Clinical Trial Protocol
Iranian Registry of Clinical Trials

04 Jun 2026

Evaluation of the therapeutic effect of Silymarin in combination with naloxone in improving methadone poisoning

Protocol summary

Study aim
Determining the effect of co-administration of silymarin with naloxone on the improvement of methadone poisoning

Design
A clinical trial with control and intervention group, with parallel groups, not blinded, phase 3 on 64 patients, non-randomly assignment into intervention or control groups.

Settings and conduct
Methadone poisoned patients referred to Ayatollah Kashani Hospital in Shahrekord are entered the study. After obtaining written consent patients are non-randomly divided into two groups, control or intervention (even days in the control and the odd days in the intervention group). The control group receives naloxone and the intervention group receives naloxone and silymarin. Before and 3 days after the intervention, blood samples are taken from patients and finally compared in all variables in the control and intervention groups to determine the effect of silymarin Participants study groups and the principal investigator, health care personnel, and those assessing the outcome are aware of the allocation of study groups.

Participants/Inclusion and exclusion criteria
Inclusion criteria: all patients with opioid triad include decreased level of consciousness, myotic pupil, and decreased level of blood oxygen; positive test for urine methadone level. Exclusion criteria: patient dissatisfaction to participate in the study, use of supplements and drugs with similar effects; participation in interventions with Naloxone and Silymarin.

Intervention groups
The control group received naloxone and the intervention group received naloxone and silymarin.

Main outcome variables
AIT, AST, BUN, Creatinine, Uric acid, Malondialdehyde, LDH, Serum antioxidant capacity level, Blood pressure, Tempereture, heart and respiratory rate, CPK, Sodium, Potassium, PH, PO2.PCO2, HCO3

General information

Reason for update

Acronym

IRCT registration information
IRCT registration number: **IRCT20210216050377N1**
Registration date: **2022-01-16, 1400/10/26**
Registration timing: **retrospective**

Last update: **2022-01-16, 1400/10/26**
Update count: **0**

Registration date
2022-01-16, 1400/10/26

Registrant information

Name
maryam hadypoor

Name of organization / entity

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Iran (Islamic Republic of)

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Recruitment status
Recruitment complete

Funding source

Expected recruitment start date
2021-05-19, 1400/02/29

Expected recruitment end date
2021-12-20, 1400/09/29

Actual recruitment start date
empty

Actual recruitment end date
empty

Trial completion date
empty

Scientific title

Evaluation of the therapeutic effect of Silymarin in combination with naloxone in improving methadone poisoning

Public title
The effect of silymarin on methadone poisoning
Purpose
Treatment
Inclusion/Exclusion criteria
Inclusion criteria:
All patients with opioid triad include decreased level of consciousness, myotic pupil and decreased level of blood oxygen Methadone level is positive in their urine test (U / A)
Exclusion criteria:
Patient dissatisfaction to participate in the study Use of supplements and drugs with similar effects or interventions with Naloxone and Silymarin
Age
No age limit
Gender
Both

Phase
3
Groups that have been masked
No information
Sample size
Target sample size: **64**
Randomization (investigator's opinion)
Not randomized
Randomization description
Blinding (investigator's opinion)
Not blinded
Blinding description
Placebo
Not used
Assignment
Parallel
Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee
Name of ethics committee
Ethics committee of Shahrekord University of Medical Sciences
Street address
No3, 41 Ave, Parastar Blvd, Shahrekord Town,
City
Shahrekord
Province
Chahar-Mahal-va-Bakhtiari
Postal code
1234567899
Approval date
2021-05-11, 1400/02/21

Ethics committee reference number
IR.SKUMS.REC.1400.048

Health conditions studied

1

Description of health condition studied
Poisoning by methadone
ICD-10 code
T40.3X4
ICD-10 code description
Poisoning by methadone, undetermined

