

# Clinical Trial Protocol

## Iranian Registry of Clinical Trials

05 Jul 2026

### Effect of intra-articular Ozone injection on pain and function in patients with mild to moderate knee osteoarthritis

#### Protocol summary

##### Study aim

The effect of intra-articular injection of ozone on pain and function in patients with mild to moderate osteoarthritis.

##### Design

Clinical trials with a control group, parallel groups, double-blind, randomized, sample size 60

##### Settings and conduct

Emam Khomeini hospital

##### Participants/Inclusion and exclusion criteria

Patients with mild to moderate knee osteoarthritis and aged between 45 and 75 with body mass index less than 30 were included. If they started drugs they were excluded.

##### Intervention groups

Intervention group: 6 knee intraarticular injections per week, including 10 cc of 20 micrograms of Ozone were received, for 6 weeks. Control group: 6 placebo injections with an insulin syringe per week were received for 6 weeks.

##### Main outcome variables

Pain; function

#### General information

##### Reason for update

##### Acronym

##### IRCT registration information

IRCT registration number: **IRCT20111025007903N13**

Registration date: **2023-05-11, 1402/02/21**

Registration timing: **retrospective**

Last update: **2023-05-11, 1402/02/21**

Update count: **0**

##### Registration date

2023-05-11, 1402/02/21

##### Registrant information

##### Name

Zahra Alizadeh

##### Name of organization / entity

Tehran University of Medical Sciences

##### Country

Iran (Islamic Republic of)

##### Phone

+98 21 6119 2282

##### Email address

z\_alizadeh@tums.ac.ir

##### Recruitment status

##### Recruitment complete

##### Funding source

##### Expected recruitment start date

2020-01-15, 1398/10/25

##### Expected recruitment end date

2021-01-14, 1399/10/25

##### Actual recruitment start date

2020-04-08, 1399/01/20

##### Actual recruitment end date

2021-04-19, 1400/01/30

##### Trial completion date

2021-04-19, 1400/01/30

##### Scientific title

Effect of intra-articular Ozone injection on pain and function in patients with mild to moderate knee osteoarthritis

##### Public title

Effect of Ozone injection on knee osteoarthritis

##### Purpose

Supportive

##### Inclusion/Exclusion criteria

##### Inclusion criteria:

Mild to moderate knee osteoarthritis Body mass index less than 30 Pain exacerbation with walking Age between 45 and 75 years

##### Exclusion criteria:

History of knee trauma or surgery, metabolic or autoimmune diseases Knee effusion Pregnancy or

lactation Usage of anti-coagulant drugs

**Age**  
From **45 years** old to **75 years** old

**Gender**  
Both

**Phase**  
3

**Groups that have been masked**

- Participant
- Investigator
- Outcome assessor

**Sample size**  
Target sample size: **60**  
Actual sample size reached: **42**

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

**Randomization description**  
Patients were entered into the study using randomized block tables. We prepared 10 blocks, and six patients were considered for each block. Patient one entered block 1, patient two/block 2, patient 3/block 3... patient 10/ block 10. Then the rotation repeated again, patient 11/block 1...until patient 60/block 10, respectively. After that, the third person who he did not aware of the patients' groups, selected 5 blocks as the control group and 5 blocks as the injection group, according to a random sequence. This method not only caused randomization to be equal in both groups but also at each stage of the study, patients were equally assigned to the groups. These small blocks kept the balance between the two groups and made the number of people in each group the same.

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

**Blinding description**  
Patients were blinded with a shield on the knee The investigator and the outcome assessor were blinded about the type of injection

**Placebo**  
Used

**Assignment**  
Parallel

**Other design features**

## Secondary Ids

empty

## Ethics committees

### 1

#### Ethics committee

##### Name of ethics committee

Research Ethics Committees of Imam Khomeini Hospital Complex- Tehran University of Medical Sciences

