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# Early menstrual induction - Proof of concept study

**Submission date**
13/07/2021

**Recruitment status**
No longer recruiting

**Registration date**
03/08/2021

**Overall study status**
Completed

**Last Edited**
03/06/2024

**Condition category**
Pregnancy and Childbirth

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

## Plain English summary of protocol

Background and study aims
Emergency contraception (EC) refers to a method of contraception that can be used to prevent pregnancy after sexual intercourse. Currently, the available EC methods only work up until 5 days after unprotected intercourse. This means that women who have not been able to access EC, and do not wish to be pregnant, will have to wait and see if they have become pregnant and obtain an abortion if desired. In the current study, we investigate the effect of a new EC treatment which can be used between 5 days after intercourse and the day before expected menstruation.

In the proof-of-concept study, 80 women who have missed the current EC window, will be given levonorgestrel (progesterone) followed by mifepristone (anti-progesterone) 48 hours later to induce menstruation, as a form of early menstrual induction. If effective, this intervention will increase options available to women, filling an important gap in the work towards preventing unwanted pregnancies and potentially unsafe abortions.

Who can participate?
Women (18-45 years old) can join the study when they have had unprotected intercourse and were too late to use the standard emergency contraception (such as the morning-after pill). They should not have reached the day of your expected menstruation. There are some specific criteria to join the study which include: having a regular menstrual cycles (25-35 days), intend to end the pregnancy if confirmed, agree not to use other contraception methods during the study period.

What does the study involve?
The study involves the following four parts:
1. Blood is drawn from women who meet the inclusion- and exclusion criteria to measure plasma βhCG. If the value is > 10 mIU/ml the women are included in the study. If lower than 10 mIU/ml, the women are asked to come back in 5 days, if the plasma βhCG remains below 10 mIU/ml they cannot join the study.
2. Women who have a positive βhCG test result either at the first or second testing will be included in the study and receive the first intervention. The participants will receive 1.5mg levonorgestrel once as a single oral intake at the facility immediately upon enrolment.

3. After the intake of levonorgestrel, the women will be sent home and asked to return to the health facility 2 days later, where they will be given 200mg mifepristone as a single dose oral intake.
4. On Day 14 the women will be invited back to the health facility for plasma βhCG measurement. If the plasma βhCG is < 10 mIU/ml, the treatment will be regarded as successful, and no further intervention is needed. If the plasma βhCG is > 10 mIU/ml, the intervention has failed, and the woman will be offered the option of pregnancy termination.
During the 14 days, the women are asked to fill out a questionnaire.

What are the possible benefits and risks of participating?
The early menstrual induction process maybe associated with cramp-like pain and bleeding that may be heavy at times. Also, women may experience other side-effects, like fever, chills, nausea, vomiting or diarrhoea. These risks of having induced menses are the same whether women take part in this study or not.
Blood samples
The drawing of blood (5ml) will be performed by skilled and qualified medical staff. It has very limited risks, such as being uncomfortable or may give some stress.
Medication
Both medications used in the study (levonorgestrel and mifepristone) are registered and approved for usage.
The intake of 1.5 mg levonorgestrel could lead to the following side effects:
Heavier or lighter than usual menstrual bleeding; spotting or bleeding between menstrual periods; nausea; vomiting; diarrhoea; tiredness; headache; dizziness; breast pain or tenderness.
The intake of 200 mg mifepristone could lead to the following side effects:
Vaginal bleeding or spotting; cramps; pelvic pain; vaginal burning, itching, or discharge; headache.

There is a possibility that the treatment with levonorgestrel and mifepristone is not successful to prevent the unintended pregnancy and that the women will be referred for follow-up care. This can cause emotional burden for them, as they will have to consider their options to terminate or continue the pregnancy.

Where is the study run from?
Chulalongkorn University Hospital (Thailand)

When is the study starting and how long is it expected to run for?
May 2021 to December 2023

Who is funding the study?
World Health Organization (Switzerland)

Who is the main contact?
Prof. Unnop Jaisamrarn, Unnop.J@Chula.ac.th

# Contact information

### Type(s)
Scientific

### Contact name
Prof Unnop Jaisamrarn

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## Additional identifiers

### Protocol serial number
A66016

## Study information

### Scientific Title
Early Menstrual Induction (EMI): A proof of concept study on a post-fertilization fertility regulation method with a combination of levonorgestrel and mifepristone

### Acronym
EMI

### Study objectives
Currently, there is no effective medical menstrual induction method for women who have missed the Emergency Contraceptive window.
Our aim is to study the effects of a novel regimen of a combined progesterone and anti-progesterone, to induce endometrial shedding and to prevent an intrauterine pregnancy in women who have had unprotected intercourse and missed this emergency contraception window.
If effective, this intervention will increase options available to women, filling an important gap in the work towards preventing unwanted pregnancies and potentially unsafe abortions.