Primary outcomes

1

Description
Serum level of Aspartate transaminase
Timepoint
Measurement of the variable before the intervention and 3 days after the intervention with silymarin
Method of measurement
They are measured on serum by commercial kits of Pars Azmoun company Italian BT3000 auto analyzer

2

Description
Serum level of Alanine transaminase
Timepoint
Measurement of the variable before the intervention and 3 days after the intervention with silymarin
Method of measurement
They are measured on serum by commercial kits of Pars Azmoun company Italian BT3000 auto analyze

3

Description
Serum level of Blood urea nitrogen
Timepoint
Measurement of the variable before the intervention and 3 days after the intervention with silymarin
Method of measurement
They are measured on serum by commercial kits of Pars Azmoun company Italian BT3000 auto analyze

4

Description
Serum level of Creatinine
Timepoint
Measurement of the variable before the intervention and 3 days after the intervention with silymarin
Method of measurement
They are measured on serum by commercial kits of Pars Azmoun company Italian BT3000 auto analyze

5

Description
Serum level of Uric Acid
Timepoint
Measurement of the variable before the intervention and 3 days after the intervention with silymarin
Method of measurement
They are measured on serum by commercial kits of Pars Azmoun company Italian BT3000 auto analyze

6

Description
Serum level of Lactate dehydrogenase
Timepoint
Measurement of the variable before the intervention and 3 days after the intervention with silymarin
Method of measurement
They are measured on serum by commercial kits of Pars Azmoun company Italian BT3000 auto analyze

7

Description
Serum level of Creatine phosphokinase
Timepoint
Measurement of the variable before the intervention and 3 days after the intervention with silymarin
Method of measurement
They are measured on serum by commercial kits of Pars Azmoun company Italian BT3000 auto analyze

8

Description
Serum level of Sodium
Timepoint
Measurement of the variable before the intervention and 3 days after the intervention with silymarin
Method of measurement
They are measured on serum by commercial kits of Pars Azmoun company Italian BT3000 auto analyze

9

Description
Serum level of Potassium
Timepoint
Measurement of the variable before the intervention and 3 days after the intervention with silymarin
Method of measurement
They are measured on serum by commercial kits of Pars Azmoun company Italian BT3000 auto analyze

10

Description
Ferric reducing ability of plasma(FRAP)
Timepoint
Measurement of the variable before the intervention and 3 days after the intervention with silymarin
Method of measurement
In the FRAP method, triazine reagent is added to the serum sample and the resulting mixture is incubated for 10 minutes at 37 ° C and then the absorbance of the solution is measured at 593 nm by a spectrophotometer.

11

Description
level of Venues blood Hydrogen Bicarbonate
Timepoint
Measurement of the variable before the intervention and 3 days after the intervention with silymarin
Method of measurement
Blood gas analyzer

12

Description
level of blood venous oxygen pressure
Timepoint
Measurement of the variable before the intervention and 3 days after the intervention with silymarin
Method of measurement
Blood gas analyzer

13

Description
level of venoues blood Carbon dioxide
Timepoint
Measurement of the variable before the intervention and 3 days after the intervention with silymarin
Method of measurement
Blood gas analyzer

14

Description
venoues blood acidity(PH)
Timepoint
Measurement of the variable before the intervention and 3 days after the intervention with silymarin
Method of measurement
Blood gas analyzer

15

Description
Serum level of Malon dialdehyde(MDA)
Timepoint
Measurement of the variable before the intervention and 3 days after the intervention with silymarin
Method of measurement
To 50 µl of serum, 50 µl of 0.05% solution of BHT (Butylated hydroxytoluene) in 0.95% ethanol, 400 µl of 0.44 mM phosphoric acid and 100 µl of 42 mM thiobarbituric acid solution (TBA) is added for 1 hour. It is incubated at 100 ° C and then the samples are placed on ice for 5 minutes and then the absorptions are read by spectrophotometer.

