# Clinical Trial Protocol
# Iranian Registry of Clinical Trials

26 Jul 2026

## The Evaluation of the Effect of N-acetylcysteine Combined With Therapeutic Effect of Naloxone in Improving Methadone Poisoning

## Protocol summary

**Study aim**

Determining the effect of N-acetylcysteine combined with the therapeutic effect of Naloxone in improving methadone poisoning

**Design**

Clinical trial with control and intervention groups, with parallel group, not blind, non-random assignment to intervention and control group, phase 3 on 64 patients

**Settings and conduct**

Clinical and therapeutic studies are performed on methadone poisoned patients who went to Ayatollah Kashani hospital in Shahrekord ,so that after obtaining their written consent , they were included in the study and divided into two groups of control and intervention non-randomly(Even days in the control group and odd days in the intervention group). The control group is treated with naloxone the intervention group is treated with Naloxone and N_acetylcysteine. Blood samples are taken from the patients, 5 days befor and after interventing,and the variables are measured and finally all are compared in the two groups of control and intervention to determine the effect of N_acetylcysteine. Participants and the main researcher, health care personnel, those who evaluate the outcome are aware of the allocation of study groups.

**Participants/Inclusion and exclusion criteria**

Admission conditions:All patients who have a triad of opioid poisoning, including:loss of consciousness,hypoxia and Myotic pupil and have a positive methadone level in urinalysis Exclusion criteria:patient dissatisfaction and Subjects who use supplements and drugs with similar effects or interfering with Naloxone and N-acetylcysteine

**Intervention groups**

The control group is treated with Naloxone and the intervention group is treated with Naloxone and N_acetylcysteine

**Main outcome variables**

AST;AlT;BUN;Creatinine;Uric acid;Malondialdehyde;LDH;Serum Antioxidant capacity level;Blood pressure;Temperature;Heart rate;Respiratory rate;Creatinine Phosphokinase;Sodium;Potassium;PH;PO2;PCO2;HCO3

## General information

**Reason for update**

**Acronym**

**IRCT registration information**

IRCT registration number: **IRCT20210222050462N1**
Registration date: **2022-01-13, 1400/10/23**
Registration timing: **retrospective**

Last update: **2022-01-13, 1400/10/23**
Update count: **0**

**Registration date**

2022-01-13, 1400/10/23

**Registrant information**

**Name**

Zahra karimi

**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**

2021-05-20, 1400/02/30

**Expected recruitment end date**

2021-12-21, 1400/09/30

**Actual recruitment start date**

empty

**Actual recruitment end date**

empty

**Trial completion date**

empty

**Scientific title**

The Evaluation of the Effect of N-acetylcysteine Combined With Therapeutic Effect of Naloxone in Improving Methadone Poisoning

**Public title**

The Evaluation of the Effect of N-acetylcysteine in Improving Methadone Poisoning

**Purpose**

Treatment

**Inclusion/Exclusion criteria**

**Inclusion criteria:**

All patients who have a triad of opioid poisoning, including: loss of consciousness, hypoxia and Myotic pupil Have a positive methadone level in urinalysis (UA)

**Exclusion criteria:**

Patient dissatisfaction Subjects who use supplements and drugs with similar effects or interfering with Naloxone and N-acetylcysteine

**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**

Parastar Ave ;Ayatollah Kashani Hospital

**City**

Shahrekord

**Province**

Chahar-Mahal-va-Bakhtiari

**Postal code**

8814835465

**Approval date**

2021-02-09, 1399/11/21

**Ethics committee reference number**

IR.SKUMS.REC.1399.244

## 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 levels of Aspartate aminotransferase enzyme

**Timepoint**

Measurement of the variable before intervening and 5 days after beginning the treatment with N-acetylcysteine

**Method of measurement**

Measured by Pars Azmoun commercial kitson on blood serum with an autoanalyzer system (BT3000, Italy)

