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Influence of age on response to new generation blood-thinning medicines

Submission date 10/05/2016	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 20/05/2016	**Overall study status** Completed	
Last Edited 22/08/2022	**Condition category** Circulatory System	

Plain English summary of protocol

Current plain English summary as of 21/09/2020:

Background and study aims

Oral anticoagulant (blood-thinning) drugs are very useful for treating and preventing blood clots. However, with them comes a risk of bleeding if the blood gets too “thin” (too slow to clot). Currently, warfarin is the most commonly used drug for treating/preventing blood clots, however dosages must be closely monitored as it can cause several severe side effects, such as making people more prone to bleeding. A new generation of anticoagulant drugs has become available which are believed to be safer than warfarin. It is already known that older people, who are normally frailer and have other concurrent diseases, are very sensitive to the blood-thinning effect of warfarin. However, it is unknown whether these people would also more sensitive to the new drugs. This study is looking at whether the blood-thinning activity of a new drug (rivaroxaban) is influenced by age.

Who can participate?

Thirty patients over the age of 65 and thirty patients under the age of 65 who are healthy.

What does the study involve?

A sample of blood is then taken through a vein which is tested in the laboratory for how much clotting factor is present (proteins that control bleeding) so that the clotting time between the two groups of patients can be compared.

What are the possible benefits and risks of participating?

There are no direct benefits involved for those taking part in this study. There is a small risk of pain, bruising or bleeding during and after blood samples are taken.

Where is the study run from?

Royal Victoria Infirmary (Newcastle)

When is the study starting and how long is it expected to run for?

September 2013 to April 2018

Who is funding the study?
NIHR Newcastle Biomedical Research Centre (UK)

Who is the main contact?
Professor Farhad Kamali
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Previous plain English summary:
Background and study aims
Oral anticoagulant (blood-thinning) drugs are very useful for treating and preventing blood clots. However, with them comes a risk of bleeding if the blood gets too “thin” (too slow to clot). Currently, warfarin is the most commonly used drug for treating/preventing blood clots, however, dosages must be closely monitored as it can cause several severe side effects, such as making people more prone to bleeding. A new generation of anticoagulant drugs has become available which are believed to be safer than warfarin. It is already known that people who eat little vitamin K (a vitamin mainly found in green leafy vegetables which plays a key role in blood clotting), are very sensitive to the blood-thinning effect of warfarin. However, it is unknown whether these people would also more sensitive to the new drugs. Tests in animals have shown that those with little vitamin K in their diets were more sensitive to the new drugs, however as yet, no one has checked whether this is the same in humans. This study is looking at whether the blood-thinning activity of two new drugs (dabigatran and rivaroxaban) is influenced by how much vitamin K we eat.

Who can participate?
Thirty patients over the age of 65 suspected of even little vitamin K and thirty patients under the age of 65 with healthy, balanced diets.

What does the study involve?
All participants are asked to complete a questionnaire about the foods that they have eaten over the last week. A sample of blood is then taken through a vein which is tested in the laboratory for vitamin K levels and how much clotting factor is present (proteins that control bleeding) so that the clotting time between the two groups of patients can be compared.

What are the possible benefits and risks of participating?
There are no direct benefits involved for those taking part in this study. There is a small risk of pain, bruising or bleeding during and after blood samples are taken.

Where is the study run from?
Royal Victoria Infirmary (Newcastle)

When is the study starting and how long is it expected to run for?
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Who is the main contact?
Professor Farhad Kamali
farhad.kamali@ncl.ac.uk

Contact information

Type(s)
Scientific

Contact name
Prof Farhad Kamali

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Additional identifiers

Protocol serial number
2.0

Study information

Scientific Title
Investigation of the effect of age on anticoagulant response to novel oral anticoagulants (direct thrombin inhibitors and FXa inhibitors) ex-vivo

Acronym
KOALA

Study objectives
Current study hypothesis as of 21/09/2020:
Age enhances anticoagulation response to a new generation of oral anticoagulants.

