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Intramuscular tranexamic acid to prevent heavy bleeding after childbirth in women at higher risk

Submission date
22/11/2022

Recruitment status
No longer recruiting

Registration date
20/01/2023

Overall study status
Completed

Last Edited
29/04/2024

Condition category
Pregnancy and Childbirth

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

Plain English summary of protocol

Background and study aims
Vaginal bleeding after childbirth is normal. It usually stops on its own and is nothing to worry about. But some women have heavy bleeding - this is called a postpartum haemorrhage or PPH. A PPH can make women very unwell and is sometimes life-threatening. This study aims to see if a drug called tranexamic acid (TXA) can prevent PPH when it is given into the muscle. TXA is a drug that reduces bleeding. It is not a new drug. It is often used to reduce bleeding in operations and after a serious injury. In an earlier study, TXA was given to thousands of women who were having PPH. It saved the lives of about 1 in 3 women who had a PPH, and it did not cause any serious side effects. The WHO recommends that all women who are having a PPH get TXA. The team's previous studies show that TXA is most effective when given early which made the team wonder if giving TXA before the birth of the baby might prevent PPH from happening in the first place. Preventing PPH might be better than treating a PPH after it happens. This study will find out if TXA can prevent PPH from happening. TXA is usually given into a vein. But it can also be given into a muscle, like a vaccine. Giving TXA into a muscle is easier and quicker. It is hoped that this study will prove that both ways of giving TXA are equally good at preventing PPH. TXA sometimes causes mild side effects like feeling sick. This may be less likely if TXA is given into the muscle and it is also hoped that the study proves this.

Who can participate?
Adult women who have a higher chance of PPH and are admitted to the hospital to give birth to take part

What does the study involve?
Participants will be asked to fill in a consent form and then information about the woman and their labour will be collected. Just before the baby is born, participants will be given two injections into different muscles and one into a vein, which will contain either TXA or a placebo (a dummy drug that is completely safe). What each injection holds is decided randomly. The study drug and the placebo look the same, so the woman and their doctors will not know which is being given. After giving birth, how much blood is lost will be measured and information about their health and their baby, while they are in the hospital, is collected. Women who take part will be in the study until they leave the hospital, or for six weeks after having their baby, whichever is sooner.

What are the possible benefits and risks of participating?
It is hoped that TXA will reduce the amount of blood women lose in childbirth and prevent PPH. Women who take part may get TXA but there is a chance they won't (i.e. if they are in the placebo group). Women who do not take part will not get TXA before childbirth as it is not currently recommended or given in the hospital to prevent PPH. We hope women who take part will be better informed for the future and can share their knowledge with others. In the future, what we learn from this study will help doctors care for women who are having a PPH or who are at higher risk of having a PPH. If TXA prevents PPH and causes fewer side effects when it is given into the muscle, this will help women who give birth in situations where having an injection into a vein is not possible – an injection of TXA into the muscle could save their lives.

TXA is widely used. The WHO recommends TXA for women who are having a PPH. Because it is an old drug, there is reassuring safety information. Lots of studies with thousands of people suggest that TXA has clear health benefits and no serious side effects. Sometimes TXA can cause minor side effects like feeling or being sick (nausea), diarrhoea, and dizziness. Studies suggest that giving TXA into a vein or a muscle has no serious side effects. There is a small risk of redness, pain, or bruising at the injection sites. Any injections have a very rare risk of infection. A small amount of TXA can cross over to the baby through the placenta or breast milk. Earlier studies did not find any harmful effects in babies whose mothers got TXA when they were pregnant, or who were breastfed by mothers who got TXA. Your doctor will watch you and your baby and give you the best available care if there are any problems. They will also tell the people running the study if there are any problems.

Where is the study run from?
This study is being done by an international group of doctors, nurses, midwives and researchers working together to find ways to improve women's health. The study is coordinated by researchers at the London School of Hygiene & Tropical Medicine (University of London) in the UK and at a National Coordinating Centre or hospital in each country taking part.

