ISRCTN11046192 https://doi.org/10.1186/ISRCTN11046192

Efficacy of mifepristone followed by misoprostol compared to misoprostol alone in first-trimester miscarriage treatment

Submission date
04/09/2020

Recruitment status
No longer recruiting

Registration date
12/09/2020

Overall study status
Completed

Last Edited
31/07/2023

Condition category
Pregnancy and Childbirth

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
First-trimester miscarriage (FTM) is the loss of a pregnancy during the first 13 weeks of pregnancy. It is a common event, occurring in 10 to 15% of all clinically identified pregnancies. Medical treatment of FTM allows a more predictable expulsion of products of conception compared to expectant management (waiting for the miscarriage to happen by itself naturally) and avoid the risks of surgical management. Misoprostol is a drug that is widely used for that effect. Vaginal administration of 800 µg is the most suitable treatment as a single dose, with success rates reaching 85%. Several studies have been investigating the combination of mifepristone with misoprostol in FTM and suggest an improvement in success rates compared to misoprostol alone. The aim of this study is to assess the effectiveness of mifepristone plus misoprostol compared to misoprostol alone for FTM.

Who can participate?
Healthy women aged 18 years or older diagnosed with FTM up to 9 weeks of gestation

What does the study involve?
Participants start the treatment under a physician's supervision, taking orally a single-dose numbered white pill, which can contain 200 mg of either mifepristone or placebo. Participants will be randomly allocated to take mifepristone or placebo. Participants are instructed to complete the treatment with 800 µg of vaginal misoprostol 36 to 48 hours after the oral pill and another visit is scheduled in 2 to 3 weeks at the same service but not necessarily with the same physician. Demographic and clinical information is collected. The participants receive written information about FTM and medical treatment. They also complete a questionnaire about their experience, including date and time of misoprostol administration, adverse effects (nausea, vomiting, diarrhea, headache, dizziness, chills or fever), bleeding and pain intensity, pain medication use and acceptability. Vaginal misoprostol can be repeated about 48 hours later if no tissue is lost or if missed or incomplete miscarriage is diagnosed in follow-up. In each follow-up the physician performs a gynaecological exam and transvaginal ultrasound, reports symptoms or complications and the conduct adopted. In the center where the trial takes place it is common practice to reserve aspiration/curettage as a last-line treatment, although that possibility is

always discussed with the patients. All participants are followed up until miscarriage resolution (diagnosis of complete miscarriage or surgical treatment).

What are the possible benefits and risks of participating?
Many Portuguese public hospitals offer only misoprostol for FTM treatment. Half of the study participants receive mifepristone, which may have a higher success rate. The surveillance and health care offered to participants is similar to any patient diagnosed with FTM. The combination with mifepristone (200 mg) is considered safe and none of the previously referred studies reported an increased risk of adverse events compared to misoprostol alone.

Where is the study run from?
Hospital Senhora da Oliveira – Guimarães (Portugal)

When is the study starting and how long is it expected to run for?
December 2018 to December 2021

Who is funding the study?
Hospital Senhora da Oliveira – Guimarães (Portugal)

Who is the main contact?
Beatriz Bettencourt Silva
beatrizbettsilva@gmail.com

Contact information

Type(s)
Scientific

Contact name
Dr Beatriz Bettencourt Silva

ORCID ID
https://orcid.org/0000-0002-1743-4329

Contact details
Rua dos Cutileiros, Creixomil
Hospital Senhora da Oliveira - Serviço de Ginecologia e Obstetrícia
Guimarães
Portugal
4835-044
+351 (0)253 540 330
beatrizsilva@hospitaldeguimaraes.min-saude.pt

Type(s)
Public

Contact name
Dr Beatriz Bettencourt Silva

Contact details

Rua dos Cutileiros, Creixomil
Hospital Senhora da Oliveira - Serviço de Ginecologia e Obstetrícia
Guimarães
Portugal
4835-044
+351 (0)253 540 330
beatrizbettsilva@gmail.com

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
3\2019

Study information

Scientific Title
The role of Mifepristone on First-trimester miscarriage Treatment (MiFirsT) – a double-blind randomized controlled trial

Acronym
MiFirsT

Study objectives
Mifepristone followed by vaginal misoprostol is more successful at treating first-trimester miscarriage than vaginal misoprostol alone.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 26/02/2019, Ethics Committee for Health of Hospital Senhora da Oliveira – Guimarães (Rua dos Cutileiros, Creixomil, 4835-044 Guimarães; +351 253 540 330; comissaoetica@hospitaldeguimaraes.min-saude.pt), ref: 3\2019

Study design
Single-center prospective interventional randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
First trimester miscarriage (embryo without cardiac activity or anembryonic gestation) up to 9 weeks of gestation, diagnosed by transvaginal ultrasonographic criteria

Interventions
Adult women diagnosed with first-trimester miscarriage (up to 9 weeks of gestation), who are eligible and choose medical treatment, are randomized to either treatment with oral mifepristone (200 mg) or placebo, both followed by vaginal misoprostol (800 µg).

