

Clinical Trial Protocol

Iranian Registry of Clinical Trials

13 Jul 2026

Evaluation of the effect of Milk Thistle in the prevention of anti-tuberculosis drugs-induced hepatotoxicity: A randomized controlled clinical trial

Protocol summary

Study aim

Recommendation for Use of the Extract of Milk Thistle (Containing Silymarin) in Patients Receiving Anti-Tuberculosis Drugs to Reduce the Risk of Hepatotoxicity, If Positive Results Were Observed

Design

Randomized, Parallel Group, Controlled Clinical Trial

Settings and conduct

This study was performed in Al-Zahra hospital affiliated to Isfahan University of Medical Sciences. Patients who had inclusion criteria were randomly assigned to two groups of drugs and control. All patients received standard anti-TB regimen according to the national protocol. The patients of drug used liver support capsule, twice daily for 2 weeks, while patients in the control group received the standard anti-TB drugs alone. All patients were measured and recorded ALT, AST, ALP and serum bilirubin at the beginning of the study and before the start of interventions and then weekly for up to 2 weeks.

Participants/Inclusion and exclusion criteria

Age $\geq$ 18 years old; pulmonary or outer pulmonary tuberculosis; taking first line of anti-TB drugs (Isoniazid, Rifampin and Pyrazinamide); don't take first line of anti-TB drugs for the last 8 weeks; don't use of known hepatotoxic drugs (e.g., sodium valproate, methotrexate, sulfonamides); not taking acetaminophen persistently; not using systemic glucocorticoids simultaneously; don't use supplements containing Silymarin in the last 4 weeks; not using alcohol; not use antioxidants (such as vitamins E,C); lack of chronic liver or kidney disease; and non pregnant; non lactating women.

Intervention groups

Drug group: taking capsule of dry extract of Milk Thistle Seed (Liver Support) Containing 150 mg of Silymarin, twice daily from the Onset of Anti-Tuberculosis Drugs
Control group: taking Anti-Tuberculosis drugs alone

Main outcome variables

Serum Levels of Liver Enzymes (ALT, AST, ALP) and Total and Direct Bilirubin; The Number of Cases of Acute Liver Injury

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20150721023282N9**

Registration date: **2020-03-30, 1399/01/11**

Registration timing: **retrospective**

Last update: **2020-03-30, 1399/01/11**

Update count: **0**

Registration date

2020-03-30, 1399/01/11

Registrant information

Name

Rasool Soltani

Name of organization / entity

Isfahan University of Medical Sciences

Country

Iran (Islamic Republic of)

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soltani@pharm.mui.ac.ir

Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2017-03-21, 1396/01/01

Expected recruitment end date

2018-08-22, 1397/05/31

Actual recruitment start date

2017-03-21, 1396/01/01

Actual recruitment end date

2018-08-22, 1397/05/31

Trial completion date

2018-09-22, 1397/06/31

Scientific title

Evaluation of the effect of Milk Thistle in the prevention of anti-tuberculosis drugs-induced hepatotoxicity: A randomized controlled clinical trial

Public title

Evaluation of the effect of Milk Thistle in the prevention of anti-tuberculosis drugs-induced hepatotoxicity: A randomized controlled clinical trial

Purpose

Treatment

Inclusion/Exclusion criteria**Inclusion criteria:**

Age $\geq$ 18 years Pulmonary or outer pulmonary tuberculosis Taking first line of anti-TB drugs (Isoniazid, Rifampin and Pyrazinamide) No use of first-line anti-TB drugs within the last 8 weeks

Exclusion criteria:

Use of known hepatotoxic drugs (e.g., sodium valproate, methotrexate, sulfonamides) Regular use of acetaminophen Use of systemic glucocorticoids Use of Silymarin-containing supplements within the last 4 weeks Alcoholism Use of antioxidant agents (e.g., vitamins E and C) Having chronic hepatic or renal disease Pregnancy Lactation

AgeFrom **18 years** old**Gender**

Both

Phase

N/A

Groups that have been masked

- Participant
- Care provider
- Investigator

Sample sizeTarget sample size: **53**Actual sample size reached: **37****Randomization (investigator's opinion)**

Randomized

Randomization description

Simple randomization was used for patients' allocation to the groups. For this, an online random number generator was used (available at: <https://www.random.org/sequences>) so that even and odd numbers were considered for drug and control groups, respectively.

Blinding (investigator's opinion)

Double blinded

Blinding description

This study is a double-blind clinical trial (participant, researcher).

Placebo

Not used

Assignment

Parallel

Other design features**Secondary Ids**

empty

Ethics committees**1****Ethics committee****Name of ethics committee**

Ethical Committee of Isfahan University of Medical Sciences

Street address

Isfahan University of Medical Sciences, Hezar-Jerib Ave.

City

Isfahan

Province

Isfahan

Postal code

8174673461

Approval date

2016-05-29, 1395/03/09

Ethics committee reference number

IR.MUI.REC.1395.3.930

Health conditions studied**1****Description of health condition studied**

Anti-tuberculosis drugs-induced hepatotoxicity

ICD-10 code

K71

ICD-10 code description

Toxic liver disease

Primary outcomes**1****Description**

Serum level of ALT

Timepoint

Before the intervention and 7 and 14 days after initiation of intervention

Method of measurement

blood test

2**Description**

serum level of AST

Timepoint

Before the intervention and 7 and 14 days after initiation of intervention

Method of measurement

blood test

3

Description

serum level of ALP

Timepoint

Before the intervention and 7 and 14 days after initiation of intervention

Method of measurement

blood test

4

Description

serum level of bilirubin(direct/total)

Timepoint

Before the intervention and 7 and 14 days after initiation of intervention

Method of measurement

blood test

Secondary outcomes

empty

Intervention groups

1

Description

Intervention group: 150-mg oral capsules of Milk Thistle, twice daily, for 2 weeks with standard 4-drug anti-TB therapeutic regimen including isoniazid 5 mg/kg + rifampin 10 mg/kg + ethambutol 15 mg/kg + pyrazinamide 25 mg/kg

Category

Prevention

2

Description

Control group: standard 4-drug anti-TB therapeutic regimen including isoniazid 5 mg/kg + rifampin 10 mg/kg + ethambutol 15 mg/kg + pyrazinamide 25 mg/kg

Category

N/A

Recruitment centers

1

Recruitment center

Name of recruitment center

Al-Zahra Hospital

Full name of responsible person

Rasool Soltani

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Soffeh Ave.

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity

Esfahan University of Medical Sciences

Full name of responsible person

Shagayegh Haghjooy Javanmard

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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

Esfahan 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

Esfahan University of Medical Sciences

Full name of responsible person

Rasool Soltani

Position

Associate professor

Latest degree

Specialist

Other areas of specialty/work

Medical Pharmacy

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Latest degree

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Person responsible for updating data

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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

Confidentiality of patients data

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

No - There is not a plan to make this available

Data Dictionary

No - There is not a plan to make this available