

# Clinical Trial Protocol

## Iranian Registry of Clinical Trials

10 Jun 2026

### The analgesic effect of metformin in patients with fibromyalgia

#### Protocol summary

##### Study aim

Determination of the analgesic effect of metformin in patients with fibromyalgia

##### Design

Randomized, double blinded trial, phase 3, on 30 patients with fibromyalgia, with one control and two intervention groups, which are parallel. Randomization is by block method.

##### Settings and conduct

Research would take place in Boali hospital of Tehran but patients detection will not be limited to Azad University hospitals and some other hospitals would be added if needed. Patient's initial condition would be assessed by two valid questionnaire (Revised Fibromyalgia Impact Questionnaire (FIQR) and Toronto Clinical Neuropathy Scoring System (TCNS)) and some physical examinations. Then, they would be randomly placed in each of three groups. After a 3-month trial and reassessment of patients, the results before and after interventions would be compared. The trial is double blinded (outcome assessor and data analyser).

##### Participants/Inclusion and exclusion criteria

Inclusion Cr: American College of Rheumatology criteria for Fibromyalgia diagnosis - Not using any medication for fibromyalgia and metformin / Exclusion Cr: Comorbid disorders including history of CVD, RA, untreated endocrine abnormalities (except diabetes), autoimmune conditions, neuromuscular diseases, active malignancy, immunodeficiency, advanced renal failure - Taking medications associated with IR such as glucocorticoids, thiazide diuretics, atypical anti-psychotics, beta-blockers, niacin, statins and NSAID - Drug or alcohol abuse - Opium addiction or cigarette smoking - Using any medication for fibromyalgia and metform

##### Intervention groups

A. Standard medication of fibromyalgia including either Norepinephrine Reuptake Inhibitors or Membrane Stabilizing agents (control group) B. metformin alone C. Combination therapy with both medications

##### Main outcome variables

Fibromyalgia severity, Pain severity, Neuropathy severity, Tender points

#### General information

##### Reason for update

According to the method of blinding which includes the outcome assessor and the data analyser, I changed the type of blinding from single blinding to double blinding.

##### Acronym

##### IRCT registration information

IRCT registration number: **IRCT20210306050589N1**

Registration date: **2021-04-28, 1400/02/08**

Registration timing: **prospective**

Last update: **2021-05-02, 1400/02/12**

Update count: **1**

##### Registration date

2021-04-28, 1400/02/08

##### Registrant information

##### Name

Smaeil Shekari

##### Name of organization / entity

##### Country

Iran (Islamic Republic of)

##### Phone

+98 21 3660 4854

##### Email address

shekari.es.1973@gmail.com

##### Recruitment status

**Recruitment complete**

##### Funding source

##### Expected recruitment start date

2021-06-22, 1400/04/01

##### Expected recruitment end date

2021-09-23, 1400/07/01

##### Actual recruitment start date

empty

##### Actual recruitment end date

empty

**Trial completion date**  
empty

**Scientific title**  
The analgesic effect of metformin in patients with fibromyalgia

**Public title**  
The effect of metformin in fibromyalgia

**Purpose**  
Treatment

**Inclusion/Exclusion criteria**  
**Inclusion criteria:**  
American College of Rheumatology criteria for Fibromyalgia diagnosis Not using any medication for fibromyalgia and metformin  
**Exclusion criteria:**  
Comorbid disorders including history of cerebrovascular disease, rheumatoid arthritis, untreated endocrine abnormalities(except diabetes), autoimmune conditions, neuromuscular diseases, active malignancy, immunodeficiency, advanced renal failure Taking medications associated with insulin resistance such as glucocorticoids, thiazide diuretics, atypical anti-psychotics, beta-blockers, niacin, statins and NSAID Drug or alcohol abuse Opium addiction or cigarette smoking Using any medication for fibromyalgia and metformin

**Age**  
No age limit

**Gender**  
Both

**Phase**  
3

**Groups that have been masked**

- Care provider
- Investigator
- Outcome assessor
- Data analyser

**Sample size**  
Target sample size: 30

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

**Randomization description**  
Randomization method would be based on block randomization with the block size of 3. For each possible cases numbers are assigned as mentioned below: ABC(1), ACB(2), BAC(3), BCA(4), CAB(5), CBA(6) Then a number between 1-6 would be assigned for each block using random number table, so that the therapeutic group for each participant is determined.

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

**Blinding description**  
A person other than the main researcher of the project determines the intervention and control groups with the name of A, B and C, put the medications in appropriate boxes with the name of group and provide them to the main researcher as they are sealed. In fact, the main researcher who acts the role of clinical care giver, outcome assessor and data analyst as well, would be

unaware of the patients assignment to either control or intervention group until the end of the project. And would only deal with the group names A, B and C and also would not know the patients' name during clinical care in order to prevent possible bias of the project.