After eligibility and written informed consent, women initiate the treatment in the Obstetrics Emergency Service of Hospital Senhora da Oliveira – Guimarães under a physician's supervision, taking orally a single-dose numbered white pill which contains either 200 mg of mifepristone (mifepristone group) or placebo (misoprostol-alone group). The pills are randomly numbered by the hospital's pharmacy in a 1:1 proportion and assigned to the participants in ascending order. Women are instructed to complete the treatment with 800 µg of vaginal misoprostol 36 to 48 hours after the oral pill and a revaluation is scheduled in 2-3 weeks at the same service. Participants and physicians involved in recruitment and follow-up are unaware of the treatment-group assignments (only the hospital pharmacy has the information about which numbered pills contained mifepristone). Vaginal misoprostol can be repeated approximately 48 hours after the first evaluation if no tissue is lost or in follow-up if missed or incomplete miscarriage is diagnosed. All patients maintain follow-up until complete miscarriage, which can take 2 months.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Mifepristone, misoprostol

Primary outcome(s)
The success of medical treatment, defined as the complete evacuation of conception products by vaginal ultrasound and, thus, no need for surgical intervention. Treatment success is evaluated at the first follow-up appointment, 2 to 3 weeks after randomization (success rate at first follow-up) and at the second appointment, 3 to 5 weeks after randomization (success rate at second follow-up). The overall success rate and the rate of uterine aspiration/curettage is also reported.

Key secondary outcome(s))
1. Complications (namely severe bleeding or pelvic infection) evaluated by the physician at follow-up appointments or admission to emergency service
2. Adverse effects (nausea, vomiting, diarrhea, headache, dizziness, chills or fever) measured by questionnaire (binomial questions) to be answered after completing the initial treatment (mifepristone or placebo plus vaginal misoprostol)
3. Intensity of bleeding and pain measured by questionnaire (Likert-type scales) to be answered after completing the initial treatment (mifepristone or placebo plus vaginal misoprostol)
4. Acceptability of the treatment measured by questionnaire (classification of the treatment as "good", "indifferent" or "bad" and if the participant would recommend it to a friend in the same clinical situation), to be answered after completing the initial treatment (mifepristone or placebo plus vaginal misoprostol)

5. Clinical characteristics that can influence treatment success (gravidity, parity, gestational age and diagnosis – embryo death or anembryonic gestation), assessed by the physician at randomization

Completion date
16/12/2021

Eligibility

Key inclusion criteria
1. Anembryonic or missed first-trimester miscarriage up to 9 weeks of gestation by transvaginal ultrasound (diagnosis criteria according to Society of Radiologists in Ultrasound Multispeciality Consensus Conference on Early First Trimester Diagnosis of Miscarriage and Exclusion of a Viable Intrauterine Pregnancy, October 2012)
2. Healthy women aged 18 years or older

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Female

Total final enrolment
216

Key exclusion criteria
1. Diagnosis of inevitable or incomplete miscarriage
2. Suspicious of ectopic pregnancy or trophoblastic disease
3. Intrauterine device in place
4. Allergy to prostaglandins
5. Medical conditions contraindicating the treatment with misoprostol and/or mifepristone, namely intense vaginal bleeding with severe anemia or hemodynamic instability, suspicious of systemic infection, patients with hemorrhagic disorders or on anticoagulant therapy, patients with porphyria, uncontrolled heart disease, adrenal failure or on concurrent long-term corticosteroid therapy

Date of first enrolment
10/04/2019

Date of final enrolment
25/11/2021

Locations

Countries of recruitment
Portugal

Study participating centre
Hospital Senhora da Olivieira – Guimarães, Serviço de Ginecologia e Obstetrícia
Rua dos Cutileiros
Creixomil
Guimarães
Portugal
4835-044

Sponsor information

Organisation
Hospital da Senhora da Oliveira Guimarães

ROR
https://ror.org/00y0jw647

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Hospital Senhora da Oliveira Guimarães

Results and Publications

Individual participant data (IPD) sharing plan
Current IPD sharing plan as of 31/07/2023:
The datasets generated during and/or analysed during the current study will be available upon request from Beatriz Bettencourt Silva (email address: beatrizbettsilva@gmail.com).

———

Previous IPD sharing plan:
The participant-level data is not expected to be made available because participants gave

written informed consent to store the anonymized data and to share the study results with the scientific community, not specifically to share the individual data beyond the investigation team.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results		13/01/2023	13/01/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file			05/01/2023	No	No