

# Clinical Trial Protocol

## Iranian Registry of Clinical Trials

03 Jul 2026

### Evaluation of the effect of adding duloxetine to exercise therapy on pain and function of patients with knee osteoarthritis

#### Protocol summary

##### Study aim

Evaluation of the effect of adding duloxetine to exercise therapy on pain and function of patients with knee osteoarthritis

##### Design

A semi-experimental clinical trial, with a control group, randomized by a numerical random selection, unblinded, phase 3 on 60 patients

##### Settings and conduct

The participants are selected from people who come to the sports medicine department of Imam Khomeini Hospital in Sari because of knee pain. The intervention in the first group is the administration of duloxetine (Abidi company) along with exercise therapy. The intervention in the second group is exercise therapy alone.

##### Participants/Inclusion and exclusion criteria

Inclusion Criteria: Patients 40-80 years old Knee pain during the 3-month period before the first visit more than 14 days per month with an average pain score of Visual Analogue score  $\geq 4$  Osteoarthritis grade 2 and 3 based on Kallgren-Lawrence BMI  $\leq 40$  Stable knee Exclusion Criteria: Deformity of the knee Spondylolisthesis Radiculopathy Inflammatory arthritis Autoimmune disorder Septic arthritis Contraindications for duloxetine Previous exposure or allergy to duloxetine Simultaneous use of other drugs affecting the central nervous system Metabolic diseases Anticoagulation therapy pregnancy Aggressive knee treatments in the last 6 months Any knee replacement or current infection

##### Intervention groups

Intervention group: administration of duloxetine (Abidi company) along with exercise therapy Control group: exercise therapy For both groups, exercise therapy will be knee and hip isometric exercises and hamstring muscle stretching, and then progress to hip flexion and knee extension isotonic exercises in a sitting position.

##### Main outcome variables

Primary outcomes: Brief pain Inventory questionnaire, Western Ontario and McMaster Universities Arthritis

Index questionnaire Secondary outcomes include knee extension strength, Timed Up and Go test

#### General information

##### Reason for update

##### Acronym

##### IRCT registration information

IRCT registration number: **IRCT20230821059204N1**

Registration date: **2023-10-08, 1402/07/16**

Registration timing: **prospective**

Last update: **2023-10-08, 1402/07/16**

Update count: **0**

##### Registration date

2023-10-08, 1402/07/16

##### Registrant information

##### Name

Hanieh Ahmadi

##### Name of organization / entity

##### Country

Iran (Islamic Republic of)

##### Phone

+98 11 3336 6552

##### Email address

h.ahmadi@mazums.ac.ir

##### Recruitment status

**Recruitment complete**

##### Funding source

##### Expected recruitment start date

2023-10-22, 1402/07/30

##### Expected recruitment end date

2024-03-19, 1402/12/29

##### Actual recruitment start date

empty

##### Actual recruitment end date

empty

## Trial completion date

empty

## Scientific title

Evaluation of the effect of adding duloxetine to exercise therapy on pain and function of patients with knee osteoarthritis

## Public title

Effect of Duloxetine in knee osteoarthritis

## Purpose

Treatment

## Inclusion/Exclusion criteria

### Inclusion criteria:

Patients aged 40-80 years Knee pain more than 14 days per month and the average pain score Visual Analogue score (VAS)  $\geq 4$  during the 3-month period before the first visit The grade of knee osteoarthritis is 2 and 3 based on the Kallgren-Lawrence classification BMI  $\leq 40$  The knee should be stable Good cognitive status The ability to understand the study protocol and the mental ability to answer the questions of the questionnaires Willingness to participate in the study

### Exclusion criteria:

Deformity of the knee Spondylolisthesis Lumbar radiculopathy Inflammatory arthritis Autoimmune disorder Septic arthritis Any other concomitant disease such as liver and kidney disease Contraindications for duloxetine (current use of monoamine oxidase inhibitors or poorly controlled angle-closure glaucoma) Previous exposure to duloxetine Concomitant use of other drugs that affect the central nervous system (such as benzodiazepines) History of allergy to duloxetine Metabolic diseases Anticoagulation therapy pregnancy History of aggressive knee treatments in the last 6 months Knee joint replacement at any time Current infection in the affected limb

