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Use of aspirin for the prevention of preeclampsia in twin pregnancies

Submission date
05/08/2022

Registration date
22/08/2022

Last Edited
19/11/2024

Recruitment status
Recruiting

Overall study status
Ongoing

Condition category
Pregnancy and Childbirth

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Preeclampsia (PE) is a medical condition that can happen during pregnancy after 20 weeks and it is characterised by high blood pressure and the presence of protein in the urine or in its absence the finding of maternal organ dysfunction. PE is one of the leading causes of maternal and perinatal death and disabilities. There is extensive evidence that in singleton high-risk pregnancies for PE, the use of aspirin (150 mg/day from 12 until 36 weeks of gestation) reduces the chances of developing PE before 32 weeks by 89% and PE before 37 weeks by 62%. The rate of PE in twin pregnancies is about 9%, which is 3–times higher than in singleton pregnancies. Few studies investigated the use of aspirin in reducing the risk of PE in twin pregnancies, but the results are inconsistent with the findings in singleton pregnancies. Therefore, the aim of this study is to determine whether taking low-dose aspirin can reduce the risk of PE in twin pregnancies.

Who can participate?
Anyone pregnant with twins, aged over 18 years old and had a first-trimester scan between 11+2 - 13+6 weeks of pregnancy

What does the study involve?
Participants will be randomised and will take 2 tablets per day, either Aspirin or placebo, from 14+3 weeks until 36 weeks of pregnancy or delivery. There will be 3 telephone calls and 4 follow-up visits that will happen at the same time as the regular scan appointments.

What are the possible benefits and risks of participating?
The possible benefits of participating include a reduction in the chances of developing preeclampsia, which can have a positive impact on the health of both the mothers and their children. The possible risks include potential pain from the blood collection at 3 of the clinical visits (optional). From taking the tablets, there are additional risks of developing: allergic reactions, stomach ache, nausea and gastric bleeding, and increased vaginal bleeding before and after delivery. Based on currently available evidence, no major risks are anticipated.

Where is the study run from?
Fetal Medicine Foundation (UK)

When is the study starting and how long is it expected to run for?
August 2019 to October 2028

Who is funding the study?
Fetal Medicine Foundation (UK)

Who is the main contact?
Prof. Kypros Nicolaides
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Study website
https://www.fetalmedicine.org

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2019-003341-15

IRAS number
269958

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 50869, IRAS 269958

Study information

Scientific Title
Aspirin versus placebo in twin pregnancies for preeclampsia prevention: a multicenter, randomised, double-blind, placebo-controlled trial (ASPRE-T)

Acronym
ASPRE-T

Study objectives

To evaluate the effectiveness of low-dose aspirin in reducing the risk of preterm preeclampsia in twin pregnancy, the study will compare the results of the interventional group with the results of the placebo group

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 12/04/2022, London - Surrey Borders Research Ethics Committee (The Old Chapel, Royal Standard Place, HRA, Nottingham, NG1 6FS, UK; +44 (0)20 7104 8057; surreyborders.rec@hra.nhs.uk), ref: 21/LO/0757

Study design
Randomized case-controlled study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

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
Preterm preeclampsia in twin pregnancy

Interventions
Women will be recruited from their routine first-trimester scan where the eligibility criteria will be assessed. Women who accept to take part in the trial and sign the consent form will agree to have some of their blood stored for future analysis. They routinely will have bloods taken for screening of trisomies and at the same time will be consented for bloods for the research study. Routinely in the units involved, they will also have basic clinical investigations of blood pressure, height, weight and a medical history taken. Upon participation, they will then be randomised to placebo or aspirin and asked to take this until 36 weeks of gestation.

From this point on, women will continue on their normal follow-up pathway for twin pregnancies. Those with monochorionic pregnancies will actually be seen more often for clinical needs, but in terms of research follow-up, in addition to their routine scans, and clinical investigations at the 20-, 28-, 31- and 35-week time points, we will determine compliance of medication by counting their remaining tablets and assessing their diary cards for adverse events. The only additional blood sampling we will be asking for will be at the 20- and 32-week visits.

They will receive telephone interviews at 15 and 24 weeks of gestation, followed by a call 4 weeks after the last dose of the investigational medicinal product (IMP). The purpose of these will be reminders to take the medication, but more importantly to assess for adverse events.

Intervention Type
Other

Phase
Phase III

Primary outcome measure
Incidence of preeclampsia (PE) requiring delivery before 37 weeks gestation in twin pregnancies, measured by examination of hospital records and patient interviews. PE will be defined by the American College of Obstetricians and Gynecologists (ACOG 2013).

