval format

Ethics approval(s)
Riverside Research Ethics Committee approved in February 2007, ref: 07/Q0401/1

Study design
Non-randomised interventional treatment trial

Primary study design
Interventional

Secondary study design
Non randomised study

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
Topic: Cardiovascular; Subtopic: Cardiovascular (all Subtopics); Disease: Cardiovascular

Interventions
As of 01/08/2016:
Subjects will attend clinic following an overnight fast, and having abstained from tobacco, caffeine–containing drinks and alcohol for at least 12 hours. 100 ml blood will be taken from an antecubital
vein using a 19G needle, for both genotyping and platelet phenotyping. These baseline bloods will also be sent for routine haematology and biochemistry screening (full blood count, renal function, liver profile, lipid profile, glucose, HbA1c, homocysteine, hsCRP). A urine sample will also be taken for measurement of 11–dehydrothromboxane B2 and creatinine (the ratio of 11–dehydrothromboxane B2 to creatinine in urine is a well validated index of platelet activation). One week later, subjects will re–attend under the same conditions as above, for further venesection (80 ml blood) and repeat platelet phenotyping (we will not need to repeat the DNA analyses, haematology or biochemistry testing on visit 2), in order to establish a stable baseline for platelet function studies. Another urine sample will be taken for measurement of 11–dehydrothromboxane B2 to creatinine ratio. Subjects will then be given aspirin 300mg daily

for 4 weeks, at the end of which time they will re–attend once again under the same conditions as above, for further venesection (80 ml blood) and repeat platelet phenotyping and urinary 11–dehydrothromboxane B2 to creatinine ratio measurement.

Initial:
Aspirin 300 mg daily adminstered for 1 month. Follow up length: 1 month.

Intervention Type
Drug

Phase
Phase IV

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

Primary outcome measure
Presence of aspirin resistance at 1 month

Secondary outcome measures
Presence/absence of genetic polymorphisms in a number of candidate genes possibly related to aspirin at 1 month

Overall study start date
01/01/2007

Completion date
31/12/2008

Eligibility

Key inclusion criteria
Male or female aged 18 or more

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Not Specified

Target number of participants
Planned Sample Size: 100

Key exclusion criteria

1. Significant co-morbidity
2. Current regular therapy with any drug
3. Ingestion of aspirin, other non-steroidal anti-inflammatory drug, or other anti-platelet agent within the previous 30 days
4. Previous reaction to aspirin or other anti-platelet drug
5. History of dyspepsia or peptic ulceration
6. Pregnancy or female currently trying to conceive. Females of reproductive age wishing to take part will be asked to undergo a pregnancy test prior to inclusion, and will participate only if the test is negative.

Date of first enrolment
01/01/2007

Date of final enrolment
31/12/2008

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
King's College London
London
United Kingdom
SE1 9NH

Sponsor information

Organisation
Kings College London (UK)

Sponsor details
c/o Keith Brennan
1.8 Hodgkin Building
Guy's Campus
London
England
United Kingdom
SE1 1UL

Sponsor type
University/education

Website
http://www.kcl.ac.uk/

ROR
https://ror.org/0220mzb33

Funder(s)

Funder type
Research council

Funder Name
Biotechnology and Biological Science Research Council (BBSRC) (UK)

Funder Name
Heart Research UK (UK)

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?

Results article	results:	01/08/2014	Yes	No