Previous study hypothesis:
Vitamin K deficiency enhances anticoagulation response to a new generation of oral anticoagulants.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee North East- Newcastle & North Tyneside 2, 18/05/2016, ref: 12/NE/0209

Primary study design
Observational

Study design

Single-centre observational cohort study

Study type(s)
Other

Health condition(s) or problem(s) studied
Anticoagulation response

Interventions
Current interventions as of 21/09/2020:
The study will recruit 30 elderly inpatients not on warfarin and 30 young medically stable subjects not on warfarin.

A sample of 20 ml fasting venous blood is then taken for later laboratory tests. Activated partial thromboplastin time (aPTT), prothrombin time (PT) and modified PT will be measured in plasma incubated with rivaroxaban (100-500 ng/ml). The kinetics of thrombin formation in plasma in the presence of drug will be determined using the endogenous thrombin potential (ETP) test.

Previous interventions:
The study will recruit 30 subjects suspected of low dietary vitamin K intake (elderly inpatients not on warfarin), 30 elderly medically stable subjects (inpatients not on warfarin) with healthy diets, and 30 healthy younger subjects with adequate dietary vitamin K intake.

All subjects will complete a validated simple questionnaire (FFQ) which records their food intake of vitamin K containing foods on average and over the past week. A sample of 20 ml fasting venous blood is then taken for later laboratory tests Plasma fasting vitamin K levels will be measured as an indication of subjects' dietary status. Activated partial thromboplastin time (aPTT), prothrombin time (PT) and modified PT will be measured in plasma incubated with rivaroxaban (100-500ng/ml). The kinetics of thrombin formation in plasma in the presence of drug will be determined using the endogenous thrombin potential (ETP) test.

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome(s)
Clotting time

Key secondary outcome(s)
No secondary outcome measures

Completion date
01/04/2018

Eligibility

Key inclusion criteria
Current inclusion criteria as of 21/09/2020:
Older subjects:
1. >65 years old
2. Medically stable
3. Without liver dysfunction
4. Able to give informed consent

Younger subjects:
1. <65 years of age
2. Healthy

Previous inclusion criteria:
Older subjects:
1. >65 years old
2. Medically stable
3. Without liver dysfunction
4. Able to give informed consent
5. Suspected of vitamin K deficiency as evaluated by the use of dietary questionnaire

Younger subjects:
1. <65 years of age
2. Healthy
3. Having a normal healthy diet as evaluated by the dietary questionnaire

Participant type(s)
Mixed

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
66

Key exclusion criteria
1. Less than 18 years of age
2. Liver dysfunction
3. Receiving anticoagulation therapy

Date of first enrolment
01/10/2013

Date of final enrolment
01/10/2016

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Royal Victoria Infirmary
Victoria Road
Newcastle upon Tyne
United Kingdom
NE1 4LP

Sponsor information

Organisation
Newcastle upon Tyne Hospitals Foundation Trust

ROR
https://ror.org/05p40t847

Funder(s)

Funder type
Government

Funder Name
NIHR Newcastle Biomedical Research Centre

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Farhad Kamali (farhad.kamali@ncl.ac.uk).
Type of data: continuous data of haematological assay results and subject demographics.
When the data will become available and for how long: data may be available upon request after the publication of the study and without limit in the length of time after publication.
By what access criteria data will be shared including with whom: access will be granted at the discretion of the principal investigator detailed above upon request via email, only if it is

impossible to acquire the data from the publicly available report and on the basis of the reason for the request and the expected use of the data. No publication of the data should occur and data should not be shared with anyone else without the consent of the principal investigator.
For what types of analyses, and by what mechanism: any types of analysis can be agreed in advance with the principal investigator to determine the minimum amount of data that should be shared.
Whether consent from participants was obtained: participants have consented for their data to be used for data analysis and anonymous publication of the results.
Comments on data anonymisation: data have been manually anonymised and as such may be provided at the discretion of the principal investigator.
Any ethical or legal restrictions: the principal investigator may refuse to provide the data in case their expected use is against the sponsor's requirements, or if there are any other restrictions.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		17/10/2021	22/08/2022	Yes	No
Basic results		21/09/2020	21/09/2020	No	No