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

Who is funding the study?
Unitaid (Switzerland)

Who is the main contact?
Amy Brenner (Lead Investigator), imwoman@lshtm.ac.uk (UK)

Contact information

Type(s)
Principal investigator

Contact name
Miss Amy Brenner

ORCID ID
https://orcid.org/0000-0003-2017-5994

Contact details

Clinical Trials Unit - Global Health Trials Group
Department of Population Health
London School of Hygiene & Tropical Medicine
Keppel Street
London
United Kingdom
WC1E 7HT
+44 (0)20 7958 8283
imwoman@lshtm.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
NCT05562609

Protocol serial number
2021-KEP-588

Study information

Scientific Title
Tranexamic acid by the intramuscular or intravenous route for the prevention of postpartum haemorrhage in women at increased risk: a randomised, double-blind, placebo-controlled trial

Acronym
I'M WOMAN

Study objectives
Postpartum haemorrhage (PPH) causes about 70,000 maternal deaths every year. Tranexamic acid (TXA) is a lifesaving treatment for women with PPH. Intravenous (IV) TXA reduces deaths due to PPH by one-third when given within 3 hours of childbirth. Because TXA is more effective when given early and PPH usually occurs soon after childbirth, giving TXA just before childbirth might prevent PPH. We hypothesise that:
1. Giving TXA just before childbirth reduces the incidence of PPH in women at increased risk
2. Intramuscular (IM) TXA is non-inferior to IV tranexamic acid for the prevention of PPH
3. IM TXA is associated with fewer side effects compared with IV TXA

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 12/01/2023, Research ethics committee of The London School of Hygiene & Tropical Medicine (Keppel Street, London, WC1E 7HT, UK; +44 (0) 207 636 8636; ethics@lshtm.ac.uk), ref: 28252

Study design

Randomized double-blind parallel-group-assignment placebo-controlled three-arm trial

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Postpartum haemorrhage

Interventions
Women will be randomly allocated to receive either:
1. 1 gram of tranexamic acid as two 5 ml IM injections (100 mg/ml) and IV placebo (10 ml 0.9% sodium chloride)
2. 1 gram of tranexamic acid by IV injection and two 5 ml IM placebo injections
3. Matching placebo

An IT coding expert supported by a statistician will prepare a randomisation list detailing the allocation sequence using a computerised random number generator. A unique randomisation number will be linked with each treatment allocation. The required allocation ratio will be maintained by using blocking throughout the trial. The randomisation list will be sent to the clinical trial supplies company so that blinded treatment packs can be prepared. The company will produce, label and package TXA and placebo ampoules into patient treatment packs as per the randomisation list. Trial staff (coordinating centres and sites) and patients will not have access to the randomisation list until after the final database lock.

The trial treatment will be given just prior to skin incision (after draping) in caesarean births and at crowning in vaginal births. For IM administration, the 1 g dose (10 ml) is divided into two 5ml IM injections to reduce the injection volume and given into the vastus lateralis (thigh - preferred), the ventro-gluteal region (buttocks), or the deltoid (arm). Women will receive all the usual care in labour and after birth. Participation will not result in any needed treatment being withheld. Women who develop PPH should be treated in the usual way.The woman is considered to have been randomised once administration of the first IM injection has started.

