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Mild bleeding disorders caused by platelet defects

Submission date
21/03/2011

Recruitment status
Recruiting

Registration date
28/04/2011

Overall study status
Ongoing

Last Edited
17/04/2024

Condition category
Haematological Disorders

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol

Background and study aims
This study aims to understand why certain patients bleed excessively. We look at the following groups of patients:
1. Patients with mild bleeding who have been seen by a blood specialist who feels their symptoms could be due to a problem in the platelets (clinically diagnosed platelet defects)
2. Patients who have unexpectedly heavy periods with no obvious cause
3. Patients with lifelong low platelet counts in the blood with no known cause
For these populations we suspect that there may be a problem in small cells in the blood, known as platelets, but we are not certain that this is the case. This study is using new and more specialist tests in an attempt to confirm that there is a problem in platelets in these groups and to use this information to help identify the gene or genes that cause this problem.

Who can participate?
Patients aged under 85 with a platelet disorder of unknown cause

What does the study involve?
Participants are asked questions about their medical history and complete a bleeding questionnaire. Participants are also asked to give a sample of blood (between 10–50 ml). The blood sample is usually be taken at a local Haematology Clinic, ideally early in the day so that the analyses can be carried out on the same day. Depending on the results of the tests, participants may be asked to give blood on up to three further occasions. This is to carry out different types of tests on the platelets and therefore find out more information on the problem. This can be taken either during a ‘regular’ visit to the Haematology Clinic/surgery or through a specific appointment. There is a minimum of one month between the dates that the blood is taken and no upper time limit on the gap between the donations. The blood samples are sent to research laboratories in Birmingham and/or Sheffield for analysis of the platelets. A frozen sample is also kept for a maximum of 10 years, which may be used to look for gene defects that could cause the platelet problem or changes in blood proteins that may increase your chance of bleeding. The sample is destroyed at this time, or earlier if requested. The sample may be kept for this length of time in the event that we are unable to find a problem with your genes in the first set of investigations. It is possible that, as we gain more knowledge, the sample is investigated at later times to find a gene defect that may be the cause of the bleeding problem.

What are the possible benefits and risks of participating?
The study will generate important information on possible defects in the platelets and may also identify the genes that are responsible for the defects. The identification of a defect in your platelets may influence clinical treatment. If a gene defect is found, it will be possible to investigate whether one or more members of the participant's family have the same gene defect, should they wish.

Where is the study run from?
University of Birmingham (UK)

When is the study starting and how long is it expected to run for?
December 2010 to February 2027

Who is funding the study?
1. British Heart Foundation (UK)
2. Wellcome Trust (UK)

Who is the main contact?
Prof Neil Morgan
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Contact information

Type(s)
Scientific

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Additional identifiers

Integrated Research Application System (IRAS)
76061

Protocol serial number
9858

Study information

Scientific Title
Mild bleeding disorders caused by platelet defects: a non-randomised observational study

Acronym
Genotyping and platelet phenotyping (GAPP)

Study objectives
It is becoming increasingly recognised that platelet function disorders are heavily under-diagnosed and therefore under-researched. Several factors have contributed to this including:

1. The absence of a 'gold standard' point-of-care assay of platelet function
2. The generally asymptomatic presentation of patients with mild defects in platelet function who only exhibit symptoms of excessive bleeding when subject to an appropriate challenge such as surgery or severe injury
3. The considerable redundancy in the pathways underlying platelet activation such that a single gene defect may not be sufficient to give rise to excessive bleeding (but may become clinically important under challenging conditions)
4. The limited amount of mRNA that can be recovered from the anucleate platelet which severely hampers many standard approaches in molecular biology including the use of microarrays.

The Birmingham Platelet Group has an approach to gene mapping of platelet disorders based on initial evaluation of clinical and laboratory phenotypes of patients with clinically diagnosed bleeding disorders and subsequent targeted gene sequencing.

In this project, we intend to investigate populations of patients enriched for bleeding to test the hypothesis that a proportion of patients who present with excessive bleeding have a previously unrecognised impairment in platelet function which may explain their propensity to bleed in conditions which would not normally be associated with severe bleeding. The proposed research will use a combination of platelet phenotyping and targeted gene sequencing approach to identify candidate mutations underlying platelet dysfunction. The effect of a small number of missense mutations on protein function will be investigated through expression studies in immortalised cell lines.

Ethics approval required
Old ethics approval format

Ethics approval(s)
West Midlands Research Ethics Committee, original approval date 10/08/2006, substantial amendment AM 2/1 approved on 06/12/2010

Primary study design
Observational

Study design
Non-randomised observational study

Study type(s)

Diagnostic

Health condition(s) or problem(s) studied
Non-malignant haematology

Interventions
Assessment of bleeding history
1. By medical questionnaire
2. Assessment: Laboratory testing for defect, extended aggregometry, flow cytometry, protein expression studies and DNA sequencing for platelet genes

Intervention Type
Other

Phase
Not Applicable

Primary outcome(s)
Identification of defects: End of project 2016, aim to identify on a molecular basis platelet defects which cause bleeding

Key secondary outcome(s)
No secondary outcome measures

Completion date
28/02/2027

Eligibility

Key inclusion criteria
1. Patients, aged 0 - 85 years, either sex
2. Diagnosed with a platelet disorder of unknown cause
3. Willing to participate and able to provide informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
0 Years

Upper age limit
85 Years

Sex

All

Key exclusion criteria
1. Patients taking drugs that are known to influence platelet function, including nonsteroidal anti-inflammatory drugs (NSAIDs) including COX-2 selective anti-inflammatory drugs), aspirin, clopidogrel, dipyridamole, warfarin or acenocoumarol within 7 days of enrolment
2. Patients having undergone a major surgical procedure within 1 month of enrolment
3. Patients with chronic renal failure requiring dialysis
4. Patients with a platelet count outside the 100 000 to 450 000/µL range
5. Patients with severe anaemia (haemoglobin < 8g/dl)

Date of first enrolment
31/12/2010

Date of final enrolment
28/02/2027

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University of Birmingham
College of Medical and Dental Sciences
Edgbaston
Birmingham
United Kingdom
B15 2TT

Study participating centre
25+ referring centres
United Kingdom
-

Sponsor information

Organisation
University of Birmingham

ROR

https://ror.org/03angcq70

Funder(s)

Funder type
Charity

Funder Name
British Heart Foundation

Alternative Name(s)
The British Heart Foundation, the_bhf, BHF

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Funder Name
Wellcome Trust

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
International organizations

Location
United Kingdom

Funder Name
National Institutes of Health

Alternative Name(s)
US National Institutes of Health, Institutos Nacionales de la Salud, NIH, USNIH

Funding Body Type

Government organisation

Funding Body Subtype
National government

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available due to the danger of it being identifiable.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/09/2013		Yes	No
Results article	results	20/02/2014		Yes	No
Results article	results	01/05/2014		Yes	No
Results article	results	01/04/2015		Yes	No
Results article	results	01/04/2015		Yes	No
Results article	results	01/09/2015		Yes	No
Results article	results	01/10/2017		Yes	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes