Clinical Trial Protocol
Iranian Registry of Clinical Trials

09 Jun 2026

Comparison of single-dose and multi-dose methotrexate in the treatment of patients with ectopic pregnancy

Protocol summary

Study aim

In this study, we will try to examine the differences and the effect of methotrexate treatment as a single dose and several doses and identify the factors influencing the success and failure of treatment and suggest an effective diet with the lowest dose with the least risk and complications.

Design

The present study is a randomized double-blind clinical trial.

Settings and conduct

This study is a two-course clinical trial; In order to evaluate the effect of effective and safe dose of methotrexate in the treatment of ectopic pregnancy, 108 women with ectopic pregnancy referred to the obstetrics and gynecology department of Shahid Beheshti Hospital and Al-Zahra Hospital will be performed in 2017-2018.

Participants/Inclusion and exclusion criteria

Inclusion criteria will be satisfaction with participating in the study, confirmation of ectopic pregnancy by ultrasound and βHCG, stable hemodynamic status, a gestational sac with the largest diameter of, 4 cm, and the existence of low free fluid in the abdominal and pelvic cavity based on ultrasound. In the case of active hepatitis, kidney disease, use of immunosuppressive drugs, history of a severe allergy to methotrexate, leukopenia in patient CBC tests, and hematopoiesis disorder the patients will exclude.

Intervention groups

In the first group, the multi-dose regimen and in the second group, the single-dose methotrexate regimens will administer. In such a way that; in the multi-dose regimen, 1 mg/kg methotrexate will be injected on days of 1, 3, 5, and 7. And in the single-dose regimen after methotrexate injection, βHCG titers will be evaluated on days 4 and 7.

Main outcome variables

Serum βHCG levels; Outcome of treatment

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20120716010297N7**
Registration date: **2020-07-11, 1399/04/21**
Registration timing: **retrospective**

Last update: **2020-07-11, 1399/04/21**
Update count: **0**

Registration date

2020-07-11, 1399/04/21

Registrant information

Name

Leili Allahbakhshian

Name of organization / entity

Isfahan University of Medical Sciences

Country

Iran (Islamic Republic of)

Phone

+98 31 1668 7079

Email address

allahbakhshian@med.mui.ac.ir

Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2017-06-22, 1396/04/01

Expected recruitment end date

2018-08-22, 1397/05/31

Actual recruitment start date

2017-07-01, 1396/04/10

Actual recruitment end date

2018-05-05, 1397/02/15

Trial completion date

2018-05-05, 1397/02/15

Scientific title
Comparison of single-dose and multi-dose methotrexate in the treatment of patients with ectopic pregnancy

Public title
Comparison of the effect of methotrexate dose in the treatment of patients with ectopic pregnancy

Purpose
Treatment

Inclusion/Exclusion criteria

Inclusion criteria:
Satisfaction with participating in the study Confirmation of ectopic pregnancy by ultrasound and βHCG Stable hemodynamic status the gestational sac with the largest diameter of, 4 cm; Existence of low free fluid in the abdominal and pelvic cavity based on ultrasound.

Exclusion criteria:
The presence of active hepatitis The presence of kidney disease Use of immunosuppressive drugs History of severe allergy to methotrexate Leukopenia in patient CBC tests Hematopoiesis disorder

Age
No age limit

Gender
Female

Phase
2-3

Groups that have been masked

- Participant
- Outcome assessor
- Data analyser

Sample size
Target sample size: **108**
More than 1 sample in each individual
Number of samples in each individual: **54**
Women with ectopic pregnancy eligible to enter the study
Actual sample size reached: **108**
More than 1 sample in each individual
Actual sample size in each individual: **54**
Women with ectopic pregnancy eligible to enter the study

Randomization (investigator's opinion)
Randomized

Randomization description
First, eligible patients will be selected using non-probability consecutive. All the patients will randomly be assigned to two intervention groups using a computer-based random digit generator based on the consecutive admission numbers.

Blinding (investigator's opinion)
Double blinded

Blinding description
Because of the use of different doses of the drug, the researcher is aware of the type of each group, but the person following the patient's condition and the statistician will not be aware of the type of group.

Placebo
Not used

Assignment
Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee
Ethics committee of Isfahan University of Medical Sciences

Street address
Hezar Jarib Ave, Azadi Square.

