

# Clinical Trial Protocol

## Iranian Registry of Clinical Trials

29 Jul 2026

**Investigating the effects of ozone injection combined with hyaluronic acid compared to hyaluronic injection in the treatment of knee osteoarthritis in patients referred to the orthopedic clinic and the pain clinic of Fatemi Ardabil Hospital.**

### Protocol summary

#### Study aim

Investigating the effects of ozone injection combined with hyaluronic acid compared to hyaluronic injection in the treatment of knee osteoarthritis

#### Design

Clinical trial with a control group, parallel groups, double-blind, randomized, phase 3, on 60 patients. Simple randomization and lottery will be used for randomization.

#### Settings and conduct

This study aims to investigate the effects of intra-articular injection of ozone along with hyaluronic acid compared to hyaluronic acid on pain intensity, quality of life and sleep quality of patients with knee osteoarthritis in Fatemi Ardabil Hospital. One group received 2 cc of intra-articular hyaluronic acid (Nitka company, 2 mg) three times with an interval of one week, and the other group received 2 cc of intra-articular hyaluronic acid (Nitka company, 2 mg) and 10 cc They will receive 25% ozone in three times with an interval of one week. Pain, quality of life and sleep quality of patients will be evaluated. Patients and those evaluating the outcome will not know about the grouping done and the study will be double-blind.

#### Participants/Inclusion and exclusion criteria

Inclusion criteria: Patients with grade 1 and 2 osteoarthritis. Exclusion criteria: Pregnancy or breastfeeding; use of anticoagulants; use of intra-articular drugs in the last 6 months and history of knee surgery.

#### Intervention groups

The intervention groups will include patients with grade 1 and 2 osteoarthritis, in one group, ozone medicine will be injected with hyaluronic acid, and in the other group, hyaluronic acid will be injected intra-articularly.

#### Main outcome variables

Pain

### General information

#### Reason for update

#### Acronym

#### IRCT registration information

IRCT registration number: **IRCT20230823059241N1**

Registration date: **2023-09-27, 1402/07/05**

Registration timing: **prospective**

Last update: **2023-09-27, 1402/07/05**

Update count: **0**

#### Registration date

2023-09-27, 1402/07/05

#### Registrant information

##### Name

maryam asayeshi

##### Name of organization / entity

##### Country

Iran (Islamic Republic of)

##### Phone

+98 45 3373 1691

##### Email address

maryamasayeshi88@gmail.com

#### Recruitment status

**Recruitment complete**

#### Funding source

#### Expected recruitment start date

2023-10-23, 1402/08/01

#### Expected recruitment end date

2024-05-21, 1403/03/01

#### Actual recruitment start date

empty

#### Actual recruitment end date

empty

#### Trial completion date

|                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
|-----------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| empty                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| <b>Scientific title</b>                       | Investigating the effects of ozone injection combined with hyaluronic acid compared to hyaluronic injection in the treatment of knee osteoarthritis in patients referred to the orthopedic clinic and the pain clinic of Fatemi Ardabil Hospital.                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| <b>Public title</b>                           | Ozone injection combined with hyaluronic acid compared to hyaluronic injection in the treatment of knee osteoarthritis                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| <b>Purpose</b>                                | Treatment                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| <b>Inclusion/Exclusion criteria</b>           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| <b>Inclusion criteria:</b>                    | Osteoarthritis grade 1&2                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| <b>Exclusion criteria:</b>                    | Pregnancy or breastfeeding Taking anticoagulants Intra-articular drug use during the last 6 months History of knee surgery                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| <b>Age</b>                                    | No age limit                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| <b>Gender</b>                                 | Both                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| <b>Phase</b>                                  | 3                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| <b>Groups that have been masked</b>           | <ul style="list-style-type: none"> <li>Participant</li> <li>Outcome assessor</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| <b>Sample size</b>                            | Target sample size: 60                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| <b>Randomization (investigator's opinion)</b> | Randomized                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| <b>Randomization description</b>              | Patients will be randomly divided into two groups receiving hyaluronic acid and ozone with hyaluronic acid. Simple randomization and lottery will be used for randomization. Cards and envelopes are prepared according to the number of the research sample and an equal number of names of groups A and B are recorded on each card. The cards are placed inside the letter envelopes. The lid of the letter envelopes is glued and placed inside a box. At the start of the study, according to the order of entry of the participants, the patient will take one of the envelopes from the box and will be placed in one of the two study groups based on the group written on the card. |
| <b>Blinding (investigator's opinion)</b>      | Double blinded                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| <b>Blinding description</b>                   | Patients in one group will receive hyaluronic acid and patients in the other group will receive ozone along with hyaluronic acid. Patients and doctors who evaluate the outcome will be unaware of the type of drug received.                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <b>Placebo</b>                                | Not used                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| <b>Assignment</b>                             | Parallel                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| <b>Other design features</b>                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |

