M&M Trial

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON21883

Source
Nationaal Trial Register

Brief title
M&M Trial

Health condition

early pregnancy failure, miscarriage, missed abortion, medical treatment, mifepriston, misoprostol, miskraam, niet-vitale zwangerschap, medicamenteuze behandeling

Sponsors and support

Primary sponsor: Radboudumc
791 Verloskunde & Gynaecologie Stafafdeling
Postbus 9101, 6500 HB Nijmegen
Source(s) of monetary or material Support: Exelgyn (Groupe Nordic Pharma), Baarn, Netherlands
Radboudumc, Nijmegen
Canisius-Wilhelmina Ziekenhuis, Nijmegen

Intervention

Outcome measures

Primary outcome

Complete (success) or incomplete (failure) evacuation will be determined using transvaginal

ultrasonography six to nine days after medical treatment. An endometrial thickness <15mm (maximum anterior-posterior diameter) and no evidence of retained products of conception using only the allocated therapy is considered as complete evacuation.

Secondary outcome

Patient satisfaction with treatment will be measured using a standard, validated questionnaire; the Client Satisfaction Questionnaire (CSQ-8) will be filled in four weeks after treatment.

Quality of life will be measured at baseline, two days and four weeks after treatment using standard, validated questionnaires such as EuroQOL and Short Form 36.

Patients will receive a registration form to document possible side effects. The treating gynaecologist will document these side effects and complications using the case report form (CRF).

Study description

Background summary

Rationale:

Early pregnancy failure (EPF) is a common complication of pregnancy. Yearly in the Netherlands, 10.000 women with EPF do not abort spontaneously and do receive medical or surgical treatment in order to remove the products of conception from the uterus. For many years, surgical treatment has been the standard treatment. However, medical treatment is a safe and less expensive alternative. Unfortunately, the current medical treatment with misoprostol only has a 54% complete evacuation rate without additional surgery.

Medical treatment for EPF can most probably be improved. For other conditions, such as medical termination of vital pregnancy, the combination of mifepristone with misoprostol has been shown to be superior to the use of misoprostol alone. Based on retrospective data in the Radboud University Medical Centre that are compatible with data from the literature, we expect a complete evacuation rate of at least 67%. However, until now conclusive evidence is lacking.

Objective:

The goal of this study is to test the hypothesis that in early pregnancy failure the sequential

combination of mifepristone with misoprostol is superior to the use of misoprostol alone in terms of complete evacuation of the products of conception from the uterus.

Study design:

A multi-centred, prospective, two-armed, randomized, double blinded and placebo-controlled trial.

Study population:

Woman with ultrasonography confirmed early pregnancy failure (6-14 weeks postmenstrual), managed expectantly for at least one week.

Intervention:

At day one women allocated to Mifepristone will receive mifepristone 600mg, orally, before starting with the standard treatment.

Control group:

Women allocated to placebo will receive placebo tablets at day one before starting with the standard treatment.

General treatment:

Apart from the study medication, management of participants will be similar in both groups. All women will get two doses of misoprostol 400µg (four hours apart), which will be taken orally at home. One day later two more doses of oral misoprostol 400µg (four hours apart) will be taken at home.

Main study parameters/endpoints:

Six to nine days after treatment, ultrasonography will be performed to determine complete or incomplete evacuation. An endometrial thickness <15mm (maximum anterior-posterior diameter) and no evidence of retained products of conception using only the allocated

therapy would be considered as success. The secondary objectives establish patient satisfaction with treatment, side effects, complications and costs.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:

We intend to compare medical treatments that are already applied worldwide for several other indications.

The common undesirable effects mentioned in the information leaflet of mifepristone are nausea, vomiting, diarrhoea, cramping or uterine contractions and bleeding.

Ultrasonography performed six to nine days after treatment is part of the general treatment. No additional physical examination is needed for this study, nor will extra blood be taken from the subjects.

Study participants will be asked to fill in standard, validated questionnaires at three different time points.
Participants are followed in an outpatient clinic; hospital admission follows if medically necessary.
According to the risk classification of the NFU for patients participating in this study, the risk has been assessed as "negligible".

Study objective

The goal of this study is to test the hypothesis that in early pregnancy failure the sequential combination of mifepristone with misoprostol is superior to the use of misoprostol alone in terms of complete evacuation of the products of conception from the uterus.