Secondary outcome measures
All measured by examination of hospital records and patient interviews
1. Incidence of PE requiring delivery before 32 weeks, 34 weeks, 37 weeks and at any gestation,
2. For all features of severe PE the timepoint is from diagnosis of PE until maternal discharge from hospital- Features of severe PE include:
2.1. Stroke
2.2. Eclampsia
2.3. Systolic blood pressure >160 mmHg on at least one occasion
2.4. Systolic blood pressure >160 mmHg on at least one occasion
2.5. Respiratory failure
2.6. Myocardial ischemia or infarction
2.7. Pulmonary edema
2.8. Hepatic dysfunction
2.9. Hepatic hematoma or rapture
2.10. Platelet count <100 x 109/litre
2.11. Abnormal liver function enzymes (ALT or AST >67 iu/litre),
2.12. Acute kidney injury
2.13. Creatinine >150 µmol/L
2.14. Cortical blindness
2.15. Retinal detachment
2.16. Transfusion of any blood products,
2.17. HELLP syndrome,
2.18. Placental abruption
2.19. Postpartum hemorrhage
2.20. Intensive therapy or high-dependency unit admission;
2.21. Confirmed sepsis
2.22. Total number of nights in hospital
3. Gestational hypertension (GH) requiring delivery before 37 weeks' gestation defined by ACOG 2013
4. Birth before 32, 34 and 37 weeks, either:
4.1. Spontaneous
4.2. Iatrogenic for PE, GH or Fetal Growth Restriction (FGR)
4.3. Iatrogenic for other reasons
5. Death of one twin and/or both twins at timepoint before discharge from hospital
5.1. Miscarriage of the whole pregnancy or death of one twin before 24 weeks' gestation
5.2. Stillbirth or neonatal death of one or both twins at 32 weeks, 34 weeks, 37 weeks and at any

gestation
6. Birthweight <3rd, <5th and <10th percentile for gestational age measured by Fetal Medicine Foundation birthweight chart (Nicolaides et al., 2018)
7. Placental abruption timepoint at 32 weeks, 34 weeks, 37 weeks and at any gestation
8. Postpartum hemorrhage timepoint first 24 hours after delivery
9. Neonatal morbidity including any of the following measured by examination of hospital records and patients' interviews, timepoint until discharge from hospital after birth:
9.1. Intraventricular hemorrhage (IVH) grade II or above
9.2. Neonatal sepsis
9.3. Encephalopathy
9.4. Neonatal seizures
9.5. Anaemia
9.6. Respiratory distress syndrome
9.7. Necrotizing enterocolitis
9.8. Composite of any of the above
10. Neonatal therapy including any of the following measured by examination of hospital records and patients' interviews, timepoint until discharge from hospital after birth:
10.1. Neonatal intensive care unit admission
10.2. Ventilation
10.3. Composite of any of the above
10.4. Length of stay in neonatal intensive care unit

Overall study start date
08/08/2019

Completion date
31/10/2028

Eligibility

Key inclusion criteria
1. Aged 18 years old and over
2. DCDA or MCDA twin pregnancies
3. Both live fetuses at 11+2-13+6 weeks of gestation
4. Informed and written consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Female

Target number of participants
Planned Sample Size: 2400; UK Sample Size: 1200

Key exclusion criteria
1. Monoamniotic twins
2. Triplet pregnancies that had undergone embryo reduction to twins or with one vanishing twin
3. Pregnancies complicated by a major fetal abnormality or nuchal translucency thickness > 3.5 mm identified at the 11+2-13+6 weeks scan
4. MCDA twin pregnancies in which there are early signs of TTTS or sFGR defined by a 20% discordance in CRL at the 11+2-13+6 weeks' scan
5. Those who lack capacity and who are unable to provide informed consent to take part
6. Women taking low-dose aspirin regularly (administration must have ceased > 7 days prior to randomization)
7. Participation in another drug trial within the previous 7 days
8. Haemorrhagic diathesis; coagulation disorders such as haemophilia and thrombocytopenia or concurrent anticoagulant therapy
9. Active or history of recurrent peptic ulceration and/or gastric/intestinal haemorrhage, or other kinds of bleeding such as cerebrovascular haemorrhages
10. Patients who are suffering from known gout, severe hepatic impairment or severe renal impairment
11. Hypersensitivity to salicylic acid compounds or prostaglandin synthetase inhibitors (e.g. certain asthma patients who may suffer an attack or faint and certain patients who may suffer from bronchospasm, rhinitis and urticaria) or to any excipients (see section 6.1 of the SmPC for details)
12. Patients on long-term non-steroidal anti-inflammatory medication
13. Not fluent in local language and absence of an interpreter
14. Any other reason the clinical investigators think will prevent the potential participant from complying with the trial protocol

Date of first enrolment
30/08/2022

Date of final enrolment
30/09/2028

Locations

Countries of recruitment
Austria

Belgium

Bulgaria

Denmark

England

Germany

Greece

Hungary

Ireland

Israel

Italy

Poland

Portugal

Spain

United Kingdom

Study participating centre
North Middlesex University Hospital Trust
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Study participating centre
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Study participating centre
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Study participating centre
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Study participating centre
Centro Hospitalar Universitário de Lisboa Central
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Study participating centre
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Sponsor information

Organisation
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Sponsor type
Research organisation

Website
https://www.ffis.es/

ROR
https://ror.org/05m5has32

Funder(s)

Funder type
Charity

Funder Name
Fetal Medicine Foundation; Grant Codes: N/K

Alternative Name(s)
FMF

Funding Body Type
Private sector organisation

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

Location
United Kingdom

Results and Publications

Publication and dissemination plan

1. Planned publication in a high-impact peer-reviewed journal. The study protocol will be published on the Fetal Medicine Foundation website (https://www.fetalmedicine.org). Publication of study results is anticipated within one year from the study end and analysis.
2. Presentation at international conferences
3. Internal report
4. Website

Intention to publish date

31/10/2029

Individual participant data (IPD) sharing plan

The data sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No