16

Description

Blood pressure

Timepoint

Measurement of the variable before the intervention and 3 days after the intervention with silymarin

Method of measurement

Use of mercury sphygmomanometer

17

Description

Heart rate

Timepoint

Measurement of the variable before the intervention and 3 days after the intervention with silymarin

Method of measurement

Use of pulse oximeter

18

Description

Respiratory rate

Timepoint

Measurement of the variable before the intervention and 3 days after the intervention with silymarin

Method of measurement

Count chest movements in one minute

19

Description

Body temperature

Timepoint

Measurement of the variable before the intervention and 3 days after the intervention with silymarin

Method of measurement

Using a mercury thermometer

Secondary outcomes

empty

Intervention groups

1

Description

Control group:This group includes people who have been exposed to methadone poisoning and have referred to Ayatollah Kashani Hospital in Shahrekord and have the inclusion criteria and receive only naloxane for treatment, so that after taking the initial serum sample, treatment measures are taken. We start and inject 0.4 mg of naloxone every 5 minutes once in non-addicted people and 0.05 mg or one-eighth ampoule every 5 minutes in addicted people (IV) to increase the oxygen saturation rate above 93%. And then the maintenance dose with two-thirds of the wake up dose (the dose with which the patient is awake or the respiratory depression is relieved) starts as an infusion per hour for the patient and lasts for 24 hours, then we start taper naloxone so that Every 6 hours, we halve the dose of naloxone received by the patient to reach zero, and since the half-life of methadone is about 25-52 hours, the patient should be monitored and up to 24 hours after discontinuation of naloxone if the patient has no symptoms and At the end of three days after starting treatment with naloxone , we took a second blood sample from the patient. Finally, we measure and compare all the initial variables in the before and after samples

Category

Treatment - Drugs

2

Description

Intervention group: This group includes people who have suffered from methadone poisoning and have referred to Ayatollah Kashani Hospital in Shahrekord and have inclusion criteria and these people also receive silymarin in addition to naloxone for treatment. The prototype is taken and then the patient, in addition to receiving naloxone in the same way as the control group (0.4 mg naloxone once every 5 minutes in non-addicts and 0.05 mg or one-eighth ampoule once every 5 minutes in We inject addicts (IV) to increase the oxygen saturation to above 93%, and then the maintenance dose is started with an infusion of two-thirds of the wake up dose (the dose with which the patient is awake or the respiratory depression is gone) per hour for the patient to It lasts for 24 hours, then we start taper naloxone so that every 6 hours we halve the dose of naloxone received by the patient until it reaches zero, and since the half-life of methadone is about 52-25 hours, the patient should be monitored. And up to 24 hours after naloxone discontinuation if the patient has no symptoms Yilmarin, under the brand name of Livergel, receives the drug at a dose of 140 mg 3 times a day for 3 days. At the end of three days after starting treatment with naloxone and silymarin, we take a second blood sample from the patient and finally all the variables. We measure and compare the prototype in the before and after samples.

Category

Treatment - Drugs

Recruitment centers

1

Recruitment center

Name of recruitment center

Ayatollah Kashani Hospital

Full name of responsible person

Pantea Ramezan najad

Street address

Parastar Ave., Ayatollah Kashani Hospital

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity

Shahre-kord University of Medical Sciences

Full name of responsible person

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Kashani AveShahre-kord University of Medical Sciences

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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

Shahre-kord 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

Shahre-kord University of Medical Sciences

Full name of responsible person

Pantea Ramezan Nezhad

Position

Associate professor

Latest degree

Specialist

Other areas of specialty/work

Forensic Medicine

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Person responsible for scientific inquiries

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Name of organization / entity

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Position

Associate professor

Latest degree

Specialist

Other areas of specialty/work

Forensic Medicine

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Person responsible for updating data

Contact

Name of organization / entity

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Full name of responsible person

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Position

Associate professor

Latest degree

Specialist

Other areas of specialty/work

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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