##### Street address

Dr. Gharib street, Tohid square

##### City

TEHRAN  
**Province**  
Tehran  
**Postal code**  
1419733141

#### Approval date

2019-12-28, 1398/10/07

#### Ethics committee reference number

IR.TUMS.IKHC.REC.1398.211

## Health conditions studied

### 1

#### Description of health condition studied

Osteoarthritis

#### ICD-10 code

M17

#### ICD-10 code description

Osteoarthritis of knee

## Primary outcomes

### 1

#### Description

knee pain

#### Timepoint

before intervention, 6 weeks and, 6 months after injection

#### Method of measurement

Visual Analogue Scale

## Secondary outcomes

### 1

#### Description

Function

#### Timepoint

before intervention, 6 weeks and, 6 months after injection

#### Method of measurement

6minute walking test

## Intervention groups

### 1

#### Description

Intervention group: For knee injection, a 22-gauge syringe was used by the classic anterolateral approach in a supine position and at an angle of 90 degrees to the knee. In the intervention group, 10 ml of 20 µg of ozone solution was used intra-articular. A total of six intra-articular injections of ozone were given to each patient for six consecutive weeks (one injection per week). After the injection, an ice pack was used at the injection site to prevent hematoma. The patients were advised to rest for up to 48 hours and continue the exercise programs afterwards. Participants were received stretching and

strengthening exercise during the trial. Exercise program in the form of isometric multi-joint exercises of the muscles around the knee was defined, including the quadriceps, abductors and adductors of the thigh, holding for 10 seconds, ten repetitions three times a day. In addition, stretching exercises include stretching the hamstrings, gastrocnemius and soleus muscles, holding for 20 seconds in a state of painless stretching with a feeling of discomfort caused by stretching, which was done 1 set of 5 repetitions a day. After one month, concentric exercises of the thigh muscles (quadriceps, then abductors and adductors) with one set of 10 repetitions were started, then the number of repeats was increased to 12 repetitions. In the next step, the number of sets was increased to 3 sets per day, and finally, the weight was added by controlling patients' pain and symptoms. The mentioned program was monitored and re-educated by a sports medicine specialist in each injection session.

#### Category

Treatment - Other

## 2

#### Description

Control group: In the control group, an insulin syringe was used at the injection point without any injection, only for the feeling of the needle by patients. In addition, the patients were blinded during the injection. A total of six needling with an insulin syringe were given to each patient for six consecutive weeks (one injection per week). The exercise program was similar to the intervention group.

#### Category

Placebo

## Recruitment centers

### 1

#### Recruitment center

##### Name of recruitment center

Imam Khomeini Hospital Complex

##### Full name of responsible person

Zahra Alizadeh

##### Street address

Dr. Gharib street, Tohid square

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## Sponsors / Funding sources

### 1

#### Sponsor

##### Name of organization / entity

Tehran University of Medical Sciences

##### Full name of responsible person

Hajar Moamaee

##### Street address

4th Floor, The Center of Tehran University of Medical Sciences, Ghods St., Keshavarz Blvd.

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#### Grant name

#### Grant code / Reference number

#### Is the source of funding the same sponsor organization/entity?

Yes

#### Title of funding source

Tehran 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

Tehran University of Medical Sciences

##### Full name of responsible person

Zahra Alizade

##### Position

Associate Professor

##### Latest degree

Specialist

##### Other areas of specialty/work

Sport Medicine

##### Street address

Sports Medicine Research Center, No7, Opposite of Shariati Hospital, Ale-Ahmad Highway

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## Person responsible for scientific inquiries

### Contact

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Associate Professor of Sports Medicine  
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**Other areas of specialty/work**  
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## Person responsible for updating data

### Contact

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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

Yes - There is a plan to make this available

### Clinical Study Report

Yes - There is 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

### Title and more details about the data/document

Primary and secondary outcomes, and others according to researchers' request

### When the data will become available and for how long

starting 6 months after publication

### To whom data/document is available

Please contact with this e-mail: z\_alizadeh@tums.ac.ir

### Under which criteria data/document could be used

Please contact with this e-mail: z\_alizadeh@tums.ac.ir

### From where data/document is obtainable

Please contact with this e-mail: z\_alizadeh@tums.ac.ir

### What processes are involved for a request to access data/document

Please contact with this e-mail: z\_alizadeh@tums.ac.ir

### Comments