Early pregnancy failure (EPF) is a common complication of pregnancy. Yearly in the Netherlands, 10.000 women with EPF do not abort spontaneously and do receive medical or surgical treatment in
order to remove the products of conception from the uterus. For many years, surgical treatment has been the standard treatment. However, medical treatment is a safe and less expensive alternative. Unfortunately, the current medical treatment with misoprostol only has a 54% complete evacuation rate without additional surgery.

Medical treatment for EPF can most probably be improved. For other conditions, such as medical termination of vital pregnancy, the combination of mifepristone with misoprostol has been shown to be superior to the use of misoprostol alone. Based on retrospective data in the Radboud University Medical Centre that are compatible with data from the literature, we expect a complete evacuation rate of at least 67%. However, until now conclusive evidence is lacking.

Study design

Primary outcome: transvaginal ultrasonography six to nine days after medical treatment.

Secondary outcome: digital questionnaires at baseline, two days and four weeks after treatment.

Intervention

Early pregnancy failure is diagnosed using transvaginal ultrasonography. The treating gynaecologist will include patients if they meet the inclusion criteria.

After randomization the patient will receive three tablets, each containing a placebo or 200mg mifepristone (day 1). These tablets will be orally swallowed at the outpatient clinic in the presence of a physician.

Then, the standard therapy should be started. No additional procedures, sampling or laboratory tests are performed. Apart from the study medication, management of participants will be similar in both groups. All women will get two doses of misoprostol 400µg (four hours apart), which will be taken orally at home. By day 4, two more doses of oral misoprostol 400µg (four hours apart) will be taken at home. It is advised to take the misoprostol tablets together with food or directly
after any meal. The patient will use a registration form to document the amount of tablets taken at each day. This will also be entered into the case report form.

Six to nine days later ultrasonography will be performed, as part of the standard treatment, to determine complete or incomplete evacuation. An endometrial thickness <15mm (maximum anteriorposterior diameter) and no evidence of retained products of conception using only the allocated therapy is considered as complete.

Anti-D prophylaxis should be given if necessary as part of the standard treatment, following the NVOG-guideline “Erytrocytenimmunisatie en zwangerschap”. Anti-D prophylaxis should be given within 48 hours after evacuation in case of gestational age more than 10 weeks or if curettage has been performed.

At randomisation, during treatment and four weeks after treatment data collected from the clinic maternal charts will be entered into case report form. Primary and secondary outcome measures are subtracted from routine clinical parameters and questionnaires.

Contacts

Public
Canisius-Wilhelmina Ziekenhuis - A44 - Verloskunde en Gynaecologie

J van den Berg
Postbus 9015

Nijmegen 6500 GS
The Netherlands
024 - 365 8245
Scientific
Canisius-Wilhelmina Ziekenhuis - A44 - Verloskunde en Gynaecologie

J van den Berg
Postbus 9015

Nijmegen 6500 GS
The Netherlands
024 - 365 8245

Eligibility criteria

Inclusion criteria

Early pregnancy failure, 6-14 weeks postmenstrual

o Crown-rump length ≥ 6mm and no cardiac activity OR

o Gestational sac without embryonic pole, confirmed by a second ultrasound at least one week later

• At least one week after diagnosis OR a discrepancy of at least one week between crown-rump length and calendar gestational age

• Intra-uterine pregnancy

• Women aged above 18 years

• Hemodynamic stable patient

• No signs of infection

• No signs of incomplete abortion

• No high risk of thrombosis

Exclusion criteria

Interaction between study-medication and other medicine

o Medicinal products and other forms that are CYP3A4 substrates: ketoconazole, itraconazole, erythromycin, rifampicin, dexamethasone, St. John's Wort, certain anticonvulsants (phenytoin, phenobarbital, carbamazepine) and grapefruit juice

o Magnesium-containing antacids should be avoided during treatment with misoprostol as this may worsen the misoprostol-induced diarrhoea.

• Contraindications for mifepristone or misoprostol

o chronic adrenal failure

o hypersensitivity to the active substance or to any of the excipients

o severe asthma uncontrolled by therapy

o inherited porphyria

o pregnancy not confirmed by ultrasound scan or biological tests

o suspected extra-uterine pregnancy

o hypersensitivity to misoprostol or to any other prostaglandins

• Patient does not meet inclusion criteria, discovered after randomization

• Inability to give informed consent

Study design

Design

Study type:	Interventional
Intervention model:	Parallel

Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-10-2016
Enrollment:	40
Type:	Actual

Ethics review

Positive opinion

Date:	07-10-2016
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 43323
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL5929
NTR-old	NTR6109
CCMO	NL57892.091.16
OMON	NL-OMON43323

Study results