### 2

**Description**

Serum levels of Alanine transaminase

**Timepoint**

Measurement of the variable before intervening and 5 days after beginning the treatment with N-acetylcysteine

**Method of measurement**

By Pars Azmoun commercial kits Measured on blood serum with an autoanalyzer system (BT3000, Italy)

### 3

**Description**

Serum levels of Blood urea Nitrogen

**Timepoint**

Measurement of the variable before intervening and 5 days after beginning of treatment with N-acetylcysteine

**Method of measurement**

Measured by Pars Azmoun commercial kits on blood serum with an autoanalyzer system(BT3000, Italy)

### 4

**Description**

Serum levels of Creatinine

**Timepoint**

Measurement of the variable before tntervening and 5 days after beginning of treatment with N-acetylcysteine

**Method of measurement**

Measured by Pars Azmoun commercial kits on blood serum with an autoanalyzer system (BT3000, Italy)

## 5

**Description**
Serum levels of Uric acid
**Timepoint**
Measurement of the variable before the intervening and 5 days after beginning treatment with N-acetylcysteine
**Method of measurement**
By Pars Azmoun commercial kits Measured on blood serum with an autoanalyzer system(BT3000, Italy)

## 6

**Description**
Serum levels of Malondialdehyde
**Timepoint**
Measurement of the variable before the intervention and 5 days after the beginning treatment with N-acetylcysteine
**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. The temperature is incubated at 100 ° C and then the samples are placed on ice for 5 minutes and then the absorptions are read with a spectrophotometer.

## 7

**Description**
Serum levels of Lactate dehydrogenase
**Timepoint**
Measurement of the variable before intervening and 5 days after beginning of treatment with N-acetylcysteine
**Method of measurement**
By Pars Azmoun commercial kits Measured on blood serum with an autoanalyzer (BT3000, Italy)

## 8

**Description**
Serum levels of ferric reducing ability of plasma(FRAP)
**Timepoint**
Measurement of the variable before intervening and 5 days after beginning of treatment with N-acetylcysteine
**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. Then the absorbance of the solution is measured at a wavelength of 593 nm by a spectrophotometer.

## 9

**Description**
Blood pressure
**Timepoint**
Measurement of the variable before intervening and 5 days after beginning of treatment with N-acetylcysteine
**Method of measurement**
Mercury sphygmomanometer

## 10

**Description**
Heart rate
**Timepoint**
Measurement of the variable before intervening and 5 days after beginning of treatment with N-acetylcysteine
**Method of measurement**
Pulse oximeter

## 11

**Description**
respiratory rate
**Timepoint**
Measurement of the variable before intervening and 5 days after beginning of treatment with N-acetylcysteine
**Method of measurement**
Count the number of breaths by observing the movements of the chest

## 12

**Description**
Body Temperature
**Timepoint**
Measurement of the variable before the intervening and 5 days after beginning of treatment with N-acetylcysteine
**Method of measurement**
Mercury Therommeter

## 13

**Description**
Serum levels of Creatine phosphokinase
**Timepoint**
Measurement of the variable before intervening and 5 days after beginning of treatment with N-acetylcysteine
**Method of measurement**
By Pars Azmoun commercial kits Measured on blood serum with an autoanalyzer (BT3000, Italy)

## 14

**Description**
Serum levels of sodium
**Timepoint**
Measurement of the variable before intervening and 5 days after beginning of treatment with N-acetylcysteine
**Method of measurement**
By Pars Azmoun commercial kits Measured on blood serum with an autoanalyzer (BT3000, Italy)

## 15

**Description**
Serum levels of potassium
**Timepoint**
Measurement of the variable before intervening and 5

days after beginning of treatment with N-acetylcysteine

**Method of measurement**

By Pars Azmoun commercial kits Measured on blood serum with an autoanalyzer (BT3000, Italy)

### 16

**Description**

Venous blood pH

**Timepoint**

Measurement of the variable before the intervening and 5 days after beginning of treatment with N-acetylcysteine

