ISRCTN44900603 https://doi.org/10.1186/ISRCTN44900603

Oxytocin injection and misoprostol tablet compared to oxytocin-ergometrine injection and placebo tablet to prevent bleeding after vaginal delivery

Submission date
03/01/2025

Recruitment status
No longer recruiting

Registration date
14/01/2025

Overall study status
Ongoing

Last Edited
13/01/2025

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
Worldwide, severe bleeding due to childbirth is a primary cause of the death of new mothers accounting for 8 to 20% of the deaths. Severe bleeding can also cause multiple body organs to fail and removal of the womb to control bleeding. The main cause of severe bleeding is the failure of the womb to contract adequately or maintain the contracted state following separation and delivery of the afterbirth. It is standard practice worldwide to routinely give medicines that increase womb contraction immediately at delivery to reduce bleeding. Oxytocin is a natural substance (hormone) released by a part of the brain to quickly and effectively cause womb contraction but it lasts only a short time (minutes) whereas the risk of bleeding if the womb is relaxed persists for many hours. In Malaysia, oxytocin is combined with ergometrine (a slower-acting but longer-lasting medicine to maintain womb contraction) as an injection for a more sustained effect. However, ergometrine can cause side effects like increasing blood pressure which can be of concern as high blood pressure is a common complication during pregnancy. High blood pressure due to pregnancy can show itself for the first time in the hours or days after birth has occurred. Therefore, ergometrine may worsen further the unanticipated high blood pressure that is only revealed after birth.

Misoprostol is a different type of longer-lasting womb contraction-sustaining medicine that can be taken orally. Misoprostol does not appear to cause high blood pressure and likely has a different side effect profile from ergometrine. Both ergometrine and misoprostol are shown to be similarly effective at reducing childbirth-related bleeding in combination with oxytocin. A direct comparative study of oxytocin-misoprostol compared to oxytocin-ergometrine in the context of their use to prevent childbirth-related bleeding based on their side effects and effectiveness in reducing bleeding has not been performed. This study aims to evaluate oxytocin (injection) and misoprostol (tablet) compared to oxytocin-ergometrine (single injection) and placebo (tablet) immediately at vaginal delivery on side effects and blood loss.

Who can participate?
Patients expecting a vaginal delivery, age 18-45 years, term (≥37 weeks of pregnancy), single baby in head down presentation, not more than 4 previous births.

What does the study involve?
Only patients who delivered vaginally will receive the trial medicines as randomly assigned by a computer. Oxytocin injection combined with oral misoprostol tablets or fixed-dose single injection of oxytocin and ergometrine (syntometrine) with oral placebo (non-active) tablets, given one time only at the delivery of the baby and before the placenta is delivered.

What are the possible benefits and risks of participating?
Oxytocin injection combined with oral misoprostol and a fixed dose single injection of combination oxytocin and ergometrine (Syntometrine®) to prevent childbirth-related bleeding has been evaluated in other studies and shown to be effective and reasonably well tolerated. However, these combinations have not been directly compared within a study. Major benefits or differences in bleeding between them are not anticipated. Any benefit or harm is within their side effects profiles. These side effects are anticipated to be mild and short-lasting only. The study will provide high-quality comparative data to guide future care of universally applied medications during childbirth.

Where is the study run from?
Labour ward, Universiti Malaya Medical Centre

When is the study starting and how long is it expected to run for?
January 2024 to October 2026

Who is funding the study?
Department of Obstetrics and Gynaecology, Universiti Malaya Medical Centre

Who is the main contact?
Dr Hemavahthy Mani, hemavahthymani@gmail.com

Contact information

Type(s)
Public, Scientific, Principal investigator

Contact name
Dr Hemavahthy Mani

Contact details
Medical Officer, Obstetrics and Gynaecology
Pusat Perubatan Universiti Malaya
Lembah Pantai
Kuala Lumpur
Malaysia
59100
+60 01126364662
hemavahthymani@gmail.com

Type(s)

Public, Scientific

Contact name
Prof Dr Tan Peng Chiong

Contact details
Obstetrics and Gynaecology
Pusat Perubatan Universiti Malaya
Lembah Pantai
Kuala Lumpur
Malaysia
59100
-
tanpengchiong@yahoo.com

Type(s)
Public, Scientific

Contact name
Dr Wong Thai Ying

Contact details
Obstetrics and Gynaecology
Pusat Perubatan Universiti Malaya
Lembah Pantai
Kuala Lumpur
Malaysia
59100
-
thaiying.wong@gmail.com

Additional identifiers

Study information

Scientific Title
Intramuscular oxytocin & oral misoprostol versus intramuscular fixed dose oxytocin-ergometrine & oral placebo tablet for postpartum haemorrhage prophylaxis following vaginal delivery: a randomised controlled trial

Acronym
MisO Study

Study objectives
We hypothesize that oxytocin 10 IU i.m. plus oral misoprostol 600 mcg compared to fixed dose oxytocin 5 IU-ergometrine 500 mcg i.m. plus oral placebo tablet will have different impact on hypertension and fever in the one hour after delivery

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 07/11/2024, Medical Research Ethics Committee of University of Malaya Medical Centre (Lembah Pantai, Kuala Lumpur, 59100, Malaysia; +80 03-79493209/2251; iresearch@ummc.edu.my), ref: 2024117-13252

Study design
Participant-blinded parallel-group randomized trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Prevention of postpartum haemorrhage, tolerability of prophylactic agents

Interventions
Patient recruitment will take place in antenatal or labour ward of UMMC. All women admitted for a planned vaginal birth will be assessed for eligibility. A Patient Information Sheet will be provided. Oral questions about the study will be invited and answered by the recruiting provider. Written informed consent will be taken from all who agree to participate.

