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Vaginal application of acetic acid 3% gel to hasten induction of abortion in women with mid-trimestric missed abortion

Submission date	Recruitment status	[_] Prospectively registered
31/10/2010	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
10/01/2011	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
07/05/2013	Pregnancy and Childbirth	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Prof Karim Abd-El-Maeboud

Contact details
2 Mobarak St.
Off Asmaa fahmy
Ard El-Golf
Cairo
Egypt
11341
kabdelmaeboud@yahoo.com

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
Assessment of efficacy and saftey of vaginal acidity enhancement with 3% acetic acid on response to vaginal misoprostol induction of abortion in missed mid-trimesteric abortion

Study objectives
Enhacement of vaginal acidity induces cervical softening leading to more successful termination of pregnancy (TOP) with misoprostol along with shorter induction-abortion interval.

Ethics approval required
Old ethics approval format

Ethics approval(s)
The Ethics and Research Committee of Obstetrics and Gynaecology Department, Faculty of Medicine, Ain Shams University approved in September 2010

Study design
Randomised controlled single centre trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Termination of pregnancy (TOP)

Interventions
This trial took place at Ain Shams University Maternity Hospital. The participants will be randomly allocated to the following two groups:
1. Group I: Subjects (n = 24) who will be treated with acidifying vaginal gel (acetic acid 3%) applied every 12 hours, starting 2 days ahead of the planned procedure
2. Group II: Subjects (n = 24) who will be treated with neutral (placebo) vaginal gel (the base of the gel without active agent) applied every 12 hours, starting 2 days ahead of the planned procedure

During the pre-selection visit, exclusion and inclusion criteria will be applied. When the patient's consent is obtained, the investigator will receive the medication package with a label carrying

the corresponding number. Baseline investigations - ABO and rhesus blood group, complete blood count (CBC), random blood sugar, serum glutamate oxalate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), serum creatinine, and coagulation profile will be done. The investigators will supervise application of the medication (dose by dose) from the package carrying the number matching with the patient's entry number. The biometrician will keep the sealed envelopes with the numbers of order till the end of the study. The medication will be strictly allocated in the numbers order, according to the randomization plan. The randomization schedule will be constructed so that the number in each group would be balanced for every 10 women recruited. Subjects withdrawn from the study before the onset of uterine pains will not be substituted. The next patient included in the study will receive the next number.

Before digital vaginal examination, a speculum examination will be performed and vaginal pH value will be measured by using indicator paper (pH-indicator strips pH 0-14 Universal indicator paper, Merck KGbA, Darmstadt, Germany). The indicator will be held with an artery forceps against the vaginal wall in the midvagina- until it becomes wet. Then, another indicator paper will be held with an artery forceps against the vaginal wall - high up in the vagina - until it becomes wet. Colour change of the strip will be immediately compared with the colorimetric scale and the measurement of vaginal pH at the two positions, mid and high vagina, will be recorded. Digital vaginal examination will be then performed assessing three criteria only. These are dilatation, length, position (posterior, midway, anterior or central), and consistency (firm or soft).

After pretreatment with the vaginal gel for two days, induction of abortion will performed, starting at 8 am. Peri-abortion prophylaxis will entail metronidazole 1 g rectally at the time of abortion plus doxycycline 100 mg orally twice daily for 7 days, commencing on the day of abortion. All women will receive misoprostol 800 mg vaginally, then misoprostol 400 mg vaginal, 4-hourly, to a maximum of five doses in the first 24 hours. Before inserting the tablet in the posterior fornix, it will be wetted with acetic acid (7%) to assure its complete dissolution. If a woman does not have adequate uterine contractions within 8 hours following the last dose, the same regimen will be repeated over the following 24 hours and if no response was achieved, this will be considered a failure of therapy, and alternative interventions (treatment with high-dose oxytocin, administration of extra-amniotic prostaglandin F2á, mechanical cervical dilatation with a 16-French Foley balloon catheter or performing a hysterotomy) are to be carried out on the basis of judgment of the clinicians.

Vital signs of the patients including temperature, pulse rate, blood pressure and the frequency of uterine contractions will be monitored every 3 h, with a recording of the time of the onset of regular uterine contractions, and the time of the expulsion of conceptus. Pethidine hydrochloride 50 mg will be given for pain relief if women requested. After abortion, the products of conception (fetus and placenta) will be examined to see whether the abortion was complete, Evacuation of the uterus will be performed under general anaesthesia only if the placenta is found to be incomplete. The amount of blood loss during abortion will be assessed clinically. After abortion, oxytocin 50 U/ 1000 mL normal saline will be administered intravenously at the rate of 100 mL/h. The side-effects of misoprsotol therapy, including nausea, vomiting, diarrhea, fever and marked abdominal pain, will be recorded. Anti-D immunoglobulin G (250 iu before 20 weeks of gestation and 500 iu thereafter) will be given, by injection into the deltoid muscle, to all non-sensitized RhD negative women within 72 hours following termination. The abortus will be handled to the pathologist for further study.

