

# Clinical Trial Protocol

## Iranian Registry of Clinical Trials

24 Feb 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  $\beta$ HCG, 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,  $\beta$ HCG titers will be evaluated on days 4 and 7.

##### Main outcome variables

Serum  $\beta$ HCG 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  $\beta$ HCG 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

Isfahan

##### 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  $\beta$ HCG 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,  $\beta$ HCG 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,  $\beta$ HCG titers will be evaluated on days 4 and 7. If no reduction of 15% in  $\beta$ HCG 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/m<sup>2</sup> 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

Isfahan

##### 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

Isfahan

##### 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

Isfahan

##### 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**  
Isfahan  
**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**  
Isfahan

**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**  
Isfahan  
**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