

# Clinical Trial Protocol

## Iranian Registry of Clinical Trials

30 May 2026

### Evaluating the Therapeutic Effect of Theophylline and Zinc Sulfate Co-administration in Infertile Men

#### Protocol summary

##### Study aim

The aim of this study is to investigate the impact of co-administration of Theophylline and Zinc sulfate on oxidative stress, apoptosis, and inflammation, sperm capacitation and parameters in infertile men.

##### Design

Clinical trial with placebo-control group, parallel groups, double-blind, randomized

##### Settings and conduct

This study will perform on infertile men referred to Rastak infertility treatment center in Sina hospital (Markazi Province-Arak city). In this study Both participants and researchers or evaluators of the outcome are unaware of the allocation of study groups.

##### Participants/Inclusion and exclusion criteria

Inclusion criteria: Infertile men referred to the infertility treatment center who, have had at least one year of unprotected intercourse, Natural fertility has not happened in their spouse. These men will all be married These men will be between the ages of 20 and 50. According to WHO criteria, Sperm parameters abnormalities should be observed in at least two spermogram within 2 weeks. Exclusion criteria: Single men Men with varicocele or any other specific disease Men who have taken a particular drug for the past three months

##### Intervention groups

.1. Control group: they take placebo for 3 months. 2.They take Theophylline (200 mg/day) for 3 months. 3. They take zinc (zinc sulfate) (220 mg/day) for 3 months. 4. They take Theophylline (200 mg daily) and Zinc (Zinc sulfate) (220 mg daily) for 3 months.

##### Main outcome variables

Semen analysis and sperm parameters (Spermogram); Levels of LH, FSH and Testosterone; Malondialdehyde Level; TNF- $\alpha$  and Interleukin 10; DNA Fragmentation; Sperm viability; Total antioxidant level of semen; Expression of Caspase 3, BAX, BCL2 genes; Caspase-3, BAX, BCL2 proteins; Sperm maturation; Evaluation of

sperm capacitation All of the aforementioned analyzes were measured in two stages before and after the study.

#### General information

##### Reason for update

##### Acronym

##### IRCT registration information

IRCT registration number: **IRCT20190714044209N1**

Registration date: **2020-02-06, 1398/11/17**

Registration timing: **registered\_while\_recruiting**

Last update: **2020-02-06, 1398/11/17**

Update count: **0**

##### Registration date

2020-02-06, 1398/11/17

##### Registrant information

##### Name

Atena Sadat Azimi

##### Name of organization / entity

Arak University

##### Country

Iran (Islamic Republic of)

##### Phone

+98 86 3277 7300

##### Email address

a-azimi@phd.araku.ac.ir

##### Recruitment status

**Recruitment complete**

##### Funding source

##### Expected recruitment start date

2019-12-22, 1398/10/01

##### Expected recruitment end date

2020-12-21, 1399/10/01

##### Actual recruitment start date

empty

##### Actual recruitment end date

empty

**Trial completion date**  
empty

**Scientific title**  
Evaluating the Therapeutic Effect of Theophylline and Zinc Sulfate Co-administration in Infertile Men

**Public title**  
Evaluating the Therapeutic Effect of Theophylline and Zinc Sulfate Co-administration in Infertile Men

**Purpose**  
Treatment

**Inclusion/Exclusion criteria**  
**Inclusion criteria:**  
Infertile men who, despite having at least one year of unprotected intercourse, have not had fertility in their spouse. These men will all be married According to WHO criteria, abnormalities in sperm parameters should be observed in at least two sperm samples within 2 weeks. These men will be between the ages of 20 and 50.  
**Exclusion criteria:**  
Single men Men with varicoceles or any other specific disease Men who have taken a particular drug for the past three months

**Age**  
From **20 years** old to **50 years** old

**Gender**  
Male

**Phase**  
3

**Groups that have been masked**

- Participant
- Investigator
- Outcome assessor
- Data analyser

**Sample size**  
Target sample size: **120**

**Randomization (investigator's opinion)**  
Randomized

**Randomization description**  
Simple randomization

**Blinding (investigator's opinion)**  
Double blinded

**Blinding description**  
Both participants and researchers or evaluators of the outcome are unaware of the allocation of study groups.

**Placebo**  
Used

**Assignment**  
Parallel

**Other design features**  
The drugs selected in this study will not interfere in the normal course of treatment of patients.

## Secondary Ids

empty

## Ethics committees

### 1

#### Ethics committee

##### Name of ethics committee

Ethics Committee of Arak University of Medical Sciences

##### Street address

No. 6315 Upstairs Azimi shop, Shahid Haghani Street.