City
Isfahan

Province
Isfehan

Postal code
8174673461

Approval date
2018-10-24, 1397/08/02

Ethics committee reference number
IR.MUI.MED.REC.1397.082

Health conditions studied

1

Description of health condition studied
Ectopic pregnancy

ICD-10 code
O00.9

ICD-10 code description
Ectopic pregnancy, unspecified

Primary outcomes

1

Description
Serum βHCG level

Timepoint
On days 1, 3, 5 and 7 after injection of methotrexate

Method of measurement
blood test

2

Description
Outcome of treatment

Timepoint
6 weeks after starting treatment

Method of measurement
The outcome of treatment is assessed as follows: The success of single-dose treatment means a 5% reduction in serum hCG levels after one week of treatment and a serum level of less than 5 mIU / mL after 6 weeks of treatment. In the multi-dose regimen, a 15% decrease in hCG serum levels after 48 hours of treatment or after 4

therapeutic doses, or hCG serum levels less than 5 mIU / mL after 6 weeks of treatment will be regarded as success of treatment.

Secondary outcomes

1

Description
Methotrexate complications such as Hair loss, gastroenteritis, Neutropenia, Fever, and Increase in liver enzyme
Timepoint
during the treatment up to six weeks after
Method of measurement
Clinical observation and doctor's diagnosis

Intervention groups

1

Description
Intervention group: In the multi-dose regimen, 1 mg / kg methotrexate will be injected on days of 1, 3, 5, and 7. It should be noted that in these days, βHCG titer will be measured before methotrexate injection, and methotrexate is prescribed if there was no reduction of less than 15%. Leucovorin will be injected at a dose of 0.1 mg / kg on days 2, 4, 6, and 8.
Category
Treatment - Drugs

2

Description
Intervention group: In the single-dose regimen after methotrexate injection, βHCG titers will be evaluated on days 4 and 7. If no reduction of 15% in βHCG titer was observed during this period, an additional dose will be injected on the seventh day. The dose of methotrexate in the single-dose method is 50 mg/m2 intramuscularly and is not require Leucovorin injection
Category
Treatment - Drugs

Recruitment centers

1

Recruitment center
Name of recruitment center
Al-Zahra Hospital
Full name of responsible person
Behnaz Khani
Street address
Soffe Blvd
City
Isfahan
Province
Isfehan
Postal code
8174675731
Phone
+98 21 3620 2020
Email
alzahra@mui.ac.ir

2

Recruitment center
Name of recruitment center
Shahid Beheshti Hospital
Full name of responsible person
Behnaz Khani
Street address
Ostad Motahhari Street
City
Isfahan
Province
Isfehan
Postal code
8174673461
Phone
+98 31 3236 7001
Email
khani@med.mui.ac.ir

Sponsors / Funding sources

1

Sponsor
Name of organization / entity
Esfahan University of Medical Sciences
Full name of responsible person
Mojgan Mortazavi
Street address
Isfahan University of Medical Sciences, Hezar Jarib Street.
City
Isfahan
Province
Isfehan
Postal code
8179964167
Phone
+98 31 3651 3337
Email
mortazavi@gmail.com
Grant name
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
Esfahan University of Medical Sciences
Proportion provided by this source
100
Public or private sector
Public
Domestic or foreign origin
Domestic
Category of foreign source of funding
empty

Country of origin
Type of organization providing the funding
Academic

Person responsible for general inquiries

Contact
Name of organization / entity
Esfahan University of Medical Sciences
Full name of responsible person
Behnaz Khani
Position
Professor
Latest degree
Specialist
Other areas of specialty/work
Gynecology and Obstetrics
Street address
Shahid Beheshti Hospital, Ostad Motahhari Street, Isfahan.
City
Isfahan
Province
Isfehan
Postal code
8174673461
Phone
+98 31 3236 7001
Email
khani@med.mui.ac.ir

Person responsible for scientific inquiries

Contact
Name of organization / entity
Esfahan University of Medical Sciences
Full name of responsible person
Behnaz Khani
Position
Professor
Latest degree
Specialist
Other areas of specialty/work
Gynecology and Obstetrics
Street address
Shahid Beheshti Hospital, Ostad Motahhari Street, Isfahan.
City
Isfahan
Province
Isfehan
Postal code
8174673461
Phone
+98 31 3236 7001
Email
khani@med.mui.ac.ir

Person responsible for updating data

Contact
Name of organization / entity
Esfahan University of Medical Sciences
Full name of responsible person
Behnaz Khani
Position
Professor
Latest degree
Specialist
Other areas of specialty/work
Gynecology and Obstetrics
Street address
Shahid Beheshti Hospital, Ostad Motahhari Street, Isfahan.
City
Isfahan
Province
Isfehan
Postal code
8174673461
Phone
+98 31 3236 7001
Email
khani@med.mui.ac.ir

Sharing plan

Deidentified Individual Participant Data Set (IPD)
No - There is not a plan to make this available
Justification/reason for indecision/not sharing IPD
There is no further information
Study Protocol
No - There is not a plan to make this available
Statistical Analysis Plan
No - There is not a plan to make this available
Informed Consent Form
No - There is not a plan to make this available
Clinical Study Report
No - There is not a plan to make this available
Analytic Code
No - There is not a plan to make this available
Data Dictionary
No - There is not a plan to make this available