## Age

From **40 years** old to **80 years** old

## Gender

Both

## Phase

3

## Groups that have been masked

*No information*

## Sample size

Target sample size: **60**

## Randomization (investigator's opinion)

Randomized

## Randomization description

Participants are randomly divided into two groups by numerical random selection process, which are odd numbers for the first group (duloxetine combined with exercise therapy) and even numbers for the second group (exercise therapy).

## Blinding (investigator's opinion)

Not blinded

## Blinding description

## Placebo

Not used

## Assignment

Other

## Other design features

The intervention in the first group is the administration of duloxetine (Abidi company) along with exercise therapy. The intervention in the second group is exercise therapy alone.

## Secondary Ids

empty

## Ethics committees

### 1

#### Ethics committee

##### Name of ethics committee

Ethics Committee of Mazandaran University of Medical Sciences, Imam Hospital

##### Street address

Serah Joibar, the beginning of Vali Asr Highway, the headquarters of Mazandaran University of Medical Sciences and Health Services

##### City

sari

##### Province

Mazandaran

##### Postal code

3397148157

#### Approval date

2023-04-19, 1402/01/30

#### Ethics committee reference number

IR.MAZUMS.IMAMHOSPITAL.REC.1402.14934

## Health conditions studied

### 1

#### Description of health condition studied

Osteoarthritis of knee

#### ICD-10 code

M17

#### ICD-10 code description

Osteoarthritis of knee

## Primary outcomes

### 1

#### Description

The patient's pain level is based on the BPI (Brief Pain Inventory) short pain questionnaire, in the range of 0 to 10

#### Timepoint

At the beginning of the study before the start of the intervention and at the end of the fourth week and then at the end of the study at the end of the 12th week of the intervention

#### Method of measurement

The patient will be asked about her/his pain level using the BPI (Brief Pain Inventory) short pain questionnaire in the range of 0 to 10.

## 2

### **Description**

Estimating pain, stiffness and physical activity in patients with knee osteoarthritis using the WOMAC (The Western Ontario and McMaster Universities Arthritis Index) questionnaire

### **Timepoint**

At the beginning of the study before the start of the intervention and at the end of the fourth week and then at the end of the study at the end of the 12th week of the intervention

### **Method of measurement**

The performance of the patient will be measured using the WOMAC (The Western Ontario and McMaster Universities Arthritis Index) questionnaire, the level of the patient's performance will be measured in the range of 0 to 96.

## **Secondary outcomes**

### 1

#### **Description**

Knee extension strength based on 1-RM (one-repetition maximum)

#### **Timepoint**

At the beginning of the study before the start of the intervention and at the end of the fourth week and then at the end of the study at the end of the 12th week of the intervention

#### **Method of measurement**

Using the knee extension machine, we obtain the maximum weight that a person can lift in the range of 4 to 10 repetitions, then by the formula one-repetition maximum =  $\text{weight}/1 - (0.02 * \text{repetition})$  the amount of one-repetition maximum; where weight is the amount of the last weight that the person was able to lift and repetition is the number of repetitions of the lifted weight.

### 2

#### **Description**

Evaluation of patients' functional mobility during daily activities using the Timed Up and Go (TUG) test.

#### **Timepoint**

At the beginning of the study before the start of the intervention and at the end of the fourth week and then at the end of the study at the end of the 12th week of the intervention

#### **Method of measurement**

In the Timed Up and Go test, after familiarizing the person with how to do it, the patient first gets up from a standard chair (the chair does not have handles and the height from the seat of the chair to the floor is 50 cm), then walks 3 meters, then turns and goes back to the chair with the same speed as usual and sits on the chair. The time spent for this movement sequence will be recorded in seconds using a stopwatch. The best time will be recorded after three times of testing.