**Placebo**  
Not used

**Assignment**  
Parallel

**Other design features**

## Secondary Ids

empty

## Ethics committees

### 1

#### Ethics committee

##### Name of ethics committee

Ethics Committee of Tehran Islamic Azad University of Medical Science

##### Street address

Islamic Azad University of Medical Sciences, Tehran Branch, Khaghani St, Shariati Ave

##### City

Tehran

##### Province

Tehran

##### Postal code

1916893813

#### Approval date

2021-01-18, 1399/10/29

#### Ethics committee reference number

IR.IAU.TMU.REC.1399.459

## Health conditions studied

### 1

#### Description of health condition studied

Fibromyalgia

#### ICD-10 code

M79.7

#### ICD-10 code description

Fibromyalgia

### 2

#### Description of health condition studied

Idiopathic peripheral autonomic neuropathy

#### ICD-10 code

G90.0

#### ICD-10 code description

Idiopathic peripheral autonomic neuropathy

## Primary outcomes

### 1

#### Description

Pain severity

### **Timepoint**

At the first visit and 3 month after the beginning of interventions

### **Method of measurement**

Numeric Pain Rating Scale (NPRS)

## **2**

### **Description**

Fibromyalgia severity

### **Timepoint**

At the first visit and 3 month after the beginning of interventions

### **Method of measurement**

Revised Fibromyalgia Impact Questionnaire (FIQR)

## **3**

### **Description**

Tender points

### **Timepoint**

At the first visit and 3 month after the beginning of interventions

### **Method of measurement**

Counting

## **Secondary outcomes**

### **1**

#### **Description**

Neuropathy severity

#### **Timepoint**

At the first visit and 3 month after the beginning of interventions

#### **Method of measurement**

Toronto Clinical Neuropathy Scoring System (TCNS)

## **Intervention groups**

### **1**

#### **Description**

Control group (group A): The control group would be on the treatment with the standard medication of fibromyalgia (based on the latest available guidelines) including either Norepinephrine Reuptake Inhibitors (amitriptyline, duloxetine or milnacipran) or Membrane Stabilizing agents (pregabalin or gabapentin). The duration of treatment would be 3 month. (For most patients we would prescribe Amitriptyline (with the initial dose of 5-10 mg/d 3 hour before bedtime and gradually increasing the dose to 25-50 mg/d if needed and tolerated). If there is severe fatigue or depression in patients we would use either Duloxetine (with the initial dose of 20-30 mg/d in the morning and gradually increasing the dose to 60 mg/d) or Milnacipran (with initial dose of 12.5 mg/d in the morning and gradually increasing the dose to 50-100 mg twice daily if needed and tolerated) and occasionally if there is severe sleep disturbance we would use either Pregabalin (with initial

dose of 25-50 mg/d at bedtime and gradually increasing the dose to 300-450 mg/d if needed and tolerated) or Gabapentin (with initial dose of 100 mg/d at bedtime and gradually increasing the dose to 1200-2400 mg/d in divided doses if needed and tolerated)) Predicted Pharmaceutical companies: Amitriptyline: Pars Darou, Duloxetine: Dr. Abidi, Pregabalin: Sobhan Darou, Gabapentin: Razak. Because Milnacipran is not made in Iranian companies, we use Duloxetine instead.

#### **Category**

Treatment - Drugs

### **2**

#### **Description**

First intervention group (group B): The first intervention group would be on the treatment with metformin alone. The duration of treatment would be 3 month. (Metformin would be prescribed with the initial dose of 500 mg/d, and would be increased gradually until it reaches 1500 mg/d (the effective dose) if tolerated.) Predicted Pharmaceutical companies: Metformin: Razak

#### **Category**

Treatment - Drugs

### **3**

#### **Description**

Second intervention group (group C): The second intervention group would be on the combination therapy with both medications, standard medication of fibromyalgia and metformin together, according to the order of these two groups. The duration of treatment would be 3 month. Predicted Pharmaceutical companies: Amitriptyline: Pars Darou, Duloxetine: Dr. Abidi, Pregabalin: Sobhan Darou, Gabapentin: Razak, Metformin: Razak.

#### **Category**

Treatment - Drugs

## **Recruitment centers**

### **1**

#### **Recruitment center**

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

Booali hospital

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

Sara Hallaji

##### **Street address**

At the beginning of Damavand Blv, Imam Hossein Sq.

##### **City**

Tehran

##### **Province**

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**2**

**Recruitment center**

**Name of recruitment center**

Amir Al-Momenin hospital

**Full name of responsible person**

Sara Hallaji

**Street address**

In front of Sardar Jangal Park, Shirmohammadi St,  
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**Sponsors / Funding sources**

**1**

**Sponsor**

**Name of organization / entity**

Islamic Azad University

**Full name of responsible person**

Farshad Hashemiyani

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Islamic Azad University of Medical Sciences, Tehran  
Branch, Khaghani St, Shariati Ave

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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**

Islamic Azad University

**Proportion provided by this source**

100

**Public or private sector**

Private

**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**

Islamic Azad University

**Full name of responsible person**

Sara Hallaji

**Position**

Medical student

**Latest degree**

A Level or less

**Other areas of specialty/work**

General Practitioner

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**Person responsible for updating data****Contact****Name of organization / entity**

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**Sharing plan****Deidentified Individual Participant Data Set (IPD)**

No - There is not a plan to make this available

**Justification/reason for indecision/not sharing IPD**

There is no plan to publish it.

**Study Protocol**

No - There is not a plan to make this available

**Statistical Analysis Plan**

No - There is not a plan to make this available

**Informed Consent Form**

No - There is not a plan to make this available

**Clinical Study Report**

No - There is not a plan to make this available

**Analytic Code**

Not applicable

**Data Dictionary**

Not applicable