Participants will be randomised only at vaginal delivery to:
i) i.m. oxytocin 10 IU and oral misoprostol 600 mcg tablet
OR
ii) i.m. syntometrine (fixed dose oxytocin 5 IU and ergometrine 500mcg) plus oral placebo
Given at the delivery of the anterior shoulder or latest before delivery of the placenta.
These prepared interventions will be placed in the sealed opaque numbered randomization envelopes.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Oxytocin for injection (10 IU), syntometrine for injection (fixed dose oxytocin 5 IU and ergometrine 0.5 mg), oral misoprostol tablet, placebo tablet

Primary outcome(s)
One hour after delivery, the presence of:
1. Hypertension (systolic ≥ 140 mmHg and/or diastolic ≥ 90 mmHg) measured using a hospital-grade automated blood pressure device
2. Fever (body temperature ≥ 37.5 0C) measured using a hospital-grade thermometer

Key secondary outcome(s))
1. Delivery blood loss measured using data collected from participant electronic medical records (EMR) at hospital discharge

2. Use of additional haemostatic intervention (e.g., uterotonics, operative interventions) measured using data collected from EMR at hospital discharge
3. Transfer for a higher level of care (HDU or ICU) measured using data collected from EMR at hospital discharge
4. Blood transfusion measured using data collected from EMR at hospital discharge
5. Women's sense of wellbeing measured using a 0-10 Numerical Rating Scale (NRS) before hospital discharge
6. Satisfaction with the allocated intervention measured using a 0-10 NRS) before hospital discharge
7. Interval to first satisfactory breastfeeding (from maternal perspective); date and time as reported by mother as soon as satisfactory breastfeeding episode achieved
8. Shock ascertained measured using data collected from EMR at hospital discharge
9. Coagulopathy measured using data collected from EMR at hospital discharge
10. Hysterectomy measured using data collected from EMR at hospital discharge
11. Organ dysfunction measured using data collected from EMR at hospital discharge
12. Maternal death measured using data collected from EMR at hospital discharge
13. Adverse effects of hypertension, fever, vomiting, shivering, epigastric discomfort or fullness, diarrhoea, headache, chest pain, palpitation, and shortness of breath measured using data collected through direct questioning within 24 hours of birth and from EMR
14. Composite adverse effects of at least one of hypertension, fever, vomiting, shivering, epigastric discomfort or fullness, diarrhoea, headache, chest pain, palpitation, and shortness of breath measured using data collected from EMR at hospital discharge
15. Major harm measured using data collected from EMR at hospital discharge:
15.1. Haemorrhagic cerebral vascular event due to hypertension
15.2. Maternal febrile convulsion
15.3. Maternal ICU admission for bleeding complications due to uterine atony

Completion date
30/10/2026

Eligibility

Key inclusion criteria
1. Expecting a vaginal delivery
2. Age 18-45 years
3. Term gestation (≥37weeks)
4. Single fetus
5. Cephalic presentation
6. Parity <5
7. Final inclusion for randomization: have achieved vaginal delivery

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit

18 years

Upper age limit
45 years

Sex
Female

Key exclusion criteria
1. Contraindication to oxytocin, misoprostol and ergometrine
2. Known hypertension, cardiovascular, hepatic or hematologic disorders

Date of first enrolment
01/02/2025

Date of final enrolment
31/03/2026

Locations

Countries of recruitment
Malaysia

Study participating centre
Universiti Malaya Medical Centre
Lembah Pantai, 59100, Kuala Lumpur
Kuala Lumpur
Malaysia
59100

Sponsor information

Organisation
University Malaya Medical Centre

ROR
https://ror.org/00vkrxq08

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Universiti Malaya

Alternative Name(s)
University of Malaya, University Malaya, Malayan University, King Edward VII College of Medicine, Raffles College, University of Malaya in Singapore, , , , UM

Funding Body Type
Government organisation

Funding Body Subtype
Universities (academic only)

Location
Malaysia

Results and Publications

Individual participant data (IPD) sharing plan
The raw data generated during and/or analyzed during the current study are/will be available upon request from Dr Hemavahthy Mani (hemavahthymani@gmail.com) subject to institutional review board approval 6 months after publication.
The type of data that will be shared: the reported data
Whether consent from participants was required and obtained: yes
Comments on data anonymization: yes
Any ethical or legal restrictions: Data sharing will be subject to ethical review and approval

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet		09/07/2024	13/01/2025	No	Yes
Protocol file	version 3	09/07/2024	13/01/2025	No	No