Clinical Trial Protocol
Iranian Registry of Clinical Trials

16 Sep 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

Scientific title
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.

Public title
Ozone injection combined with hyaluronic acid compared to hyaloronic injection in the treatment of knee osteoarthritis
Purpose
Treatment
Inclusion/Exclusion criteria
Inclusion criteria:
Osteoartitis grade 1&2
Exclusion criteria:
Pregnancy or breastfeeding Taking anticoagulants Intra-articular drug use during the last 6 months History of knee surgery
Age
No age limit
Gender
Both

Phase
3
Groups that have been masked

- Participant
- Outcome assessor

Sample size
Target sample size: **60**
Randomization (investigator's opinion)
Randomized
Randomization description
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.
Blinding (investigator's opinion)
Double blinded
Blinding description
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.
Placebo
Not used
Assignment
Parallel
Other design features

Secondary Ids

empty

Ethics committees

1

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

Health conditions studied

1

Description of health condition studied
Osteoartritis in knee
ICD-10 code
M17
ICD-10 code description
Osteoarthritis of knee

Primary outcomes

1

Description
Pain
Timepoint
The moment of entry, the second week, the second month and the sixth month after the intervention
Method of measurement
Visual Analog Scale

Secondary outcomes

1

Description
Quality of Life
Timepoint
The moment of entry, the second week, the second month and the sixth month after the intervention
Method of measurement
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
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5614733775
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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
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5618985991
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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 ansthesiology
Latest degree
Medical doctor
Other areas of specialty/work
Anesthesiology
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Position

Resident of ansthesiology

Latest degree

Medical doctor

Other areas of specialty/work

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Person responsible for updating data

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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