**Method of measurement**

Blood gas analyzer

### 17

**Description**

Venous blood levels of Partial oxygen pressure (PO2)

**Timepoint**

Measurement of the variable before intervening and 5 days after beginning of treatment with N-acetylcysteine

**Method of measurement**

Blood gas analyzer

### 18

**Description**

Venous blood levels of Partial pressure of carbon dioxide (PCO2)

**Timepoint**

Measurement of the variable before intervening and 5 days after beginning of treatment with N-acetylcysteine

**Method of measurement**

Blood gas analyzer

### 19

**Description**

Venous blood levels of Bicarbonate ion ( HCO3)

**Timepoint**

Measurement of the variable before intervening and 5 days after beginning of treatment with N-acetylcysteine

**Method of measurement**

Blood gas analyzer

## Secondary outcomes

empty

## Intervention groups

### 1

**Description**

Intervention group:In this group, treatment performed by using Naloxone and N-acetylcysteine . N-acetylcysteine is applied in therapeutic doses which used in acetaminophen poisoning, with the initial injection dose of N-acetylcysteine being infused at 150 mg / kg in 200 cc of 5% dextrose within 1 hour, followed by 50 mg / kg immediately is infused in 500 cc of 5% dextrose for 4 hours and immediately after that 100 mg / Kg in one liter of 5% dextrose is infused for 16 hours. Therapeutic intervention with 0.4 mg injectable dose of naloxone in non-addicts and 0.05 mg in addicts is administered every 5 minutes until the patient's concentration reaches above 93% and then the maintenance dose with 2.3 doses of wake up (dose that the patient with It wakes up or the patient's respiratory depression resolves) starts per hour for the patient and lasts up to 24 hours, and then we start taper naloxone so that every 6 hours we halve the dose of naloxone received by the patient to zero and eventually 5 days after beginning of treatment, blood samples are taken from patients again.Finally, all variables are compared separately in two groups of case and control to determine the effect of N-acetylcysteine.

**Category**

Treatment - Drugs

### 2

**Description**

Control group:In the control group, treatment performed just by Naloxone . Intervention therapy with 0.4 mg injectable dose of naloxone in non-addicts and 0.05 mg in addicts is administered every 5 minutes until the patient's concentration reaches above 93% and then the maintenance dose It starts with 2/3 dose of wake up (the dose that the patient wakes up with or the patient's respiratory depression goes away) per hour for the patient and continues for 24 hours and then we start taper naloxone so that every 6 hours the dose We halve the naloxone intake of the patient to zero and finally, after 5 days from the start of treatment,Blood samples are taken from the patient again. Finally, all variables are compared separately in case and control groups to determine the effect of N-acetylcysteine.

**Category**

Treatment - Drugs

## Recruitment centers

### 1

**Recruitment center**

**Name of recruitment center**

Ayatollah Kashani Hospital in Shahrekord

**Full name of responsible person**

Pante A Ramezannezhad

**Street address**

Parastar Ave ;Ayatollah Kashani Hospital

**City**

Shahrekord

**Province**

Chahar-Mahal-va-Bakhtiari

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5891588167

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+98 38 3226 4841

**Email**

drzahrakarimi@gmail.com

**Web page address**

http://kashanihp.skums.ac.ir/

## Sponsors / Funding sources

**1**

**Sponsor**
**Name of organization / entity**
Shahre-kord University of Medical Sciences
**Full name of responsible person**
Mehraban Sadeghi
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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**
Pante A Ramezannezhad
**Position**
Assistant Professor
**Latest degree**
Specialist
**Other areas of specialty/work**
Forensic Medicine
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Parastar Ave ;Ayatollah Kashani Hospital
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## Person responsible for updating data

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**Latest degree**
Specialist
**Other areas of specialty/work**
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**Province**
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**Phone**
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**Email**
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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