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Investigating the effects of steroids given in pregnancy on infant stress responses

Submission date
29/04/2022

Recruitment status
No longer recruiting

Registration date
20/07/2022

Overall study status
Completed

Last Edited
29/05/2025

Condition category
Pregnancy and Childbirth

[ ] 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
The use of ACS in late preterm (35-36 weeks gestation) and early term (37 weeks gestation) is an area of substantial controversy in obstetrics. There is evidence that ACS reduce serious breathing difficulties and neonatal unit admission but there is potential for both short (e.g. low blood sugar levels) and long-term harms (e.g. brain development) in some exposed babies. Practice is highly variable regarding ACS administration at later preterm and early term gestations.
STOPPIT-3 is a multicentre placebo-controlled trial to evaluate the effectiveness of ACS (dexamethasone phosphate) prior to planned birth of twins in an NHS setting. The primary outcome is respiratory support within 72 hours of birth. STOPPIT-M is a linked study to explore the mechanisms underlying ACS effects on the infant's endogenous HPA axis responses, and resultant effects on neonatal outcomes.

Study aims:
We will use these samples to compare the stress axis in infants with
1. early adverse health (need for respiratory support; low APGAR score; low blood sugar; jaundice), in babies exposed and non-exposed to ACS
2. developmental delay aged 2 years (from the main STOPPIT-3 trial)

A secondary aim is to explore whether these outcomes differ in boys and girls.
Gaining a better understanding of the mechanisms of action of ACS is essential to improve targeted delivery of ACS – ensuring administration to mothers and babies who will benefit from ACS, but avoiding harm in those who will not benefit.

Who can participate?
STOPPIT-M will aim to recruit 543 women pregnant with twins enrolled in the STOPPIT-3 (ISRCTN59959611) trial across 50 sites.

What does the study involve?
Women who have agreed to take part will have the following samples collected at delivery of

twins: paired maternal and cord blood samples, amniotic fluid sample and a placenta sample. In a subset of infants in Edinburgh the following samples will be taken: a saliva sample and a hair sample.

What are the possible benefits and risks of participating?
The researchers cannot promise the study will directly help you or your babies. Information the researchers obtain from your participation in the study may help inform on the future healthcare of other patients. Taking part will help create much needed evidence on the use of ACS prior to a planned birth of twins which will help women and babies in future.

Where is the study run from?
University of Edinburgh and NHS Lothian (UK)

When is the study starting and how long is it expected to run for?
November 2021 to February 2025

Who is funding the study?
National Institute for Health and Care Research (NIHR) The Efficacy and Mechanism Evaluation (EME) Programme (UK)

Who is the main contact?
The trial management team at the University of Edinburgh Clinical Trials Unit (ECTU)
STOPPIT.Trial@ed.ac.uk

Contact information

Type(s)
Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
309594

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
AC21185, NIHR133388, IRAS 309594, CPMS 52586

Study information

Scientific Title
Infant hypothalamic-pituitary-adrenal axis responses following antenatal corticosteroids and perinatal outcomes: a mechanism of action of health intervention study

Acronym
STOPPIT-M

Study objectives
1. Late preterm/early term born infants who have respiratory morbidity despite ACS treatment (non-responders); or who have other morbidities (hypoglycaemia; low Apgar score; jaundice; effects on neurodevelopment) have suppressed cord blood cortisol levels and reduction in glucocorticoid signalling
2. In infants who do not receive ACS, immaturity of the HPA axis with low endogenous cortisol levels in cord blood and reduced glucocorticoid signalling is associated with increased rates of morbidity and neonatal care requirements

Ethics approval required
Old ethics approval format

Ethics approval(s)

Approved 28/02/2022, North of Scotland Research Ethics Service (Summerfield House, 2 Eday Road, Aberdeen, AB15 6RE, UK; +44 1224 558458; gram.nosres@nhs.scot), ref: 22/NS/0017

Study design
Observational/mechanistic study linked to STOPPIT-3 trial (ISRCTN59959611)

Primary study design
Observational

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Effects of antenatal corticosteroids on infant stress responses

Interventions
The site clinical team will be asked to take the following samples at delivery of twins:
• Paired maternal and cord blood samples (about 10mls)
• Amniotic fluid sample
• Placenta sample

In a subset of infants, in Edinburgh, the following samples will be taken:
• a saliva sample
• a hair sample

Intervention Type
Other

Primary outcome(s)
1. Measurement of endogenous glucocorticoids, dexamethasone and its metabolites in maternal and cord blood and amniotic fluid in samples collected at birth.
2. Measurement of glucocorticoid receptor in cord blood leukocytes collected at birth.
3. Measurement of placental genes regulating glucocorticoids in placenta samples collected at birth.

Key secondary outcome(s))
1. Salivary cortisol pre and post heel-prick at 5 days
2. Hair cortisol at 5 days

Completion date
28/02/2025

Eligibility

Key inclusion criteria
1. Women with a twin pregnancy with a planned caesarean birth scheduled between 35+0 and 38+6 weeks gestation who are enrolled in STOPPIT-3 (ISRCTN59959611)
2. Women aged 16 years or older and able to provide electronic or written consent

Participant type(s)

Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
16 years

Sex
Female

Total final enrolment
17

Key exclusion criteria
1. Women taking prescribed corticosteroid medication (orally, injected, inhaled or topical) within the last 3 months.
2. Women with planned vaginal birth.

Date of first enrolment
01/05/2022

Date of final enrolment
24/11/2024

Locations

Countries of recruitment
United Kingdom

England

Scotland

Wales

Study participating centre
NHS Lothian
Waverley Gate
2-4 Waterloo Place
Edinburgh
United Kingdom
EH1 3EG

Sponsor information

Organisation
University of Edinburgh

ROR
https://ror.org/01nrxwf90

Organisation
NHS Lothian

ROR
https://ror.org/03q82t418

Funder(s)

Funder type
Government

Funder Name
NIHR The Efficacy and Mechanism Evaluation (EME) Programme

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

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
Participant information sheet	version 1.0	22/02/2022	16/05/2022	No	Yes
Participant information sheet	version 2.0	25/11/2022	20/11/2023	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes