ISRCTN14693054 https://doi.org/10.1186/ISRCTN14693054

What happens to low doses of aspirin (75 and 150 mg) and how it affects certain blood particles in pregnant women at risk of pre-eclampsia?

Submission date
12/01/2021

Recruitment status
No longer recruiting

Registration date
09/03/2021

Overall study status
Completed

Last Edited
24/10/2024

Condition category
Pregnancy and Childbirth

[X] Prospectively registered

[X] Protocol

[_] Statistical analysis plan

[X] Results

[_] Individual participant data

Plain English summary of protocol

Background and study aims
Problems with the proper functioning of the heart and blood vessels, also known as cardiovascular disease (CVD), are one of the main causes of death in the North East of England. In addition to the widely known risk factors, pregnancy-related problems affecting blood pressure predispose many young women and their children to CVD later in life. It is important to prevent women from developing high blood pressure conditions such as pre-eclampsia during pregnancy in order to improve the health-related outcomes for both them and their babies.

Use of low-dose aspirin (75 mg -150 mg) is recommended to prevent blood pressure complications in pregnancy. The effects of aspirin on blood (and specifically platelets – the cells that help blood clot), and the way aspirin is broken down and removed from the body, have been studied in non-pregnant people. However, surprisingly, no such studies have been performed in pregnant women, even though both measures are expected to change greatly in this population.

This study will measure the disappearance of the aspirin from the body and its effects on blood clotting function in pregnant women, for two different doses of aspirin. Knowing the effects of aspirin in pregnant women will help doctors to optimise the dose of aspirin given to pregnant women and support a more personalised use of aspirin for effective CVD prevention in this population.

Who can participate?
Pregnant women at risk of pre-eclampsia

What does the study involve?
Pregnant women, who have been prescribed aspirin, because of their increased risk of developing high blood pressure in pregnancy, will be asked to take two aspirin doses in a

random order (chosen by chance) and to donate blood samples at regular intervals to measure the disappearance of the drug from the body and the drug's effects on blood clotting function in pregnant women.

What are the possible benefits and risks of participating?
There will be no direct benefit to participants from this trial. However, the study team recognise that participation in this trial is time-consuming, therefore all effort will be made to ensure participant comfort during their research visit. This includes a comfortable space to rest and the provision of standardised meals. To show gratitude to women who complete the study schedule in full, a complimentary 28 weeks 4D scan will be offered.

All women will be prescribed aspirin for clinical reasons. Monitoring of adverse effects will be performed in person during the first 4 hours following aspirin ingestion and again at 24 hours. All women will be given emergency contact numbers to ensure access to medical care in case needed outside of their research visits.

Where is the study run from?
Newcastle upon Tyne Hospitals NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
March 2019 to March 2022

Who is funding the study?
Newcastle Upon Tyne Hospitals NHS Charity (UK)

Who is the main contact?
Mrs Raya Vinogradov
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Contact information

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Public

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Additional identifiers

Clinical Trials Information System (CTIS)
2021-000071-36

Integrated Research Application System (IRAS)
253665

Study information

Scientific Title
A randomised crossover design study comparing the pharmacokinetics and pharmacodynamics of two single Doses of ORal Aspirin (75 mg v 150 mg) in pregnant women at risk of pre-eclampsia (DORA)

Acronym
DORA

Study objectives
To compare aspirin pharmacokinetics (plasma salicylic acid concentrations) and pharmacodynamics (serum thromboxane B2 concentrations) in pregnant women at 11-16 weeks gestation' following the administration of a single oral dose of either 75 mg or 150 mg aspirin.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 30/03/2021, Wales REC 1 (Health and Care Research Wales Support and Delivery Centre, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, UK; +44 (0)2920 230457; Wales.REC1@wales.nhs.uk), ref: 21/WA/0066

Primary study design
Interventional

Study design
Randomized crossover study

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Pre-eclampsia

Interventions
Online non-blinded envelope randomisation will be performed. The lab will be blinded to the randomisation. Participants will be randomised to either a sequence of a single dose of 75 mg aspirin followed by a 7-day washout period and then a single dose of 150 mg aspirin, or a single dose of 150 mg aspirin followed by a 7-day washout period and then a single dose of 75 mg aspirin.

Blood sampling will be performed to assess levels of salicylic acid and thromboxane B2. Participants will be asked to abstain from taking aspirin for 7 days between the doses.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Acetylsalicylic acid

Primary outcome(s)
1. Pharmacokinetics and pharmacodynamics measured using serum salicylic acid concentration and serum thromboxane B2 concentration from blood samples taken at baseline, 1, and 8 days

Key secondary outcome(s)
1. Time to the detection limit of salicylic acid in plasma measured from blood samples taken at baseline, 1, and 8 days

Completion date
31/03/2022

Eligibility

Key inclusion criteria
1. Pregnant women at risk of pre-eclampsia according to NICE criteria

Participant type(s)
Other

Healthy volunteers allowed
No

Age group
Adult

Sex
Female

Total final enrolment
16

Key exclusion criteria
1. Hypersensitivity to aspirin, salicylic acid compounds, or prostaglandin synthase inhibitors (e.g. certain asthma patients who may suffer an attack or faint)
2. Active, or history of, recurrent peptic ulcer and/or gastric/intestinal haemorrhage, or other kinds of bleeding such as cerebrovascular haemorrhage
3. Haemorrhagic diathesis or coagulation disorders such as hemophilia and thrombocytopenia
4. Severe hepatic or renal impairment
5. Gout
6. Taken aspirin over the preceding 4 weeks
7. Current anticoagulant therapy
8. Unable to give informed consent
9. Multiple pregnancy
10. Known fetal anomaly
11. Vegetarian/vegan diet

Date of first enrolment
01/07/2021

Date of final enrolment
31/03/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
The Newcastle upon Tyne Hospitals NHS Foundation Trust
Clinical Research Facility
Level 6 Leazes Wing
Royal Victoria Infirmary
Queen Victoria Road
Newcastle
United Kingdom
NE1 4LP

Sponsor information

Organisation
Newcastle upon Tyne Hospitals NHS Foundation Trust

ROR
https://ror.org/05p40t847

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Newcastle Upon Tyne Hospitals NHS Charity

Results and Publications

Individual participant data (IPD) sharing plan
The datasets (anonymised) generated and analysed during the current study will be available upon request from S Robson (s.c.robson@newcastle.ac.uk)/ R Vinogradov (raya.vinogradov@ncl.ac.uk) subject to ethical approvals. We reserve our right to review sharing policy depending on a nature of the request.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		21/10/2024	24/10/2024	Yes	No
Basic results		07/07/2023	07/07/2023	No	No
HRA research summary			28/06/2023	No	No
Protocol file	version 1.9	08/03/2021	11/08/2022	No	No