Intervention Type
Drug

Phase
Phase III

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

Primary outcome(s)
Postpartum haemorrhage measured using clinical diagnosis through an estimated blood loss of more than 500 ml in a vaginal birth, more than 1000 ml in caesarean birth, or any blood loss sufficient to compromise haemodynamic stability within 24 hours of birth

Haemodynamic instability is based on clinical judgement and assessed using clinical signs (low systolic blood pressure, tachycardia, reduced urine output)

Key secondary outcome(s))
Specific to caesarean births:
1. Intraoperative blood loss measured by quantifying the amount of blood in sponges and drapes used in surgery and blood loss from suctioning, excluding amniotic fluid
2. Surgery duration measured using patient records
3. Intraoperative whole blood/red cell transfusion measured using patient records
4. Postoperative haemoglobin (Hb) or packed cell volume (PCV) measured using patient records up to the end of the second postoperative day, if known

All births:
1. Postpartum blood loss measured using a calibrated obstetric drape starting immediately after vaginal birth or once the women are shifted to a bed in the observation area after CS surgery, for 1 hour, or up to 2 hours if bleeding continues after 1 hour and the woman remains in bed
2. Blood pressure and heart rate (lowest recorded blood pressure reading and associated heart rate) measured using patient records up to 24h after birth
3. Interventions for bleeding (uterotonics, non-trial TXA, blood transfusion, surgical and non-surgical interventions) measured using patient records within 24 hours of birth
4. Nausea, vomiting, dizziness (when the calibrated drape is removed, the woman will be asked about her nausea, vomiting and dizziness during and since the birth) measured using a score from 1-10 and/or patient medical records
5. Pain or adverse skin reactions at injection sites (when the calibrated drape is removed, each injection site will be inspected for local reactions and the woman will be asked about pain at her injection sites) measured using patient records
6. Prespecified maternal adverse events up to 42 days postpartum (thromboembolic events, seizure, sepsis, organ dysfunction, coagulopathy) measured using patient records
7. Other maternal adverse events up to 42 days postpartum measured using patient records
8. Maternal mortality up to 42 days postpartum (all-cause, cause-specific, narrative) measured using patient records
9. Length of hospital stay measured using patient records
10. Days in ICU/HDU measured using patient records
11. Transfer to another hospital measured using patient records
12. Prespecified neonatal outcomes up to discharge, death or 42 days (breastfeeding, intracranial haemorrhage, pulmonary haemorrhage, bruising, thromboembolic event, seizure, stillbirth/intrapartum death, neonatal death, cause of death, congenital and genetic abnormalities, adverse events) measured using patient records

Completion date
30/09/2025

Eligibility

Key inclusion criteria
1. Women thought to be aged 18 years and over admitted to the hospital for a vaginal or caesarean birth
2. One or more known risk factors for PPH

Participant type(s)
Patient

Healthy volunteers allowed

No

Age group
Adult

Lower age limit
18 years

Sex
Female

Key exclusion criteria
The fundamental eligibility criterion is the responsible doctor's 'uncertainty' about whether to use tranexamic acid in a particular woman. Women should not be randomised if the responsible doctor believes that tranexamic acid is clearly indicated (e.g., tranexamic acid has been given within 12 hours or planned to be given) or clearly contraindicated (e.g., known allergy to tranexamic acid).

Date of first enrolment
22/04/2024

Date of final enrolment
14/09/2025

Locations

Countries of recruitment
United Kingdom

England

Kenya

Nigeria

Pakistan

Tanzania

Study participating centre
London School of Hygiene and Tropical Medicine
Keppel Street
London
United Kingdom
WC1E 7HT

Sponsor information

Organisation
London School of Hygiene & Tropical Medicine

ROR
https://ror.org/00a0jsq62

Funder(s)

Funder type
Research organisation

Funder Name
Unitaid

Results and Publications

Individual participant data (IPD) sharing plan
Publications will only contain anonymised data. We are committed to sharing data for ethical research with justified scientific objectives. Until all planned analyses are completed by the LSHTM CTU Global Health Trials Group, data will be shared through a controlled access approach whereby researchers can make formal applications for data sharing. Afterwards, the anonymised dataset will be shared via the LSHTM CTU Global Health Trials Group data-sharing platform at https://freebird.lshtm.ac.uk/.

All trial materials including training materials, CRFs and Protocol will be made available on the trial website and team YouTube channel.

IPD sharing plan summary
Stored in publicly available repository, Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		03/12/2023	04/12/2023	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes