Clinical Trial Protocol
Iranian Registry of Clinical Trials

10 Jun 2026

Effect of Methotrexate on Symptoms and Nasal Polyp Size in Patients With Recurrent Chronic Rhinosinusitis With Nasal Polyps (CRSwNP): A Double-Blind Randomized Pilot Clinical Trial

Protocol summary

Study aim

Effect of Methotrexate on Symptoms and Polyp Size in Patients With recurrent Chronic rhino sinusitis with nasal polyposis (CRSwNP)

Design

This study is a Phase III randomized, double-blind, placebo-controlled Pilot clinical trial conducted on 40 patients. Randomization and allocation of participants into two groups were performed using the website https://sealedenvelope.com/randomisation .

Settings and conduct

This is a randomized, double-blind, parallel pilot clinical trial (1:1) conducted in adult patients with recurrent CRSwNP at Imam Khomeini Hospital, Ahvaz. Participants are randomly assigned to oral methotrexate or placebo group, with 12-week follow-up. Both patients and outcome assessors are blinded, and the placebo is matched in appearance and dosing schedule.

Participants/Inclusion and exclusion criteria

Inclusion criteria: Age ≥18 years; diagnosis of recurrent CRSwNP based on EPOS 2020 criteria (European position paper on Rhinosinusitis and Nasal polyps) ; no use of biologics in the past 6 months; written informed consent. Exclusion criteria: Active liver disease ; severe hematologic abnormalities (WBC <3,000/µL or PLT <100,000/µL); renal impairment (CrCl <50 mL/min); active infection (TB, HBV, HCV); known hypersensitivity to methotrexate.

Intervention groups

Intervention: oral methotrexate (Nanovalond) 15 milligrams weekly for 12 weeks. Control: oral methotrexate placebo 15 milligrams weekly for 12 weeks. All patients: weekly folic acid five milligrams (Shefa), intranasal fluticasone spray (Koushan Pharmed), and nasal rinse (Sgalesh).

Main outcome variables

Primary outcome: Nasal endoscopy score (Lund–Kennedy); Secondary outcomes: SNOT-22 score, Symptom severity score

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20120404009375N2**
Registration date: **2026-05-10, 1405/02/20**
Registration timing: **registered_while_recruiting**

Last update: **2026-05-10, 1405/02/20**
Update count: **0**

Registration date

2026-05-10, 1405/02/20

Registrant information

Name

Soheila Nikakhlagh

Name of organization / entity

Ahvaz Jondishapoor University of Medical Sciences

Country

Iran (Islamic Republic of)

Phone

+98 61 3292 1838

Email address

nikakhlagh-s@ajums.ac.ir

Recruitment status

recruiting

Funding source

Expected recruitment start date

2026-03-10, 1404/12/19

Expected recruitment end date

2026-09-21, 1405/06/30

Actual recruitment start date

empty

Actual recruitment end date
empty
Trial completion date
empty

Scientific title
Effect of Methotrexate on Symptoms and Nasal Polyp Size in Patients With Recurrent Chronic Rhinosinusitis With Nasal Polyps (CRSwNP): A Double-Blind Randomized Pilot Clinical Trial

Public title
Effect of Oral Methotrexate on Improvement of Nasal Polyps
Purpose
Treatment
Inclusion/Exclusion criteria
Inclusion criteria:
Age18 or greater than Diagnosis of recurrent Chronic Rhinosinusitis With Nasal Polyps (CRSwNP) based on the European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS 2020) criteria No use of biological medications during the past six months Written informed consent for participation in the study
Exclusion criteria:
Presence of active liver disease Severe leukopenia or thrombocytopenia, defined as White Blood Cell count (WBC) less than 3,000 per microliter or Platelet count (PLT) less than 100,000 per microliter Significant renal dysfunction defined as Creatinine Clearance (CrCl) less than 50 milliliters per minute Active infection with Mycobacterium tuberculosis (TB), Hepatitis B virus (HBV), or Hepatitis C virus (HCV) Alcohol abuse Known hypersensitivity to methotrexate
Age
From **18 years** old to **60 years** old
Gender
Both

Phase
3
Groups that have been masked

- Participant
- Outcome assessor

Sample size
Target sample size: **40**
Randomization (investigator's opinion)
Randomized
Randomization description
Participants will be randomly allocated into two study groups using the SealedEnvelope.com/randomisation website. Block randomization with variable block sizes (4 or 6) with a 1:1 allocation ratio will be used. The randomization process will be performed by an epidemiologist
Blinding (investigator's opinion)
Double blinded
Blinding description
This study will be conducted in a double-blind manner (participants and outcome assessor/examining physician). The study drug and placebo will have identical packaging and labeling. Participant assignment will be concealed using alphanumeric codes (concealment). The randomized code list will be kept in two copies by the study epidemiologist and the principal investigator, and will only be broken in case of emergency.
Placebo
Used
Assignment
Parallel
Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee
Name of ethics committee
Ethical Committee of Ahvaz Jundishapur University of Medical Sciences
Street address
College Town, Golestan
City
Ahvaz
Province
Khouzestan
Postal code
6135715794
Approval date
2026-02-21, 1404/12/02
Ethics committee reference number
IR.AJUMS.REC.1404.656

Health conditions studied

1

Description of health condition studied
Patients With Recurrent Chronic Rhinosinusitis With Nasal Polyps
ICD-10 code
J33.0
ICD-10 code description
Polyp of nasal cavity

Primary outcomes

1

Description
Nasal endoscopy score base on Lund–Kennedy score
Timepoint
At baseline (prior to the start of the intervention, week 0), and subsequently at weeks 4, 8, and 12 after the initiation of the intervention
Method of measurement
Endoscopic evaluation of the nasal cavity scored using the Lund–Kennedy index

Secondary outcomes

1

Description
Sino Nasal Outcome 22 questionnaire score
Timepoint
At baseline (prior to the start of the intervention, week 0), and subsequently at weeks 4, 8, and 12 after the initiation of the intervention
Method of measurement
Sino-Nasal Outcome Test-22 Questionnaire

2

Description
score of severity of symptoms (nasal congestion, nasal discharge, decreased sense of smell, and facial pain or pressure)
Timepoint
At baseline (prior to the start of the intervention, week 0), and subsequently at weeks 4, 8, and 12 after the initiation of the intervention
Method of measurement
Patient-reported symptom severity will be measured using the Visual Analog Scale

Intervention groups

1

Description
Intervention group: Patients will receive oral methotrexate at a dose of 15 mg per week for 12 weeks, administered as divided doses over two consecutive days (Thursday and Friday). The methotrexate used is Trexoma® 2.5 mg tablets (Nano Alvand Pharmaceutical Nanotechnology Company). In addition, folic acid 5 mg will be administered once weekly (Shafa Pharmaceutical and Hygienic Company).All patients will receive standard therapy, including intranasal fluticasone spray twice daily (Koushan Pharmed Company) and nasal and sinus irrigation with saline solution 1–2 times daily (SGALESH Nasal and Sinus Irrigation Solution).In case of severe exacerbation of symptoms, a short course (up to one week) of oral prednisolone (Aburaihan Pharmaceutical Company) may be prescribed. The dose and duration of prednisolone use will be recorded and considered in the data analysis.
Category
Treatment - Drugs

2

Description
Control group: patients will receive placebo tablets matching oral methotrexate at a dose equivalent to 15 mg per week, administered as divided doses on two consecutive days (Thursday and Friday) for a duration of 12 weeks. The placebo tablets will be prepared to resemble Trexoma 2.5 mg tablets manufactured by Nano Alvand Pharmaceutical Nanotechnology Company. Additionally, folic acid 5 mg will be prescribed once weekly. The folic acid used in this study is manufactured by Shafa Pharmaceutical and Hygienic Company. All patients will also receive standard therapy, including intranasal fluticasone spray twice daily manufactured by Koushan Pharmed Company, and nasal and sinus irrigation with saline solution one to two times daily using SGALESH Nasal and Sinus Irrigation Solution. In case of severe exacerbation of symptoms, oral prednisolone manufactured by Aburaihan Pharmaceutical Company may be prescribed for a short course of up to one week. The dose and duration of prednisolone use will be carefully recorded and considered in the data analysis.
Category
Treatment - Drugs

Recruitment centers

1

Recruitment center
Name of recruitment center
Imam Khomeini Hospital, Ahvaz
Full name of responsible person
Soheila Nikakhlagh
Street address
Otorhinolaryngology Department, Imam Khomeini Hospital, 24-Metri Street, Ahvaz, Khuzestan Province, Iran
City
Ahvaz
Province
Khouzestan
Postal code
61357-15794
Phone
+98 61 3222 1838
Fax
+98 61 3222 1838
Email
nikakhlagh-s@ajums.ac.ir

Sponsors / Funding sources

1

Sponsor
Name of organization / entity
Ahvaz University of Medical Sciences
Full name of responsible person
Abdollah Rafiei
Street address
Vice-Chancellor for Research and Technology, Ahvaz Jundishapur University of Medical Sciences, Golestan Boulevard, Ahvaz, Iran
City
Ahvaz
Province
Khouzestan
Postal code
6135715794

Phone
+98 61 3373 8383
Email
rafiei-a@ajums.ac.ir

Grant name
Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Grant code / Reference number
HRC-0405

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

Title of funding source
Ahvaz 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
Ahvaz University of Medical Sciences

Full name of responsible person
Soheila Nikakhlagh

Position
Professor

Latest degree
Specialist

Other areas of specialty/work
Ear, Nose, and Throat

Street address
Otorhinolaryngology Department, Imam Khomeini Hospital, 24-Metri Street, Ahvaz, Khuzestan Province, Iran

City
Ahvaz

Province
Khouzestan

Postal code
61357-15794

Phone
+98 61 3222 1838

Fax
+98 61 3222 1838

Email
Nikakhlagh-s@ajums.ac.ir

Person responsible for scientific inquiries

Contact

Name of organization / entity
Ahvaz University of Medical Sciences

Full name of responsible person
Soheila Nikakhlagh

Position
Professor

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Khouzestan

Postal code
61357-15794

Phone
+98 61 3222 1838

Fax
+98 61 3222 1838

Email
Nikakhlagh-s@ajums.ac.ir

Person responsible for updating data

Contact

Name of organization / entity
Ahvaz University of Medical Sciences

Full name of responsible person
Soheila Nilakhlagh

Position
Professor

Latest degree
Specialist

Other areas of specialty/work
Ear, Nose, and Throat

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Province
Khouzestan

Postal code
61357-15794

Phone
+98 61 3222 1838

Fax
+98 61 3222 1838

Email
NikaKhlagh-s@ajums.ac.ir

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
Yes - There is a plan to make this available

Statistical Analysis Plan

Yes - There is 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

.

When the data will become available and for how long

.

To whom data/document is available

.

Under which criteria data/document could be used

.

From where data/document is obtainable

.

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

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Comments