### Ethics approval required
Old ethics approval format

### Ethics approval(s)
Approved 20/05/2021, Institutional Review Board Faculty of Medicine, Chulalongkorn University (1873 Rama 4 Road, Pathumwan, Bangkok 10330, Thailand; +66 2-256-4493; eccu@chula.ac.th), ref: COA No. 637/2021, IRB No. 309/64

### Primary study design
Interventional

### Study design
Single-centre single group open label phase I intervention study

### Study type(s)

Treatment

### Health condition(s) or problem(s) studied
To prevent an intrauterine pregnancy in women who have had unprotected intercourse and missed the emergency contraception window

### Interventions
1. Blood is drawn from women who meet the inclusion criteria to measure plasma βhCG. If the value is >10 mIU/ml the women are included in the study. If lower than 10 mIU/ml, the women are requested to come back in 5 days, if the plasma βhCG remains below 10 mIU/ml they cannot join the study.
2. Women who have a positive βhCG test result either at the first or second testing will be included in the study and receive the intervention. The participants will receive 1.5 mg levonorgestrel once as a single oral intake at the facility immediately upon enrolment.
3. After the intake of levonorgestrel, the women will be sent home and asked to return to the health facility 2 days later, where they will be given 200 mg mifepristone as a single dose oral intake.
4. On Day 14 the women will be invited back to the health facility for plasma βhCG measurement. If the plasma βhCG is < 10 mIU/ml, the treatment will be regarded as successful, and no further intervention is needed. If the plasma βhCG is > 10 mIU/ml, the intervention has failed, and the woman will be offered the option of pregnancy termination or continuation. The pregnancy will be followed up until it ends by the investigators in failed cases.

### Intervention Type
Drug

### Phase
Phase I

### Drug/device/biological/vaccine name(s)
levonorgestrel, mifepristone

### Primary outcome(s)
Effect of the intervention measured by plasma βhCG on Day 14

### Key secondary outcome(s)
1. Amount of uterine bleeding after treatment measured using a self-recording questionnaire for day 1-2, and day 3-14
2. Length of post-treatment menstrual cycle measured using a self-recording questionnaire for day 1-2, and day 3-14
3. Satisfaction using the intervention measured using a self-recording questionnaire for day 3-14
4. Side-effects of drugs measured using a self-recording questionnaire for day 1-2, and day 3-14

### Completion date
31/12/2023

## Eligibility

### Key inclusion criteria

1. Women aged 18 - 45 years
2. Regular menstrual cycles (duration of 25 – 35 days)
3. Intend to end the pregnancy if confirmed
4. Unprotected intercourse > 5 days but before expected menstruation
5. Positive plasma βhCG (>10 mIU/ml)
6. Agree not to use any other contraception method during the study period
7. Literacy to read and understand the study procedures

### 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. Irregular menstrual cycles
2. Breastfeeding
3. Unknown date of last menstrual period
4. Use of emergency contraception during the current menstrual cycle
5. Known allergy or any contraindication to levonorgestrel or mifepristone
6. Any systemic illness that requires the use of regular medications or any other serious medical disease
7. Any cases where the woman indicates pregnancy caused by rape, as the woman may need additional support and care. These women will be referred for appropriate services, including for termination of pregnancy where desired.

### Date of first enrolment
01/09/2021

### Date of final enrolment
31/08/2022

## Locations

### Countries of recruitment
Thailand

**Study participating centre**
**Chulalongkorn University**
Faculty of Medicine
1873 Rama 4 Road
Bangkok
Thailand
10330

# Sponsor information

**Organisation**
Concept Foundation

**ROR**
https://ror.org/039k72k82

# Funder(s)

**Funder type**
Research organisation

**Funder Name**
World Health Organization

**Alternative Name(s)**
, , Всемирная организация здравоохранения, Organisation mondiale de la Santé, Organización Mundial de la Salud, WHO, , ВОЗ, OMS

**Funding Body Type**
Government organisation

**Funding Body Subtype**
International organizations

**Location**
Switzerland

# Results and Publications

**Individual participant data (IPD) sharing plan**

The datasets generated during and/or analysed during the current study will be stored in a non-publically available repository. The data will be collected in REDCap (www.project-redcap.org), and access is only given to a strict number of researchers from Chulalongkorn University and Concept Foundation. The data entered in REDCap is completely anonymous, and only the PI has the decoding to document.

## IPD sharing plan summary