Following termination of pregnancy, women will be given a written account of the symptoms they may experience and a list of those that would make an urgent medical consultation necessary. They will be given a 24-hour telephone helpline number to use if they feel worried

about pain, bleeding or high temperature. Urgent clinical assessment and emergency gynaecology admission will be available when necessary. Also, each woman will be offered a follow-up appointment within 2 weeks of the termination. On discharge, each woman will be given a letter that includes sufficient information about the procedure, with referral for further genetic counseling if necessary. Future contraception will be discussed before discharge following termination.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Acetic acid (3% gel), misoprostol

Primary outcome measure
Efficacy will be assessed on the basis of improved cervical softening as evidenced by success of induction and its duration. The main outcome measures are
1. Successful abortion rate (defined as expulsion of fetus within 12, 24 and 48 h after administration of misoprsotol)
2. Induction-to-abortion interval (defined as the duration between the application of the first dose of misoprsotol and the time of the expulsion of the fetus)
3. The total dose of misoprsotol used

Secondary outcome measures
1. Drug tolerability as judged by the investigator will be collected and analyzed
2. Side-effects of misoprostol, including vomiting, diarrhoea, fever (defined as a single temperature reading exceeding 38°C), marked abdominal pain along with the need for analgesic and its total dose
3. Blood loss will be estimated visually by the attending obstetrician and excessive bleeding will be defined as an estimated blood loss of 500 ml or more
4. The rate of incomplete abortion (the need for surgical evacuation of the uterus)

Overall study start date
10/11/2010

Completion date
10/03/2011

Eligibility

Key inclusion criteria
1. Aged 18 - 40 years
2. Missed abortion
3. Singleton pregnancy
4. Gestational age ranging between 14 and 26 weeks of pregnancy (by calculation, examination and/or ultrasound)
5. Uterus and cervix apparently normal on clinical examination
6. Cervix not dilated with absence of effacement

7. Absence of uterine activity
8. Written and signed informed consent by the patient to participate in the study

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Female

Target number of participants
48

Key exclusion criteria
1. A contraindication to medical termination of pregnancy, e.g. placenta praevia
2. Evidences suggesting onset of spontaneous abortion (uterine contractions with or without cervical changes)
3. Presence of vaginal bleeding
4. Presence of intrauterine contraceptive device (IUCD) in situ
5. Presence of ruptured membranes and/or suspicion of septic abortion as evidenced by maternal temperature of 38°C or more, uterine tenderness or foul-smelling vaginal discharge
6. Previous trial to induce abortion or the use of pre-induction agent during the current pregnancy
7. Any contraindication to receiving prostaglandins, including known hypersensitivity to misoprostol or other prostaglandins (PGs), history of asthma, glaucoma, cardiac or cardiovascular disease
8. Parity six or more
9. Multifetal pregnancy
10. Polyhydramnios
11. Uterine anomaly, previous two or more caesarean sections, previous uterine surgery, e.g., myomectomy or trauma, e.g., uterine perforation
12. History of any cervical surgery or manipulation: cervical cerclage during current pregnancy history thereof during a previous pregnancy, previous cauterization of cervical erosion, previous cervical dilatation or operation with resultant apparent cervical tears or lacerations
13. Associated collagen or autoimmune medical disorder
14. Metabolic acidosis as a result of a medical disorder
15. History of adverse effects to vaginally administered medications
16. Likelihood of requiring treatment during the study period with drugs not permitted by the study protocol which include all vaginal forms of medications
17. Mental condition rendering the patients unable to understand the nature, scope and possible consequences of the study

Date of first enrolment
10/11/2010

Date of final enrolment

10/03/2011

Locations

Countries of recruitment
Egypt

Study participating centre
2 Mobarak St.
Cairo
Egypt
11341

Sponsor information

Organisation
Ain Shams University Maternity Hospital (Egypt)

Sponsor details
c/o Prof Karim H I Abd-El-Maeboud
Abbassia
Cairo
Egypt
11566
obsgyn.asu@gmail.com

Sponsor type
Hospital/treatment centre

Website
http://med.shams.edu.eg/index.php

ROR
https://ror.org/00p59qs14

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Ain Shams University Maternity Hospital (Egypt)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/12/2012		Yes	No