##### City

Arak

##### Province

Markazi

##### Postal code

3815166315

##### Approval date

2019-08-07, 1398/05/16

##### Ethics committee reference number

IR.ARAKMU.REC.1398.179

## Health conditions studied

### 1

#### Description of health condition studied

infertile men

#### ICD-10 code

N46

#### ICD-10 code description

Male infertility

## Primary outcomes

### 1

#### Description

semen analysis

#### Timepoint

Before intervention

#### Method of measurement

CASA (Computer-aided sperm analysis) system

### 2

#### Description

Hormones analysis

#### Timepoint

Before intervention

#### Method of measurement

ELISA Kit

### 3

#### Description

Malondialdehyde (MDA) level

#### Timepoint

Before intervention

#### Method of measurement

ELISA Kit

## 4

### **Description**

total antioxidant capacity (TAC)

### **Timepoint**

Before intervention

### **Method of measurement**

ELISA Kit

## 5

### **Description**

DNA fragmentation

### **Timepoint**

Before intervention

### **Method of measurement**

SDFA (Sperm DNA Fragmentation Analysis) kit

## 6

### **Description**

Levels of inflammatory factors

### **Timepoint**

Before intervention

### **Method of measurement**

ELISA Kit

## 7

### **Description**

sperm viability

### **Timepoint**

Before intervention

### **Method of measurement**

Eosin-Negrosin Staining

## 8

### **Description**

sperm maturation

### **Timepoint**

Before intervention

### **Method of measurement**

Aniline blue staining kit

## 9

### **Description**

Investigation of changes in gene expression level

### **Timepoint**

Before intervention

### **Method of measurement**

Real-time polymerase chain reaction (RT-PCR)

## 10

### **Description**

Protein levels measurement

### **Timepoint**

Before intervention

### **Method of measurement**

Western blot

## **Secondary outcomes**

empty

## **Intervention groups**

### 1

#### **Description**

Intervention group: Theophylline (200 mg/day for 3 months period)

#### **Category**

Treatment - Drugs

### 2

#### **Description**

Intervention group: Zink sulfate (220 mg/day for 3 months period)

#### **Category**

Treatment - Drugs

### 3

#### **Description**

Intervention group: Theophylline (200 mg/day for 3 months period) and Zink sulfate (220 mg/day for 3 months period) at the same time

#### **Category**

Treatment - Drugs

### 4

#### **Description**

Control group: just placebo for 3 months period

#### **Category**

Treatment - Drugs

## **Recruitment centers**

### 1

#### **Recruitment center**

##### **Name of recruitment center**

Sina Hospital-Rastak Infertility Clinic

##### **Full name of responsible person**

Dr. Alireza Noushad Kamran

##### **Street address**

Rastak Fertility Clinic, Sina Hospital, Next to Imam Khomeini Stadium, Hepko Ave.

##### **City**

Arak

##### **Province**

Markazi

##### **Postal code**

3818853558

##### **Phone**

+98 86 3340 5343

##### **Fax**

+98 86 3340 5339

##### **Email**

info@araksinahospital.ir

## Sponsors / Funding sources

### 1

#### Sponsor

**Name of organization / entity**

The University of Arak

**Full name of responsible person**

Dr. Malek Soleimani Mehranjani

**Street address**

Arak University, Karbala Ave., Basij Square

**City**

Arak

**Province**

Markazi

**Postal code**

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**Phone**

+98 86 3417 3403

**Fax**

+98 86 3277 4031

**Email**

m-soleimani@araku.ac.ir

**Grant name****Grant code / Reference number****Is the source of funding the same sponsor organization/entity?**

Yes

**Title of funding source**

The University of Arak

**Proportion provided by this source**

25

**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**

Arak University

**Full name of responsible person**

Atena Sadat Azimi

**Position**

PhD student

**Latest degree**

Ph.D.

**Other areas of specialty/work**

Others

**Street address**

No. 6313 , At the top of Azimi shop, Haqqani Street

**City**

Arak

**Province**

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**Phone**

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**Fax****Email**

a-azimi@phd.araku.ac.ir

## Person responsible for scientific inquiries

#### Contact

**Name of organization / entity**

Arak University

**Full name of responsible person**

Atena Sadat Azimi

**Position**

PhD student

**Latest degree**

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## **Sharing plan**

### **Deidentified Individual Participant Data Set (IPD)**

Undecided - It is not yet known if there will be a plan to make this available

### **Study Protocol**

Undecided - It is not yet known if there will be a plan to make this available

### **Statistical Analysis Plan**

Undecided - It is not yet known if there will be a plan to make this available

## **Informed Consent Form**

Undecided - It is not yet known if there will be a plan to make this available

### **Clinical Study Report**

Undecided - It is not yet known if there will be a plan to make this available

### **Analytic Code**

Undecided - It is not yet known if there will be a plan to make this available

### **Data Dictionary**

Undecided - It is not yet known if there will be a plan to make this available