## **Intervention groups**

### 1

#### **Description**

Intervention group: The prescription of Duloxetine (Abidi Company) is 20 mg per day for one week, then 30 mg per day for the next week, and finally 40 mg per day for the continuation of the study, which is done along with exercise therapy. After the end of 12 weeks of therapeutic intervention, in order to reduce the side effects of drug discontinuation, patients enter the drug tapering phase and receive duloxetine 20 mg for one week, and finally the drug is discontinued. Exercise therapy will be knee and hip isometric exercises and hamstring muscle stretching, and then progress to hip flexion and knee extension isotonic exercises in a sitting position with ankle weights at 50-70% of one repetition maximum. Exercise is home-based, where basic training will be given by the doctor in the clinic, and a booklet containing the form and explanation of how to do the exercises will be provided to the patients as a guide for doing the exercises at home. A phone number will also be provided to patients so that they can contact their doctor if they have any questions or problems about taking medicine or exercising. Exercises are for 4 weeks and 5 times a week. Each exercise is performed in three sets with 10 repetitions until exhaustion. Exercises include (1) seated isotonic exercise for the quadriceps, (2) isometric exercise for the quadriceps, (3) supine isotonic exercise for the hip extensors, (4) isometric seated exercise on the chair for the hip adductors, (5) side-lying isotonic exercise for the hip abductors, (6) low-distance squats, and (7) the seated hamstring stretch.

#### **Category**

Treatment - Drugs

### 2

#### **Description**

Control group: Exercise therapy will be knee and hip isometric exercises and hamstring muscle stretching, and then progress to hip flexion and knee extension isotonic exercises in a sitting position with ankle weights at 50-70% of one repetition maximum. Exercise is home-based, where basic training will be given by the doctor in the clinic, and a booklet containing the form and explanation of how to do the exercises will be provided to the patients as a guide for doing the exercises at home. A phone number will also be provided to patients so that they can contact their doctor if they have any questions or problems about taking medicine or exercising. Exercises are for 4 weeks and 5 times a week. Each exercise is performed in three sets with 10 repetitions until exhaustion. Exercises include (1) seated isotonic exercise for the quadriceps, (2) isometric exercise for the quadriceps, (3) supine isotonic exercise for the hip extensors, (4) isometric seated exercise on the chair for the hip adductors, (5) side-lying isotonic exercise for the hip abductors, (6) low-distance squats, and (7) the seated hamstring stretch.

#### **Category**

Treatment - Other

## Recruitment centers

1

### Recruitment center

**Name of recruitment center**

Department of Sports Medicine, Mostafavian Clinic,  
Sari Imam Khomeini Hospital

**Full name of responsible person**

Hanieh Ahmadi

**Street address**

Sports Medicine Department, Mostafavian Clinic, Razi  
No. 3 Alley, Razi St.

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4816868890

**Phone**

+98 11 3336 6552

**Email**

h.ahmadi@mazums.ac.ir

## Sponsors / Funding sources

1

### Sponsor

**Name of organization / entity**

Mazandaran University of Medical Sciences

**Full name of responsible person**

Pedram Ebrahimnejad

**Street address**

Department of pharmaceuticals, Faculty of Pharmacy,  
Mazandaran University of Medical Sciences, Sari, Iran

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Sari

**Province**

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**Email**

pebrahimnejad@mazums.ac.ir

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

Yes

**Title of funding source**

Mazandaran 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**

Mazandaran University of Medical Sciences

**Full name of responsible person**

Hanieh Ahmadi

**Position**

Associate professor

**Latest degree**

Specialist

**Other areas of specialty/work**

Sport Medicine

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## Person responsible for scientific inquiries

**Contact****Name of organization / entity**

Mazandaran University of Medical Sciences

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**Position**

Associate professor

**Latest degree**

Specialist

**Other areas of specialty/work**

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## Person responsible for updating data

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### Contact

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**Other areas of specialty/work**

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**Email**

## 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