|                                          |                                                                |
|------------------------------------------|----------------------------------------------------------------|
| <b>Secondary Ids</b>                     | empty                                                          |
| <b>Ethics committees</b>                 |                                                                |
| <b>1</b>                                 |                                                                |
| <b>Ethics committee</b>                  |                                                                |
| <b>Name of ethics committee</b>          | Ethics committee of Ardabil University of Medical Sciences     |
| <b>Street address</b>                    | Ardabil University of Medical Sciences, Daneshgah Ave, Ardabil |
| <b>City</b>                              | Ardabil                                                        |
| <b>Province</b>                          | Ardabil                                                        |
| <b>Postal code</b>                       | 5618985991                                                     |
| <b>Approval date</b>                     | 2023-07-22, 1402/04/31                                         |
| <b>Ethics committee reference number</b> | IR.ARUMS.REC.1402.108                                          |

## Health conditions studied

|                                                |                        |
|------------------------------------------------|------------------------|
| <b>1</b>                                       |                        |
| <b>Description of health condition studied</b> | Osteoarthritis in knee |
| <b>ICD-10 code</b>                             | M17                    |
| <b>ICD-10 code description</b>                 | Osteoarthritis of knee |

## Primary outcomes

|                              |                                                                                                   |
|------------------------------|---------------------------------------------------------------------------------------------------|
| <b>1</b>                     |                                                                                                   |
| <b>Description</b>           | Pain                                                                                              |
| <b>Timepoint</b>             | The moment of entry, the second week, the second month and the sixth month after the intervention |
| <b>Method of measurement</b> | Visual Analog Scale                                                                               |

## Secondary outcomes

|                              |                                                                                                   |
|------------------------------|---------------------------------------------------------------------------------------------------|
| <b>1</b>                     |                                                                                                   |
| <b>Description</b>           | Quality of Life                                                                                   |
| <b>Timepoint</b>             | The moment of entry, the second week, the second month and the sixth month after the intervention |
| <b>Method of measurement</b> | SF-36 questionnaire                                                                               |

## 2

### Description

Sleep quality

### Timepoint

The moment of entry, the second week, the second month and the sixth month after the intervention

### Method of measurement

Pittsburgh Questionnaire

## Intervention groups

### 1

#### Description

Intervention group: 2 cc of intra-articular hyaluronic acid (Nitca company, 2 mg) on three occasions with an interval of one week

#### Category

Treatment - Drugs

### 2

#### Description

Intervention group: 2 cc of intra-articular hyaluronic acid (Nitca company, 2 mg) and 10 cc of 25% ozone in three sessions with an interval of one week.

#### Category

Treatment - Drugs

## Recruitment centers

### 1

#### Recruitment center

##### Name of recruitment center

Fatemi Hospital in Ardabil

##### Full name of responsible person

Maryam Asayeshi

##### Street address

Fatemi hospital, Imam Khomeini street, Ardabil

##### City

Ardabil

##### Province

Ardabil

##### Postal code

5614733775

##### Phone

+98 45 3323 2520

##### Email

fatemi@arums.ac.ir

## Sponsors / Funding sources

### 1

#### Sponsor

##### Name of organization / entity

Ardabil University of Medical Sciences

##### Full name of responsible person

Farhad Pourfarzi

##### Street address

Vice chancellor for research, Ardabil University of Medical Sciences, Daneshgah Ave, Ardabil

##### City

Ardabil

##### Province

Ardabil

##### Postal code

5618985991

##### Phone

+98 45 3353 4757

##### Email

research@arums.ac.ir

##### Grant name

##### Grant code / Reference number

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

Yes

##### Title of funding source

Ardabil 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

Ardabil University of Medical Sciences

##### Full name of responsible person

Maryam Asayeshi

##### Position

Resident of anesthesiology

##### Latest degree

Medical doctor

##### Other areas of specialty/work

Anesthesiology

##### Street address

Fatemi hospital, Imam Khomeini street, Ardabil

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##### Phone

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##### Email

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## Person responsible for scientific inquiries

#### Contact

##### Name of organization / entity

Ardabil University of Medical Sciences

**Full name of responsible person**

Maryam Asayeshi

**Position**

Resident of anesthesiology

**Latest degree**

Medical doctor

**Other areas of specialty/work**

Anesthesiology

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**Phone**

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**Email**

maryamasayeshi88@gmail.com

**Person responsible for updating data**

**Contact**

**Name of organization / entity**

Ardabil University of Medical Sciences

**Full name of responsible person**

Maryam Asayeshi

**Position**

Resident of anesthesiology

**Latest degree**

Medical doctor

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**Email**

maryamasayeshi88@gmail.com

**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